TOOLISED MEDICINE:
An anthropological study of 'experimental' cell therapy during a period of regulatory change in China

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Submitted for the degree of Doctor of Philosophy in Social Anthropology

University of Sussex

June 2019

DECLARATION

I hereby declare that this thesis has not been and will not be, submitted in whole or in part to another University for the award of any other degree.

Signature:

For my grandmother HUANG Xueying (黄学英)

SUMMARY

Between December 2011 and autumn 2015, Chinese health authorities developed new regulations for stem cell clinical research. During this period, all pre-existing stem cell clinical research and practices were halted, and no permission was given to new project applications. Nevertheless, other biotechnologies, including immunotherapy, continued to be developed and offered in China. My fieldwork, from early 2014 to mid-2015, allowed me to learn how this regulatory change affected the life and work of some Chinese patients, researchers, health care professionals, biotech entrepreneurs, industry analysts and investors, and how differently each group understood, valued, and in some cases, used stem cell- and immune cell- therapy. Nevertheless, I noted then, and contend in this thesis that what the developers and users of 'experimental' cell therapy all valued and worked with was the medicinal potentiality of these cells. In the making and use of cell-based medicinal products, the users and developers integrated their own values and purposes that derived both from within, and outside of, the medical arena. In other words, the developers and users conceptualised and used cell-based medicine like a "tool" to address particular issues rising from specific situations - not just for health reasons. I develop the concepts of "toolised medicine" and "tooling work" to depict and analyse this "tool-like" feature and use of biomedicine, and use these concepts to reassess China's recent regulatory change in this field. In so doing, I contribute to social science theorisation and studies of biomedicine.

CONTENTS

ABBREVIATIONS OF ORGANISATIONS AND PROGRAMMES[1]

AMMS	Academy of Military Medical Sciences
ATMPs	Advanced Therapy Medicinal Products
APF	Armed Police Force
CAE	Chinese Academy of Engineering
CAS	Chinese Academy of Sciences
CCP	Chinese Communist Party
CCPCC	Chinese People's Political Consultative Conference Annual Conference
CCTV	China Central Television
CFDA	China Food and Drug Administration
EMA	European Medicines Agency
FYP	Five-Year Plan (for Economic and Social Development)
ISSCR	International Society for Stem Cell Research
MLP	The National Medium- and Long-term Program for Science and Development (2006-2020)
MOE	Ministry of Education
MOF	Ministry of Finance
MOH	Ministry of Health
MOHRSS	Ministry of Human Resources and Social Services
MOST	Ministry of Science and Technology
NDRC	National Development and Reform Commission
NHFPC	National Health and Family Planning Commission
NIH	National Institutes of Health in the United States
NPC	National People's Congress
NSFC	National Natural Science Foundation of China
PRC	People's Republic of China
PLA	People's Liberation Army
SAIC	State Administration for Industry & Commerce
SAT	State Administration of Taxation
SC	State Council
SEIP	Strategic Emerging Industries Plan (2012-2015)
SFDA	State Food and Drug Administration
S&T	Science and Technology
US FDA	United States Food and Drug Administration

[1] Except shown as otherwise, all are Chinese originations and programmes.

ACKNOWLEDGEMENTS

I thank all my research participants and those who conversed with me during my fieldwork, from January 2014 to April 2015, in China. In this thesis, I can only include some of them and a portion of what I learned from them all. To protect their confidentiality and privacy, I cannot address my thanks directly to my interlocutors, and I used pseudonyms and masked the place and, sometimes, the time of our encounter.

I am indebted to my supervisors Professor Margaret Sleeboom-Faulkner and Dr Rebecca Prentice for their artful guidance, sharp feedback and continuous support in helping me transit from bioscience into anthropology and they patiently read and gave me rigorous advice on how to improve the thesis. Any omissions and mistakes in the final submission are mine.

Margaret sets a high bar in this field that I am studying. I am grateful for her generous sharing of her intellect, reflection and research experiences with me and her confidence in my potential to become an anthropologist. If not for Margaret's encouragement and her successful co-application for funding from the European Research Council, I would not have come to England and pursue my research interests beyond genomics and bioethics. I am indebted thus also to ERC for funding my doctoral research (ERC: 283219).

I am grateful that Becky agreed to co-supervise me, after hearing out my research plan at our first coffee meeting in February 2013. Over these years, Becky has taught me how to write for a wider readership who may be interested in, yet know little about biomedicine and China. Becky's feedback and suggestions have helped me clarify my thoughts, sharpen my argument and improve my writing. Becky has also taught me how to teach with passion and inspiration. Like those students we taught, I am often uplifted by Becky's smile and moved by her kindness. I only wish I start to learn how to tweak from her earlier.

During writing-up, I am grateful for the Brocher Foundation providing me with a tranquil writing space and stimulating intellectual encounters, from August to October 2015. Some of the books and articles recommended to me by Nina Hallowell, Laura Mamo, Françoise Baylis have found their way into this thesis. Conversations with all Brocher fellows and workshop participants who I met in that autumn have helped me map out my thesis and some key ideas.

In my years writing-up, colleagues and friends in Brighton have helped me overcome challenges and setbacks at work and life. Special thanks to Achim Rosemann, George Byrne, Clare Rogers, Wen-Ching Ting and Po-Han Lee. Achim has known me since 2007 and, when I joined the Centre for Bionetworking in 2012, we worked together for three years. During my transition into anthropology and relocation to England, on many

occasions, Achim is among a few who I can talk to and consult in times of crisis. I am grateful that each time, Achim is there for me and gives me his valuable advice and warm support.

George and I started a Master of Social Research Methods together and we bonded with our shared interest in interdisciplinary research. After we returned from fieldwork in different parts of the world, our research and life experiences pulled us closer. To be able to share some of my deepest concern and most far-fetched thoughts, George assures me that I am not alone in encountering life changes. The warm friendship that I have received from Clare, Wen-Ching and Po-Han gives me further strength to choose to believe that light will shine through, after even the darkest moments.

I also want to thank Frances Thomson for making a writing-pact with me, Abraham Navarro Garcia for stressing determination in completing a thesis, and Gemma Houldey for approaching and sharing with me her experiences of loss and mourning, after seeing my sudden withdrawal from university life that resembled what she recently had gone through. Those friendships I have gratefully received make it possible for me to live up to my beloved grandmother's teaching: 'To strive against hardship.'

In the University of Sussex, many staff from the School of Global Studies, International Student Support, Research Student Administration Office, Student Life Centre and Health Centre have helped me. I sincerely thank Jayne Paulin, Rachel Gould, James Gordon, Joanne Chee, Ann, Charlie, Katie Walsh and Sarah Longstaff.

I would also like to thank my housemates Basil, Alex and Riyad for their support and tolerating my odd work hours. In the last ten months, I go to Ground Coffee House almost every workday to work on my thesis. I am grateful for the support and companionship from those who work(ed) at the Ground - Rick, Jamie, Ole, Lemon, (another) Alex, Nick, Pauline, Luise, Christian and Ryan - and my fellow regulars - Senka, Brad, Ty, Moran, Andrew and Kathrine.

Among those outside England, my deepest gratitude to my parents, my aunts Hui Su and Lilia Wang and my sister-like friend Xiaoxiao Wang who not only supported me but also took care of my grandmothers. I am also indebted to Professor Huanming Yang, my former doctoral supervisor in genomics who led me into interdisciplinary research. Although I decided to leave that Ph.D half way through in order to formally pursue interdisciplinary research, Huanming continuously supports me. He insists that I owe him a doctoral degree. He has further inspired me with his experiences in encountering and overcoming obstacles, and taught me a poem of Alexander Pushkin to stay hopeful and keep working. I also thank Ole Döring and Yali Cong for their continuous support of my pursuit of interdisciplinary research.

Last but not least, I thank Tim Lay, my copy-editor, without whose support and guidance this submission would not be possible.

CHAPTER ONE. Introduction

Biomedicine is a generic term that refers to the application of bioscience to medical research and practices. Social sciences researchers, who approach biomedicine as an applied science and practices, have long been interested in studying local variations of knowledge production and practice (Whyte et al., 2002; Lock, 2008). Some further investigate the stabilisation and travel across institutional and national borders of scientific hypotheses and principles, technical standards and protocols, and disciplinary norms and practices (Fujimura, 1992; Keating and Cambrosio, 2003; Petryna, 2009). As genetic testing, gene therapy and cell therapy[1] move into clinical trials and health markets, social science researchers have recently started to also investigate the value production and the materiality of gene- and cell- based medicine (Franklin and Lock, 2003; Waldby, 2002; Vermeulen et al., 2012).

My fieldwork, which followed a recent regulatory change to stem cell clinical research and practices in China, led me to focus on the conceptualisation and use of 'experimental' cell therapies in varied situations by different people and their families, institutions and associations. From learning about how cell therapies are conceptualised, developed and used by practitioners, patients and patient families and the Central and the local governments in China, I came to notice the difference and distance between a cell's materiality and its potentiality in medical and non-medical domains. This distance between biological capability and medicinal potentiality enables one to approach and use cell therapy as a "tool" to achieve specific purposes, including non-medical ones such as (re)constructing one's identity. Meanwhile, those using cell therapy like a tool need to carry out "tooling work" to help cells fulfil their medicinal and non-medicinal potentialities in specific ways. In this thesis, I focus on comprehending this "tool-like" feature of cell therapy. Since this difference and distance between biological capability and medicinal potentiality corresponds to the difference and distance between bioscience and medicine, I further use cell therapy as an example to think through what

[1] I use 'cell therapy' to denote more abstract conceptualisation of, and discussion about, using or integrating cells in developing medicinal products. I use its plural form - cell-based therapies - when I introduce multiple visions and approaches that exist and compete in reality to develop, administer, organise and use cell therapy. I apply the same distinction in discussing cell and cells, stem cell and stem cells, and two specific types of cell therapy - stem cell therapy, immunotherapy - and their clinical practices and evolving regulatory situations in China.

"tool-like" biomedicine means for practitioners, patients and patient families, health care systems and markets, and the nation-state.

In this chapter, I first introduce the general background that prompted my interest in studying China's recent regulatory change to stem cell clinical research and practices. I elaborate on two related aspects: the stem cell and its connection with 'regenerative medicine' and 'translational research', and specific unorthodox stem cell clinical practices in China prior to the regulatory change. I then introduce how studying this 'Chinese' case led me to note the "tool-like" feature of cell therapy, and briefly discuss the analytical value and potential use of the concepts of "toolised medicine" and "tooling work". Finally, I present a chapter overview of the thesis.

General research background

A stem cell has the capacity to reproduce itself and differentiate and produce other types of cell and so presents a new version of medicine that may regenerate and rejuvenate damaged, failing or ageing human bodies or parts of bodies. Nevertheless, scientists have emphasised that it will take decades to transform knowledge that they first gather from the laboratory into effective therapy. At the beginning of the 21st century, certain Chinese clinician-researchers and biotech companies deviated from this path: in the absence of scientific evidence and regulatory approval, they started to offer patients stem cell therapy that they developed from their own laboratories. With the aid of the internet, patients and patient families around the world found experimental stem cell therapy that for varied reasons, was not available in some countries but was on offer in some others, including China. Some contacted these Chinese providers and decided to travel to China to receive experimental stem cell therapy. By 2010, stem cell therapy was widely advertised and sold to patients in Chinese hospitals, while journalists, scientists, bioethicists both in, and outside, China continued criticising such 'unscientific, unethical' clinical practice and called for regulatory intervention. In late 2011, the Chinese health authorities responded to these criticisms and calls: the Ministry of Health (MOH) ordered all involved in stem cell clinical research and practice in China to stop their relevant activities and to start a procedure of 'self-

examination and self-rectifying' (MOH, 2011)[2]. Meanwhile, the authorities convened an Expert Committee to assist them in developing specific regulations to regulate stem cell clinical research (MOH, 2013). In March 2013, the first draft of a set of three regulatory documents was published for public comment (MOH and SFDA, 2013a).

In summer 2013, I proposed to study the unfolding regulatory change, specifically the changing mode and practice of regulating biomedical research in contemporary China. My research outline was approved by the examination board, and after obtaining approval from the ethics committee of the University of Sussex[3], I embarked on my fieldwork in January 2014. As events turned out, little happened with regard to this regulatory change while I was in China for the next fourteen months. While the health authorities underwent restructuring during China's recent government reform (Xinhua, 2013a), they seemingly put on hold this particular regulatory change to stem cell clinical research. In March 2015, National Health and Family Planning Commission (NHFPC) and China Food and Drug Administration (CFDA) published a second draft for consultation from relevant agencies and professional bodies (NHFPC and CFDA, 2015a). New regulations were published in August 2015. Bound by my ethics committee approval, I could only stay in the field until the end of April 2015.

Due to access constraints during fieldwork, I could not obtain first-hand observations about how Chinese technocrats and regulators developed the new regulations on stem cell clinical research. My research participants lived through the period of 'regulatory impasse' during which they could not know how long the regulatory changes would take, what the new regulations would look like and how the regulations would affect their health care, work and life. I was able to observe, discuss and learn from them other issues during the impasse. I learnt that patients or patient families considered pursuing cell-based therapies and integrated this possibility into their care practice, even though they knew that such therapies were experimental and unapproved. I also found out that clinician-researchers argued passionately against the drug-like regulatory route that China was about to take, and stressed the indispensability of medical knowledge,

[2] I record the dates of those regulatory events as appeared on the official documents (i.e. on paper), rather than the dates of their publications online.

[3] During my fieldwork, I was asked by local hosts to undergo an independent ethics review of my research. I obtained the approval from the Independent Ethics Committee at Shanghai Clinical Research Center in August 2014.

clinical skills, and professional care in treating patients with cell-based therapies. Additionally, I encountered ambivalence about seemingly opposite options, for example, whether or not to pursue experimental therapy; whether to continue running a unit that provided patients with experimental therapy or to close it down; whether to remain or leave a stem cell research enterprise; or, to regulate cell based therapy as drug or medical technology.

It seemed, on these occasions, my research participants, and those I observed in this study, were using the possibility that stem cells, or other types of cell, present to medicine by achieving something else in addition to medicinal potentiality. My research participants worked hard in this process to conceive and help to actualise the varied potentialities that cell-based therapies presented to them, while constantly weighing cell therapy against other options that might assist them in obtaining what they valued. I came to see the distance and difference between a cell's biological capability and its varied potentialities beyond medicine. I started to ponder over what this difference and distance means to current understandings of biomedicine and the regulation of biomedicine, and to rethink a set of propositions regarding the science, ethics and value of stem cell therapy that instituted this regulatory change in China, yet had been challenged in the past years both within, and outside of, China.

Stem cell research and recent regulatory change to stem cell clinical research in China

The book '*Stem cells: scientific facts and fiction*' (Mummery et al., 2014a) is authored by leading stem cell researchers primarily from Europe. Its publisher recommends the book to 'non-stem cell expert,' and Amazon lists it in 'ancillary services' for 'medical & healthcare practitioners' under the category of 'health, family & lifestyle'. A keynote speaker at a high-end, science conference, which I attended during my fieldwork, recommended the book during their speech. It has become one of my main reference books for 'scientific facts.' The success of its first edition led to the publication of the second edition four years later. In the preface of the second edition, the editors wrote,

> 'As is often the case when science opens a new door, things can go wrong…Just as in many other professions, personal integrity and the attraction of fame and fortune can all influence individual behavior, and stem cell research has already been among those areas with serious cases of fraud. *Mala fide* stem cell

> practices continue to grow at epidemic rates and this growth of what has become known as "stem cell tourism" shows no signs of stopping, however much the experts warn patients of their lack of effect or even risks' (Mummery et al., 2014a: x).

The editors continued: '[the book] distinguishes truth from fiction and empty promises from fact for non-experts in the field.'

Since the early 2000s, science journals, policy briefings, and, increasingly, the media framed science as contrary to falsehood. They did this alongside what became known as the criticisms of 'stem cell tourism' and 'marketing of unproven stem cell–based interventions.' Articles were authored, individually or collectively, by scientists, bioethicists, legal scholars, and policy researchers and alike who took a firm stand against 'unscientific and unethical' practice, and called for further action from professional bodies, regulators and policy makers to better inform the patients and to curtail the aforementioned market activities (Levine and Wolf, 2012; Bowman et al., 2015; Dominici et al., 2015; Caulfield et al., 2016; Sipp et al., 2017; Lee et al., 2017). For instance, Caplan and Levine condemned the 'fraudulent, deceitful and inept practitioners of counterfeit and sham cellular therapies,' and urged that 'patient advocacy organisations, cellular therapy professional and clinicians, professional societies, and international regulatory bodies must act in a concerted, responsive, and responsible manner if patients are to be made capable of distinguishing hope from hype' (2010: 24-25).

In my study on China's regulatory change to stem cell clinical research and practice, I encountered similar criticisms of direct-to-patient marketing and provision of experimental stem cell therapy by Chinese clinician-researchers and biotech companies. I also heard concerns and complaints about how such activities had damaged the reputation of Chinese stem cell science and hindered real translational research. I also heard criticism of Chinese regulators' (in)action, and those with vested interest in either maintaining or breaking the status quo.

In this section, I take a closer look at these 'scientific facts' and 'fiction' about stem cell, stem cell therapy and the 'Chinese' practices, that together instituted China's recent regulatory change to stem cell clinical research and practice.

Stem cell, regenerative medicine and translational research

Prima facie, the definition of stem cell in science literature is unambiguous. For instance, Mummery et. al. wrote,

> '[t]he common definition of a stem cell is "a cell that can divide to give rise to both a new copy of itself and at least one specialized, differentiated, cell type".'(Mummery et al., 2014b: 54)

Definitions of a stem cell from official portals such as the United States Food and Drug Administration (USFDA) or EuroStemCell (the European knowledge hub of stem cells), state,

> 'Stem cells are cells that have the ability to divide and develop into many different cell types in the body during early life and growth. Stem cells may also help repair the body by dividing to replenish cells that are damaged by disease, injury, or normal wear…' (USFDA, 2015)[4]

> 'Stem cells are the body's natural reservoir – replenishing stocks of specialized cells that have been used up or damaged….Stem cells have the unique ability to produce both copies of themselves (self-renewal) and other more specialized cell types (differentiation) every time they divide…' (EuroStemCell, 2016)

After providing generic introductions, the science literature often presents different types of stem cells, and they start to differ in their use of categories and descriptions of those cells. For instance, Mummery et. al. continued to say that: '…it is conceptually easiest to divide stem cells into two types: embryonic stem cells and adult stem cells' (ibid.). The USFDA (2015) report that 'three types of stem cells have been identified: 1. adult stem cells; 2. human embryonic stem cells; 3. induced pluripotent stem cells.' Although EuroStemCell agreed with the USFDA that there were three types of stem cell, and shared a similar definition on the second and third types, EuroStemCell introduced another concept of 'tissue stem cells' in their own 'three categories [of stem cells]'.

Though the distinction between 'human embryonic stem cell' and 'induced pluripotent stem cell' is commonly used in science literature, these two types of stem cells and their research are intricately linked. Yamanaka's lecture, given upon his reception for the *Nobel Prize in Physiology or Medicine 2012,* illustrates this point. Yamanaka recalled

[4] USFDA's website no longer shows the material. A possible explanation is that the 21st Century Cures Act - signed into law by US's former President Obama in December 2016 - established a new category of 'Regenerative Medicine Advanced Therapy' that rendered such information outdated.

how he came to set the goal of his new laboratory to 'establish ES [embryonic stem] cell-like pluripotent stem cells that were not derived from embryos, but from differentiated somatic cells' (Yamanaka, 2012: 272). He recounted how the successful development of a human embryonic stem cell line, by Thomson and colleagues (1998), excited and convinced him to continue working with embryonic stem cells. Yet, the 'ethical obstacle regarding the use of human embryos,' made human embryonic stem cell research a 'distant and forbidden world' to him (ibid.: 271).

This 'controversial' feature of human embryonic stem cell research makes the distinction between human embryonic and non-human embryonic stem cell research meaningful, particularly in policy discussions and societal debates. Policy changes in the United States, at the federal and state levels, also have far-reaching effects on stem cell research, product, industry development, and policymaking in other countries. In the United States, questions about the status of human embryo were closely linked to religious, societal and political contests on, for example, the issue of abortion (Thompson, 2013: 8-9; Hurlbut, 2017). These questions led President George W. Bush to introduce restrictions on the use of federal research funding for human embryonic research in August 2001 (Bush, 2001). Bush's restrictive policy subsequently changed the landscape of human embryonic stem cell research not only in the United States (Cohen, 2004; Karmali et al., 2010), but also around the world (Editorial, 2004; DeRouen et al., 2012). To some extent, 'Bush's ban' also contributed to the discovery and instant popularisation of induced pluripotent stem cell. While Yamanaka acknowledged that, 'I was well aware of the ethical issues over the human embryonic stem cells and wanted to find a method to circumvent the problem' (Mummery et al. 2014c: 98), scientists around the world soon joined and advanced the research on, and with, induced pluripotent stem cells (Scudellari, 2016). Celebrated, in particular, for by-passing 'ethical' issues that foreshadowed human embryonic stem cell research, the induced pluripotent stem cell has in turn profoundly changed stem cell worldwide research, products, industry development and policy making (Editorial, 2010a).

The link between the controversy of human embryonic stem cell and the celebration of the discovery of induced pluripotent stem cell illustrates some of the tensions that fill the evolving terrain of stem cell research with complexity and uncertainty. Although the use of human embryonic cells as research materials triggers and sustains multifaceted

controversies around human embryonic stem cell research, other types of non-human embryonic stem cells have been used in stem cell research and 'regenerative medicine' for a longer period of time (Franklin and Kaftantzi, 2008). For instance, mesenchymal stem cells have gained popularity among researchers and industrialists (Uccelli et al., 2008; Squillaro et al., 2016), including those working in China (Yuan et al., 2012) - a point I return to in chapter three.

Before giving an overview of stem cell research and regulatory change in China, I briefly introduce two concepts, regenerative medicine and translational research. These are important terms in worldwide discussions about stem cell research and regulation. In the current configuration of biomedical research and industry, which originated in the United States and travelled around the world (Maienschein et al., 2008), stem cell research, regenerative medicine, and translational research are intricately linked.

The textbook '*Translational Regenerative Medicine'* (Atala and Allickson, 2015) provides a useful introduction to these concepts. In this textbook, which was compiled by leading figures in the field in 2015, the director of United States National Institutes of Health (NIH) Centre for Regenerative Medicine restated the view of the NIH on regenerative medicine,

> 'The application of treatments developed to replace *tissues* damaged by injury or disease. These treatments may involve the use of biochemical techniques to induce tissue *regeneration* directly at the site of damage or the use of transplantation techniques using differentiated *cells* or *stem cells*, either alone or as part of a bioartificial tissue' (Rao, 2015: 3, original emphasis).

After giving an overview of the field, Rao emphasised that regenerative medicine 'should not be considered as a unified field but, rather, as a set of subfields that focus on different cells and different indications and that are regulated by diverse regulatory pathways' (ibid.: 7). It is a field that is 'united conceptually' and developed 'several business models' that all posed regulatory authorities varied challenges (ibid.: 7). Rao further expected that as a field 'in a state of flux,' new discoveries and technologies, such as gene engineering, three-dimensional printing technologies, will probably 'chang[e] the field yet again' (ibid.: 8).

Notably, neither Rao, nor others in the textbook, provide a specific explanation about why and how 'translational' is added to 'regenerative medicine'. According to the

Index, the term ‘translational medicine’ appears once in this textbook in a chapter on how to derive commercial values from biomaterials (Prestwich and Mann, 2015). The authors start their discussion with a ‘bench-to-bedside’ conceptualisation of the ‘translational’ process, which they suggest needs to be modified into a ‘bench-to-business-to-bedside’ process to better mirror the real-world (ibid.: 185-186). In another chapter, ‘*Translation of regenerative medicine products into the clinic in the United States’,* officials from the USFDA further confirm this ‘translational’ direction (Lee et al., 2015). This ‘bench-to-bedside’ flow is used as a default mode of ‘translation’ by the contributors to this textbook.

Yet, ‘translational’ research is a fuzzy concept that has caused lasting confusion since it was first reported in genetic research (Butler, 2008). Recently, the director of the United States National Centre for Advancing Translational Sciences published a comment piece on *Nature Reviews Drug Discovery* to address particularly the confusion between ‘translational science’ and ‘translational research’ (Austin, 2018). ‘Put simply, basic and translational research in the biomedical field seek to “understand” and “fix”, respectively,’ Austin (2018: 456) stated. He further pointed out that ‘translation is bidirectional’ and cautioned against underestimating the research and operational challenges involved in the translational process (ibid.: 455).

Social science researchers have also noted the confusions around translational research and the complexities involved in regenerative medicine and stem cell research. For instance, historian Maienschein pointed out that,

> ‘Stem cell research, with its public promises of significant clinical applicability, has become a poster child for translational research. The slogan “regenerative medicine” works well for public interests, NIH translational needs, and a growing research community’s interests’ (Maienschein, 2011a: 204)

In other words, the close relation between stem cell research, translational research and regenerative medicine was forged because scientists and politicians believed in, and wanted to capitalise on, the ‘tremendous promise for valuable applications’ of ‘translation, stem cells, and regeneration’ (Maienschein, 2011a: 219). Yet, ‘too simplistic pictures of how development works’ (Maienschein, 2011a) were not the only contribution to the misconception recognised by Austin (2018), Maienschein and

colleagues further warned that 'the widespread push to translation distorts the science...and bioethical discussions' (2008: 43).

The future of stem cell's medicinal and economic-political values is a matter of worldwide consideration (Caulfield, 2010; Morrison, 2012). This speculation not only affects how stem cell research is organized and conducted at present, but also influences how the past and the future of stem cell research is (re)constructed. On the one hand, at the expense of fostering 'historical amnesia' which neglects the traditional notion of stem cells, these contemporary predictions created a 'pre-disciplined set of futures' for stem cell research and industry (Brown et al., 2006). On the other hand, these predictions create a sense of political urgency that leads policy makers to prioritise and quickly respond to '*short-term* putative clinical and economic opportunities and expectations' and undertake 'reflex regulation' (Brown and Beynon-Jones, 2012: 224, original emphasis).

In chapters three, six and seven, I return to this issue when I discuss stem cell research, clinical practices, business activities and regulation in China. In particular, I will examine the connection between stem cell research, regenerative medicine and translational research, and the neglected past and the promissory future of stem cell research-enterprise in China. Meanwhile, in the section below, I set out an overview of China's regulatory change to stem cell clinical research and practices.

Recent regulatory change to stem cell clinical research and practices in China

Here I chronologically introduce China's recent regulatory change on stem cell clinical research and practice - a chronology that is commonly presented in the media, and in relevant scholarly work and serves as part of the background of this study. This chapter examines material primarily from news reports, statements issued by professional organisations, and commentaries published in science journals. In the next chapter, I detail relevant social science studies.

The initiation: the troubling 'Chinese' practice

As I mentioned earlier, stem cell research is a battleground fought at subnational, national and international levels and fuelled by interlinked scientific, religious, ethical and political interests. It is widely noted that stem cell related sciences started to rise in China around the turn of the 21st century (Dennis, 2002; Yang, 2004). China's interest in investing and supporting stem cell research is rooted in stem cells' potential in developing regenerative medicine for 'the national interests and the needs of the people' (Qiu, 2017: 552). The 'rise' of stem cell science in China thus benefits from the Chinese government's substantial, continuous funding and supportive policies (Liao and Zhao, 2008; Yuan et al., 2012; Qiu, 2017). The notable return of Chinese-born stem cell scientists from their established positions in American universities and research institutes, nevertheless, is partly attributed to the restrictive research policy imposed and sustained during the Bush administration (Dennis, 2002; Levine, 2010). The rise of stem cell related sciences in China, in turn, accelerated global competition in stem cell research (DeRouen et. al., 2012; Salter and Faulkner, 2011).

In the same period of time, from 2000 to 2010, an unorthodox clinical practice and business model around stem cell therapy started to prevail in Chinese hospitals. To address clinical questions that they encountered in China, some practitioners adopted scientific knowledge and laboratory techniques that they acquired from literature or training abroad. They did not conduct clinical trials and, instead, directly applied those freshly developed cell-based 'therapies' in 'treating' patients, thereby skipping the 'translation' phase in the 'translational research' model. They treated both Chinese and foreign patients, charging patients considerable amounts of money for the cell-based therapies.

These practitioners, who bypassed the 'translational' phase in developing stem-cell based therapy and attracting patients from overseas, effectively blurred the boundaries between science, medicine and commerce, and between nation-states. Their unorthodox clinical practices, thus, fell squarely into the ongoing international contest on stem cell research, product and industry development, yet raised some new questions that led to scrutiny worldwide. Specifically, their operation reconfigured their practitioner roles and the roles of their patients, which, consequently, also changed the relation between them and their patients. Depending on circumstances, their patient became a consumer, a client-patron, an investor, a research subject, or simultaneously acquired some or all

of the aforementioned roles. Similarly, these practitioners acquired multiple identities and duties as doctor, clinician-researcher, and biotech entrepreneur. A particular controversy arose regarding the allure their practice created for foreign patients. Some of these patients travelled to China for 'controversial and scientifically unproven' cell therapies (Judson, 2006) because in their home countries stem cell research was clouded by turbulent policy changes and stem cell therapy was not available in clinics. This phenomenon, which became known as 'stem cell tourism,' has been forcefully criticised by scientists, bioethicists, as well as doctors, insurers, regulators and policy-makers in those patients' home countries.

Commentators writing in those other, often Western, countries, stressed that researchers from countries outside China 'wouldn't dare' (Einhorn, 2006) use cells that were derived from human embryos or aborted foetuses, while '[s]tem-cell research in China is unlikely ever to be prone to the intense moral politicking that characterizes the field in the West, particularly in the United States' (Murray and Spar, 2006: 1194). Cast in this light, Dennis (2002: 335) reported that against the rise of stem cells research in China, critics were concerned that some of the studies were proceeded in a 'morally bankrupt "Wild East" of biology'.

The common belief that, in China, there are less religious or moral objections to human embryonic stem cell research is a view loosely linked with ideas about Chinese 'tradition' or 'culture' (Yang, 2004). The discrepancy between stem cell research practices and policies in, and outside, of China has also been attributed to 'cultural conflict' (Salter and Qiu, 2009) and the Chinese state's 'political strategy' in developing its bioeconomy (Salter et al., 2006; Salter, 2009). Yet, with findings generated from more in-depth social science investigation (Nie, 2005; Sleeboom-Faulkner, 2008), such binary portraits of practice either in China, or in the 'West', become untenable.

On the one hand, recent studies have noted, in contrast to narratives of a 'Chinese' problem, 'the practice of unproved stem-cell therapies in China' had been effectively curtailed by the Chinese health authorities (Qiu, 2017: 552). On the other hand, despite the medical and scientific communities repeatedly warning about danger, patients worldwide have continued pursuing experimental cell therapy, either in their home countries or by travelling to other countries. The list of regions and countries where

patients could obtain such experimental therapy includes the United States, the United Kingdom, Australia, and Japan (Sipp, 2011; Berger et al., 2016; Turner and Knoepfler, 2016; Munsie et al., 2017). Nonetheless, despite Chinese scientists' objections (Sipp and Pei, 2016), the image of China being a 'Wild East' in stem cell research continues to haunt Chinese practitioners.

Under these conditions, at the end of 2011, the MOH initiated a regulatory intervention to bring order and guidance to stem cell clinical research and practice in China (MOH, 2011). It was an initiative championed by Chinese scientists and bioethicists who felt that 'unscientific and unethical' stem cell related clinical practice of some of their countrymen had tarnished the reputation of Chinese science, and the Chinese nation. They wanted to restore the reputation by bringing China in line with internationally acknowledged 'translational' research model (Editorial, 2009; Döring, 2004). In the following years, this translational model failed to provide easy answers for Chinese practitioners and regulators, or their counterparts in other countries. When I embarked my fieldwork in early 2014, I observed the dissatisfaction of Chinese practitioners who were aggrieved as they witnessed how, in contrast to China, policies and regulations in other countries were becoming more friendly towards stem cell research, regenerative medicine and biomedical industries. In the next section, I introduce the regulatory changes in China, as recorded in official documents.

The process and early appraisal of the regulatory change

In December 2011, the MOH intervened in stem cell clinical research and practice in China when it issued a cease-and-desist order to halt all related activities until further notice (MOH, 2011). Meanwhile, the regulatory agency started to prepare a new regulation specifically addressing stem cell clinical research that had been designated as a type of 'medical technology' in an earlier regulation (MOH 2009b)[5].

The development and finalisation of this new regulation took nearly four years. The key new regulation is called 'Management Measures on Stem Cell Clinical Research (Interim, 2015)' (NHFPC and CFDA, 2015c). Two consultative versions were published in March 2013 and March 2015 (MOH and SFDA, 2013a; NHFPC and

[5] I will introduce more in detail in chapter two on this earlier regulation on medical technologies.

CFDA, 2015a). Noticeable modifications between the two consultative versions occurred in the title of the key document, which went from 'clinical trials research' to 'clinical research' and in the reduced number of regulations: from three to two. Except for the expansion of defining *ex vivo* manipulation to include the gene level (clause 2), the finalised version (NHFPC and CFDA, 2015c) is identical to the second consultative version (NHFPC and CFDA, 2015b). In the Appendixes, Table 1 summarises the main differences between the first consultative version and the finalised and now implemented new regulation.

Rosemann and Sleeboom-Faulkner (2016)'s early appraisal of the interim regulation is rather illuminating[6],

> 'The promise of greater dependability of approval procedures for the clinical development of stem cell treatments and greater compatibility with international procedures should be a relief to many stem cell scientists in China.
>
> The draft regulation…promises to create congruence with both, the benchmarks set out in the "Guidelines for the Clinical Translation of Stem Cells" of the International Society for Stem Cell research, and the standards for clinical stem cell research handled by the US FDA and the EMA [European Medicines Agency].
>
> The focus of this new regulation, however, is exclusively on the governance of clinical research. It does not stipulate any details on how the transition from clinical trials to routine clinical use and market approval shall be handled.' (pp7-8)

The set of questions that Rosemann and Sleeboom-Faulkner (2016) identified include the lack of transparency regarding the status of stem cell-based products, the clinical research procedures, the possibility to allow for experimental clinical intervention, and the affordability of stem cell trials (p8). They further ask whether China's health regulators left these questions 'deliberately open, so as to have the flexibility to follow the current Japanese model rather than the USA or EU model' (ibid.).

Some of these questions were heatedly debated among Chinese stem cell practitioners and I will return to these issues in chapter three. Here, let me underscore three points regarding this regulatory initiative that are important in this thesis.

[6] In the next chapter, I will introduce some additional social science studies that investigated and evaluated this regulatory change in China.

First, prior to the regulatory change, Chinese practitioners did not operate in a regulatory vacuum. Since 2009, an earlier regulation had existed that regulated certain types of stem cell-based therapies as 'category three' medical technologies (MOH 2009b). According to this earlier regulation, category three medical technologies were deemed as containing unresolved techno-scientific or ethical questions, which therefore required additional regulatory scrutiny and sanction, before they could be used in clinical settings (MOH, 2009a). Yet, partly due to its weak implementation, this earlier regulation retrospectively enabled, rather than circumscribed, the proliferation of those yet to be approved medical technologies across China.

Second, because stem cell clinical research and product development spans different terrains of science, medicine and business, and blurs the public and the private spheres, it essentially floats above these terrains. In contemporary China, this enterprise is loosely held in a complex and evolving web of scientific, economic and political initiatives that intersect, and sometimes contradict, one another.

During the regulatory change, the existing regulation on medical technologies (MOH, 2009) that I just mentioned created a notable barrier for the health authorities to introduce a new regulation on stem cell clinical research. The parallel provision of health care services by civilian hospitals and military and armed police hospitals created a further challenge for the health authorities to carry out this regulatory reform in stem cell clinical research and practices across the board. As notable providers of experimental stem cell therapies, military and armed police hospitals are not regulated by the NHFPC, but by the General Logistics Departments within, respectively, the People's Liberal Army (PLA) and the Armed Police Force (APF). Those who (once) provided and sold experimental stem cell therapies to patients in hospitals also liked to cite relevant local policies that, in their interpretation, provided them with a regulatory and administrative basis to establish and operate these practices. They would often refer to the local health-care services pricing policy that, within each of their operational jurisdictions, enlisted cell-based therapies as marketable and chargeable items (also see Huang and Chen, 2015). Since biotech industries were regulated and monitored by the local administrations of both taxation and industry and commerce, those working in stem cell related industries keenly observed how these other regulators would respond to the health authorities' interventions into stem cell clinical research and practices.

Drawing from a wider regulatory landscape to support developing stem cell-based therapies and related industries, practitioners readily directed me to a series of policies, regulations and guidance documents that were issued by other ministries, regulatory agencies and governments at provincial and local levels. For instance, the Ministry of Science and Technology's (MOST) consecutive research funding for stem cell science and reproductive health research since the 1990s was frequently referred to as definitive evidence of governmental support (also see Yuan et al., 2012). Similarly, practitioners cited the National Medium- and Long-term Program for Science and Development (2006-2020) and the Chinese Academy of Sciences (CAS)'s Innovation 2020 as evidence of stem cell science and reproductive health research being recognised and supported by the Central government as a strategic research area that is of national health, economic and security importance (also see Fu and Zhao, 2011; Zhou, 2015).

Figure 1 in Appendixes gives a snapshot of these intersecting terrains and web of initiatives amid which the MOH launched this regulatory change to stem cell clinical research and practices. In chapter three, I will return to the question about the dual regulation of medical institutions. In chapter five, I will discuss how health care services policies, in particular reimbursement policies, affected the organisation and operation of immunotherapy in hospitals. In chapter six, I will also discuss how biotech entrepreneurs sought support and endorsement from local governments to help them survive the industry's 'winter' and (re)position their companies in burgeoning biotech industries in China. Given the complexity of the regulatory situation, this four-years regulatory impasse should not, as some practitioners do, be equated to a kind of regulatory 'inaction' that resulted from a mixture of regulators' incompetency and from the conflict and tension between different groups of stakeholders. Rather, I suggest that anchoring this floating enterprise in these intersecting terrains and evolving web is a challenging task for the regulators who, like the regulated, recognised that making this new regulation could neither be reduced to, nor resolved through, techno-scientific or ethical-regulatory questions.

Compared with the initial goal to regulate stem cell clinical research in a similar way to drug clinical trials, the making of this new regulation became a process of prioritising and gaining justification and legitimacy that directed stem cell towards actualising and maximising its economic and political potential over, and through, the attainment of its

medicinal potential. More concretely, both the regulated and the regulators came to see the establishment and implementation of this new regulation as an essential step to develop a Chinese stem cell research-enterprise, which would secure China's national security and competiveness in the global biomedical research and industry. The timing of such change not only paralleled the end of China's 12th Five-Year Plan (2011-2015), but also, and more importantly, it became part of a new wave of state-led innovation initiatives that were called to fulfil a 'Chinese Dream'. As such, this regulatory change mirrored a substantial change towards developing and normalising a state-led entrepreneurial science model for Chinese biomedical industries in general. I will deepen the analyses of this regulatory change and its effects on different people and their families, institutions and networks in chapters six and seven.

Thirdly, during this regulatory impasse, Chinese practitioners repeatedly pointed out that other nation-states (including the United States, Europe, Canada, and Japan) had been adjusting their policies and regulations to accommodate biological-entity based medicine. Therefore, these jurisdictions had created a more friendly environment for developing new medicines and related industries. Their observations have been documented and analysed by social science scholars in these other countries (von Tigerstrom, 2008; Caulfield et al., 2009; Faulkner, 2012; Hogarth and Salter, 2010). It is, therefore, crucial to consider this larger, turbulent movement of contemporary biomedicine in the world where it resides and whose future it helps to shape.

This brief overview of stem cell clinical practices and regulatory change in China starts to show that, even when reviewed in a chronological order, China's recent regulatory change to stem cell clinical research and practice did not unfold according to the translational research path. One way to comprehend the regulatory change, I suggest, is to put to one side narrowly defined questions of science and ethics. Instead, I propose considering the possibility that the varied and sometimes conflictual 'Chinese' practices are indicative of something other than the 'Chinese' or 'neoliberal' context, or the power and work of (bio)capital or political economy of (bio)innovation.

Toolised medicine and tooling work: what China's regulatory change to stem cell clinical research tells us about biomedicine

In this thesis, I explore how, by reorienting the analytical focus towards the essence and practice of biological entity-based medicine, I can achieve new understandings of both biomedicine and China's recent regulatory change in this field. Using this reorientation, China's regulatory change becomes part of the research context that enabled me to learn about biomedicine from those who lived, worked, and made sense and use of cell-based therapies and this regulatory change (I will elaborate on this point in chapter two).

To learn from my research participants, in this thesis, I restrain myself from binary thinking of the right versus the wrong, the scientific versus the maverick, or the hopeful versus the folly. The portrait of science and fiction, and of scientist-as-hero and maverick clinician-as-villain[7] has prevailed in the media, science journals, and has also preoccupied social science researchers with phenomena such as 'stem cell tourism'. Yet, as I mentioned earlier, these dichotomies do not explain why, despite receiving repeated warnings from scientists, doctors and regulators against experimental stem cell therapy, some patients and their families continue to seek these therapies. Nor do those dichotomies explain why debates on defining stem cells and their regulation persist among practitioners and regulators in, and outside, China, despite having in place a scientific model of translational research and an established regulatory framework arranged around clinical trials. If one follows scientific and bioethics principles, these questions should have been easy to resolve.

Nevertheless, these debates have persisted for nearly two decades and, more recently, became subjects of social science inquires. For instance, after following recent research and regulatory endeavours in developing stem cell therapies and industries in the United States, Europe and China, Haddad and colleagues (2013) point out that the dichotomisation between an 'ethical' and an 'unethical' stem cell industry 'fails to capture the messy worlds of the stem cell industries' (p104). Furthermore the construction of the 'unethical side of stem cell treatments' as 'an ethical, regulatory, and political problem' is itself a strategic problematization by 'unstable and informal alliances of researchers, science journalists, and most notably bioethicists' (ibid.: 113). Instead, Haddad et. al. suggest that stem cell therapy is an 'unruly biomedical field of

[7] See for example this quote from Ellison (2011:617):'Finding themselves between the Scylla of scientific complexity and the Charybdis of legislative restriction, scientists like [Doug] Melton, [Kevin] Eggan, [James] Thomson, [Hans] Keirstead, [Harold] Varmus, and [Shinya] Yamanaka become the Ulysses to cheer for, the hero you want to see win by the book [Park (2011)]'s conclusion.'

heterogeneous practices,' and as such, stem cell therapies are 'fluid sites of regulatory science struggles' that can be used to study the 'very political dimensions of governing science, technology, and innovation' (ibid.:110-111). Similarly, Sleeboom-Faulkner (2016) has posed the question 'why "stem cell tourism" to some is "stem cell therapy" to others'. Sleeboom-Faulkner uses the example of a Chinese stem cell company, Beike Biotech, to describe how local conditions matter to the construction of 'ethicality' of stem cell research, clinical practice and market activity, and to our understanding of the existence and persistence of an 'ethically grey area of stem cell experimentation combining research and treatment in various forms' (ibid.: 78). This messy, grey area was the site of some of the persistent, yet evolving, complexities, uncertainties and ambiguities that I mentioned earlier around experimental stem cell therapy.

Nevertheless, the clue to unravel the complexities, uncertainties and ambiguities does not lie in the 'grey area' (Sleeboom-Faulkner, 2016), nor in the realisation that stem cell therapy is an 'unruly object' (Haddad et al., 2013). Rather, I suggest, the clue lies in what I came to notice during the fieldwork: the distance and difference between a cell's biological capability and its varied potentialities in science, medicine, commerce and politics. I suggest that this distance and difference enables varied imaginations about the usefulness and value of cell therapy, yet, at the same time, requires a concrete contribution from its users to bring the varied potentialities of cell therapy into fruition. In other words, I suggest that the difference and distance between a cell's biological capability and varied potentialities makes stem cell therapy unruly and makes the grey area of experimentation, which simultaneously combines research and treatment, sustainable.

I develop the concepts of "toolised medicine" and "tooling work" to capture a dual process and an evolving relation and interaction between biological entity-based medicine[8] and its users. On the one hand, the concept encompasses the multiple meanings and values presented by biological entity-based medicine to different people, their families, institutions, associations and networks and, on the other hand, the necessity and importance of the user's work to realise the potential of this new form of

[8] This difference and distance between biological capability and medicinal potentiality applies also to other biological-entity based medicine, such as gene therapy, whereas my research revealed to me first through cell therapy.

medicine. By naming it "toolised medicine," I want to underscore that the user of "toolised medicine" can be a patient, patient family, scientist, clinician-researcher, biotech entrepreneur, or nation-state. As I observed during this study in China, even though in principle everyone can be a user of toolised medicine, not everyone had the economic or political means to become a user. Moreover, users did not view each other as equal contributors to the making of new medicine, and not all 'usership' (Faulkner, 2008b) is equal. For instance, in chapter seven, using the lens of toolised medicine and tooling work, I suggest that China's recent regulatory change to stem cell clinical research and practice could be viewed as a case when a nation-state took its primary usership in (re)forming and (re)directing a nationalist stem cell-based research enterprise to compete with other nation-states in a increasingly intensified global competition. In this process, the need and preferences of other users - in particular patients and clinician-researchers - were, nevertheless, rendered secondary.

Nevertheless, once other users for instance, patients, health care professionals, and biotech entrepreneurs, are treated with equal scholarly attention as to the nation-state, then it will be seen that this regulatory exercise is not a typical case of the 'co-production' between knowledge and state power (Jasanoff, 2004). Nor is it a pure exertion of the power of 'biocaptial' (Sunder Rajan, 2006) and an instance of political economy of (bio)science and (bio)innovation (Tyfield et al., 2017). Despite the powerful role of the nation-state and of the primacy of political and economic interest in directing and formulating a 'Chinese' stem cell research-enterprise, my research shows other users such as patients and clinician-researchers have also influenced how cell therapies are conceptualised, practised and used collectively. Even though the resulting new regulations reflect the preferences of the party-state, it is important to note that other values, motives, emotions and affects continue to persist and resist the assimilation into the grand dreams of science, markets or politics. So, in social science analysis, one can choose not to be captivated by the power of science, markets or politics, but pay more attention on how those other views and practices shape the future of biomedicine.

Additionally, I suggest biomedicine has become "toolised" because I noticed that the usefulness and value of a particular kind of biomedicine, including the cell therapy studied here, is relative. While a user engages with cell therapy as a tool to achieve

specific purposes, a user is likely to have other tools at their disposal to achieve the same purposes. This "tool-like" feature explains how competing definitions, claims, and values can be assigned to cell therapy. It also helps to explain how, a patient or a biotech entrepreneur, at one time actively pursued cell therapy and, at another time, decided to switch to another remedy or business. In the thesis, I explore, under what conditions, these users changed their minds.

Science fiction novelists, futurologists and ethicists have speculated the coming of a 'tipping point'[9] of biotechnology that will fundamentally or even irreversibly change our understanding of what it means to be human (Huxley, 1931; Fukuyama, 2003; Wallach, 2015). Now the reality is catching up. Human genome editing technology *CRISPR-Cas9* has raised worldwide enthusiasm, concern and debate in science, religion, ethics and policy communities (the Economist, 2015; National Academies of Sciences, Engineering, and Medicine, 2017; Nuffield Council on Bioethics, 2018). Existing and emerging biotechnologies are converging (Wen and Tang, 2016; Sweet, 2017; Pulecio et al., 2017), so are biotechnologies and other technologies, such as three-dimensional printing (Lieben, 2016) and nanotechnology (Coccia and Wang, 2015). These technologies facilitate one another's development and applications.

Compared with standard modern medicine, toolised medicine is more fluid in its form, movement and usage. Any particular kind of toolised medicine, such as cell therapy, is simultaneously versatile in its function and possibly ephemeral in its actualisation now and in the future (Rao, 2015). Developing a particular kind of toolised medicine could still take its developers and investors decades to reach the health market. But it is no longer fictional to suggest that toolised medicine(s) will likely alter humanity and human societies in the 21st century. Critical questions must be asked, and if possible, resolved at this 'inflection point'[10]. Questions about the affordability, accessibility and reimbursement mechanism of cell therapy have been contested among scientists, industry analysts, health economists, regulators and insurers (Romero, 2018), and preliminary solutions are put to the test (Medmeme, 2017). More fundamental questions

[9] A tipping point is 'an event whereby one simple alteration forces a complex system to reorganizes' (Wallash, 2015: 37).

[10] Wallash introduced 'inflection points' as 'turning points in history followed by either positive or negative consequences. They provide windows of opportunity that allow us to assert a degree of control over the future we create' (2015:10).

that require wider societal debates are pending. Whose vision and preference takes precedence in the envisioning, developing and actualising future medicines, and for what purpose? How will the desirability, usability, and value of a particular future medicine be defined, evaluated, and decided - and who, or what, will make those decisions?

"Toolised medicine" and "tooling work" are thus concepts that I develop to think through a key feature of contemporary biomedicine that is built upon the difference and distance between a biological entity's biological capability and its varied potentialities. In following chapters, I want to highlight how different users and tooling work contribute to the making and remaking of contemporary biomedicine and its industries. In so doing, I want this thesis to serve as a reminder that, no matter how science, markets and politics seem to dominate the envisioning, development and organisation of biomedicine, there always are multiple options to forge future medicine and our shared future.

Overview of the following chapters

Chapter two illustrates the context of my fieldwork, and how my fieldwork led me to go beyond following China's regulatory change to stem cell clinical research and practice and focus more on biomedicine. I provide a literature review of social science studies of stem cell research, clinical practice and regulation in China in the past decades. I introduce my fieldwork and describe the following three, interlinked aspects of the regulatory situation that also constituted a significant part of my fieldwork situation. First, regulatory change had severely affected clinical practice and business activities around stem cell therapy; second, regulatory change had fallen into an impasse with no clear clue when and how it would end; and third, while experimental stem cell therapy was brought into regulatory scrutiny, other novel biomedical interventions, including immunotherapy - a 'sister' therapy to stem cell therapy - continued being developed and practised in China. The chapter concludes as I reflect on how studying patients' and practitioners' views and experiences with experimental cell therapy and regulatory change had gradually nudged me to rethink biomedicine, in particular its translational research and regulation model.

From chapter three to chapter six, I recount and analyse how regulatory change, to varied degrees and in different ways, affected different groups of people, and how those people viewed and responded to those changes. In sequence, I focus on clinician-researchers, patients and patient families, health care professionals, and biotech entrepreneurs. I illustrate how, through understanding those people in their specific lifeworlds, I saw that their views on and experiences with experimental cell therapy could not be explained away by the 'Chinese context', though some of their life and work strategies were developed in responses to the changing regulatory situation.

Chapter three introduces stem cell practitioners' perceptions and contestations of an 'leading edge' in a Chinese stem cell enterprise set within the context of global research and industry competition. Clinician-researchers and biotech companies claimed that their previous work had helped to create this 'Chinese edge'. This edge was dismissed by stem cell scientists whose work had been, so far, primarily conducted in the laboratory. In observing and analysing those debates, and relevant documents and literatures, I take the first step to conceptualise "toolised medicine". Specifically, I distinguish between a biological entity's biological capability and its medicinal potentiality, and anchor "toolised medicine" in this process of actualising a biological entity's potentiality from its materiality.

In chapter four, I introduce some of my research participants - patient and patient families who valued (and sometimes pursued) experimental stem cell therapy for specific reasons, despite their knowledge of the experimental status of stem cell therapy that was undergoing regulatory scrutiny. Literature on stem cell tourism has repeatedly documented this apparent contradiction, and suggests that patients and patient families are mostly driven by desperation and hope in their stem cell therapy journeys. Yet, for those patients and patient families who I met in this study, the medicinal potentiality of a stem cell is intricately linked with the possibility that it offers to help (re)construct identity, family relations and social standing. These possibilities although medically related are, essentially, non-medical. For those patients and patient families in particular situations, this possibility to insert their own meaning and value into their pursuit of stem cell therapy paradoxically resides in the 'experimental' status of stem cell therapy. Like those clinician-researchers who underscored the importance of clinical work in actualising stem cell's medicinal potentiality, those patients and patient families also understood that their work of hope and care was part of the process that helps to attain

stem cell's varied potentialities that correspond to their need. In other words, what those patients and patient families valued and acted upon is stem cell's varied potentialities, and they devoted their "tooling work" in the process of attaining those potentialities. Critically, patients' and patient families' tooling work reveals, simultaneously, agency and vulnerability - a theme that I revisit in the following chapters.

In chapter five, through recalling my participant observation, I introduce how immunotherapy was perceived and used by health care professionals and patients in a cancer hospital in early 2015. Since being listed together as 'category three medical technologies' by the MOH in 2009, immunotherapy and stem cell therapy are referred as 'sisters' by practitioners in China. Nevertheless, for various reasons, while stem cell therapy had been brought under regulatory scrutiny since late 2011, immunotherapy continued to be administered to cancer patients in public hospitals until early 2016. The nationwide downturn of immunotherapy is often attributed to the public outcry over questionable practices around immunotherapy that gained momentum after a young cancer patient, Wei Zexi, passed away.

My participant observation in a biotherapy unit allowed me to observe how immunotherapy was administered by doctors and used by patients in a nearly ordinary manner while also known as a yet-to-be-proven therapy. This practice was sustained amid a set of evolving clinical, health care insurance, and regulatory uncertainties that were brought to public attention during the events around Wei Zexi's death in mid-2016. On the one hand, those uncertainties were known to, and seemingly accepted, by both patients and doctors in that biotherapy unit in early 2015. On the other hand, towards late 2014, those uncertainties had prompted leading clinician-researchers to take proactive measures to prevent immunotherapy from going down the same path that they had witnessed in experimental stem cell therapy in the previous years. These proactive measures included strengthening self-regulation and asking regulators to strengthen the oversight and regulation of immunotherapy clinical practice. Amid accumulative and changing uncertainties, that biotherapy unit closed its immunotherapy programme in mid-2015.

Chapter five, therefore, deals with this ambiguous situation that was co-constructed and maintained by patients, health care professionals and relevant institutional

arrangements, and in which yet-to-be-proven immunotherapy was practised and used rather ordinarily. Those understandings of experimental therapy and the ambiguous situation helped me to rethink and reassess, in chapters six and seven, China's recent regulatory change to stem cell clinical research and practice.

In chapters six, I consider the perspectives, experiences and actions of biotech entrepreneurs during this period of regulatory change. I include in my analyses those people that I talked to during the study, and some others whose business activities were documented in the public domain. These biotech entrepreneurs had all ventured into stem cell therapy and related industries prior to the regulatory change, and were among the most affected by it. They, accordingly, devised varied strategies to survive this winter of their industry, and to prepare themselves for rising opportunities amid multifaceted risks. I analyse those strategies as tooling work that biotech entrepreneurs exerted through reorienting the development of biomedicine towards maximising its economic and political values. To secure their business survival and prepare the future, biotech entrepreneurs devised their strategies primarily responded to 'signals' that were sent from the Chinese party-state. But their tooling work also had consequences on other users, such as the patients.

In chapter seven, using the lens of toolised medicine and tooling work, I examine the effects of different users' tooling work that they exerted during regulatory change on one another, and reassess this recent regulatory change to stem cell clinical research and practice in China. I contend that this recent regulatory change provided the leading practitioners, regulators and various mediators with an opportunity and venue to exercise their joint tooling work to make biomedicine into a tool to aid China's nation-building in the 21st century. While their joint tooling work prioritised actualising stem cell's potentialities in economic and political domains, this in-the-making Chinese stem cell research-enterprise has varied effects on other users and user groups who have different visions and preferences for stem cell-based medicine.

CHAPTER TWO. Contexts

This chapter provides the general background to this study. First it introduces social science literature on stem cell research and regulation in China and then it introduces the fieldwork. It also takes a closer look at the regulatory situation that allowed me to study alternative interpretations of the regulatory change outlined in the previous chapter and to examine the varied experiences of ordinary Chinese people during this period of change. This regulatory situation contained a discordancy wherein immunotherapy, which was perceived as a 'sister' to stem cell therapy in China, was able to continue its clinical life, whereas stem cell therapy was cut short. I further explain how I came to realise this regulatory change to stem cell clinical research and practices in China opened a window for me to study biomedicine.

Literature on stem cell research and regulation in China

In the previous chapter, I mentioned that policy changes to stem cell research in the United States had far-reaching and long-term effects on stem cell research and policy making in other nation-states, including China. Like the United States and Europe, the Chinese government has, since the 1990s, identified stem cell research as a critical area that holds potential for bettering public health and generating economic returns, so the government offers political support (Fu and Zhao, 2011).

In the first decade of the 21st century, two aspects of 'Chinese' stem cell practices attracted the attention of stem cell researchers, bioethicists, and patients in countries outside of China. On the one hand, while the US President Bush introduced federal restrictions on human embryonic stem cell research in 2008, the Chinese government's unwavering investment and support for stem cell research attracted Chinese-born, established stem cell scientists working outside China to return and work in China (Dennis, 2002; Yang, 2004). These returnee-scientists in turn contributed to the rise of stem cell science in China (Yuan et al., 2012). On the other hand, patients and scientists noticed the advertising by Chinese hospitals and biotech companies promoting their provision of stem cell therapy to patients in and outside of China. Despite its 'unproven' status, in the 2000s, the 'experimental' cell therapy that was on offer in China attracted

a large number of foreign patients. The media soon reported on the international travel of patients and families in pursuit of stem cell therapy - an activity commonly defined as 'offshore' treatment or 'stem cell tourism' in subsequent scholarly and policy discussions (Kiatpongsan and Sipp, 2009; Ryan et al., 2010; Cohen and Cohen, 2010). Chinese clinician-researcher Huang Hongyun and biotech company Beike Biotech were among the first of these providers of experimental cell therapy and, in the following years, they were scrutinised as operators of stem cell tourism (Watts, 2005; Judson, 2006; Einhorn and Weintraub, 2007; Qiu, 2008; Kiatpongsan and Sipp, 2009; Editorial, 2010b).

The Economist reported that: '...in the field of stem cells, China is showing that it can do world-class science. It is a shame, then, that so many fraudsters operate and that officialdom turns a blind eye' (the Economist, 2010). Against this background, social science researchers started to investigate stem cell research, clinical practices, business activities and regulatory changes in China. They soon witnessed the efforts of Chinese scientists and bioethicists to establish scientific standards, research procedures, and ethical guidance in China that were internationally comparable. For instance, writing for a special issue on *Human embryonic stem cell research: international and U.S. public policy,* Döring (2004) introduces an initiative taken by Chinese leading researchers in life sciences and bioethics to promote 'scientifically and ethically satisfactory regulations on human embryonic stem cell research' in China (pp42-44). Döring observes how this proposed regulation, nevertheless, had a particular purpose, 'the currently discussed ethical standards are embedded in the shared purpose of facilitating the life science by increasing their regular performance and raising the level of acceptance within the public' (ibid.: 45). Döring further points out that, despite its merit, this initiative reflected 'the visions and interests of a limited but influential group of people [researchers and bioethicists] in China' (ibid.: 45), however, the views from ordinary Chinese people were still missing.

Döring's early observations on the efforts of China's leading scientists and bioethicists, and their dominant role in developing internationally acknowledged standards in China, is echoed by social science researchers investigating stem cell research and related regulatory change in China later on. Zhang's work on the 'cosmopolitanization of science' and Rosemann's investigation into transnational stem cell clinical research

consider the process of bringing Chinese research practices, guidelines and regulation closer to international standards. Based on her interviews with Chinese stem cell scientists and bioethicists who partook in international collaboration, Zhang suggests that the interaction of Chinese researchers with the international science community did not lead to 'Westernization'. Rather, Chinese researchers reflectively participated in international collaboration, and continuously negotiated with their local and international colleagues, institutions, and other stakeholders, on designing and organising research projects as well as everyday laboratory activities (Zhang, 2010, 2012). Similarly, in his anthropological study of the China Spinal Cord Injury Network, Rosemann illuminates how stem cell scientists and clinician-researchers from China, Hong Kong, Taiwan and the United States developed and sustained a 'transcontinental clinical research infrastructure' to conduct stem cell clinical trials to treat spinal cord injury (Rosemann, 2013, 2014). Rosemann suggests that the science world is undergoing 'multipolarisation' (2013), wherein to make multi-country stem cell trials work, scientists and clinical researchers needed and were able to tailor international standards to specific regulatory, institutional and epistemic-cultural situations (2014). Notably, this situation-specific standardisation practice is not peculiar to China. Rather, as demonstrated in Rosemann's later joint research with researchers from Thailand, Argentina and Mexico, the practice of 'alter-standardisation' exists in various transnational research and business activities in the development and practices of stem cell-based medicine (Rosemann et al., 2016; Rosemann and Chaisinthop, 2016).

Both Cong's (2007) philosophical reflection on the practices in China around the turn of the 21st century and Sleeboom-Faulkner's (2010a, 2010b) long-term fieldwork address the influential role of scientists and bioethicists in the construction of standards in China, and the subsequent consequences. Cong (2007) tackles a critical question on 'Chinese values of life' that is pertinent to human embryonic stem cell research. Cong stresses the multiplicity and ambiguity in Chinese people's views towards using human embryos in biomedical research, and provides an insider's critique of stem cell research practices both within and outside China. For instance, Cong notes that although certain experiments by Chinese researchers - for instance, creating human-animal chimeras - were heatedly debated internationally, they did not draw much attention in China (ibid.:18-19). Noting the eagerness of Chinese researchers for 'quick success and instant benefit' in pursuing science and technology advancement in and for China (ibid.: 26-

27), Cong further cautions against potential exploitation, by both Chinese and western researchers, of varied ethical standards and research practices between China and other countries (ibid.:28).

Sleeboom-Faulkner's work has further deepened our scholarly understanding of the introduction and adaptation of international standards, in particular ethical standards in leading laboratories in China. Sleeboom-Faulkner (2010b) points out that stem cell scientists in China were aware of the differences that existed in the understanding of 'risk' involved in human embryonic stem cell research between China and the United States and Europe, and different research conditions in urban and rural China. Those scientists further integrated this form of 'double reflexivity' into their 'strategic reasoning' for research that they conducted in particular institutional settings in China (Sleeboom-Faulkner, 2010b), and in constructing boundaries between 'ethical' and 'non-ethical' science (Sleeboom-Faulkner, 2010a). Since leading Chinese stem cell scientists are also active members in the international stem cell research community, they applied similar reflexivity and reasoning in preparing for and conducting international scientific collaborations (Sleeboom-Faulkner, 2013). Salter and colleagues (Salter, 2008; Salter and Qiu, 2009), and Wahlberg (2012) have observed this awareness and utilisation of existing differences in research, regulation, social-economic and political conditions between different regions in China and between China and other countries. Whereas Sleeboom-Faulkner and Wahlberg, as anthropologists, pay more attention to the reasoning and actions of people, Salter, a political scientist, interprets the situation through the lens of political economy and stresses the role and function of the nation-state in heightened global competition in biomedical research and innovation (also see Salter et al., 2006; Salter, 2009).

Social science researchers have studied thus the views and practices of Chinese stem cell scientists and bioethicists in constructing and promoting standards of 'good research practice' in stem cell research and (bioethical) regulation in, and for the benefit of, China. Yet, most of those scientists who conversed with social science researchers and who were able to contribute to the making of national research policy and regulation, nevertheless, worked in elite institutions. So when social science researchers turned attention to the other side of the 'Chinese' practice - stem cell *clinical practice* - their studies revealed a different and more complex picture.

As I mentioned earlier, this 'entrepreneurial' aspect of cell therapy in China was first reported by science journalists as examples of 'stem cell tourism'. Noting that 'stem cell tourism' is criticised on both 'scientific' and 'ethical-regulatory' grounds, this tourism framing, especially in the early days, steered the attention of social science towards the 'wrongness' of 'Chinese' practices. Over time, the accumulative social science studies into clinical practice, in particular patients' experience, started to challenge this one-dimensional diagnosis of 'stem cell therapy…[being exploited] by frauds, kooks, apostates and those willing to do whatever it takes to earn large sums of money from the desperate' (Caplan and Levine, 2010: 24). Particularly, studies exploring patients' views on experimental cell therapy repeatedly reveal that, patients and healthy adults alike consider traveling to destinations that offer experimental treatment even when they know about the risk and have received warnings from their doctors about the potential dangers (Brophy, 2017; Einsiedel and Adamson, 2012).

To unravel why patients pursue experimental cell therapy, social science researchers began to use 'hope' as a key explanatory concept (Murdoch and Scott 2010). Later, more empirically grounded studies enriched scholarly understanding of the perspectives and experiences of patients and patient families. For instance, Song (2010) illuminates how American patients and their families consider that part of individual's 'salvation,' is travel to China and undergo experimental cell treatment. Song proposes the concept of 'biotech pilgrim' to capture this religious-spiritual dimension of stem cell travel for patients and their families. Based on their interviews with patients who travelled to Beike Biotech in pursuit of experimental stem cell therapy, Chen and Gottweis (2013) illustrate how patients see themselves as 'well-informed and pursuing treatment options intelligently' (ibid.: 14), and in seeking experimental treatment, these patients also act as 'voluntary research subjects and even *de facto* funders of research' (ibid.: 3). As such, Chen and Gottweis suggest that we might be witnessing a reconfiguration of contemporary patienthood, that is closely interwoven with reconfigurations in global bio-economy and health care.

Salter et al. (2014), Song (2010), and Petersen et al. (2017) use the lens of political economy to analyse this wider social-economic and political context in China as well as the global dynamics that enabled both the 'rise of stem cell science' in China and the phenomena of 'stem cell tourism'. Sleeboom-Faulkner and colleagues' work on

‘bionetworking’ and ‘bionetwork’ focuses on translocal and transnational stem cell research and business activities. They provide further insight into how different social actors, institutions and organisations forge dynamic relations in the pursuit and advancement of a particular project. Sleeboom-Faulkner and Patra (2011) propose the concept of ‘bionetwork’ in their study of a transnational network between Japanese and Indian researchers, medical professionals, managers and patients who brought and transformed Japanese stem cell technologies into experimental stem cell therapy in India. In this context, ‘bionetwork exploits differences and similarities in the provision of healthcare, levels of wealth, standards of scientific development, and research regulatory regimes and their implementation’ (ibid.: 647). A related concept of ‘bionetworking’ that was first proposed in Patra and Sleeboom-Faulkner (2009) emphasises ‘the entrepreneurial aspects of scientific networks that engage in creating biomedical products’ (Sleeboom-Faulkner，2016). Pertinent to my study, Sleeboom-Faulkner and colleagues demonstrate how regulatory capacity building is intrinsic to ‘bionetworks’ and ‘bionetworking activities’ (Sleeboom-Faulkner et al., 2018). Additionally, they examine how China’s regulatory change to stem cell research and clinical practice affected, and was affected by, ‘bionetworking’ activities in research and business arenas (Sui and Sleeboom-Faulkner, 2015; Sleeboom-Faulkner, 2016).

So far, I have introduced literature that investigates different facets of stem cell science, clinical practice, and business activities in China. The role and function of national regulation and governance is stressed in almost all this literature. Therefore, it is unsurprising that China’s evolving regulatory landscape in the field of stem cell research, clinical practice and industry draws attention from scientists and social scientists in, and outside of, China. Yet, this literature also suggests that the regulation of Chinese practice is a complicated task that creates conceptual and methodological challenges for social science researchers. In the next section, I will introduce how I tackled some of the theoretical and methodological challenges that arose in my study.

Fieldwork: timing, sites, research participants and constraints

Chinese health authorities initiated regulatory changes in late 2011, and in March 2013 published three regulatory documents for consultation (MOH and SFDA, 2013b, c, d). During summer 2013, I proposed a 14-months long fieldwork study on the finalisation

and implementation of the new regulation in China, to understand how the new regulation was evaluated by practitioners and patients. Given that stem cell research and industries are concentrated in the most prominent and innovative regions in China, I planned to construct my field sites and travels around Beijing, Shanghai, and Guangdong province[12]. My main research methods were conducting interviews, participant observation in hospitals and research institutions, and archival research. I felt this range of methods would address the need to include different groups of people working in different types of institutions and living in different regions in China. I considered practitioners, regulators, and patients as my main research participants. My research proposal was approved by academic and ethics reviews from the University of Sussex in autumn 2013, and January 2014, respectively. Accordingly, I conducted my fieldwork.

Yet, when I was traveling around in China for my fieldwork from January 2014 to by the time my fieldwork ended, in April 2015, the regulatory changes were still incomplete. What I witnessed and documented was a period of regulatory impasse. Apart from a second consultative version of the new regulation published in March 2015, a month before I left the field, the new regulations were still pending to be announced. As such, I witnessed how those affected by the regulatory change lived through this ambivalent time and how some of them continued to pursue experimental cell therapies.

In May 2015, I returned to the University of Sussex with 95 interview records, 14 field notebooks, a box of documents that I collected during my field visits of research institutes, hospitals, biotech companies and conferences, and about 35 gigabytes of digital materials stored in my laptop.

The 95 interviews were conducted after my research participants gave their written informed consent[13] and lasted, on average, about 45 minutes. The shortest lasted under

[12] I chose these sites based on both research and my own work experiences. Between 2002 and 2012, I had studied bioscience, and worked in a genomics institute in Beijing and Shenzhen, Guangdong province, and nearly yearly visited Shanghai in attending professional conferences. When the science journal *Nature* published its *China Index 2014* (Campbell and Grayson, 2014), I noted that there is a significant overlap between *Nature*'s list of innovation centres and my field travels.

[13] Acquiring signatures to document one's consent to partake in research is an 'informed consent' model used by biomedical research and recommended by research ethics guidelines, yet contested by social

just half an hour, and the longest lasted three and a half hours. Largely corresponding to my research plan, I interviewed 36 practitioners (12 scientists, 9 clinician-researchers, 15 biotech entrepreneurs)[14], 10 health care professionals, 5 officials, and 20 patients and patient families. These semi-structured interviews were themed around: i) my research participants' views on, and experiences with, stem cell research and stem cell-based medicine; ii) their views on, and responses towards, the regulatory change and the proposed new regulation; and iii) how the regulatory change had, so far, affected their work and life.

Partly because of the aforementioned regulatory impasse, I changed my plan in two ways. First, not long after I started my fieldwork in January 2014, I realised that I had underestimated the difficulty of obtaining first-hand insight into regulators' work on this regulatory change. Studying policymaking in China is a well recognised scholarly challenge (Wu, 2013). Prior to doing fieldwork, my years of studying and working with senior geneticists and bioethicists in China had, nevertheless, made me relatively optimistic about the possibility to reach the regulators in the health authorities. Yet, I could not have anticipated how fundamentally the recent political and governmental reform would affect the health authorities' work on this regulatory change, and how in turn, it changed the outlook of my proposed research in studying this regulatory change.

I had anticipated that the restructuring of the health authorities would create a complicated coordination challenge for the two key regulatory agencies. During the fieldwork, I further realised that the heightened innovation rhetoric in today's China had effectively repositioned the proposed regulation on stem cell clinical research in a wider political context. While the new regulation shifted towards the intersection of stem cell science, health care system, and market and political aspirations, the health authorities needed now to carefully weigh competing interests and demands from these domains against one another. My query about the ongoing regulatory deliberation thus acquired unanticipated political weight, and my affiliation to a British university increased the sensitivity of my research.

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science researchers (Sleeboom-Faulkner et al., 2017) and was alien to some of my research participants. The 95 interviews did not include off-record and daily conversations.

[14] Though a considerable number of practitioners worked in different domains, I use here my interviewees' self-assigned primary identity. I will discuss in chapter three, and again in chapters six and seven, the association, disassociation and changing relation between these groups, and what I suggest could be learned in attending to these changes.

For instance, in early 2014, a regulator in the health authority told me during my visit to her office that they had already commissioned a group of Chinese bioethicists to conduct an internal review on how stakeholders saw this proposed regulation, which in her opinion, was similar to my study. Moreover, the regulator foreclosed the possibility that I could ask about questions regarding their regulatory deliberation, citing that the State Council had recently stressed to all officials working in the Central Government to be vigilant against foreign forces attempting to steal state secrets. In the following months, I was explicitly reminded of the sensitivity of my study a couple more times, and my interview requests were rejected for this very reason on two other occasions.

Second, I developed more interest in understanding less studied groups, in particular patients and patient families, and practitioners working in less known institutions or emerging industries. Similarly, I identified new research venues, such as conferences (and, occasionally, semi-professional and semi-social gatherings), science parks, consultancy firms, and start-up cafes. So, in addition to the aforementioned main research groups, I also interviewed four science managers, six consultants and four investors whose work, which remained mostly behind the scenes, became important for the stem cell research-industry. I also interviewed a journal editor, a retired ethicist, and some students and company employees who worked at the periphery of stem cell research or industries. Among all those who I interviewed, about twenty still remain in contact with me.

In addition to interviews, I conducted participant observation in two civilian public hospitals, each for about three months. In autumn 2014, I followed Dr Hua[15], a neurologist who specialises in motor neurone diseases, in his daily work in a renowned hospital located in a cosmopolitan city in the Yangtze River Delta. In early 2015, I shadowed Dr Jiang, an oncologist at a melanoma-biotherapy department in a megacity in the Pearl River Delta. The two regions are among the most developed in China, and, respectively, the two hospitals are ranked among the top centres for neurology and cancer treatments. My participant observation was orally granted by the chiefs of these departments and I abided by the agreement made between me and the two doctors prior

[15] In this thesis, I use pseudonyms to protect the identity of my interloctours. The surnames are chosen from the book *Hundred Family Name* (*baijia xing*) that has been used by Chinese people since the Song Dynasty. Some authors that I cite may have the same surnames, but there is no overlapping between those authors and my interlocoturs that share the same surnames.

to shadowing them. In both hospitals, the core of our agreements was that patients' benefits, privacy and confidentiality came first. In practice, it meant that I would not interfere with health care practice, that as doctors saw patients in consultation rooms and hospital wards I would try to be 'a fly on the wall', and I would not approach patients without the doctor's approval and introduction. On occasions when it was most convenient for the patients, I was allowed to conduct interviews and focus group discussions on-site with patients upon receiving their consent. In the neurological department, I conducted three interviews with patient families inside the hospital after their consultation meetings with Dr Hua and two more outside of the hospital when they found that more convenient. In the cancer hospital, I conducted two focus groups with cancer patients. I had another focus group discussion with a group of spinal cord injury patients and their families in another site.

There were two main constraints to my research. First, the choice of my field sites, as I mentioned earlier, was based on my research on the locations of biomedical research and industry hubs in China, and where also I expected to best observe the regulatory deliberation about the new regulations. These hubs attract substantial research and education, health care, finance and investment resources to support their development. In the context of significant unequal development in China (Sun and Guo, 2013b), I mainly travelled in the most developed regions and cities in China and met those who lived or travelled to those places. Even though I made additional efforts to widen the reach of my field visits and research participants, to increase the diversity inside each group, and to query how things were in other parts of China, my first-hand understanding of stem cell research, clinical practice and regulatory debate in less developed regions is limited. Second, my inquiry into China's regulatory change together with my affiliation to a British university occasionally caused doubts and suspicions from those I encountered during the fieldwork. Nevertheless, as a Chinese citizen who had previously studied and worked in biosciences and bioethics with senior researchers in China I also carried much credibility too. I will revisit these constraints in later chapters.

Gazing at the regulatory situation

The regulatory situation constitutes the general background for my fieldwork and my subsequent inquiry into stem cell-based medicine. The people I met in the field lived through three intertwined aspects of the regulatory situation. First, the stem cell research-industry had largely dwindled; second, the regulatory change fell into an impasse; and third, immunotherapy - a 'sister' therapy to stem cell therapy - continued to be provided to cancer patients around China. Practitioners told me about these aspects with notable frustration. While the first two were directed at stem cell clinical research and practices, the third appeared to have only a remote link with regulatory change to stem cell therapy. Yet, all three aspects informed how I understood the regulatory situation, its effects on my research participants, and my own research situation.

The 'enterprise' and its 'winter'

During my fieldwork, I sporadically read news about how patients were sold 'experimental' stem cell therapy. These reports stoked waves of criticism about 'unethical' practices of 'greedy' practitioners who created and sustained the 'messy' situation that trapped Chinese stem cell research and industry (see also Sui and Sleeboom-Faulkner, 2015). Nevertheless, I learned soon after I started the fieldwork that, to a large extent, commercial activities around experimental stem cell therapy had dwindled. Since the publication of the cease-and-desist order in 2011 (MOH，2011), Chinese health authorities not only halted all stem cell clinical research and practice, but also stopped reviewing new applications to conduct stem cell clinical research.

Many of the practitioners I met in this study thus refereed to this regulatory order as a 'total ban' on stem cell related research or business activity at, or near, the 'bedside'. Constrained by this 'total ban', those once working with stem cell, either at or close to the 'bedside', were put into a mode of 'standing by'. This working condition was described by many of my practitioner-research participants, as 'the winter for the [stem cell] enterprise'. I first heard the phrase from Dr Bai in May 2014.

Dr Bai has a doctorate degree in bioengineering and is a senior executive at a new media company that reports on life sciences and industries. The media company, which developed out of a bulletin board for life science students, was one of the first science

communication ventures established in China at the turn of the twenty-first century. Although it still maintains professional services to life sciences researchers, the company has expanded into publication, conference organisation and consultancy. It has built its reputation as reliable news source and intermediary between the academia and the biopharma, biotech, and investment industries.

At our first meeting, Dr Bai struck me as a cautious interviewee who aligned himself with the image of the company. Although he gave me succinct answers, and confined the topics to those we had agreed on prior to the meeting, he frequently used the term of 'stem cell enterprise'. Dr Bai, like other practitioners I met, referred to 'enterprise,' using two Chinese terms - *hangye* (行业) and *chanye* (产业) - He used them synonymously, although there are certain critical differences between the two terms. The former, *hangye*, is more close to the concept of 'field', and is mostly used discussing research and clinical practice. While the latter, *chanye*, is used almost exclusively to describe industry, and is mostly used talking about business activities or national and local economies.

In our second meeting, I picked up this question about 'enterprise,' and asked him about the annual conferences his company had been co-organising with various research and clinical partners since 2009. Dr Bai seemed pleased that I noted this particular work they had done for the stem cell research community and industry in China, and commented,

> 'Yes! We were the first to organise such a conference/workshop in China. It's kinda [of our conference] tradition now. [Though] someone else [the Chinese Medical Doctor Association] stole our conference's title [that was developed for the annual conference], practitioners still give us face[16] [*smile*], [and] always come to our conferences and workshops.'

He then stepped out of the meeting room and asked me to wait for him. He returned from his office with a pile of conference books and put them one by one on the table: 'See, we started the annual conference in 2009, and we kept all of them [the conference books]!' I was quite amazed at this collection. Dr Bai soon used these records to map the past and present of the field, and even give an educated guess about its future.

[16] Face (*mianzi*, 面子) is associated with one's social status and network (Hu, 1944). In this context, by attending the conferences organised by Dr Bai, the senior practitioners gave their recognition of Dr Bai and its company's expertise and contribution to biotech research and industries in China.

Dr Bai looked at those conference books with a big smile, which I rarely saw on him, and said,

> 'Look at the [title of] first one: *the Spring of Stem Cell*! Then we all thought that soon the spring of the industry would come, and organised this very first workshop, and provided training for the participants. It [stem cell technology] was new then, and we collaborated with scientists from the Chinese Academy of Sciences and other renowned universities.'

I smiled and nodded. I noticed one conference book featured Dr Zhou Qi, a leading cell biologist who in recent years had become a leading voice of China's stem cell science in the international arena. I pointed at the cover and asked Dr Bai, 'Isn't that Zhou Qi?'

> 'Yes, that's him! We were close [collaborators]…'. After a brief pause, Dr Bai did not complete his sentence[17], instead he started a new topic of the industry trajectory,
>
> 'Look at them [*pointing at the conference books*]. Back then, everyone was excited and anticipating [the coming of] the *spring*. Who would know the *winter* come so suddenly and last so long till today! [*sigh*]'
>
> I noted he used the analogy of 'winter' to describe the situation the industry was then enduring and asked him to elaborate.
>
> 'Well, not so many companies are active in stem cell [research and clinical practice] now. Both the number [of biotech companies] and the sheer volume of the enterprise have shrunk. Especially when the [then] MOH took a harder line on its ban [on clinical practice] after the Jilin case made the headlines [in 2012]. It's said that the Jilin case was the trigger, but it's the *Nature* report that first exposed it and infuriated Chen Zhu [the former Minister of Health] who made a direct order to speed up the regulatory reform. [*pause*] He probably did not expect that the regulatory reform would be stagnated. Well, he had left [the office in 2013].'

Nevertheless, it is important to note that this 'winter' affected to a large extent only those working on or close to the 'bedside'. This was also pointed out by Dr Bai but at our first meeting,

> 'In the past years, the "downstream" of stem cell business (therapeutics) went downward spiral, the "middle-range" (suppliers and research contractors) and "upstream" (research and banking business) kept developing and diversifying rather steadily, and immunotherapy was the most eye-catching area.'

It was not difficult to detect disappointment in his tone when speaking about the 'winter' or 'downturn' of stem cell clinical research and related business, although most

[17] I did not ask Dr Bai why the collaboration between his company and Dr Zhou discontinued, partly because Dr Bai's pause and body language suggested that this question might further discomfort him. It was also because I had noted during my fieldwork that laboratory-based scientists, especially the elite ones like Zhou, apparently disengaged themselves from the private sector, whereas Dr Bai's company operates in a non-public domain.

of the time, especially during our earlier conversations, Dr Bai refrained from giving me his personal opinions but presented factual content such as statistics as an industry observer and consultant.

I will return to these discussions in chapters six and seven when examining practitioners' various responses towards this regulatory change, and the strategies they devised for surviving this regulatory impasse. Here I want to look at the two cases Dr Bai cited - the 'Jilin case' and the '*Nature* report'.

The 'Jilin case' was reported by journalists Zhao and Pan (2012) in the *People's Daily* (the official newspaper of the Chinese Communist Party (CCP)). The story concerned a hospital in Jilin province called '*Guigu*' (a Chinese translation of 'Silicon Valley') that continued advertising and selling experimental stem cell therapy to patients after the health authorities had ordered all practitioners to stop stem cell related clinical practice. Moreover, Guigu hospital claimed that its practice was sanctioned by the health authorities (ibid.). Soon after, the health authorities investigated, revoked the hospital's licence for medical practice, and published a letter of denouncement condemning the malpractice of implicated personnel and ordered the lower-level health authorities to strengthen their regulation and monitoring of medical institutions under their jurisdiction (MOH and SFDA, 2012).

The Jilin case is among a few cases that were taken up by news agencies affiliated with China's party-state and resulted in direct response from the health authorities (MOH and SFDA, 2012). Its significance to stem cell clinical practices and regulation in China was noted also in Sui and Sleeboom-Faulkner (2015)'s analysis of the 'three-stage evolution of stem cell regulation in China'. During my fieldwork, a similar news event occurred in March 2014 when, during China's Consumer Rights Day, China Central Television's (CCTV) primetime *Focus Report* aired an investigatory report on a cell company. The company offered experimental stem cell therapy directly to cancer patients and used stem cells from an illegal source of aborted fetuses (CCTV13, 2014). During Consumer Rights Day, a key component of CCTV television shows is the 'naming and shaming' of companies that dishonour consumers' rights. The event is keenly watched by consumers and companies alike (Jourdan and Cai, 2017). The exposure of that cell company on *Focus Report* also affected my research. Stem cell

practitioners became nervous and a few cancelled or postponed our previously agreed meetings. Additionally, it helped to construct a situation where, over time, the 'experimental' nature of stem cell therapy and the 'illegitimacy' of stem cell clinical practice became widely known among ordinary people in China.

The '*Nature* report' Dr Bai referred to is an investigatory piece titled '*China's stem-cell rules go unheeded*' (Cyranoski, 2012). The article reveals how experimental stem cell therapy was still on offer in various places in China, even though Chinese health authorities had ordered all practitioners to stop their clinical activities (ibid.). Practitioners, who I met in this study, commonly considered reports by foreign science journalists on China's 'stem cell tourism' and ineffective regulatory measures had made China 'look bad' and pressured the health authorities to 'clean up' the 'mess'. Chinese practitioners associated *Nature* with Britain[18] - a country, they often pointed out, that also leads and invests heavily in stem cell research. My interlocutors sometimes cited *Nature* reporter Cyranoski's reporting on China as examples of foreign forces intervening in Chinese stem cell research enterprise. As a kind of collateral damage, my 'British' association was sometimes raised as doubts about my ('true') research intention.

A regulatory impasse

Following the cease-and-desist order in 2011, the health authorities convened an Expert Committee to draft new regulation(s) (MOH, 2013). They published two consultative versions in March 2013 (MOH and SFDA, 2013a) and March 2015 (NHFPC and CFDA, 2015a) but, apart from that, the health authorities kept quiet about their work-in-progress on this particular matter and failed to set a deadline for publishing a new regulation. These years were thus experienced by practitioners and other affected people, institutions and associations as a "regulatory impasse", which also constituted an important aspect of my fieldwork.

During this regulatory impasse, while clinical research and business activities were constrained by the 'total ban,' many practitioners still tried to prepare themselves for the

[18] Although *Nature* was founded in London, it was owned by a private firm prior to be merged with Springer in 2015 (Van Noorden, 2015).

publication of this new regulation whose content remained obscure to most of them. Indeed, at industry conferences, networking events and social gatherings, the collective spirit of practitioners was high, at least in public settings, as they spoke about how 'risk and opportunity [always] coexist' (*jiyu yu tiaozhan bingcun*, 机遇与挑战并存).

This phrase 'risk and opportunity coexist' appeared in conference titles, panel discussions, presentations, news reports, and practitioners' conversations with me. It is, nevertheless, a superficial description of their situation. When I asked my interlocutors to elaborate, they were often perplexed. A few suggested vague answers such as 'well, one needs to identify [situational] risk and seizing opportunity'. Indeed, this phrase has been used so generically to describe a wide range of political, economic and social issues in 'post-Mao' China that some practitioners questioned my 'Chineseness' because I asked them about the specificities of such a generic phrase. Meanwhile the majority simply ignored my question altogether. I will take a closer look at my interlocutors' use of this phrase in chapter six when I discuss how they devised varied strategies to survive the regulatory impasse.

Towards the end of 2014, when news leaked that the new regulation would likely align more with the pathway for drug development and authorisation, another phrase gained popularity among practitioners who referred to 'a different game in town now'. Sometimes, this phrase was used together with 'reshuffling the cards' (*chongxin xipai*, 重新洗牌), a reference to the changing landscape and composition of the stem cell industry in China that unfolded during the regulatory.

The process was reported in media and consultancy reports as 'raise the entry bar' and 'let the good ones stand out, and eliminate the bad ones' (Mu et al., 2015; Xiang, 2015b). In this narrative, small businessmen and ordinary clinician-researchers who used to actively work in stem cell clinical research and practices were portrayed as the 'bad ones', whereas the 'good ones' were those getting themselves ready for joining this 'new game' under the new conditions. Yet, expatriation, retreat and loss on the part of small businessmen and ordinary clinician-researchers were seldom mentioned either in the media or among the practitioners themselves in public. In chapters six and seven, I will take a closer look at those different actors and this 'new game'. I will reveal that

some of those practitioners closing down or selling their business to the ‘big players’ were no less serious than the commentators about stem cell research and enterprise. It is equally doubtful that the big players’ practices are ‘good’.

During the prolonged regulatory impasse, there was a consensus among most stem cell practitioners, including those who had experienced considerable loss during this regulatory change, that it was time for Chinese stem cell research enterprise to march to its promising future, and the earlier years’ association with experimental stem cell therapy must now be put behind.

In the relation and interaction between the regulators and the practitioners during the regulatory change, the position of scientists and clinician-researchers was different to that of more ordinary practitioners. On the one hand, Chinese health authorities relied on an Expert Committee to develop a blueprint of the new regulations. The committee’s membership list, which I obtained in early 2014, showed that except for one specialist in law and another in bioethics, the rest were scientists and clinician-researchers (including two working in a research institute affiliated to CFDA). All expert committee members are well connected, high-profile figures, who work closely with both Chinese and foreign researchers in their research areas. They are extremely busy in their work, and, like the regulators, most of them kept quiet about the new regulations in-the-making. On the other hand, regulators had little contact with ordinary stem cell practitioners. When the health authorities published draft regulations for consultation, they only invited feedback from certain professional organisations and other regulatory agencies that had influence over, or a stake in, the regulation on stem cell clinical research.

This relationship between the regulators and the regulated meant that most stem cell practitioners had no official channel to either give their input or receive timely updates on the regulation process. In turn, these more ordinary practitioners had to rely largely on their professional and personal networks to obtain necessary intelligence to help them devise strategies to survive the winter of their enterprise, as part and parcel of preparing for uncertain future(s).

Nevertheless, this regulator-regulated relation is neither static, nor a straightforward representation of each other's power. The regulators initiated the regulatory change, selected the Expert Committee members, and had the final say on the new regulation. Yet, during my fieldwork, I discovered that, no person or institution was entirely in control of making the new regulation. Although the regulators, and to a lesser degree the Expert Committee, appeared to be in a powerful position, they were subject to multidirectional pressures and criticisms, which in parallel to the fate of practitioners, made their future just as uncertain and hard to prepare for. The regulators were constrained by their own working conditions and relations, which had been in flux since China's new leadership took office in March 2013 and launched a series of political-economic reforms. Practitioners could, and did, openly criticise the regulatory impasse and attributed the 'inaction' (*bu zuowei*, 不作为) of health authorities to the regulators 'being lazy' or 'not daring to take responsibility'. By contrast, the regulators could not respond to these accusations.

The regulatory impasse was not due to 'inaction' by Chinese health authorities. Rather, both the 'unruly' nature of stem cell-based medicine (Haddad et al., 2013) and the larger socio-economic and political context in China contributed to the instituting, the prolongation and, eventually, the ending of the regulatory impasse. During the regulatory impasse, the working relation between the regulators and the regulated, and among practitioners, changed - a point that I will return to in the next section. Questions remained about what the new regulation should address, what mattered, and who could be blamed or celebrated, and for what. Such altercations, as I will demonstrate in chapters six and seven, were influenced also by those working with, investing in, and regulating other biotechnologies inside, and outside of, China.

A discordant regulatory situation and a second cell-based, 'sister' therapy to stem cell therapy

My interlocutors often referred to immunotherapy as a 'sister' to experimental stem cell therapy in China. They had used this term ever since the MOH issued the *List of*

Category Three Medical Technologies for Clinical Applications (MOH, 2009b)[19] with the two types of cell-based therapy listed side by side.

Though my interlocutors talked about immunotherapy mainly as a novel therapy for cancer treatment, immunotherapy is neither a single therapy nor specific to cancer treatment. It is a therapeutic approach that has developed into a range of concrete mechanisms to use, mobilise and modify patients' immune systems to treat diseases (Elert, 2013). Although it has received worldwide attention as a likely cure of cancer from researchers, patients, biopharma and investment industries (Scientific American, 2017; Coontz, 2013; Regalado, 2016), this innovative research area remains a field of heated debate (Cohen, 2017; Prasad et al., 2018).

I was told that in China, cancer hospitals, and cancer departments in major hospitals, started to incorporate immunotherapy in their care of cancer patients ever since immunotherapy was listed as a category three medical technology. Citing this list, immunotherapy was featured as a novel medical technology by those hospitals, while its designative feature of being a 'category three' medical technology was conveniently overlooked. Recalling literature that I introduced earlier, experimental stem cell therapy was practised in similar way in China, before the health authorities halted its clinical practice in December 2011. As I observed during the fieldwork, the validity and usefulness of conceiving stem cell therapy as a 'medical technology' for regulation was one of the most debated questions among the practitioners during regulatory change. Therefore, I am going to examine further this regulation on medical technology and the list of category three medical technologies.

The regulation on clinical applications of medical technologies was issued by MOH in March 2009 (MOH, 2009a). The regulation gives a generic definition for 'medical technology': 'any diagnostic or treatment measures adopted by medical institutions or health care professionals in making diagnoses, alleviating pain, bettering [bodily]

[19] In July 2015, NHFPC issued *Announcement Regarding Cancelling Licence-Approval of Category Three Medical Technologies for Clinical Applications and other Related Work* (NHFPC, 2015) in response to the State Council's order to streamline administrative measures and deepen economic reform (Lu, 2015). It repealed the *List* on category three medical technologies that emphasised licensing and intended to strengthen procedure regulations instead. The main regulation on medical technologies remain intact and source of contestation. I will return to this point in discussing the interim nature of the new regulations in chapter seven.

function, prolonging life, or aiding healing' (Clause 2, *my translation)*. Acknowledging that medical technologies involve different kinds and degrees of techno-scientific, clinical, and ethical risk, MOH adopted a categorisation-licensing approach in this new regulation. According to MOH (2009a), 'category three' medical technologies are those involving the most risk or uncertainty, in needing the use of scarce medical resources, or otherwise requiring the strictest regulation by the health authorities. This regulation also stipulated the procedures for medical institutions to apply for licences to introduce and practice category three medical technologies.

The aforementioned list (MOH, 2009b), published in May 2009, was a follow-up to the regulation published two months earlier (MOH 2009a). The list introduced the first group of category three medical technologies with clinical application permissions. It delineated a sequence of five medical technologies that may involve the use of cells: i) autologous immunological cell (including T cells and NK cells) technology; ii) cell transplantation technology (excluding stem cell); iii) umbilical cord blood stem cell technology; iv) haematopoietic stem cell technology (excluding umbilical cord blood stem cell); and v) tissue engineering and tissue transplantation technology. Yet, the publication did not explain why it categorised cells and cell-based medical technologies in this particular way.

In December 2011, when the MOH halted stem cell clinical research and practices, it left stem cell therapy's 'sister' - immunotherapy - alone. Immunotherapy, thus, continued to be offered to cancer patients in hospitals across China until mid-2016. The shutdown of all immunotherapy programmes in China, in mid-2016, is often attributed to the public outcry caused by the death of cancer patient, Wei Zexi, and by hospitals outsourcing and e-marketing unauthorised immunotherapy. In response to the public outcry, the heath authorities soon launched an investigation into the online advertising and clinical practice of immunotherapy. Citing their regulation on medical technologies, the health authorities clarified that they had never issued a licence for the practice of immunotherapy to any medical institution in China. Thus, in addition to the hospital where Wei received immunotherapy, all the other providers of immunotherapy had also transgressed the regulation (Xinhua, 2016c). The health authorities further clarified that immunotherapy was still in need of 'clinical research', such that all clinical practice related with immunotherapy must stop (Wen et al., 2016).

It appears that Wei's case had a definitive effect on how immunotherapy was brought under public and regulatory scrutiny. For instance, J. Y. Zhang (2017) calls the response of Chinese health authorities to Wei's case an example of '*post hoc* pragmatism', wherein the authorities used the issuing of a 'blanket ban' to 'quiet social discussion' and 'offer…answers to (political) accountabilities' (pp: 649-650). Nevertheless, as I will reveal in chapter five, prior to Wei's case, immunotherapy had long been practised in an ambiguous regulatory and clinical situation whose end was to various degrees anticipated by both patients and practitioners. Like the aforementioned CCTV's *Focus Report* television show, Wei's case was a notable event for cell therapy clinical practices and regulation in China and, thus, relevant to my study, and requiring further exposition.

According to accumulated news reports and other public records,[20] Wei died in April 2016 at the age of 22 from synovial sarcoma, a rare form of cancer with no effective treatment. The following recollection of Wei and his family's experiences with immunotherapy was posted by Wei in February 2016 on *Zhihu,* one of the most popular question-and-answer websites in China. In answer to the question 'what is the most evil in humanity?', Wei wrote 'I decided to write this down. I hope my answer prevents more patients being deceived.' He then described what had happened to him,

> As a last resort, Wei's family purchased immunotherapy from a hospital in Beijing in 2014 and 2015. They heard about immunotherapy and that hospital after using China's most popular search engine, *Baidu*[21], to search novel treatment for Wei. At Wei's father's preliminary visit to the hospital, the doctor told Mr Wei that the treatment was developed by researchers in Stanford University and would give Wei a guaranteed extra twenty years to live. Wei subsequently received immunotherapy at that hospital. Wei's family paid more than 200,000 yuan (about £20,000) for the therapy, but it was ineffective in Wei's case. Later, Wei learned from his friend living in the United States that the kinds of immunotherapy he received and advertised as 'novel' therapy in China - dendritic cell and cytokine-induced killer cell based therapy - were 'outdated' in the United States.

To 'avoid unnecessary trouble', Wei did not name the hospital nor the doctor who had assured his father that immunotherapy would prolong Wei's life. But he decried search

[20] Including investigators news reports such as Han (2016), Wen et al. (2016), Lau (2016), and in social media, Wei's own records of his treatment journey and evaluation (Wei 2016).
[21] *Baidu* is the most popular search engine in China, especially after Google retreated from the Chinese market in 2010. Direct-to-consumer advertising of medicinal products is not allowed in China, yet, the monitoring of online advertisements was weak.

engine *Baidu's* 'evil' bid-for-advertisement-listing business model that promoted such dubious medical practices.

Wei's *Zhihu* post grabbed the attention of Chinese netizens who cared about Wie's predicament. When Wei passed away two months later, Wei's online followers called for accountability from the hospital - which was then revealed as Beijing's Second Armed Police Hospital - and from the search engine *Baidu*, and ultimately, from the regulatory agencies. Within days, Wei's case became headlines in almost all major news agencies and a most trending topic on social media.

Journalists and regulators pursued *Baidu* and the hospital, which Wei had named as culpable parties. The media criticized the contract between Beijing's Second Armed Police Hospital and Shanghai Claison Biotech Company, on the sale of immunotherapy and its subsequent administration to patients, and they criticized *Baidu*'s advertisement business too. In early May 2016, Chinese authorities[22] conducted two separate investigations into Beijing's Second Armed Police Hospital and *Baidu*. Both investigations concluded that they had broken regulations and institutional policies, conducted malpractice and jeopardised public trust. The authorities ordered the hospital and *Baidu* to correct their organisational work and routine practice (Xinhua, 2016a, 2016c). After the publication of the official investigation reports, media and public attention around Wei's case dwindled.

In China, between late 2011 and mid-2016, one type of cell therapy had been brought into regulatory scrutiny, while another was still routinely administered to patients as novel therapy. They were treated differently by researchers, patients and investors alike. Yet, what made these two cell-based therapies siblings was not their juxtaposition on a list but their 'experimental' status, which at different times became subject for regulatory intervention. My fieldwork between January 2014 and April 2015 overlapped with part of this discordant regulatory situation. Stem cell practitioners openly criticised this 'unfair [regulatory] treatment' in conferences and in conversations with me. In turn, studying the two types of cell-based therapies in their evolving regulatory situations

[22] The investigation into the hospital was coordinated between civilian and military health authorities, and the investigation into *Baidu* was coordinated between the authorities in charge of health, commerce, and cyberspace matters.

during this peculiar time thus allowed me to observe, compare and assess how regulation affected the development and practices of novel biomedical products in China. I will introduce this particular aspect of my research in chapter five.

Learning from my research participants: an anthropological response and reorientation

So far, I have introduced social science studies of stem cell research, clinical practice and regulation in China, provided an overview of my fieldwork, and introduced three linking aspects of the regulatory situation that were significant to my fieldwork and later analysis. In this section, I reflect why I chose to look at China's recent regulatory change through the lens of those affected by the regulations, who lived through and responded to accumulated research, clinical, regulatory and market uncertainties. I explain how, by studying these individual and collective experiences and responses, I gained insight into biomedicine, as well as China. Patients (and patient families), who used or were interested in using experimental cell therapy, as well as clinician-researchers who engaged in entrepreneurial-like activities, presented me with intricate views that cast doubt on the mainstream portrait and critiques of 'desperate' patient being exploited by 'corrupted' doctors and 'greedy' businessmen. As I focused on these individuals' relationships with experimental cell therapy, I gradually reoriented my scholarly attention towards biomedicine.

'Duped' patients, 'hyped' consumer?

In mid-2013, while preparing my research proposal, I developed an interest in patients' viewpoints and experiences with experimental stem cell therapy for the following three reasons. First, during my training in genetics and bioethics, I became interested in the public engagement of biosciences (Su, 2009), and my prior research into consumers' views on direct-to-consumer genetic testing had revealed the value of learning from the end-users of new biotechnology (Su et al., 2011, 2013).

Second, when conducting a literature review for my research proposal, two limitations struck me. Despite sustained criticism and calls for regulatory action against the commercial provision of 'experimental' stem cell therapy in the past decades, empirical

investigation into phenomena such as ‘stem cell tourism’ was underdeveloped (Ryan et al., 2010). Among the few who looked into patients’ experiences and decision-making, most investigators analysed patients’ reasoning as irrational and typically took the form of hope as first suggested in Murdoch and Scott (2010). For instance, Einsiedel and Adamson (2012) conducted a study on ‘future stem cell tourists’ and showed that, in Canada, healthy adults were sympathetic to patients who travelled overseas for experimental stem cell therapy. These prospective patients who were well informed of the risks and uncertainties entailed in this process were further willing to consider taking similar action if they were in similar situations. Yet, following Murdoch and Scott’s (2010) suggestion of ‘the power of hope’, Einsiedel and Adamson (2012: 42) view their research participants as decision-makers who might be affected by ‘a similarly enticing and powerful mix of hope and possibility’. Einsiedel and Adamson (2012) further suggest that the market for stem cell therapy is ‘for the twin imperatives of desperation and hope’ and they expect to see continual growth of this market.

This approach might be due to researchers’ taking the translational research model as a truth claim, and its accompanied scientific and ethical principles as a benchmark to assess both the claims of the providers of ‘experimental’ stem cell therapy and the rationality of patients. Such an *a priori* approach presents a potential methodological fallacy.

Another limitation in existing scholarly work is that, in comparison with patients travelling to a foreign destination in pursuit of experimental stem cell therapy, knowledge about local patients’ experiences with such therapy was sparse. For instance, except Chen and Gottweis (2013), and Sui and Sleeboom-Faulkner (2015), who did pay specific attention to Chinese patients’ encounters with, and evaluation of, experimental stem cell therapy that was offered by Chinese clinician-researchers or biotech companies in China, little else in this has been explored.

Finally, after considering that clinical trials require patients to volunteer as research subjects, it seemed logical to me to explore patients’ views on the design, organisation and conduct of stem cell clinical trials. Therefore, I included patients as potential research participants in my research proposal.

Being considered as having a ‘regenerative’ function, stem cell therapy is conceived and accordingly developed to treat diseases and disabilities that are triggered or affected by deficient cells or loss of normal cells. Spinal cord injury, diabetes, cardiovascular diseases, knee injury, blindness, and motor neurone diseases such as Parkinson’s disease and amyotrophic lateral sclerosis (ALS) are among those attracting most attention from the research community, biopharma industries and patients and patient organisations (Li et al., 2014). A critical component in the Bionetworking in Asia projects (which also funded my doctoral research) is to understand patient recruitment mechanisms in stem cell clinical research and related business. Working as part of the Bionetworking research team, my doctoral research proposal included the same groups of patients that the team planned to study in other countries: patients with spinal cord injury, type 1 diabetes, motor neurone diseases, and cardiovascular diseases.

Early on in my fieldwork, in parallel to my research, my colleagues and I organised a public event for the Centre for Bionetworking to elicit patients’ views towards stem cell therapies. The contextual and organisational conditions led us to collaborate with a local residential community that was originally built for housing faculty members and their families working for a local university. There I visited and became acquainted with a dozen residents who are in their 70s and live with chronic diseases, such as type 2 diabetes, hypertension, heart disease, and post-stroke conditions. Those residents were interested in learning from the invited speakers about current stem cell therapy research and the ongoing regulatory change to stem cell clinical research. During the discussion, the patients talked more about the existing constraints in accessing health care services that affected their daily living with and management of these chronic conditions. They made further suggestions to the speakers that rather than concentrating resources on developing yet-to-come ‘high-tech’ medicines, policy makers would serve patients better if they could improve the accessibility, affordability and quality of existing health care services.

This early lesson stayed with me throughout the fieldwork. Yet, due to practical opportunities as well as constraints that accompanied my frequent field travels, I started to work more with patients living with spinal cord injury, type 1 diabetes, and motor neurone diseases.

Contrary to what I had read about patients' enthusiastic pursuit of experimental stem cell therapy, once in the field I found that Chinese patients and patient families, who I met, were cautious about both experimental stem cell therapy and the providers of such therapy. Compared with these earlier reports and scholarly work on the surge of foreign patients traveling to China for experimental stem cell therapy before 2010, I only met a few Chinese patients who had similarly travelled abroad. My interlocutors were familiar with those investigatory news reports that I mentioned earlier when introducing the winter of stem cell enterprise. They could easily list scientific and ethical reasons when condemning those advertising or charging patients fees for unauthorised and unproven stem cell therapy. Their reasons were nearly identical to those listed by reporters, and they particularly liked to quote the *Focus Report* investigation into the dubious operation around stem cell therapy (CCTV13, 2014). They considered this particular report represented the official opinion of the Chinese government and applauded CCTV's naming and shaming of dubious business activities that protected their 'consumers'' rights.

Investigatory news reports that had in the past years questioned dubious, for-profit operation of unproven and unauthorised stem cell therapy in China had achieved an educational function. Nevertheless, despite their vigilant assessment of the then on-offer stem cell therapy, those patients and patient families who I conversed with during the fieldwork did not foreclose the possibility of using stem cell therapy to better one's - and often also one's family's - conditions. As mentioned earlier, the regulatory impasse caused a significant downsizing of stem cell clinical practice and business nationwide. On rare occasions, when my research participants did decide to pursue experimental stem cell therapy, their action seemingly contradicted what they knew about the undesirability of what they were arduously pursuing, which perplexed me. Similar confusion arose during my participant observation at a biotherapy department in a cancer hospital in early 2015. Here, patients and health care professionals both acknowledged the lack of definite evidence of the therapeutic benefits of immunotherapy, yet, they used and practised this novel therapy in a nearly ordinary way. In chapters four and five, I will revisit these issues.

My interlocutors often cited terms such as ‘the [Chinese] national context’ (*guoqing*, 国情) and ‘the system institutional or systemic flaw’ (*tizhi wenti*, 体制问题) in explaining their views and decision-making around the ambiguous situations wherein they took similarly contradictory actions. Nevertheless, my interlocutor rarely responded to my query about what exactly they meant by *guoqing* or *tizhi wenti*. In their wry smiles or questioning my Chineseness, my interlocutors nevertheless showed me that they understood and took those generic terms as ‘officialese’ (Hansen, 2017) that originate in governmental discourse and have little substance. Their swift navigation and strategic use of the ‘Chinese’ context, nevertheless, highlighted to me that amid those uncertainties and ambiguities there was something that made them want to take actions that were sometimes contradictory.

The ‘wrong-doing’, the regulation, and changing relations among practitioners

Not long into my fieldwork, I started to note a kind of dissociation between different groups of stem cell practitioners. In addition to how my interlocutors liked to identify themselves according to the kind of institution where they worked (research institute, or hospital, or biotech company), they exhibited this dissociation most tellingly at professional conferences. That is, among the conferences, workshops and networking events that I attended during the fieldwork, except a number of leading researchers, I rarely saw those working at the ‘bench’ attending professional events that were organised by those working at the ‘bedside’ or the industry, and vice versa.

In addition to their professional achievements, a leading researcher holds a prominent position in their respective institutions and professional organisations, wherein their leadership is formally acknowledged by institutions and their peers. Notably, most of those leading researchers had collaborations with laboratory-based scientists and clinician-researchers, and some of them had opened or sat on advisory, consultancy or directive boards of biotech companies. A few of them were also members of the Expert Committee. As such, on occasions that those leading researchers were not themselves the conference organisers, they attended conferences as keynote speakers or panellists in ‘high-end dialogues’ that, regardless of the topic, all touched upon the regulatory aspect of stem cell clinical research.

In listening to practitioners' discussions at those professional events, I gradually noted that, on the one hand, clinician-researchers closely followed advances in stem cell science, and spoke with similar passion about progress in their own studies, as laboratory-based scientists. On the other hand, laboratory-based scientists had, to various degrees, a component in their 'basic' research that was directed at clinical applications. Like clinician-researchers and biotech entrepreneurs, the leading scientists often emphasised the value of stem cell science in improving public health and contributing to China's future development. In other words, there was no fundamental difference between the three groups of practitioners - laboratory-based scientists, clinician-researchers, and biotech entrepreneurs - over the importance and value of stem cell science in developing stem cell-based medicine and related industries.

Nevertheless, the three groups differed on how to achieve the potential of stem cell science, and what their respective roles and functions should be in this process. Those differences corresponded to their views and evaluations upon the regulatory change that was affecting their daily work. As Döring (2004) noted, elite researchers were early advocators for regulating stem cell research in China according to internationally acknowledged scientific and ethical principles. I also observed that laboratory-based scientists were often opposed to past clinical practices, and supported any regulatory change that brought stem cell research and practices in China closer in line to international standards.

In the public speeches and discussions of clinician-researchers, and in their conversations with me, they defended the existing regulation on medical technologies, rather than the specific ways some of them had practised 'experimental' stem cell therapy. It appeared that in defending this regulation, those clinician-researchers simultaneously defended their past - and in a few cases, ongoing practices of offering experimental cell therapies to their patients. They believed that the regulation on medical technologies and the *List of Category Three Technologies for Clinical Applications* (MOH, 2009a, 2009b) had effectively acknowledged a readiness to introduce stem cell therapy into clinical settings. While being criticised for transgressing regulations by practising without obtaining a licence from the health authorities, the clinician-researchers pointed out that no institutions had been put in place to authorise such a licence. What those clinician-researchers described to me was

thus an ambiguous regulatory situation that in practice conditioned the proliferation of unauthorised stem cell theory in Chinese hospitals. This ambiguous situation has recently been documented in the literatures as a 'grey area' (Sleeboom-Faulkner, 2016), and I argue, in chapters five and six that it is key for comprehending the entrepreneurial-like clinical practices and business activities in the rising biomedical field in China.

The last group of stem cell practitioners - biotech entrepreneurs - were, as mentioned earlier, the most affected by regulatory change. Businesses tried to survive the regulatory change. Before I started my fieldwork the sector had experienced a 'reshuffling' of businesses. Compared with people who primarily worked in research institutes and hospitals, full-time biotech entrepreneurs seemed less concerned about what direction the new regulation was taking. Rather, they more forcefully and urgently called for regulators to end the regulatory impasse so that they, as individual business and a collective Chinese stem cell research-enterprise, could move on.

This urgency to end of the impasse was shared by stem cell researchers too. While in defending their proposition to keep intact the regulatory designation of stem cell therapy as a medical technology, clinician-researchers and biotech entrepreneurs had always cited the fact that there was no 'international' consensus on how to regulate the research and development of stem cell-based medicine. The proposition was taken up by elite scientists much later, when they advocated that the new regulation ought to be designed for 'Chinese' stem cell research-enterprise. This reframing of what the purpose of the new regulation is, nevertheless, arose from the innovation-driven development strategy that the new Chinese leadership had promoted since early 2013. Yet, in order to develop Chinese stem cell research-enterprise for future competition at the global level, they started to forge new partnerships between laboratory-based scientists, biotech industrialists, investors, and clinician-researchers. Thus, the reframing denoted a recomposition of biotech entrepreneurship and the relation between the regulated and the regulators. I will elaborate on this matter in chapters six and seven.

Regulatory change was premised on the idea that what Chinese clinician-researchers and biotech companies had done was wrong and that new regulation rectify measures for scientists, patients and the reputation of Chinese stem cell science and the Chinese

nation. My observations and conversations with various groups of stem cell practitioners led me to rethink this premise. Instead, I started to consider the boundary and relation between 'science' and 'medicine,' between the 'wrongdoing' and the 'rule-biding' and between the subject and object of regulating biomedical research.

From ambiguity to multiplicity: from the 'Chinese context' to "toolised medicine"

This chapter's overview of the literature, my fieldwork and aspects of the regulatory situation has been set against two observations that puzzled me. On the one hand, patients considering undertaking experimental cell therapy and, on the other hand, clinician-researchers' insistence that clinical research and medical practices are of equal importance to basic research in the development of stem cell therapy.

I gradually realised that my previous scientific studies of bioscience and bioethics might have created a blind spot to my field observations; the discrepancy that existed between the model of 'translational research' and what 'stem cell therapy' really is and how it can be developed and used by patients. I started to question the validity of the scientific and ethical discourse around stem cell research and product development even though I was unsure where this route would take me.

In May 2015, I returned to the University of Sussex and started the 'writing-up'. While re-examining the literature, I noted that recent empirical studies have shown two interlinked phenomena. First, patients' interest in, and travels to pursue 'experimental' stem cell therapy are sustained (Petersen et al., 2017). Second, the stem cell therapy market has expanded at the global level (Sipp, 2011; Turner and Knoepfler, 2016; Munsie et al., 2017), including in countries that 'tend to have more stringent regulatory infrastructures governing health products and medical practice' (Berger et al., 2016: 162). These studies corresponded to my fieldwork observations. and similarly questioned the approach of critics of 'stem cell tourism'. Most of these researchers used their findings as evidence for strengthening regulatory oversight, and patients' education, to counteract the global expansion of stem cell therapy market (Sipp et al., 2017). Yet, their research findings strengthen my resolve to step away from the translational research model of developing stem cell-based medicine and industry in

order to rethink about the development of China's new regulation on stem cell clinical research.

The translational research model used in social science critique supported research analysis of the exploitation of 'desperate' patients and 'gullible' consumers by 'rogue', 'greedy' practitioners, and of a global stem cell therapy market rapidly expanding from the margins of science and pharmaceutical industries. Nevertheless, the translational research model, including the design of clinical trials, has in recent years been challenged by scientists, clinician-researchers, pharmaceutical industry, and social science researchers (Summerskill, 2005; Lauer and D'Agostino, 2013; Lenfant, 2003; Gardner and Webster, 2016). The existing regulatory framework that was developed for the pharmaceutical industry falls short when regulating research and development of biopharmaceuticals, including and in particular cell- and gene- based medicines (Dolsten, 2016). This reconceptualisation of where, and how, 'translation' fails, makes existing regulations appear as a 'barrier' for contemporary biomedical innovation and reframes the relation between regulation and biomedical enterprise (Isasi and Knoppers, 2011; Ginty et al., 2011).

Though this reframing was observed in early policy and regulation discussions in the United States and Europe (Hogle, 2009; Faulkner, 2009), increasing global competition in biomedical research and business has normalised the incorporation of a global-competition perspective in national policy and regulation deliberations around the world (Hogarth and Salter, 2010; Salter and Faulkner, 2011). Research policy and regulatory bodies in North America, Europe and Asia, in turn, have started to make specific adjustments or reforms to their jurisdictions (Sleeboom-Faulkner et al., 2016). While the most notable 'innovation' first occurred in Asia (Lysaght, 2014; Azuma and Yamanaka, 2016), this 'flexible' trend has affected policy and regulation discussions and development in both leaders and followers in this global biomedical research-enterprise (Faulkner, 2017; Rosemann et al., 2016). This 'flexible' trend in making regulation for biomedical industry was also observed by Chinese stem cell practitioners who worked and lived with the regulatory impasse in China and who criticised the inaction of Chinese regulators. They used this observation to argue for 'Chinese' regulations that would aid the development and international competition of Chinese' stem cell research-enterprise.

I become increasingly convinced that the juncture between the ‘Chinese context’ and stem cell-based medicine held the key to comprehending the multifaceted uncertainty, ambiguous clinical, regulatory and market situations, and contradictory claims and actions that I had observed in the fieldwork. In subsequent years, I thus focused my inquiry on locating and comprehending this juncture.

CHAPTER THREE. Tooling stem cell: from biological capability to medicinal potentiality

This chapter explores how and why the majority of stem cell clinician-researchers[23] who I met believed that stem cell therapy should continue to be regulated and practised as a 'medical technology' in China. It further explains how exploring the arguments of clinician-researchers' provided a foundation for me to develop the concept of "toolised medicine". That is, a biological entity, such as stem cell, offers a possibility to become a tool to achieve certain medicinal purposes.

Soon into fieldwork, I noted the dissociation between different groups of stem cell practitioners. During the regulatory impasse, laboratory-based scientists and clinician-researchers, in particular, debated questions such as defining stem cell-based medicine and the best way to develop it in China. Researchers, biopharmaceutical companies and regulators around the world want to understand how to develop stem cells into stem cell-based medicine and what types of stem cells best serve this purpose. Debates around human embryonic stem cell research, which I discussed in the introduction chapter, exemplify the issues. In addition, Eriksson and Webster (2008), Hauskeller and Weber (2011), Beltrame (2013), and Kraft and Rubin (2016) have illustrated how stem cell's biological features such as 'pluripotency' and 'plasticity' are debated, negotiated and (re)defined within science communities.

What was distinctive about the debates among Chinese practitioners was that they debated those questions in response to the MOH's plan to replace an existing regulatory mode (regulating stem cell therapies as a category three medical technology) with another mode (adopting drug clinical trials to regulate stem cell clinical research and product development). Their debates lasted almost throughout the entire regulatory impasse, but if it was not for the change in institutional structure that also interrupted MOH's execution of the original plan, their debates probably would not have happened. At least not that publicly.

[23] In the literature, 'clinician-scientist' is more often used. In China, medical training and scientific training has only recently been integrated, yet through obtaining advanced training, often overseas, some clinicians have learned about how to do science. To better capture these characteristics, I used the term of 'clinician-researcher' in this study.

Social science researchers have also shown that debates around the science of stem cells have more at stake than advancing stem cell research and sustaining its research field because of the social, economic and political expectations of what stem cell-based medicine and related industries can offer to local and national health care, businesses and political power (Caulfield, 2010; Mittra, 2016). Those debates have performative effects on influencing how stem cell research and related products and industries are seen and developed (Faulkner, 2008a; Eriksson and Webster, 2015; Gardner, Higham, et al., 2017).

Participating in policy-related debates around stem cell research and product development is thus a political act. Parry (2009) and Marks (2010), for instance, illustrate how through joining in policy-related debates, stem cell scientists in the United Kingdom and Europe are able to claim and assert their cognitive authority and influence public making and funding in stem cell research and product development. Metzler (2011) and Benjamin (2013) show how mobilised citizens and voters can influence national and local research policies and agenda, respectively, in Italy and in California.

While in policy-related debates, stem cell scientists generally stand out as powerful figures (Marks, 2010), clinician researchers are gradually marginalised (Martin et al., 2008). The marginalisation happens because not only are clinicians considered as users or gatekeepers of new medicinal products and technologies rather than co-developers (Moran, 1999), but also because questions are unresolved regarding who is a clinician-scientist and what clinician-researchers should do in contemporary biomedical research (Snyderman, 2004; Wainwright et al., 2006). Clinician-researchers, as I will elaborate in this chapter is a fuzzy figure in China.

The political flavour in Chinese practitioners' debates is that while this regulatory change was championed by laboratory-based scientists (Döring, 2004), it aimed to correct the 'wrong' clinical practices that had occurred in China. In effect it positioned the two groups at the opposite sides of the regulatory change. So, while defending the existing regulation on medical technologies, Chinese clinician-researchers were also struggling to claim merit and maintain autonomy in their clinical research and practice. They argued that their previous work had created a 'leading edge' for China in

intensified global competition in stem cell clinical research and product development. They also stressed the value and necessity of integrating medical knowledge and clinical skills in treating patients with novel therapies.

This chapter starts with the kernel of the regulatory impasse that was debated between the two groups. I will take a closer look at the dissociation of the two groups that is moulded by the social-economic and political context in China and stem cell research and product development. I will explain how clinician-researchers claimed that their work contributed to earning China a leading edge in global stem cell research-enterprise, while laboratory-based scientists denied their claim.

Hearing over and over again clinician-researchers' claims and laboratory-based scientists' denial about China's leading edge in stem cell clinical research, I noted that clinician-researchers stressed the necessity and value of clinical work in developing stem cell therapies and use in various clinical settings. I realised that clinician-researchers clearly distinguished stem cells' biological capabilities and its potential usage in medicine. My research with other groups, in particular patients and patient families, further evidenced the difference and distance between stem cells' biological capabilities and its potential in medicine and other domains. These practitioners' debates thus helped me to conceptualise biological entity-based medicine as "toolised medicine" - a point I will elaborate at the end of this chapter.

The kernel of the regulatory impasse

> 'Whatever the regulation is, we can follow. What we want is simple: give me the regulation!'
> -- Dr Lv, CEO of a public company

I met Dr Lv in December 2014. His biotech company went public a couple of years ago in a foreign stock market, with its core business areas listed as stem cell research and product development. Yet, in recent years, this company had refocused its investment, and research and development activities from stem cell therapy to immunotherapy.

When Dr Lv said 'whatever the regulation' he referred to a long debate among stem cell practitioners about whether stem cell-based medicine should be regulated as 'medical

technology' or 'drug' in China. This was also a choice between modifying or replacing China's existing regulation on medical technologies with the one originally developed for pharmaceuticals - drug research and development - and partly adopted by the translational research model. In Dr Lv's assessment, this choice between regulating stem cell-based medicine as medical technology or drug made little sense,

> 'What's the fuss? Medical technology or drug? Does it matter? They both require *clinical trials*! And that is *the same* standards!'

In some way, this question about which mode to choose had not existed when MOH initiated the regulatory change. Then, the aim of the MOH's regulatory intervention was to bring stem cell clinical research and regulation in China closer to that of drug clinical trials (Chen et al., 2012). But, when China's new leadership took office in March 2013, the key architect of this regulatory change - Health Minister Chen Zhu - left the MOH to take a seat at the Standing Committee of the National People's Congress (NPC). In that spring, China's new leadership launched a series of social-economic and political reforms that started with restructuring the Central Government, which separated the state-level drug regulatory agency (SFDA) from MOH and lifted it into CFDA (Xinhua, 2013a). While the two ministry-level agencies sorted out their regulatory responsibilities and working relationship, the regulatory change to stem cell clinical research lost its regulatory priority and the question of how to regulate stem cell clinical research in China opened up for debate.

Mr Tao works for a professional society that was among a few entrusted by Chinese health authorities with channelling communications between the regulatory agencies and the practitioners during the regulatory change. We met in March 2014 and discussed, among other things, how defining stem cell therapy in the new regulations had become a persistent bottleneck at Expert Committee meetings. When practitioners had told me about the importance of defining stem cell they rarely mentioned the law, but Mr Tao thought the definition should be settled by law. Mr Tao's comment on the regulatory situation left a lasting impression on me, and it is worth introducing part of it in full length,

> '[P]eople talk about translational research, but that is just talk. How to do it? What's the best type [of stem cell] to use in clinical settings? What's the best way to inject [the product]? There is no consensus. Then you see anything goes and the field gets messier and messier. [In current debate in China] Is it a drug? Is it a medical technology? Each side gets its valid point, yet the weakness in its

> application. We talk a lot about *translation*, but it is easier said than done. Everyone thinks he/she gets the best approach, and disagrees with the others. What is right? Well, you don't know at this stage. There is no consensus among the experts. They are *all* authorities [on relevant yet different fields] and *all* present strong scientific evidence [to support one's claim]. Who do you listen to? Who do you dare to challenge? And they are, [*short pause*] well, some have their own interest in industry. But that is how it is nowadays.
>
> …each country has its own calculation in regulating this novel thing in biomedicine [i.e., stem cell therapy], and there is no international agreement on this question either. Look at the U.S., it's defined as a '[biological] drug'; in Europe, it's a 'medical product [advanced therapy medicinal products]'; and [South] Korea and Japan have developed their own regulations. I understood why they [the practitioners] warned us that we [China] are losing in this competition [in stem cell research and industry development] with other countries…but to figure out how best to regulate the industry is not an easy task [for the regulators]. [*long pause*]
>
> I had long suggested that we are at a critical point that we must define "what stem cell is" in law. I would insist that we must first have a law, then discuss how to regulate it. Otherwise, the debate will continue.'

At that meeting, I was dazzled by the amount and quality of the information Mr Tao gave me. In the following years, with my deepened understanding of the regulatory impasse, I become more impressed by how effortlessly Mr Tao identified and drew connections between the most heatedly debated questions: between the difficulty of doing translational research and ongoing debate among Chinese practitioners on defining stem cell therapy as drug or medical technology; between how the other nation-states had been confronted with and resolved the question of defining stem cell in their regulations and Chinese practitioners' concern on China's losing competitive edge; and between Chinese regulators' apparent inaction and the intrinsic challenge of regulating stem cell therapy. Mr Tao's observation and reflection of each issue and their interconnections had led him to conclude and suggest that law, rather than regulation, was what needed to resolve the regulatory impasse and direct future development of stem cell research and industry in China.[24] Nevertheless, as his long pause evinced, given the complexity of this regulatory task mingled with competing interests and high stakes, he doubted that the regulators would consider his proposal.

[24] See Sleeboom-Faulkner et al. (2016: 242-243)'s discussion on various terms used in regulatory documents and practices in China and in comparison with other countries.

In this chapter, I focus on the tension that he observed persisted among leading practitioners at the Expert Committee meetings. In chapter seven, I will revisit Mr Tao when discussing the interim feature of the new regulations.

The dissociation between science and medicine

As Mr Tao pointed out, this kernel of the regulatory impasse to some extent reflects the professional and institutional power struggle between medicine and science in China. The unbalanced intra-institutional and working relationship is important for grasping what was at stake behind the debates among different groups of practitioners and for understanding the unfolding and temporary closure of the regulatory change to stem cell clinical research in China. Yet, the historical and socio-political contexts in China only partly explain the heated debates between clinician-researchers and laboratory-based scientists, a point I will return to towards the end of the chapter.

The superior position held by science over medicine is commonly seen in contemporary biomedical research (Löwy, 2011). While the 'translational research' model was first proposed in the United States to bring science and medicine closer, worldwide, it is used to promote translating scientific knowledge into clinical practice more than clinical practice into scientific knowledge (Maienschein, 2011a). As a result of translational research policies and practices, Roberts et al. (2012) note that the hierarchy between the two sides has consolidated and the role of clinician-scientists in the medical research enterprise has declined. In China, the historical development of science and medicine and their more recent institutional transformation make it even harder for clinician-researchers to claim their scientific expertise and contribution to biomedical research.

While the clinician-researcher is a hard-to-define figure in other countries (Snyderman, 2004; Kluijtmans et al., 2017; Wilson-Kovacs and Hauskeller, 2012), this figure is to a large extent in development in China. Today, half of the doctors in China do not have bachelor degrees (Editorial, 2017). Influenced by its various origins (Gao, 2014) and disrupted by the Cultural Revolution and health care reforms (Wu et al., 2014), medical education in China exhibits a notable regional disparity that is now undergoing harmonisation and reform (Zhu et al., 2016). Yet, Chinese doctors are increasingly pressured by their institutions to conduct clinical research and publish in science

journals (Yuan et al., 2013). This unrealistic expectation on Chinese doctors' research outputs led young doctors to question 'Is this [SCI articles] more important than clinical competence?' (ibid.). The pressure of publication further cultivates a fast-growing lucrative business of ghost writing that when uncovered, led medical journals to question 'China's medical research integrity' (Editorial, 2015).

In addition to the challenge of organising and conducting clinical research in China, is patients' general distrust of medical institutions and doctors. This distrust partly resulted from China's health care and hospital reforms in the 1980s and 1990s. Those reforms were launched as part of China's social-economic reform, wherein Central Government demolished universal health care for Chinese people and reduced public funding for hospitals (Blumenthal and Hsiao, 2015). As hospitals were steered towards the marketplace, patients were made into consumers and doctors started to prescribe for bonus incomes that compensated for the loss of public funding for their institution and their relatively low basic salaries (Ran et al., 2013). Physician-patient relationships worsened, and violence against health care professionals increased (Nie et al., 2017; Zheng et al., 2006; Xu, 2014).

In comparison, science and technology has been linked with China's nation-building project since the early twentieth century (Schwarcz, 1986; Wang, 2002). Though severely attacked during the Cultural Revolution, the working environment and social-political status of scientists and engineers were soon restored once Deng Xiaoping launched social-economic reforms in 1978. A decade later, Deng (1988) further endorsed science and technology as 'a primary productive force'. Chinese leaders after Deng have continued putting science, technology and innovation high on the political agenda. After President Hu Jintao initiated the 'indigenous innovation' project in 2006 (Xinhua, 2006), his successor President Xi Jinping reinforced the role of innovation in directing China's development in the 21st century (Xinhua, 2013c). Accordingly, scientists, engineers and, more recently, scientist-entrepreneurs are all granted substantial political support and social-economic resources at the national, provincial and local levels to advance their research, careers, spin-offs and start-ups (Xinhua, 2015; State Council, 2016b; Xinhua, 2016f).

The general professional and institutional practices and hierarchy between medicine and science were manifested during this regulatory change to stem cell clinical research. Stem cell sciences in China are funded with a clear orientation towards clinical applications (Liao and Zhao, 2008). During China's 12th Five-Year Plan (FYP) (2011-2015), in addition to increasing research funding on stem cell and reproductive sciences, specific funding was given to the Chinese Academy of Sciences (CAS) to coordinate and organise stem cell scientists from various institutions to conduct science-led translational research (Zhou, 2016). Those scientists work in line with the translational research model and are confident in leading a nationwide network to promote, coordinate and conduct stem cell research and clinical applications (CAS, 2016). They were the champion of the regulatory change (Döring, 2004; Zhang, 2012).

In contrast, clinician-researchers were put at the opposite side of the regulatory change: they were ordered to 'self-examine and self-correct' their stem cell related clinical research and practices (MOH, 2011). Most leading clinician-researchers and industry leaders admit that there were some doctors and clinician-researchers who oversold stem cell therapies to patients prior to the regulatory change in China. They nevertheless contest that this wrongdoing should not be burdened upon all Chinese doctors. Practitioners like themselves, they stressed, had followed existing regulations in their clinical work, and their work and reputation was also damaged by the out-of-control proliferation of stem cell therapies across Chinese hospitals. As I will introduce in the next section, they further emphasised that their work had helped to create a leading edge for China in intensified global stem cell research-enterprise, yet their claims were largely disregarded by stem cell scientists.

Further fractures were created by a dual institutional system that separates the governance and regulation of military and armed police hospitals from civilian hospitals. In December 2011, the MOH ordered all medical institutions to stop stem cell related clinical practices, but its order did not reach those governed by the General Logistic Departments of the PLA - the equivalence of the MOH in the military system. Whether or not the regulatory change would also discipline stem cell clinical practices in non-civilian hospitals persistently concerned the advocates and observers of regulatory change (Yuan et al., 2012; Rosemann and Sleeboom-Faulkner, 2016; Qiu, 2017).

During my fieldwork, I visited some military and armed police hospitals that kept running their cell therapy programme, which partly confirmed the critics' concern about the scope and effectiveness of this regulatory change. Yet, I also started to note a more complicated dichotomy of stem cell research practices in military and non-military systems.

I first noted that almost all clinician-researchers who sat on the Expert Committee worked in military research institutes and affiliated hospitals. Additionally, at clinician-researchers' professional conferences, I met military clinician-researchers who had received their academicianship for their work on stem cell research or tissue engineering. These academicians are in their 80s, and some were among the first to obtain advanced training overseas in medical research. Clinician-researchers often addressed them as the founding fathers of stem cell research in China. I further noted that stem cell research is not only actively pursued in relevant military science institutes (AMMS, 2011), but also studied in diverse ways as part of regenerative medicine (Cheng et al., 2016). The outputs of these studies are well documented in science journals (Tang et al., 2017; Liao and Zhao, 2008). Stem cell research has its historical root in military research worldwide (Kraft, 2009). Yet, partly due to the same dual institutional systems, this recent past of stem cell science in China is hardly documented outside of the military.

Furthermore, despite certain military and armed police hospitals continued practising of stem cell therapies, I learned that the scope and scale of their practices had significantly reduced. A young doctor explained to me in summer 2014,

> 'It is a little complicated. We report to our Department of Health (DoH within GLD) and do not need to follow the rules of the NHFPC, but their rules have direct effects on ours. Given the change of our leadership and the anti-corruption campaign, the DoH and our hospital administrators have become more cautious [*short pause*] I suppose if you make a strong case [for your practice] and you get the support from your hospital, you can still do it. But there are rumours that our new leader is considering halting all [stem cell clinical] practices…so in general people [working in military hospitals] are more cautious now.'

Indeed, those military clinician-researchers and Expert Committee members had been advocating bringing military hospitals' governance and regulation on stem cell therapy more into line with the civilian hospitals. Their position was not only in response to the

aforementioned criticism, but also because they noted that, to take the successful research projects of military clinician-researchers' to the marketplace, they would have to go through the same regulatory route as their civilian counterparts.

Taking into consideration these facets of stem cell clinical research and regulatory practices in China, I contend that the practices and rationales of clinician-researchers should not be gauged too readily against scientific criteria. Rather, there is much to be learned from their experiences with, and perspectives on, cell therapies and the regulatory change in China.

The Chinese leading edge: perception and contestation

Stem cell clinician-researchers, who had used regulation to guide their clinical practices, defended the existing regulation on medical technologies. Though some of the leading clinician-researchers who I met started, or joined, other biotech companies that specialise in developing stem cell related products, they often stressed to me that their primary identity was as a doctor.

When those practitioners heard about my research interest on China's recent regulatory change to stem cell clinical research and practice, they presumed that I was investigating 'ethics' and, almost reflexively, clarified that they were not working with human embryonic stem cells.

The clarification about not working with human embryonic stem cell, as I mentioned in the introduction to the thesis, reflected how the debate on using human embryos as research materials, which had persisted mostly in the United States, had influenced stem cell clinical research and regulation in China. It was also linked to Chinese clinician-researchers' preferences for using 'adult' (*chengti*, 成体) stem cell-based products for 'autologous' treatments (*ziti zhiliao*, 自体治疗). 'Adult' clarifies that the source of the stem cell is not from human embryos. Its range spans from bone marrow and adipose tissue to (aborted) foetus, cord blood and placenta. Nevertheless, in professional conferences and in clinician-researchers' interviews with me, the term 'mesenchymal stem cell' was used almost interchangeably with the term 'adult stem cell'. 'Autologous' refers to using cells that are originally extracted from a patient's body and

developed into cell-based medicinal products to treat the same person. While adult stem cell-based products can be used for allogeneic treatment (to treat patients other than the one whose cells were made into the products), autologous treatment was often the focus of Chinese clinician-researchers' discussions when they defended the preservation of this treatment for clinical practice.

While in more recent years clinical trials using pluripotent stem cells started to proceed in countries such as the United States, the United Kingdom and Japan (Trounson and DeWitt, 2016; Atala, 2012), Chinese clinician-researchers have been working more often with other types of stem cells such as mesenchymal stem cells. The pluripotent stem cells are also favoured by leading laboratory-based scientists in China who, during the regulatory change, advocated the adoption of the translational research model and the regulation of stem cell clinical research more akin to drug clinical trials. Leading laboratory-based scientists advocated developing pluripotent stem cell-based medicinal products that can be manufactured, traded and used like other drugs and, therefore, could expand the industry. They often hinted that clinician-researchers preferred to develop autologous stem cell therapy because of their lack of scientific expertise and their commercial interests. This suspicion about why autologous stem cell therapy is populated by clinician-researchers is also seen in other countries (Munsie and Hyun, 2014; Lysaght et al., 2013). Yet, the way Chinese clinician-researchers collectively defended their work is closely linked with regulatory change, and with their perspective about how, enabled by the existing regulation on medical technologies, their work had helped to create a leading edge for Chinese stem cell clinical research and industry development.

In this section, I explain the link between clinician-researchers' choice of what types of cells to work with, their views on the 'Chinese edge' that they helped to create, and their defence to China's existing regulation on medical technologies. I also introduce laboratory-based scientists' counterarguments and in some cases, their dismissal of clinician-researchers' claim to propel the leading edge for Chinese.

In the debates about which cell would be optimal for developing medicinal products and related industries, rather than attributing the position of practitioners to their personal, professional and institutional interests, I contend that practitioners took positions that

had a material base in the cells that they chose to work with (or abstain from working with). In other words, the biological capabilities of the cells served as the base for practitioners to design, conduct and coordinate their work, and to ally themselves with the regulatory choices of regulating cell-based products as a medical technology or drug. I will elaborate this point in the last section.

The 'leading edge' in clinical research

At professional conferences that featured stem cell, biotherapy or bioindustry, keynote speakers often compared stem cell clinical research between China and leading countries of biomedicine, such as the United States and the United Kingdom. These comparisons were presented in numbers of publications, patents, registered clinical studies, and approved products - some by year, and some in total - and countries were accordingly ranked in tables. Drawing from these numbers, graphs and tables, the speakers then diagnosed the strength and weakness of China's stem cell clinical research and related industries, and suggested how practitioners, industrialists, investors and regulators should work together to advance China's stem cell clinical research, product and industry development amid intensifying global competition (see also analysed by Fu (2011), Chen and Qian (2011)). Dr Xu, a pioneering stem cell clinician-researcher, academician of Chinese Academy of Engineering (CAE) and member of the Expert Committee, was among the most invited keynote speakers.

According to Dr Xu, mesenchymal stem cell, is the most promising type of stem cell for clinical research and product development wherein Chinese clinician-researchers had made notable contributions.[25] As introduced in *Nature*, mesenchymal stem cells 'are multipotent adult stem cells that are present in multiple tissues, including umbilical cord, bone marrow and fat tissue. Mesenchymal stem cells can self-renew by dividing and can differentiate into multiple tissues including bone, cartilage, muscle and fat cells, and connective tissue' (Nature, n.d.).

[25] Like many other conference participants digitally recording those presentations, I took photos of lectures' powerpoint slides for my research use. To protect the identity of the speakers, in recalling the content of those lectures, I do not include those photos that I took in the fieldwork. Instead, I add relevant references that support those speakers' claims. The authors of the cited articles were not the speakers of those lectures.

In his keynote lectures, Dr Xu often compared mesenchymal stem cells with pluripotent stem cells (embryonic stem cell and induced pluripotent stem cell), and listed a number of reasons why mesenchymal stem cells are more suitable for clinical research. One highlighted advantage of using mesenchymal stem cells for clinical research is that they can only differentiate into a limited number of other types of cells and thus reduce the risk of developing unwanted cell types, especially tumour cells. Furthermore, because mesenchymal stem cells are more often used in autologous treatment, Dr Xu added its clinical value of avoiding adverse immune reactions after transplantation and having additional benefits of mediating the immune system.

Dr Xu highlighted the immune-related clinical benefits of mesenchymal stem cells-based therapies, nevertheless, he presented a simplified picture of the 'risks' involved in developing, delivering and monitoring these therapies (Herberts et al., 2011; Lepperdinger et al., 2008). The way Dr Xu's comparison between mesenchymal stem cells and pluripotent stem cells is an explanation commonly seen in the literature (Uccelli et al., 2008; Stoltz et al., 2015; Wei et al., 2013). The literature also reports on the potential uses of mesenchymal stem cells in treating chronic diseases (Ullah et al., 2015) and immune-mediated diseases (Abdi et al., 2008), and as drug-loaded particles (Parekkadan and Milwid, 2010). Given the multiple functions and relative stable safety profile of mesenchymal stem cells, mesenchymal stem cell-based therapy continues to attract research and commercial interests, and mesenchymal stem cell-based clinical trials and patents continue to outperform other types of stem cells in relevant databases (Bersenev, 2015; Trounson and McDonald, 2015).

After showing the clinical value of mesenchymal stem cell therapies, Dr Xu highlighted that mesenchymal stem cell-based therapies have, so far, the most successful track record of gaining market authorisations in countries that develop them (Yano et al., 2015). Countries such as South Korea, Canada and Australia were cited as exemplars of being 'market friendly' towards stem cell-based medicine and industry development. When the European Medicines Agency (EMA) approved Holoclar as 'corneal diseases stem cell transplantation' in early 2015, Chinese clinician-researchers immediately used the approval to advocate for developing adult stem cell-based products and appeal to the regulators to end the regulatory impasse (as observed also in Sui and Sleeboom-Faulkner, 2015).

After convincing his audiences about the clinical and market value of mesenchymal stem cells Dr Xu often showed a table that highlighted the regulatory situation. The table compared mesenchymal stem cell related research activities and market approvals in China and in other countries. On the one hand, mesenchymal stem cells are the most studied type of stem cells in China and Chinese clinician-researchers had made a considerable contribution to this subfield of stem cell clinical research (Fu and Zhao, 2011; Liu et al., 2016). Yet, on the other hand, so far, Chinese authorities had not approved any mesenchymal stem cell-based product in China whatsoever and, since the MOH intervened in stem cell clinical research and practices in late 2011, the authorities had stopped accepting new applications for clinical research.

After presenting these numbers, graphs and tables, Dr Xu concluded that,

> 'We have made significant progress in the past years and are not far behind the US… In fact, we can say that we [China] are among the leading countries in stem cell clinical research (and regenerative medicine).'

It was often at this point that some keynote speakers transmitted to showcasing their own contributions to making China a leading country in mesenchymal stem cell clinical research. Their publications in high impact journals evidenced their role as leading researchers in the field of stem cell research and regenerative medicine. Yet, the majority of ordinary Chinese clinicians were still unable to publish in English language journals, and could not integrate clinical studies into their clinic work.

Leading clinician-researchers, such as Dr Xu, knew that stem cell therapies, which were administered in Chinese hospitals prior to the regulatory change, had created a mess that undermined the reputation of Chinese stem cell research. Yet, unlike laboratory-based scientists or bioethicists who had championed the regulatory change to stem cell clinical research in China, Dr Xu and other leading clinician-researchers disagreed with the proposed approach of regulating stem cell clinical research more like drug clinical trials. Rather, they often urged their audiences - most were clinician-researchers, doctors and hospital administrators - to learn how to do their studies properly and to collectively improve the quality of stem cell clinical research in China. For instance, at the *10th Workshop on Regenerative Medicine* held in June 2014, after listening to a junior researcher's presentation on a case report on potential use of mesenchymal stem cell in pain management, a leading clinician-researcher commented that,

> ‘You’ve gotten very interesting findings. But you must learn how to improve your research skills and get the result published. For example, you need to improve your research design, to be more specific about the inclusion/exclusion criteria and do some follow-ups (with the patients). And is it possible to run more tests in your hospital? You need to think about multiple ways to assess the observational results. It will take some time, but it’s worth it. Because once your publish [your research results], your work will be on the record. And even if you publish in Chinese, the foreigners [non-Chinese researchers] will recognise it! For which we must give them credit.’

Dr Xu was also sympathetic towards clinician-researchers’ complaints that their work was too often dismissed by scientists and regulators and that regulatory change had significantly harmed China’s stem cell clinical research. So, even though Dr Xu presented an optimistic picture of stem cell clinical research in China through a series of comparisons with performance of the leading countries, he often ended his lectures with a cautious note, ‘While we are stuck [in the regulatory impasse], others are moving fast! We are about to lose the edge we have created for China!’

Nevertheless, Chinese authorities were aware of the ‘damage’ that this regulatory impasse had introduced to stem cell clinical research in China and they supported stem cell clinical research that aimed to develop stem cell-based medicine and related industries. The market success of mesenchymal stem cell-based products in other countries had caught the attention of CFDA’s in-house scientists. Some of the technocrats were also invited as keynote speakers at clinician-researchers’ conferences. In their presentations, they not only echoed Dr Xu’s assessment of the clinical and market value of mesenchymal stem cell-based products, but also introduced their ongoing studies on developing quality control standards for mesenchymal stem cell-based clinical research and product development.[26] In other words, these technocrats were preparing for the development of mesenchymal stem cell-based medicine in China, once the new regulation was put in place.

Laboratory-based scientists criticised the choice made by Chinese clinician-researchers’ to work with mesenchymal stem cells. Notably, those scientists also denied the clinician-researchers’ claim that stem cell clinical research in China had created a leading edge for China in global stem cell research and industry development.

[26] See also evidenced in Yuan (2015).

What leading edge?

Those who work or have worked in 'basic' science - such as molecular biology, developmental biology and genetics - were not convinced that clinician-researchers had earned China a leading edge in stem cell clinical research. In contrast to clinician-researchers' enthusiasms about stem cell clinical research and applications, they emphasised to me that there is still a long way to go to understand the biology of cells, not to mention to use cells in the clinic. They generally denied that clinical observational studies had the status of scientific research and provided me with examples of real scientific breakthroughs made by Chinese scientists. They stressed the technical, scientific and engineering complexities involved in developing and delivering stem cell-based medicinal products into the human body to treat specific diseases or conditions. Above all, they all referred to the translational research model as the scientific route to develop stem cell-based medicine.

The three laboratory-based scientists who I introduce here spend most of their time in and around the laboratory. Although they had elaborate views about the ongoing debates among Chinese stem cell practitioners on how to regulate stem cell clinical research in China, none of them took part in those debates, and they thought the debates were only remotely linked with their work. In different ways, they all asked me why I needed to learn about their views on stem cell research and regulation when I had studied genetics and bioethics before. They doubted my interviews with them would add anything new to my research findings. Although they considered it was a waste of time to conduct research on the opinions of 'basic scientists', like them, about how to regulate stem cell 'clinical' research in China, they all stressed that regulators should understand science properly, if they want to make sensible regulations in this fast-evolving field.

Although to a large extent their views on how stem cell research might contribute to medicine are close to what I had read in science literature, their counterarguments against clinician-researchers' claim about the Chinese edge were more nuanced and contextualised than the narrative I often heard from leading scientists in science conferences. Similarly, their understandings of, and experiences with, basic and clinical

research were also more fluid and thus illuminating for me in thinking about translational research.

In September 2014, I met Dr Yun, a cell biologist who pioneered heart cell and tissue repair. In the late 1980s, Dr Yun returned to China from her postdoctoral training in Europe and soon after that made a breakthrough in developing heart cells in a dish. When I interviewed her, Dr Yuan was about to reach retirement age and had reoriented her attention from research to teaching and training younger researchers. Her years of research experience made her ready to share her views with me on stem cell clinical research,

> 'It [stem cell] is far from mature to be used in the clinical settings. We only barely started to decipher the mystery of stem cell in the lab. More research is needed to fully understand how it functions in a human body. There are just so many questions: how to deliver the cells to the targeted organ? What is the niche like? For how long will the injected cells survive? How will they behave once injected? Just think about it. We are far away from the clinical applications! Whoever says otherwise just lies.'

Dr Yun's research into heart tissue repair was motivated by the desire to find more effective treatment for cardiovascular diseases. Compared with those eager to unearth stem cell's therapeutic potential, Dr Yun considered the most effective way of using cells is to develop a disease model for drug screening, yet she acknowledged that it requires substantial resources and patience to work out how to do this.

In another interview with a geneticist-immunologist, the scientist elaborated a particular complexity that Dr Yun mentioned: the stem cell niche. In science literature, stem-cell niche is defined as 'an area of a tissue that provides a specific microenvironment, in which stem cells are present in an undifferentiated and self-renewable state. Cells of the stem-cell niche interact with the stem cells to maintain them or promote their differentiation' (Nature, n.d.). In Dr Pan's account, to include stem cell niche into scientific inquiry about stem cell is a logical step towards understanding why and how (stem) cell functions in particular *in vivo* context. Without filling this knowledge gap, Dr Pan expressed doubts, 'How would you expect to design a [cell] therapy that will function in the way you want it to inside of a human body? And [to function] in at a specific time and position?"

Given his research background in genetics, Dr Pan wanted to uncover genetic factors that contribute to the regulation of microenvironment-stem cell interactions that had drawn increasing attention from the international science community (Moore and Lemischka, 2006; Jones and Wagers, 2008). Collaborating with his scientist-colleagues and long-term collaborators from local hospitals, Dr Pan recently co-authored a research grant to apply for funding from the China National Science Foundation (CNSF) to study stem cell niche in and around the liver. As a laboratory-based scientist, Dr Pan admitted to me that he was not interested in exploring how the knowledge about stem cell niche would help develop concrete therapeutic strategies to treat the patients. Nor, in this case, were his collaborators from hospitals who wanted to join a basic research project led by a group of scientists.

Dr Yun's and Dr Pan's analyses of the complexities involved in understanding the biology of stem cells and in conducting stem cell clinical trials were often echoed in responses from other laboratory-based scientists who I met during the fieldwork, and are well documented in science literature (Ankrum et al., 2014; Squillaro et al., 2016; Trounson and McDonald, 2015). Contrastingly, the view of Dr Dou, the director of the central laboratory of a children's hospital, was unexpected and revealed an episode in the recent past of stem cell research in China that alerted me to the evolving nature of this research field and its changing institutional, national and international norms.

I met Dr Dou in autumn 2014. After some small talk and hearing about my previous research in genetics, she suddenly recalled an old frontier research,

> 'If they [clinician-researchers] tell you that they are leading China's stem cell research, they are delusional! Working with what? Mesenchymal stem cell? There is so much [scientific] debate on what "mesenchymal stem cell" actually is. There is certainly no *scientific* edge in what they do! [*short pause*] Well, what Dr Sheng did was a *real* breakthrough, but it is a shame that it went down that way.'

The study by Dr Sheng Huizhen, which Dr Dou referred to, was on creating hybrid embryos through fusing rabbit eggs and human skin cells (Dennis, 2003). Though Dr Sheng aimed to develop an alternative route to provide alternatives to human embryonic stem cells for research, the methods she developed raised concern about creating 'human-animal chimera', which led to the study becoming controversial outside of China (Cong, 2007). Around the time the news broke and the controversy started, Dr

Dou was doing doctoral research in Dr Sheng's laboratory. Dr Dou recalled in particular how the heated international attention had effectively changed both Dr Sheng's and her own research careers,

> 'Before the journalists rushed into the lab, it was such an exciting [research] time. I genuinely respect her [Dr Sheng] and felt lucky that I was mentored by her. But the external attention was so disruptive and she soon left. [*pause*] I heard she moved back to the US, [and] maybe that is the best. [*longer pause*] I had already graduated by then, and decided not to follow that line of [chimera] research. [There is] too much attention and so many [scientific] questions remain unsolved.'

Later when commenting on her current work, Dr Dou returned to the point of 'so many questions remain[ing] unsolved',

> 'I like my work here. Busy but rewarding. Running the lab, looking after our hospital's small biobank and teaching leave me little time to do my own research. But I still like research, probably the interest was seeded from the time I worked with Dr Sheng. [Yet] I now research mainly iPS cells and genetics. It feels safer this way than [researching] embryonic stem cells. I guess I am not that scientifically ambitious any way, and I find working with patients very rewarding: a sense of making my research meaningful for them right here and now, rather than who knows how many years down the road.'

Having transited to clinical research, Dr Dou's reflection on the value of clinical research echoes what clinician-researchers stressed in their conferences and in their conversations with me. Nevertheless, Dr Dou maintained that her core identity was as a scientist. A closer reading of Dr Yun, Pan and You's arguments against the work and claims of clinician-researchers suggests that their views on what stem cell-based medicine is and on how best to use stem cells in medicine were closer to the views of clinician-researchers than they might like to admit. Critically, they all agreed that stem cells are not a singular, static thing, but change in their natural environment, during laboratory experimentations and in the human body. They agreed also with clinician-researchers that science alone would not address the technical, scientific, manufacturing and clinical complexities involved in developing cells into cell therapies. The divergence between laboratory-based scientists and clinician-researchers pivots around what constitutes clinical research and what knowledge and expertise matter more when developing cells into cell-based medicinal products.

Tooling stem cells: the essence and necessity of clinical work

Having presented various topics that were debated by different groups of stem cell practitioners during China's recent regulatory change to stem cell research, in this section, I introduce Dr Wei and his defence of his clinical work and the existing regulation on medical technologies. Those years of conversation with Dr Wei, and some other practitioners whose practices are commonly considered controversial prompted me to reconsider the premises underpinned in the translational research model and led to my conceptualisation of "toolised medicine".

Dr Wei: a diehard defender of the existing regulation on medical technologies who denies working with stem cells

In addition to well recognised leaders such as Dr Xu, a few other clinician-researchers were also active in defending the regulation on medical technologies during this regulatory change. Among them Dr Wei stood out because he denied working with stem cell at all. At first, his argument confused me. In news reports and literature on stem cell tourism, Dr Wei's practice is often cited as an example of how Chinese clinician-researchers attracted foreign patients to pursue experimental cell therapies in China. So his talking about upholding highest the principle of caring for patients in his clinical practices with cell therapies sounded, at first, superficial to me.

I have now known Dr Wei for over four years during which time I have had intense discussions and sometimes arguments about the science and ethics of cell therapies. He remains controversial, and his strategies and manoeuvres to get around institutional and regulatory hurdles still unsettle me. But he is no more strategic than many other practitioners who I met in this study. His determination to 'speak the truth' made him a good informant to me, even after being challenged by me, he was willing to carry on our conversations.

In what follows, I will not discuss the ethics or legality of Dr Wei's practices, or the risks Dr Wei's practices might have posed to his patients. There are plenty of news reports, commentaries and analyses of what went wrong with Chinese practitioners' stem cell clinical practices (Qiu, 2008; Kiatpongsan and Sipp, 2009; Editorial, 2009). Dr Wei's practices were not far off from what have been reported and criticised, and I agree with some of those analyses.

I choose not to repeat these criticisms, nor defend his practices.[27] I recount what Dr Wei thinks about the science and ethics of cell therapies that he practises, how he sees others practicing cell therapies, and how he recounts the origin and unfolding of this regulatory change. Like those patients who used experimental cell therapies, who I introduce in the next two chapters, maverick researchers such as Dr Wei have important things to say about cell therapies and the unfolding regulatory situation that deserve scholarly attention.

During the regulatory change, Dr Wei repeatedly clarified in public, and in private conversations with me, that he only works with adult cells and the therapy he uses is a different type of cell therapies to stem cell therapy. This distinction matters scientifically and in regulation. In conferences packed with clinician-researchers, he repeatedly reminded his peers what stem cell is, 'By definition, it *must* have the *full* capacity to develop into all kinds of cells, in addition to having the ability of self-renewal.' He further cautioned his audiences about the use of terminologies:

> 'Ask yourself: does the cell you use have such ability [of stem cell]? You may think stem cell is high-tech, fancy, and tell your patients that it is stem cell therapy. But we are not using stem cell in our work! I would say whoever in our field claims we are working with "stem cell" is either a *liar* or *ignorant*!'

He was annoyed by the 'indecisiveness' of other senior clinician-researchers. In our first meeting, he recalled a recent workshop we both attended and commented on a former colleague and friend who organised that workshop,

> 'Old[28] Zhang is all right. He is just not decisive [on his use of terminologies]. He would not dare to say that [fatal and progenitor cells are stem cell] to my face, but I know that sometimes he would say otherwise to others. It comes down to courage: whether you can stick to and speak the *truth* aloud!'

As he spoke, Dr Wei clenched his fists and kept raising his voice. He then paused and looked at me, 'You said you studied biology before, so you must understand what is stem cell?'

> 'Yes, I did. I think I know what you mean,' I nodded.

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[27] I have my personal stance on the science and ethics of cell therapies that is neither the position of Dr Wei's nor that of the critics of stem cell tourism. In chapter seven, I reflect on these questions.

[28] Dr Wei and Dr Zhang are among the first to work on cell therapies in China. 'Old' (*lao*, 老) here denotes both age, experiences and the two doctors' close relationship. Senior researchers are otherwise refer to one another with their academic or administrative titles such as 'Professor' or 'Chief'.

> ‘So the question is not a s*cientific* one. Some of us in this community stupidly think that claiming to work with “stem cell” would add credit to their work. See what has happened? They dug a hole for themselves to be regulated! I don’t care about the regulation! It is not for me. [Because] I never worked with stem cell, not now and not ever. What is stem cell? By definition it has to have *fully* developmental and regeneration potential. So far, only hESCs, and to some degree iPSCs, are qualified. But for the same reason, they are unsafe, [and] far away from clinical applications. Not to mention hESCs have ethical problems…’

The type of cells Dr Wei works with, as he persistently clarified, is what the MOH regulation on medical technologies categorises as ‘cell transplantation technology (excluding stem cell)’ (MOH, 2009b). The list included three other cell-based technologies, using respectively, ‘immune cell (T cells and NK cells)’, ‘umbilical cord blood stem cell’, and ‘haematopoietic stem cell (excluding umbilical cord blood stem cell)’. Tissue engineering and tissue transplantation is categorised as another technology in the same list. He clarified the situation further in medical journals and health magazines.

During the regulatory impasse, Dr Wei’s was determined to correct the misunderstanding about stem cell among clinician-researchers and regulators. Yet, his argument was disdained by scientists and was unpopular among clinician-researchers who he often publicly challenged. In private, several senior clinician-researchers told me he was a ‘big mouth’ and advised me to ‘just listen and ignore [his comments].’ Nevertheless, during the regulatory change, they selectively used Dr Wei’s argument to craft their own defence of the existing regulation on medical technologies. Because no matter how unpopular Dr Wei made himself among some leading clinician-researchers, his arguments are foremost grounded on cell biology and stress the value of clinical work.

During our four years of conversations, I gradually noted that Dr Wei’s obsession with the details in the *List of Category Three Medical Technologies for Clinical Applications* (MOH 2009b) extended beyond using those definitions to defend his practices. His obsession linked with his past involvement in the development of the MOH’s regulation on medical technologies. Dr Wei once mentioned that he and some other clinician-researchers were consulted as experts during the making of the then new regulation on medical technologies. As leaders of professional societies, the regulators further asked

them to develop technological guidance documents for these medical technologies once the MOH published the list. He was proud with the draft technological guidance documents that he and others developed and submitted to the MOH for review. Yet, although those draft guidance documents were published for public comment (MOH, 2009c), Dr Wei was disappointed that, 'Unfortunately, nothing happened afterwards (*meiyou xiawen*，没有下文)!'

In Dr Wei's recollection, a golden opportunity was opened up by this 'really genius' regulation to allow Chinese clinician-researchers to research and practice cell therapies. But at the same time, weak implementation of this regulation and the lack of follow-up guidance unleashed unmonitored, uncontrollable proliferation and practices of cell therapies across China. The resulting 'mess', as commonly reported in media and literature, now endangers the regulation on medical technologies. I will revisit Dr Wei's recollection of these regulatory events in chapter seven.

Dr Wei's passionate defence on this regulation is also rooted in his belief that cell therapies must be integrated into patient care through medical practice. This belief comes from his primary identity as a doctor. So did his interest in cell biology. Dr Wei told me that he earned a sponsorship from his institution for his advanced training abroad, around the time that human embryonic stem cell was first successfully derived, making worldwide news. As a relatively young, yet senior neurosurgeon, Dr Wei was immediately fascinated by the prospect of making stem cells useful for treating patients. He thus narrowed his search for laboratories that could train him for his future clinical research and practices. He was accepted to work for a couple of years as a postdoctoral researcher in a renowned stem cell research laboratory in the United State. Those days and nights culturing and studying cells, under the microscope and with mice in the laboratory, convinced him of the potential of cell therapy to treat neurological injuries. At the same time, this advanced scientific training alerted him to the lack of integration between medical expertise and laboratory-based research. In particular, he noted that the question of how to make cell biology meaningful in patient care through clinical practices had received too little attention from stem cell scientists. He decided then that once he returned to China, he would prioritise actual clinical practices and patient care in his work with cell therapies.

Dr Wei was aware of the techno-scientific unknowns around cell biology and the clinical uncertainties involved in developing and administering cell therapies. Yet, considering himself primarily a doctor, Dr Wei valued the treatment of his patients more than the advancement of the science of stem cell research, 'The concept of cell therapy or regenerative medicine is scientifically interesting, but it means nothing to my patients unless it is put into use for them.'

So after completing his advanced training abroad and returning to his hospital, Dr Wei proposed to the hospital leaders to introduce a cell therapy programme there. He gained institutional support, received the approval of the hospital's ethics committee, and started clinical research that focused on the safety of using cell therapies on humans. After receiving reassuring results about the safety of the type of cell therapy that he developed, he then started, step-by-step, to integrate cell therapies into patient treatment. Yet, his early studies on safety were too rudimentary to convince stem cell scientists in the North America and Europe that the results were valid. While patients from these regions started to seek treatment with Dr Wei in China, his critics publicly condemned his practices as reckless and said that he put patients in danger.

Dr Wei did not deny that he diverted from the translational model and skipped the standard three-phases clinical trial in developing cell therapies. He argued that this 'bench-to-bed' image of developing cell therapies is flawed. Not only because 'Cell is so delicate and malleable to be standardised the way a drug is,' but also because 'Each patient is different, and [as a doctor] one needs always to assess the patient in front of you, and choose the best mechanism to administer cell [therapy]'. For the same reason, Dr Wei advocated a more holistic approach to use cell therapy as part of a patient's treatment plan and to tailor cell therapy for an individual patient's specific conditions.

Dr Wei's argument against translational research and his holistic approach in treating patients with cell therapies is similar to reports of other practices of experimental cell therapies (Bharadwaj, 2014; Patra and Sleeboom-Faulkner, 2013). Like those already being documented (Hyun et al., 2008), Dr Wei's perspectives as a doctor were commonly dismissed by stem cell scientists because, for them, stem cell-based medicinal products must first be standardised, before being applied in clinical setting. Stem cell-based therapies also must be tested not only for safety, but also for efficacy

and efficiency, independently and preferably through double-blind randomised controlled trials. Dr Wei's clinical practices did almost the opposite, and made it nearly impossible to assess the therapeutic value of cell therapies that he administered to his patients in different ways, thus making his observational studies of little interest to most stem cell scientists.

From the beginning, Dr Wei was aware that prioritising clinical practices meant his work would have little pure scientific value. Once he became a target of stem cell tourism criticism, he realised the importance of building up a scientific reputation for his work. He started to organise more standardised clinical research and publish results in journal articles. He further noted the importance of reaching out to like-minded practitioners and set up professional networks and societies that standardised practices among themselves and developed a strong collective image of cell therapy practitioners[29]. He was strategic. But in his defence, he had to 'play the game',

> 'If that is what it takes to continue practising cell therapy, I have to do it. I know how the game [of science] works, and I was stupid to not have thought about it earlier to use science to protect my work [*pause*] It's just not fair to duplicate the work only for producing journal articles. Isn't it ironic that we subject patients to [clinical] trials for the sake of gathering data, but not for treating them?'

Dr Wei is not alone among clinician-researchers who were pragmatic about 'using science'. In answering my question about their views on translational research, some senior clinician-researchers cited the unknowns, such as those listed by Dr Yun, and asked me rhetorically, 'How much we have to know before we can use stem cell in the clinic?' Like Dr Wei, instead of chasing after science, they highlighted the clinical nature of using cell therapies. That is, one cannot just take a product made of cells out of the laboratory and apply it in the clinical setting. Rather, it requires substantial investment and work on adopting and continuously improving those therapies for the individual patients they are treating. For them, the reduction of cell therapy to a mechanic use of techniques and knowledge developed in science laboratories is a too simplistic view of cell therapy and imposing this view onto clinical practice could harm patients.

[29] Sleeboom-Faulkner (2016) analysed similar responses from BeiKe Biotech amid international and national criticism for its involvement in stem cell tourism. Rosemman also documented 'alter-standarisation' practices in stem cell research and clinical practices (Rosemann, 2013; Rosemann and Chaisinthop, 2016).

Tooling stem cells: from biological capability to medicinal potentiality

How to develop stem cells into stem cell-based medicine and what types of stem cells best serve the purpose are questions that confront researchers, biopharmaceutical companies and regulators worldwide (Mount et al., 2015). Scientists, manufacturers, industry analysts and social science researchers have noted the particularity of making 'living' entities such as cells into medicinal products (Franklin and Kaftantzi, 2008; French et al., 2014; Gardner et al., 2015). In this chapter, I grapple with the transformation and process of making a biological entity such as cells into technologies and new products. I learned this from studying how, during the regulatory impasses, Chinese stem cell practitioners debated questions such as what is a stem cell and which type of (stem) cells deserve more investment to be developed into new medicinal products. They presented multiple, yet few, answers to those questions. Following Mol and Law's (2002: 11) definition of 'multiplicity' - 'be more than one and less than many' - I suggest that how and where those practitioners narrowed down their answers is as important as how they diverged from one another.

Laboratory-based scientists and clinician-researchers did share some common beliefs. For instance, they all agreed that stem cells can be developed into stem cell-based medicine. Yet, this premise is a hypothesis about whether the biological capabilities of stem cell, such as differentiation and self-renewal, can be harnessed and made into medicine that has similar features. The hypothetical nature of the translational research that guides stem cell research and product development is often neglected by scientists and research funders (Maienschein, 2011), including those in China.

The debates among laboratory-based scientists and clinician-researchers illustrate the conundrum they both faced about how to handle techno-scientific, engineering and clinical uncertainties embodied in a (stem) cell as a living entity. Clinician-researchers who advocated for mesenchymal stem cell-based therapy stressed that they used clinical safety as the primary criteria. In the clinical setting, the limited differentiating and self-renewal capabilities of somatic cells, such as mesenchymal stem cell, become favourable to them, although research and clinical observations suggest that those cells function more like an aid rather than a key factor in tissue or organ repair or regeneration. Clinician-researchers place high priority on reducing the risk of inducing

tumour formation. In many cases, those cells were derived from and used on the same individual in the form of autologous treatment. So further benefits include reducing ethical concerns, especially compared with using human embryonic stem cells, and avoiding immune responses after transplantation.

Scientists commonly see the most effective way to ensure safety when using living cells (as part of the medicinal product) is to standardise manufacturing, delivery, prescription and administering practices. They, thus, advocated for the establishment of stem cell banks and manufacturing standardised stem cell-based products. The measure they used for manufacturing safety focuses on identifying, managing and assessing known risk. More importantly, their preference for pluripotent stem cells reflects trust in a vision of utilising techno-scientific-engineering knowledge to construct standards, protocols and infrastructure to manufacture stem cell-based products for a range of conditions at the industrial scale and for a bigger market. This rationale explains why developing stem cell-based medicine is considered a manufacturing project (Martin et al., 2014; Lipsitz et al., 2016), and why using stem cell-based medicine is a challenge for health care system and health market that requires interdisciplinary and cross-sector coordination and collaborative intervention (Martell et al., 2010; Bayon et al., 2014, 2015; Ginty et al., 2011; Bubela et al., 2015; Gardner and Webster, 2016).

Making stem cells into stem cell therapies illuminates the changing relation between, and mutual transformation of, biology and technology. As Franklin suggests in *Biological Relatives*,

> '[B]iology is itself increasingly understood as technology - and thus something that can be made…[and] the use of biological bits and pieces as tools…also means that technology is becoming more "biologized"'(2013: 3).

This transformation of stem cells into stem cell-based medicine and related industries can also be viewed as undergoing 'bio-objectification', 'different life forms are created and are given life, and perhaps, multiple lives' (Webster, 2012: 2). It is a process that often involves classification, governance, regulation and the creation of new social, economic and political relations (ibid.).

Yet, stem cells need not to go through this industrialisation route to become useful for medicine. For instance, Hopkins (2006) shows that clinician researchers and their

professional bodies are able to utilise the 'hidden research system' that is embedded in health care systems to develop new medical technologies such as cytogenetics without industrial support. Webster (2013) also notes that hospitals are likely to be a vital space for developing and adopting regenerative medicine, especially in hospital-based treatment. It is thus important not to dismiss the originality of the work presented by the clinician-researchers or to ignore their sentiment regarding their status in science. Rather, what those clinician-researchers did in the clinic goes beyond translating laboratory science into clinical practices. Their clinical research and practices is better captured in Amsden and Tschang (2003)'s definition of 'applied research'. That is, their work was centred in 'the world of science [and] requires the transformation, variation and reapplication of a known concept to an unknown end' (ibid.: 558). Thus, as those clinician-researchers stressed, their work has its own value and is essential for developing and using cell therapies.

Their work, I contend, brings to the fore the distance between a cell's biological capabilities and medicinal potentiality. This distance is acknowledged in the translational research model as a 'valley of death' between the laboratory and the clinic, and is revealed in the increasing use of stem cell-*based* medicine replacing stem cell therapy in science literature. As the word 'base' suggests, to be transformed into a medicinal product and used in the clinical setting, a cell needs to be extracted from its origin, cultured - and sometimes engineered and manufactured - collected, packaged, stored and delivered to the clinic. In other words, biological entity-based medicine will be developed from biological entities such as cells, but not in their original *in vivo* form, nor constituted solely by those biological entities. Yet, the work of clinician researchers effectively challenged this linear conceptualisation of developing stem cell-based medicine. They emphasised that clinical work is more than clinical research, and that the effort to actualise a biological entity's medicinal potentiality is neither guaranteed for success nor must follow a singular path. Considering the accelerated speed of technological innovation and convergence in a broadly defined health industry (Dolsten, 2016; Andrianantoandro, 2014), clinician-researchers were not wrong to suggest that developing cell-based therapies is an ongoing process and each intermediate version will bring stem cell closer to its full potential of becoming (part of) such medicine.

In her work on how cells are made into and used as laboratory technologies, Landecker (2007, 2010) underscores the importance of analysing how the living biological entities are made into biotechnology. Landecker reminds her reader that biotechnology foremost changes 'what it is to be biological' before it 'changes what it is to be human' (Landecker, 2007: 233). Similarly, Löwy (2011) notes that the 'invisible hyphen' in biomedicine has tilted more scholarly attention towards 'bio' rather than 'medicine'. There is a need now to understand more how *bio* becomes *medicine* and 'the life of the clinics'. I suggest that between the laboratory life and the clinic life of cell therapies, rather than a process of translation, there is an attempt to actualise the medicinal potentiality of cells from the biological capabilities of cells. 'Potentiality', as Taussig et al. (2013: s4) first introduced in study of biomedicine, also has multiple meanings: a hidden force determined to manifest itself, genuine plasticity, and a latent possibility imagined as open to choice. In actualising a biological entity's medicinal potentiality from its biological capabilities, an experimental space opens up, and will remain open, for developing and using a (possibly) improved version of biological entity-based medicine.

On this basis, I suggest that biological entity-based medicine is becoming toolised and tooling work is essential for actualising the potential of a biological entity in medicine. For its developer, the process of designing and making toolised medicine is accompanied by the acknowledgement of current limitations, as well as the expectation of improving and launching a next-generation product. For its different users, the process of tooling biological entities into biomedicine also grant them the opportunity to give and compete with one another in assigning different values and meanings in the process of making biological entities into biomedicine. As I have illustrated in this chapter, developers and users of cell therapies spoke about the necessity of clinical work in developing and administering cell therapies for individual patients, and clinician-researchers essentially talked about care practices and 'shared doctoring', in order 'to seek what can be done to improve the way in which we live with our diseases' (Mol, 2008: 56). I consider care practices and shared doctoring are critical examples of tooling work that I will introduce in the next two chapters and revisit in chapter seven.

CHAPTER FOUR. Assessing, choosing and experimenting with stem cell therapy

This chapter illustrates how patients and their families, who I met during this research, valued stem cell therapy for its potential to help them cope with both medical and non-medical issues. I first met these patients and patient families in hospitals or through social media. Although my interlocutors came from varied geographic locations and social-economic backgrounds, I do not claim they are representatives of Chinese patients and patient families. I mentioned in chapter two that, all the patients and patient families who I met in this research knew that stem cell therapy was in an 'experimental' status, and that the health authorities had intervened in unauthorised clinical use of experimental stem cell therapy. In this chapter, I will introduce a few patients and their families who taught me something significant about "toolised" feature and "tooling" process of stem cell therapy.

I met one ALS patient who had been using stem cell therapy since 2006. A more recently diagnosed ALS patient and his family considered, for nearly a year, whether he should try experimental stem cell therapy, eventually using it in January 2015. In both cases, the patient families carefully pondered over both the medical and non-medical value of experimental stem cell therapy, and made considerable efforts to access the therapy that they considered useful to their specific situations. My research participants who live with type 1 diabetes or spinal cord injuries also valued stem cell therapy because it provides the possibility to resolve non-medical problems, such as fractured identity and family relations, that were induced by their diseases or disabilities.

The experiences of stem cell therapy by patients and their families revealed three insights. First, stem cell therapy is conceived and valued differently by different people. Second, these patients and patient families were aware of the difference and distance between stem cell's biological capability and its potentiality in medicine. Third, patients and patient families could deliberately use the difference and distance to integrate their preferences and bring stem cell therapy closer to their preferred use through their work of hope and care (Mol et al., 2010). I suggest that these patients and patient families were able to use stem cell therapy as a "tool" to manage life challenges arising with

diseases and disabilities. Additionally, they used their work of hope and care as part of the "tooling work" that helps to actualise stem cell's potentiality in medicine and in other domains.

Searching, assessing, and using experimental stem cell therapy

In this section, I introduce two ALS patients - Mr Xie and Mr Shen - whose wives were my main interlocutors. I initially came to know Mr Xie through his book about his fight against ALS, with which he was diagnosed in 2006. I visited Mr and Mrs Xie at their daughter's home[30] in September 2014. I first met Mr Shen and his family at their visit to a neurologist, Dr Hua, who I was shadowing in the autumn of 2014. I interviewed Shen's family a few weeks later, and visited them in January 2015 in another hospital where Mr Shen received 'experimental'[31] stem cell treatment.

ALS is a rare, degenerative neurological disease. Riluzole is the only drug that has, so far, proven useful in delaying the progression of ALS. Unfortunately, there is no treatment to restore the lost neuro-motor function or to stop the degenerative process. Stem cell's ability to reproduce itself gives researchers, doctors and patients alike hope for making 'regenerative' medicine that will someday treat ALS. In China, ALS is not well known, including among neurologists working at the township-level hospitals (Wei et al., 2015). As a rare disease, ALS is not covered by public health care insurance in China. The monthly cost of Riluzole is around 4000 yuan (£400) in China, while the average household disposable income in China in 2015 was about 21,000 yuan (£2,100) (Wen, 2018).

The shortage of clinical expertise and the absence of public health care support have, thus, significantly delayed the diagnosis and treatment of ALS patients in China,

[30] In summer 2014, at Mr Xie's request, the couple moved out of the hospital and into their daughter's home. Multiple generations living together is not unusual in China, but usually the younger generation live in the elder's home. In the case of Xie's family, Mr and Mrs Xie sold their apartment years ago to pay for treatment fees, including experimental stem cell therapy and expenses associated with long-term patient care. Their daughter and son-in-law bought this apartment partially for its short distance to the hospital where Mr Xie used to stay. Mrs Xie told me this story as an example of her daughter and son-in-law's filial piety.

[31] 'Experimental' carries two meanings here: 1) the controversial nature of stem cell therapy as a process of active experimentation 2) my intention to challenge the mainstream view of seeing the therapy as 'experimental'.

especially those from socially and economically disadvantaged backgrounds. In summer 2015, the 'ice-bucket challenge' - a worldwide chain of fundraising events dedicated to ALS - was introduced to China and, like other parts of the world, made news headlines. Chinese internet users, however, soon lost interest in ALS as the 'ice-bucket' trend faded. Nor did the moment of heightened public awareness translate into public policy change that Dr Hua and ALS patients and their families so desired.

Pursuing novel treatments on top of standard care for ALS patients was unthinkable to families that never managed to get their affected family members properly diagnosed, or could not afford the basic medical and daily care of ALS patients. Later in this chapter, I will discuss this critical question of how wider political and socio-economic contexts influence patients and patient families' medical experiences, including their experiences with experimental therapy. In this section, I focus on delineating the examples of the two families, Xie and Shen, and how their assessment and use of experimental stem cell therapy that taught me more about "tooling work".

Home: 'It helps him anyway'

In autumn 2014, I visited Mr and Mrs Xie at their daughter's home. During that visit, Mrs Xie's reluctance to talk about stem cell therapy allowed me to see the wider context of assessment that patients and their families make when considering stem cell therapy. I also learnt something about stem cell therapy that was utterly unexpected - anyone could potentially become an operator of experimental stem cell therapy. This insight became a pivotal moment in my fieldwork.

Prior to the visit, I had read Mr Xie's book on his and Mrs Xie's experiences with ALS. It included the couple learning about, searching for, and traveling to another city for experimental stem cell therapy in late 2006.

My conversation with Mrs Xie lasted about three hours. During most of our conversation, I sat at the dining table in the living room. Mrs Xie talked with me while carrying out daily care work for Mr Xie who lay in an adjustable bed at the other end of the room. A curtain separated the area where Mr Xie stayed from the rest of the living room. About forty minutes after my arrival, Mrs Xie invited me to come to see her husband.

Before seeing Mr Xie with my own eyes, I was rather anxious about how to connect with someone who could no longer express himself. The average survival time for most Chinese ALS patients is, on average, five years. At the time of my visit, Mr Xie had lived with ALS for eight years. According to his book, by 2007 he had lost almost all his bodily motion function, except his eyeballs. Mr Xie was only able to write his book with the help of Mrs Xie and a spelling board.

When I was led to see Mr Xie behind the curtain, I was joyfully surprised to see Mr Xie in a solid shape: his chubby, rosy face made me nearly forget for a moment that he had ALS. This first uplifting impression immediately eased me. After Mrs Xie introduced me to Mr Xie, I started to talk to Mr Xie about how his inspirational book had brought me here and what an honour it was to visit him in person. Mrs Xie's encouraging smile further calmed me down.

For the next hour or so, I was invited to stay with Mr Xie while Mrs Xie continued coming in and out to do her care work. When Mrs Xie was in the kitchen preparing a meal[32] for Mr Xie, she asked me whether I would be interested in watching some videos collected by their daughter for Mr Xie. 'They are his [Mr Xie] favourite, in addition to watching news,' she smiled. 'Of course!' I happily agreed. The flash drive that Mrs Xie opened on the smart television preserved both public and private memories of Mr Xie's ALS journey. It contained a collection of local and regional news reports on Mr Xie and their family's fight against this intractable disease. There were also family photos, a song written by Mr Xie the year before and sung by their cousin-in-law, and probably most special among all, a video made by their daughter for Mr Xie's birthday the previous year. To make this birthday gift, their daughter contacted and recorded birthday wishes from a range of people, from family members to Mr Xie's school classmates and former colleagues, from doctors and nurses who had treated Mr Xie to patient families who became friends with the Xie's. I was instantly moved by this special video, and thought about what Mrs Xie had mentioned several times in passing since I came: their daughter's filial piety.

[32] Mrs Xie had developed a customised diet for Mr Xie: seven small-portion meals throughout the day, with traditional Chinese medicine, fruit juice and other supplements.

In addition to their daughter's care and help, Mrs Xie told me about a long list of people who had helped them in this 'fight against ALS'. Some of them were also contributors to the birthday video. Mrs Xie gave me examples of how, at critical moments, their family and friends had helped them. For instance, when an unexpected breathing failure almost killed Mr Xie in early 2007, a doctor-friend of Mrs Xie's quickly helped her reach an expert who gave Mrs Xie critical advice on whether or not to use tracheostomy ventilation.

More examples that Mrs Xie gave me were about how their extended families, friends and employees helped to secure the medical care that Mr Xie needed to sustain his life. Some of the help came in a monetary form to alleviate the couple's financial pressure.[33] Some gave Mrs Xie an extra hand in caring for Mr Xie. Additionally, their employees' annual visits, around the Spring Festival, gave the couple 'institutional' best wishes and respect.[34] In this context, Mrs Xie repeatedly said how lucky she felt to have this support system and that she felt even more obligated to care for Mr Xie: 'to work myself to death [*pingle laoming*, 拼了老命], I will care for him'.[35]

In passing, we also talked about the recently populated 'ice-bucket challenge', contrasting the viral video to the general lack of societal awareness and policy support of ALS patients and families. Although, as an integrated part of their experiences with ALS, this larger societal context surfaced from time to time in our conversations, Mrs Xie always ended the discussion short. Once she had started to compare nowadays with the era of Chairman Mao when they were young[36], 'at that time, everyone lived alike

[33] To give an idea about the financial burden: the monthly cost of Riluzole, the only drug available for treating ALS and not covered by public health insurance in China, takes away nearly 60% of the couples' joint pension income.

[34] In Adams and colleagues' research on blood donation practices in urban China, their research participants cited examples of home visit by people sent by their work unit as an acknowledgement for their blood donation. Whereas Adams and colleagues suggested through such act, the work unit helped to forge a relation of caring and reciprocal obligation between the state and its subjects (Adams et al., 2010).

[35] To take care of Mr Xie, Mrs Xie took an early retirement from her job with the customs, and mastered the nursing skills to care for her husband. According to local news report, over these years, Mrs Xie had become an 'exemplary nurse' that 'even the department chief asked the nurses to come to learn from her'. This moral obligation to take care of one's spouse even at the expenses of one's own health and wellbeing, in particular in case of wives taking care of husbands, is considered a part of traditional family values in China, and was observed by me in various cases during this study.

[36] See Zavoretti (2017)'s analysis of how the demolishing of universal health care that had once be provided during the Mao's era has varied effects in family life in China. See also in Steinmüller (2015), how in central China, ordinary Chinese still hold affective emotion and respect towards Mao Zedong and refer to him as their 'old man,' or 'father Mao'.

and did not need to worry about medical bills' - she abruptly changed the topic: 'oh, no, I shouldn't been talking like this. My husband is such as good person that he would not like hearing me complain [about the government]'.

I later realised that, for the similar reasons, Mrs Xie had been reluctant to talk about their experiences with experimental stem cell therapy. By the time Mrs Xie eventually engaged with this topic, almost two hours had passed since I first asked her, during which time I had tried a few more times to engage with the subject but without success. So when Mrs Xie suddenly asked me, 'What do you think of stem cell [therapy]?' my mind went blank,[37] even though I had been asked the same question by other patient families before and had a standard answer at hand. After a second or so, I gave Mrs Xie this standard answer, 'It is hard for me to speak about its science or state-of-the-art practice. I am not a stem cell scientist, nor a doctor. But I have learned from them in my fieldwork, like I am learning from you right now. I heard a lot about stem cell's potentials, but also deep concerns. The regulation I am following is on stem cell clinical trials which suggests that the regulators want to assess its safety and effectiveness'. I then paused.

Mrs Xie nodded: 'I too want to find out, *does it work?* There must be some way to test it [the efficacy]. But what we know so far is that "it may help". I wish there were studies giving me a more *definitive* answer. But it is important for my husband…to see we give him [stem cell therapy] a few times a year, to see that there is some new [treatment] coming, and we are not giving up. Every time [when the practitioner came to treat Mr Xie], I would say to him, "See, they bring stem cell to treat you" …'

This was one of the most unexpected patients' experiences with stem cell therapy that I could ever imagined beforehand. I was so surprised that I heard myself asking aloud: 'Really? How did you get it [stem cell]? Is it even possible [to have someone giving him stem cell therapy here]?'

[37] Not to intervene in patients' health care and their life in general was one of the principles that guided my fieldwork. But because these patients and patient families knew that I also interviewed researchers, from time to time, I had to face such 'ethically important moments' when I had no good answer to respond to my research participants' question. Guillemin and Gillam (2004: 262) defined an 'ethically important moment' as 'the difficult, often subtle, and usually unprepared situations that arise in the practice of doing research'.

‘The doctor [we used to see] cannot come [to treat Mr Xie] any more. For the same reason you mentioned - the regulation became strict and they wouldn’t like to take the risk [to treat him]. But I managed to find a friend who knows people who can come down to treat him a few times a year…It looks like a normal injection solution. The product is easy to transport and process. I probably could inject it myself,’ she paused then continued, ‘sometimes I think isn’t it *paying for hope*? Who knows whether it works or not. It’s like Traditional Chinese Medicine, isn’t it? But without hope, we are left with nothing. Without it, we are just waiting for [his] death to come. He wants it [stem cell treatment], so if it helps him, I would do my best to continue providing it.’

While she talked about ‘hope,’ Mrs Xie swiftly used the syringe to feed Mr Xie’s the meal she just prepared. Following her movement, I looked back and forth between the syringe in her hand and the tube linked to Mr Xie’s body. My mind started to replace the meal with a solution containing stem cells in a smaller syringe, and even more oddly, I recollected seeing a businessman walking out of a cell company’s VIP Room, where with a glance, I saw a bed and next to it an emptied intravenous therapy bag swinging on its stand. The fieldwork encounters seemed to come together, and I heard myself mumbling: ‘ha, it was easy [to take a treatment]’.

Mr and Mrs Xie’s experiences alerted me to how experimental stem cell therapy could be easily used by patients and their families. The way Mrs Xie described their routine use of experimental stem cell therapy sounded nearly identical with how she got a prescription of Chinese herbal medicine from her friend and cooking it at home for her husband. It was clear that Mrs Xie had doubt about the efficacy of experimental stem cell therapy that her husband received, and that she wanted researchers to find out more and give her a ‘definitive answer’ about the usefulness of stem cell therapy. It was also clear that Mrs Xie was aware that this ‘experimental’ stem cell therapy was now under regulatory scrutiny, and that those who had treated Mr Xie before were unable to continue treatments. Despite her cautious assessment of the situation, Mrs Xie found a way to continue getting that treatment for her husband, because ‘it is important for my husband’. Mrs Xie even acknowledged that they were purchasing ‘hope,’ because without hope, ‘we are left with nothing’. Later in the discussion section, I will return to Mrs Xie’s critical reflection on her cautious use of experimental stem cell therapy for sustaining the hope that was so critical for her husband and family.

Cautiously experimenting with stem cell therapy: when life is counted down

I first met Shen's family in September 2014 when they came to visit Dr Hua, who I was shadowing. Dr Hua worked at one of the top three neurological departments in China. Mr Shen was diagnosed with ALS nearly a year before in a reputable hospital, close to their home, in northern China. During the visit to Dr Hau, Shen's family asked Dr Hua for his 'expert opinion' on what they had learned from the internet about stem cell therapy. Dr Hua gave them the same answer that he told his other patients who asked him the same question: worldwide stem cell therapy is still in an experimental status; it is constrained by the regulatory situation in China; clinician-researchers in the hospital currently had no plan to organise stem cell clinical trial, although they might in the future. Shen's family appeared unsurprised but disappointed.

I interviewed Shen's family about two weeks after first meeting them. In that two weeks, Shen's family had visited a number of hospitals and biotech companies that were in their shortlist of providers of stem cell therapy and located in that or nearby cities. For reasons that I will elaborate on shortly, at that time they decided not to proceed further with experimental stem cell therapy.

I visited them about three months later at a hospital in a megacity in northern China. Shen's family went to that hospital for (stem) cell therapy[38]. They knew the therapy was 'experimental', but, by then, had decided to 'give it a try'. I learned weeks later that Mr Shen had initially responded well to the first treatment, which excited Shen's family, relatives and friends. Unfortunately, that immediate effect dwindled, so Shen's family went back to get a second treatment that took a different approach. The doctor used Mr Shen's own cells and injected them through Mr Shen's neck. When this treatment took place I was about to leave the field, so Mrs Shen and I agreed to keep contact on WeChat – a popular messaging and social media App in China. As Mr Shen's condition worsened our communication reduced too.[39]

[38] The doctors that provided Shen's family with the therapy used the term 'cell therapy' than 'stem cell therapy,' for similar reasons that were explained by Dr Wei (see chapter 3). Shen's family used the two terms interchangeably. In introducing and discussing the case of Shen's family, I will follow their doctors and call it 'cell therapy'.

[39] Mrs Shen posts less and less news on WeChat about the status of Mr Shen. With the birth of their grandson in 2016, Mrs Shen became busy looking after the baby. Given the physical distance between me

I explain this family's experiences with ALS and with experimental stem cell therapy, including my accidental involvement in their eventual pursuit of experimental cell therapy, in the section below.

Shen's family lived in a mid-sized city 'A' in northern China. Mr and Mrs Shen were in their mid-50s, and both held leadership roles in public institutions. Miss Shen did her master-level study in management in the United States. Upon her return to China, Miss Shen moved to city 'B', where she continues living, and started a fashion company with a few friends. At Shen's family's visit to Dr Hua, Dr Hua recognised Miss Shen, after she mentioned that earlier that year she had taken her father's medical records for Dr Hua's review.

Dr Hua is a specialist in motor neurone diseases. He completed his medical training in China, and went to the United States in late 1990s for advanced research training. After nearly a decade's medical research and practice in the United States, Dr Hua returned to China in late-2000s, and has since worked as a clinician-researcher in that hospital in city 'B'. Dr Hua's research interests reside in the intersection between neurology, immunology, and genetics, meanwhile he is known among patients more as a doctor specialised in diagnosing and treating ALS and MS (multiple sclerosis).

The first examination consisted of tracing Mr Shen's medical history, examining the progress of condition, and checking the usage of current medication and supplementary nutrition, exercise, diet and general care. Shen's family were well prepared and had done thorough research on ALS. They smoothly answered Dr Hua's questions and raised their own. One of the main questions they had was about experimental stem cell therapy. After telling them that neither 'experimental' stem cell therapy nor stem cell clinical trial was available in the hospital, Dr Hua mentioned a research project that he was then developing in collaboration with some German researchers on

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and Shen's family and ALS's degenerative nature, overall, I find it ethically troubling and emotionally difficult to ask Mrs Shen about Mr Shen's status. In mid-2018, during our general chat about each other's lives, I finally asked her about Mr Shen, but she did not answer me on this particular question. I have bad feelings about this, but to honour their privacy and our research relation, I decided not to press on with this question.

neuroprosthetics[40], and asked whether Mr Shen would be interested. Shen's family immediately agreed.

While Dr Hua asked his assistant to take contact information of Shen's family for future communication, he introduced me to Shen's family as 'someone you may like to talk to about the status of stem cell [therapy].' Until then, I had been doing my observing part of participant observation: sitting in the corner of the consultancy room, quietly observing and jotting about what happened in that room. I stood up and smiled at Shen's family.

After they completed their consultation with Dr Hua, I led them out of the consultancy room, and had a brief chat about my research. Shen's family knew about the regulatory change to stem cell clinical research. After hearing Dr Hua mention the regulatory effects, they became more interested about this topic and said that in principle they would meet me for an interview. We exchanged contact information and I handed them a hard copy of my research reading materials, then I asked them to read it and raise any questions they had before our next meeting.

We met again after two weeks. Shen's family had returned from visiting companies and hospitals that they preselected from their search for viable providers of experimental stem cell therapy. Shen's family were unimpressed by those companies' qualifications and expertise, but considered this 'educational tour' useful for improving their understanding of the current status of stem cell therapy. Nevertheless, they did appreciate one clinician-researcher who specified the limitations and potential risk of stem cell therapy that he offered in a military hospital.[41]

We discussed the various types of stem cell they had newly learned in this 'educational tour'. Though still confused about these different stem cell therapies, they easily listed common risks, such as inducing tumour and immunological reaction after transplantation. 'Of course we are not asking for 100% safety,' Mrs Shen immediately

[40] Neuroprosthetics is proposed by researchers as 'linking the human nervous system to computers' that would 'provid[e] unprecedented control of artificial limbs and restoring lost sensory function' (Leuthardt et al., 2014).
[41] See chapter three for the reference on why and how for some time clinical practices continued in military and armed police hospitals, after Chinese health authorities banned stem cell clinical practice.

added. Drawing from her experiences working as a hospital administrator in their hometown, Mrs Shen elaborated, 'It is impossible [to ask for 100% safety] in any medical procedure. There are risks we ought to take, but it's a matter of whether the operation is worth taking the risk. We trust Professor Hua[42] the most and we think we'd like to be on Professor Hua's clinical trial. If he runs a stem cell clinical trial, that will be the best. The other [neuroprosthetics] sound alright too. My husband is in an early stage and seems to be responding well to the medication, [so] we may just wait and see.'

We then discussed the family's experiences with ALS. Shen's family said little about the hardships of living with ALS. Instead, Mrs Shen recalled the support that they had received from friends and colleagues back home. She mentioned how her colleagues had given them useful advice on coping with ALS and helped them find 'real experts' in this field, such as Dr Hua. She cited examples of how Mr Shen's colleagues convinced him to stay in the leadership role in a local state-owned factory, after Mr Shen told them about his diagnosis of ALS and his plan to resign.

Mr Shen laughed, 'That's because I am a good manager! [*pause*] but as agreed with the board, I will resign once it [ALS] affects my work performance…'

> 'Don't think too much ahead!' Mrs Shen interrupted her husband, while reaching her hand to his.
>
> Miss Shen then entered the conversation, changing the subject to tell me what a big fan of car racing her father was, and how good he was at many other sports. Mr Shen loudly laughed when heard about 'car racing,' yet, added that, 'Well, I stopped driving a month ago. [*pause*] Now, look: [I have to use] walking stick! I just hate it!'

Mr Shen spoke the least in our meeting, while attentively listening to his wife and daughter's recollection. For most of the time, he carried a big smile on his face. Occasionally, he added some details. Yet, Mr Shen spoke to me a few times about his wife's patience, care and love, and his daughter's filial piety during this unexpected transition of their family life. Mrs Shen also spoke highly of their daughter, and recalled

[42] The title of 'Professor' is used generically to refer senior, respected doctors, regardless of one's actual accreditation.

how, upon hearing of her father's diagnosis with ALS, Miss Shen instantly contacted her classmates in the United States to collect information on the 'most advanced' ALS treatments there. Mrs Shen also said how much effort her daughter had devoted since in seeking the best expertise and treatment available in China, including arranging this visit to Dr Hua.

That first meeting with Shen's family left me with warm memories. Till this day, I vividly remember seeing Miss Shen walking off alongside her father, arm in arm with Mr Shen's laughing. Meanwhile, Mrs Shen stayed with me because she wanted to talk about 'one last thing' - her concern about the heritability of ALS and her request not to let anyone know about the development of ALS in Miss Shen's father. I reassured her that I protect the privacy and confidentiality of all my research participants, and added that geneticists and clinician-researchers continue to question how far ASL is a heritable disease.

Some time later, I interviewed Miss Shen. She mentioned that it was Mrs Shen who first read about experimental stem cell therapy on the internet, and asked her to check the situation in the United States. She told me that during that early research, they had learned about the regulatory 'ban' on medical institutions' offering patients experimental stem cell therapy. Nevertheless, through internet searches and friends' recommendation, they identified a few potential providers that were 'worth a site visit' in this region, and combined these visits with the visit to Dr Hua. In passing, I also learned that, 'In thinking about my parents,' Miss Shen started to consider settling down with her boyfriend. I told her 'You are really a good daughter. [43] Miss Shen replied with a smile: 'I do my best.'

Things remained relatively steady in the following months, until late 2014 when Mrs Shen left me a voice message on WeChat. Mrs Shen asked me for update about Dr Hua's department - a topic we frequently talked about - adding that 'your Uncle[44] Shen

[43] In China, there remains relatively strong family and societal expectation on young people to have a family and build a career (*chengjia liye*, 成家立业). In both families, Mr Xie's and Mr Shen's daughters took the decision, as part of their filial piety, to get married and have families 'in time' for their fathers. Additionally, given Mrs Shen's concern on the inheritability of ALS, Miss Shen's settling down might have also eased her mother's mind. In 2015, Miss Shen married and had her son in 2016.

[44] In China, once a social relationship is established, it is common to refer one another with titles similar to one's family member. In this case, as Miss Shen and I are about the same age, Mrs Shen and I refer to

is progressing quite rapidly recently.' Hearing her anxious voice, I typed out, deleted, and typed out my reply again and again. I wished there was something I could update her. In the end, I sent: 'Sorry, Aunt Shen, not yet. How is Uncle Shen? And how are you?' Mrs Shen did not reply.

Some time later, I attended a conference for the establishment of a national professional association for neurorestoratology - an interdisciplinary speciality that 'studies neurorestorative strategies and mechanisms of neural regeneration, repair and replacement of damaged components of the nervous system, neuroplasticity, neuroprotection, neuromodulation, vasculogenesis, and immune regulation' (Huang et al., 2015). Taking a holistic approach in neurorestorative interventions, neurorestoratologists are expected to provide patients with tailored treatment, including cell therapies that 'may become a key clinical therapeutic option' (ibid.). Local media television reported on this conference, in particular testimonies from two patients on their positive experiences with 'cell therapy'.

When I read a news report on that conference, I forwarded the news to Mrs Shen. Given that Shen's family had been following news related with ALS and possible treatment, I introduced the news report with a message: 'you may have read this.' It turned out they had not. Mrs Shen was excited by the news, and asked me how they could contact doctors who might be able to provide such therapy. I panicked. I noted that by introducing the news, I might have accidentally influenced their treatment plan, and broken a 'research ethics' principle that I had been rigidly following. The more excited Mrs Shen became in reading the news, the more concerned I became. Neurorestoratology was, after all, a marginal discipline that had not earned much recognition outside a group of practitioners working mainly in hospitals for military and armed police. To slow down Mrs Shen's train of thought, I reminded her of the 'experimental' status of cell therapy and the ongoing regulatory change in this field. I further suggested that she consult her colleagues at the hospital and friends who can find more about this neurorestoratology and give a second opinion. I then said, 'If you

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Mr Shen as 'Uncle Shen' in our conversation. Similarly, Mrs Shen addresses Mrs Han, who appears later in the thesis, as 'big sister Han'.

like, I can ask Mrs Han,[45] the wife of the ALS patient featured in the news, to see whether she is willing to share with you their experiences with the treatment.' When Mrs Shen agreed to search and think more about this experimental treatment, I felt slightly relieved. Later, I introduced the two wives to one another. After a few days, Mrs Shen told me that they had decided to contact Dr Lang who treated Mr Han.

In January 2015, Shen's family sought their first treatment with Dr Lang who arranged Mr Shen's treatment in an armed police hospital. Two years after the MOH issued the ban on stem cell clinical practice, his hospital was one of the few hospitals that continued providing cell therapy. Dr Lang told them that for many years he trained the neurorestoratologists there. Dr Lang specified that all the medical technologies were established and used under his supervision, and that he would personally visit Shen's family once they were admitted in that hospital. Shen's family readily accepted Dr Lang's arrangements and directed their energy to making other arrangements like taking sick leave, getting train tickets and arranging Mr Shen's travel with wheelchair.

When I arrived, Mr Shen had just settled in the ward. The rest of Shen's family was about to have some takeaways for lunch, which were brought back by Miss Shen and her fiancé. Mrs Shen told them to have lunch first, while she needed to finish mopping the floor. Mrs Shen apologised to me for keeping me waiting and mentioned that they had to stay in a hotel last night, due to 'some arrangement issue'. 'Well, it all worked out now,' Mrs Shen smiled: 'look at this room: how spacious it is! We have a double bed, television, fridge, sofa and so on. It's said that this [VIP] ward is usually preserved for generals. No wonder it is slightly dusted, but we have to clean it first!'

In the four months since I last saw Mr Shen he had changed. Most of his hair was gone and what remained had turned grey. He could still lift his legs and stand for a few minutes but he could no longer walk. At lunch, he could barely hold the bowl to drink the noodle soup from it. His loud laughter and cheerful voice, nevertheless, remained the same.

[45] Mrs Han also took part in my research. Unfortunately, her husband died unexpectedly in November 2015.

When two doctors came to see Mr Shen, Mrs Shen introduced me as a visiting friend and thanked the senior doctor for making arrangements for their stay. The senior doctor briefed us, and asked Shen's family for their opinion on the treatment arrangements. The discussion went smoothly, within half an hour Shen's family agreed with the doctors for Mr Shen to have the following arrangements. He would take some blood and imaging tests in order to assess his suitability for receiving cell therapy. If the tests went well, Mr Shen would be treated with the cell product developed from the cell line cultivated in the laboratory. Depending on the result of this first treatment, Shen's family would consider having a second treatment with a different approach. It was estimated that the first treatment, including the pre-operative assessment and post-operative observation, would take about ten days. Before they left, the senior doctor reassured Shen's family that Dr Lang would come to examine Mr Shen later that night and answer the family's questions.

After the two doctors left, I asked Mrs Shen about the 'arrangement issue' she had referred to earlier. 'Oh, it was nothing,' she said, 'the first night we were told that there was some problem with finding a bed for us in the neurosurgical ward. We contacted Dr Lang immediately. Soon after, Dr Lu [the senior doctor we had just seen] phoned us and apologised. He told us that he managed to get a bed here [in a VIP ward] instead, so we moved here this morning.' Behind these arrangement issues, Shen's family were aware that, in addition to almost reaching the limit of its bed capacity to accommodate Shen's family, the neurosurgical ward was also reluctant to be involved in providing Shen with experimental cell therapy.

Soon after, Shen's family got ready for Mr Shen's medical examination, and we said goodbye outside of this VIP building. For a while, I stayed and watched Miss Shen's fiancé pushing the wheelchair around, while Miss Shen led the way and Mrs Shen walked alongside Mr Shen in his wheelchair. I heard again Mr Shen's loud laughter, and wished I would hear more in coming years.

Eighteen months later, in June 2016, I asked Mrs Shen again about the family's views on cell therapy. 'It didn't work at all the second time,' Mrs Shen said upfront, 'Professor Lang contacted us earlier this year to recruit us for a clinical study. We decided not to go. It's not that we blame Professor Lang. We don't. Professor Lang has

been nice to us and patient in answering our queries. We understand it doesn't work for everyone, and everyone responds differently….It's more that your Uncle Shen is too fragile to travel now, and we had planned to move south to be with our daughter. The weather is better here, and it is easier to see Professor Hua. We still want to get enrolled into Professor Hua's clinical study, if he runs it…"

Like Mrs Xie, who I introduced earlier, Shen's family understood that cell therapy was experimental and lacked scientific evidence to demonstrate its medical benefits, or to specify its risk. Unlike Xie's family that started to use stem cell therapy when it was classed as a 'category three medical technology,' Shen's family made their decision amid regulatory change of which they were aware. Shen's family had first-hand experiences with this 'experimental' status of cell therapy and the regulators' intervention into this field. From their initial search for information on stem cell therapy to their 'educational tour' of a few candidate providers, from Dr Hua's answer to their inquiry about stem cell therapy to the reluctance of Dr Lu's colleagues to admit Mr Shen for cell therapy, they knew that the medical option they were pursuing was not optimal.

So why did Shen's family's use an experimental therapy which they knew might not help Mr Shen's medical condition? One may suggest that it was 'hope' that 'blinded' Shen's family in their final decision making. Yet, for most of the time, Shen's family restrained themselves from enacting such 'hope' presented by experimental stem cell therapy. Instead, they preferred waiting for a clinician-researcher who they trusted as an ALS specialist to organise a clinical trial that might include Mr Shen as a trial-subject. When Mr Shen's condition worsened, the parameters of their consideration also changed. In their eventual pursuit of cell therapy, they chose to follow the understanding that, 'it doesn't work for everyone and everyone responds differently'. Nevertheless, they decided 'to give it a try'.

I, therefore, suggest that what Shen's family valued and used in their stem cell journey was not hope per se, but the space that was opened up by stem cell therapy that made hoping possible. Stem cell therapy offered to do *something* with the situation they were facing. Their research for and enactment of 'hope' resembles what Miyazaki (2006) describes in Suvavou people's use of 'hope' as a 'method of self-knowledge' (p26). I

will return to this comparison in the discussion section, but make two points here. First, the use of 'hope' is a family endeavour. Shen's family used hope as something concrete that they could take into their hands to ponder, to try out and to willingly live with the consequences of Mr Shen's treatment together. This possibility of being able to do something about the current situation for one another is also what mattered to Xie's family - to not just 'wait for death to come'. Second, the two families' continuous research for and enactment of 'hope' also made it clear that their search is not confined to experimental stem cell therapy. As a family, they kept this hope going through different routes and in multiple domains, from Traditional Chinese Medicine to their daughters getting married. In this process, their use of experimental stem cell therapy reveals how stem cell therapy can be used as a "tool" to address one's problems and respond to particular situations.

Living with hope presented by experimental stem cell therapy

Type 1 diabetes derives from the destruction of the β-cells in the pancreas, and often starts to affect one's health in childhood or adolescence (Maahs et al., 2010).[46] Damage to the spinal cord impairs sensory function and mobility of arms, legs, and sometimes other parts of body (WHO, 2013). Although both conditions can be medically managed and mitigated over time, their features of chronicity, reduced mobility (spinal cord damage), and increasing life-threatening risk (diabetes), have made a 'cure' appealing to both patients and researchers. The 'regenerative' potential of stem cell presents such a hope of developing a 'cure'.

For this study, I interviewed a dozen type 1 diabetes patients in various places in China and held a group discussion with spinal cord injury patients and family members in a mid-sized, coastline city C. Unlike the two ALS families who I just introduced, none of these patients tried 'experimental' stem cell therapy, but they had all learned about stem cell therapy that was widely promoted on internet search engines. Moreover, they all knew or heard about patients in similar conditions who had done so.

[46] Researchers have recently suggested further differentiating types of diabetes (Ahlqvist et al., 2018), and developed diet-based treatment that challenges conventional understandings of diabetes (Forouhi et al., 2018). Given that new discoveries have not affected routine clinical practice in China, I use the common typology of diabetes.

Their views towards stem cell therapy were similar: ‘wait and see’. On the one hand, they valued the ‘regenerative’ possibility of stem cell therapy that, someday, might help them to recover from their current constraining bodily conditions. On the other hand, they were sceptical about the provision of stem cell therapy that had been denounced by health authorities as ‘experimental,’ yet, was still advertised on the internet. These patients talked about increasing negative news coverage on the business and clinical practices of ‘experimental’ stem cell therapy. Moreover, they cited first-hand unsatisfactory results reported by their ‘patient-friends’ or circulated in their social media patient groups as evidence that current stem cell therapy was not a viable solution to resolve their problems.

Nevertheless, while these patients resisted the option of using stem cell therapy or partaking in clinical trials until the treatment ‘is ready’, they had already integrated this option into managing problems that were induced by their bodily conditions. As such, I suggest that their ‘anticipatory’ use of stem cell therapy has real-time and real-life effects on these patients, and often on their families too. The ‘anticipatory’ use of stem cell therapy is conditioned by these patients’ lifeworld, wherein type 1 diabetes or spinal cord injury plays a significant role. In the following section, I embed my analysis and reflection of these patients’ anticipatory use of stem cell therapy in their lifeworld.

No need to hide on a ‘lonely island’: Zou and his patient-friends living with type 1 diabetes

I first met Zou in early 2014 in his hometown in northern China. Prior to that face-to-face meeting, we had corresponded through text messages and phone calls for about one and a half months. During that period, together with some colleagues, I was organising a patient forum on stem cell therapy for the Centre for Bionetworking. During preparation for that patient forum, we searched for someone who could speak about patients’ experiences. We found Zou through the internet. Zou had posted a series of essays on an internet forum dedicated to type 1 diabetes patients and patient families. Zou wrote about his medical history and life experiences as a type 1 diabetes patient, gave readers advice and tips on growing up with and bringing up a child with type 1 diabetes, and called for governmental attention on existing barriers for patients to access health care, higher education and employment.

In one of our early phone calls, Zou told me that an investigatory report on their experiences with type 1 diabetes would soon be aired on a national television programme. The episode used as its title a quote from a patient's interview: 'people who live on a lonely, visible island' (H. Wang, 2014). In our first meeting, in tracing his experiences of growing up and living with type 1 diabetes, Zou simultaneously explained to me why this 'island' is both 'invisible' and 'lonely'.

One of the first things Zou told me was that in China, most people do not even know that children can be affected by diabetes. This lack of knowledge, which is acknowledged by doctors (M. Li, 2016), delayed the diagnosis and treatment of many patients he knew. Zou said he was 'lucky' because his grandmother was a doctor who spotted his symptoms and found experts who could diagnose and treat him in mid-1980s. He was grateful for other family members who helped him to develop and stick to a healthy lifestyle and keep a rigid routine to monitor blood glucose level and, accordingly, self-medicate insulin. Almost all patients that I interviewed, who were in their late 20s and older, had experienced this delayed diagnosis. Those in their early 20s or younger and living in cities encountered less of this problem. Zou warned me against being too optimistic about this 'generational' change. 'In rural areas, it remains a serious problem,' Zou stressed. 'There, doctors at the township or even city-level hospitals still know little about type 1 diabetes. Parents [of paediatric patients] there also know little about how to help their kids, once they get the diagnosis. Medication is also a problem. In many places, one can only get animal insulin. Even today!'

But after crossing the first hurdle of diagnosis and treatment, these young, city residents still face essentially the same hurdles as their elderly and rural counterparts: restricted access to higher education, discriminative treatment in the job market, and difficulty in finding boyfriends or girlfriends whose families are willing to accept them as type 1 diabetes patients.[47] Because of these hurdles, Zou and his patient-friends often talked about the necessity to conceal their conditions from those around them. Meanwhile, they acknowledged that in choosing concealment and making oneself 'invisible,' one also loses many opportunities in life and may even confines oneself in one's own 'lonely island'.

[47] See also documented in Jaacks et al. (2015).

Most of the patients and parents of paediatric patients that I spoke to found themselves in this dilemma. As the aforementioned discriminative treatment a type 1 diabetes patient is likely to be experienced from childhood to early 20s in China, many parents of paediatric patients teach their children to conceal. My interlocutors referred to 'luck' for occasions when a person meets a knowledgeable doctor, a compassionate headmaster, a good employee, a supportive lover, or an understanding family who welcomes a 'diabetic' to join their family.

It is these life conditions and challenges that make the internet particularly useful for these patients and patient families, and also made stem cell therapy attractive, especially to the parents of newly diagnosed paediatric patients. The internet helped Zou and other patients to leave the 'lonely island' and find each other on internet forums and on social media. In the cyberspace, patients and parents of paediatric patients discovered their 'biosociality' (Rabinow, 1996): they formed their groups where they called each other 'patient-friend' (*bingyou*, 病友) and considered their group gave them a 'big family'.

Zou, for example, discovered the first Chinese internet forum dedicated to diabetes patients soon after its establishment in early 2000s. Zou immediately joined. Choosing his online username, he thought about his years living with diabetes, and named himself, 'Zou, the big brother'. Since then, Zou became increasingly concerned about the life obstacles induced by type 1 diabetes. He decided to 'do something about it,' so that those growing up now would no longer need to 'live in this lonely, invisible island.' Now, Zou is known among fellow patients for his volunteering work on peer education and support, as well as advocacy work for bettering public policies for type 1 diabetes patients. These patients often refer to him simply as their 'big brother'. A 'big brother' in the Confucian sense: one who looks after the siblings and in return earns their respect.

Although these patients often 'thanked' the internet for helping them to find 'a big family' and for helping them to cope better with life obstacles, their attitudes towards stem cell therapy and other biomedical innovations were ambivalent. Zou told me that

most members in their WeChat groups[48] were no longer avid for 'experimental' stem cell therapy. He recalled that from about 2005 - 2010, when stem cell therapy was widely advertised on the internet, he saw some patient-friends reported their experiences in the internet forums. 'Almost all were disappointed,' Zou said: 'one or two said it worked, but all in all, we [old patients] don't think it is worth the money…and look at what was just exposed on the Consumers' Day by the CCTV![49] No one should be providing stem cell therapy [to patients] now!'

Yet, these unsuccessful cases and the negative news coverage, on the transgressive clinical and business practices related with experimental stem cell therapy, did not dissuade all the forum members from considering using experimental stem cell therapy, 'especially the parents of the newly diagnosed patients'. Zou paused before continuing. 'It may be one of those things you do after receiving the diagnosis. In shock and dismay you look for a *cure*. Then, when they type in "cure for type 1 diabetes" in *Baidu*[50], they will see stem cell [therapy] popping up. But once they come to [ask] us, we will talk them into senses. This is exactly what we [as more experienced patients] are here for - to help them with that learning curve.' While discouraging queries on experimental therapies, such as stem cell therapy, Zou and others would give new members practical tips on managing type 1 diabetes and further changes that patient and patient families need to adjust to, for example, how to use a blood glucose metre or what to eat and how to exercise. Mastering these little things are 'what really matter for us to have an as-*normal*-as-possible life'.

Relying on these little things, Zou recently crossed the threshold of living with type 1 diabetes for thirty years – a span of time seen less frequently among Chinese patients than those living in the United States and Europe (Holmes, 2014). Zou had also managed to bypass some of aforementioned life hurdles[51]. Due to his diabetes, he could not enrol into medical school as he wished, but he learned some medicine as an

[48] WeChat sets limits on the number of members per group. Zou opened and ran dozens of groups to reach patients in different regions in China, and also joined groups run by other people.
[49] See chapter two for details.
[50] See chapter two on *Baidu* and the events around Wei Zexi. I will revisit those events in the next chapter.
[51] One thing we barely talked about is that Zou was not in a relationship and remained single. I read once, in an internal news report on a patient's event, that he had found a girlfriend who assisted him organising that event first as a volunteer. I congratulated him, but he did not show much interest in expanding the topic, and I did not persist. This relationship lasted for about half a year.

apprentice with a diabetes expert who had treated him when he was a child. Later, he joined his father in their small family business and employed two other patients with type 1 diabetes, Zou has taught himself how to manage type 1 diabetes, and built a 'as-normal-as-possible' life under these conditions. Compared with finding a 'cure' such as stem cell therapy, Zou considers it more desirable and urgent to reform public policies and improve societal acceptance of type 1 diabetes patients.

This 'as-normal-as-possible' life that Zou advocates for type 1 diabetes patients is 'too conservative' for some younger patients such as Ms Yu. Born in a cosmopolitan city in the late 1980s, Ms Yu was initially devastated by the disease and once suicidal. But 'due to some luck,' she became a representative of young Chinese patients for an international diabetes patient organisation and regularly attended conferences and events overseas. In our meeting, she sometimes used English terms such as 'human rights' and '(anti)discrimination,' and described to me a recent youth-leader meeting she had just been to in Europe. She spoke about the bicycling tour they did together, and stressed how by attending those meetings for a few years, she learned from her American and European peers, 'There shall be no difference between us and those who don't have diabetes. What others [young people] can do, we can! Full stop.'

Yu thus distinguished her approach from Zou's, which she considered focused too narrowly on managing daily life. Yu stressed to me that for the younger generation, 'To be who I am and live the life I want is the goal. And it is for everybody. [Having] Diabetes or not!' As a representative of Chinese young diabetes patients, Yu considered herself as an 'activist,' and joined researchers in publicising and recruiting patients in a survey project called *Coverage, cost and care of type 1 diabetes in China* (McGuire et al., 2011). As a 'young leader,' Yu also felt a responsibility to set an example for younger patients about how they can pursue their life 'free from diabetes'.

Yu's wish to be entirely 'diabetes free' resonated with other young patients who I interviewed. The three young men were in their early 20s. One was doing his graduate study. One was a high school dropout, due to economic constraints. He first did some labour work in his cousin's village factory but decided to leave his village to look for jobs in neighbouring cities. By the time I met him, he had been relying on odd jobs to linger in cities for two years. The third one was a college graduate. He briefly worked at

an IT company, and was considering starting an e-business related to providing services for patients like him. They all knew Zou personally through patient events that Zou routinely organised. They all met one another at those events, but they did not know each other well. They all heard of Yu, or more precisely, Yu's role in that international patient organisation. The college graduate was close to Yu, and referred her as a role model. Yu also mentioned to me in our separate interview that she considered that young man as a good candidate to be her successor in that organisation, 'After all, you need to have seen the world and have good command of English [to join that international organisation].'

In speaking about their life conditions, these young men mentioned 'luck' on various occasions: meeting supportive teachers who helped the pursuit of education; meeting Zou and other patient-friends from the cities, whose experiences convinced them to come to cities to search for better life opportunities; or meeting a supportive girlfriend and her family. In speaking about these 'luckiness,' they often simultaneously recounted the difficulties involved in the same process.

In passing, one boy joked that he was probably maturer than his 'diabetes free' peers, because life had taught him hard lessons from early on. But even if living with type 1 diabetes makes one 'maturer,' the boy ended his joke with a rhetorical question: 'Who would voluntarily choose to be a diabetic?' Even for Yu, who considered herself no different from 'diabetes free' young people, she preferred living free from the constraints of diabetes. 'It [monitoring and managing blood sugar level five times a day] is such a hassle. As young people, no party, not stay-night, we lose lot of fun!'

Compared to Zou and other 'older' patients, these young people displayed to me a stronger desire to be 'diabetes free'. They had just started their adulthood and now faced new social and family responsibilities that, compared with their 'diabetes free' peers, were more challenging to them because of their diabetes. Zou and other 'older' patients, who had passed this life-stage, had already found their coping mechanisms and often shared with the younger ones their experiences and tips. As Zou said, learning to live with type 1 diabetes is a lifelong course; and as the 'older' patients, they are there ready for helping the younger ones to adjust. In this regard, Yu acknowledged that Zou's work on peer education and support for 'living as normally as possible' is 'fundamental.'

Nevertheless, because current approaches to managing diabetes does not liberate a patient from the condition and the accompanying life challenges, these young people still want to have something that would free them from the disease. Emerging therapies, such as stem cell therapy, offers them such a promise. Because they were young, they also considered 'on-the-horizon' therapies may yet cure their diabetes and change the outlook for their lives.

Nevertheless, like Zou, they were aware of the 'experimental' status of stem cell therapy, and were not interested in 'trying' at this stage. Instead, they planned to wait until 'it's ready'. They were also interested in other technologies that are in development. Moreover, none of these young people, nor their older patient-friends who I also interviewed for this study, was interested in partaking in clinical research. Precisely because they could manage their conditions, they saw little point of trying something that is still in development. The idea of being assigned into the placebo group in a randomised controlled clinical trial further discouraged them.

For instance, Mrs Liu, a patient in her late 30s, was rather shocked at learning about this particular design of clinical trial. She had overcome almost all aforementioned life obstacles with her strong determination and a dose of 'luck'. She had built a life in a big city together with her husband, who she first met in the university thousands of miles away from her hometown. She was employed as a patient alliance worker in an IT company that provides linkages between patients, doctors and other providers of health-related commodities and services. She considered that she managed her condition well with currently available technologies and was not in a hurry to try anything new, only when the treatment 'is proven mature'. The way that the therapy was still 'under development' in clinical trials made participation unappealing for Mrs Liu. Instead, she considered that, '[since] legitimate clinical trials are free of charge, it will attract some patients to be "guinea pigs".' 'Who', she added, 'of course, are also brave and altruistic.' In hearing about the design of randomly assigning enrolled patients into a placebo or a control group, Mrs Liu was first baffled. After giving it some thought, she suggested that, 'Well, in that case, you have to give people [trial subjects] incentives, right? You know, it is kind of unfair.' I asked her why. She said, 'It's unfair because we are all suffering from the same disease, and if the purpose of a clinical trial is to test out [potential] benefits, why can't everyone have the same possibility to benefit?' After I

explained the scientific rationale behind the design of double-blind randomised trials, she leaned back in her chair, thought about it, and resumed, 'I guess it makes sense to have two groups and to compare the results…but maybe it's better to let the patients [trial subjects] choose. Maybe, for those who are willing to pay, let them join the experimental group [*pause*] and the others join the other [placebo] group.'

Most patients I met, like Mrs Liu, hoped clinical trials on new therapies would proceed, but are reluctant to be volunteers for the trials themselves. Instead, they either wanted to wait until a reliable therapy was ready, or, if there was not enough time - like in Shen's case - they would take the risk to give experimental therapy a try. Only two patients I met expressed their willingness to be a 'guinea pig' for clinical trials. One was the high-school dropout that I mentioned earlier. He told me that he didn't think, as Mrs Liu had suggested to me, that being a volunteer was an action of bravery. He wanted to volunteer because it was the right and honourable thing to do. 'Just imagine, we are all free from the control of type 1 diabetes!' he smiled. Describing volunteering for clinical trials as 'honourable' was also mentioned by Cao, a spinal cord injury patient I will introduce in the next section. These two patients had another thing in common: they were the most socially and economically disadvantaged among all patients who I met in this study. In contrast to Mrs Liu's thinking, their aspiration to attend clinical trials was not attributed to economic constraints. Instead, I learned that in anticipating to partake in stem cell clinical trials, they were working on their identities and relations with their peers, family and the society.

Overall, type 1 diabetes patients saw their lives as constrained by their bodily conditions and so looked for medical solutions, including stem cell therapy. Even in its 'anticipatory' form, stem cell therapy had been integrated into these patients' coping strategies, to varying extents. These patients understood some of their life obstacles were conditioned in the wider social-economic-political conditions - the 'Chinese context' - and could be resolved through non-medical means. I will return to this critical point in the discussion section.

Reconstructing life after spinal cord injury: the case of Cao

I first met Cao in a rehabilitation centre in a mid-sized coastline city in April 2014. In the following years, Cao was a key interlocutor and 'little brother' to me. Prior to my discussion with them on stem cell clinical research and regulation, Cao and some other patients in that rehabilitation centre had learned about stem cell therapy from the internet. Indeed, like those type 1 diabetes patients, these patients with spinal cord injury were also aware of the 'experimental' status of stem cell therapy and were not keen in partaking in stem cell clinical trials - except Cao. As I mentioned earlier, Cao was among the least advantaged who I encountered in my study. Although he noted the 'free-of-charge' condition of attending a stem cell clinical trial, Cao's interest in volunteering for a clinical trial was not, as Mrs Liu suggested, a choice by default. Instead, I suggest, Cao used the prospect of attending a stem cell clinical trial as part of his ongoing work on regaining his identity as a capable man and restructuring his family and social relations. To understand Cao's use of stem cell therapy as a "tool" to aid his life-reconstruction project, one needs to understand his lifeworld.

In August 2013, Cao fell from the roof when doing electrical maintenance in a village factory. His employer immediately called co-workers to transport him to the closest township hospital. But this transportation induced a secondary injury that led to Cao's paraplegia. His medical bills were paid by his employer. By the time I met Cao, the employer was becoming reluctant to continue payments for Cao's rehabilitation.

At my home visit to his parent-in-laws (some time after the group discussion), Cao recounted his work accident and his dispute with his employer about compensation. By then, his employer had stopped paying the medical bills and, subsequently, Cao had been discharged from the rehabilitation centre. It took me about three hours and three bus-and-taxi journeys to travel from the city to the village road where Cao's grandmother-in-law was waiting for me. She thanked me for visiting Cao, and thanked me again when walking me back to that road conjunction. Before we were about to say goodbye, she reached to my hands and told me how much pity she felt for her grandson-in-law, and found 'not right' the way Cao's employee, and her son and daughter-in-law treated Cao since his injury.

By then, I had developed a better idea of Cao's 'anger towards the world'. During a previous phone call, Cao told me that he was considering taking self-immolation as a

form of protest, 'Nowadays, the government's fear the most such protest. It will certainly make them notice [about my case]…' That phone call unsettled me and prompted me to visit him again. The first thing I asked Cao at that home visit was to promise me again not to resort to such extreme methods. In the following years, Cao never mentioned extreme action in his continuous 'fight' for gaining compensation for his work accident. Whereas, at the back of my mind, I worried about his unpredictable action that may put him in danger, and found myself often speaking with him about 'positive thinking'.

Cao stayed in a small room at his in-laws that was separated from the main house where the rest of the family lived. His old bedroom was on the second floor where his wife still lived. Where he stayed now used to be a storage room. It was on the ground, and close to the kitchen and the front gate. Cao's wheelchair and other exercise equipment were next to his single bed. The downside of having this relatively easy access to the outdoors was that Cao painfully felt being distanced by the rest of the family, except his grandmother-in-law.

That small room, nevertheless, provided us some privacy to talk about his life before and after the fall. Cao was not local. He migrated to that city from western China in his early 20s. He taught himself electrics and earned a comfortable life as a self-contractor. He fell in love with a local girl and married into her family. Agreeing to marry into one's wife's family also means the man agrees to obey his father-in-law and let their offspring take the wife's family name. In a society that is traditionally patriarchal and remains so today, this marital practice is called '*ruzhui*' (入赘) and is uncommon. Cao emphasised to me that in where he is from – western China – if a man agrees to ruzhui, they would be looked down upon for giving up man's pride. If he did not love his wife so much, and his wife was not the only child of her parents, he would never have imagined that he would have settled down in this way.

'I had a good life then,' Cao smiled, 'I was good at what I was doing, and earned a lot of money. I always bought good clothes and beauty stuff for my wife, and gifts for my in-laws. I had a lot friends who all liked hanging around with me. I was generous and took them out for dinner, karaoke, playing cards etcetera. [*pause*] Then you know, all these are superficial! None of these fair-weather friends stuck with me [after the

accident]. I was such a fool then to consider these *jiurou pengyou*[52] as my friends!' Cao's voice fluctuated with laughter, sneer, frown, sigh, and clenched fists.

He lowered his head and fell into silence. He seemed to be bothered by his blanket that partly fell over the bed. He reached to the loosened part and pulled it back along his upper body and legs. Meanwhile, flies hovered at the other end of the bed. He noted the flies and apologetically looked at me.

> 'Summer is annoying.' I said to him.
> 'Yeah, flies are everywhere' he replied. 'I do my best to keep clean,' he lowered his head again, 'Granny helps me…she is the only one. But she has a lot chores to do, so I need to wait…I cannot lift my body myself…yet…I am exercising, building up my muscles…you know…I am very strong, but still…'
> He fell into silence again, and then resumed,
>
> 'My wife recently got a job in a garment factory. It's hard work. Everyday I see her leaving home in early morning, and exhausted when she comes back in late night. I know she is tired. I feel so bad, [because when I worked] she never needed to work before [my fall]. I can see her through the window, but she hasn't visited me [here] for some days now. I know she is tired from work, but…it's also her parents! You know, you rarely know how people are until things like this happen! My parents-in-law, look like good people, don't they? We had no problem before. I treated them well, helped them to expand this property and decorate the indoors. From time to time, I bought them gifts. Not to mention in festivals. They were nice to me too. But that's all in the past. Don't even think that they are nice in keeping me here. They haven't thrown me away, only because they want my compensation [from the employee]!They've already talked to my boss about compensation. When I heard about it, I warned them and told my boss that nothing counts unless agreed by me! I know they are also talking to my wife about divorcing me…That's why she is distanced now. She loves me, I know. But she also listens to her dad…she is still young, and now I am in this status…'

Cao's voice and tightened fists were trembling heavily and made me worried. I asked him whether he'd like to have some water and take some rest.

'I am OK,' he looked at me and gave me a smile,

> 'I have no one to speak to [about these]. It's good you are here…[*pause*] you know, they [parents-in-law] want to take my son. You met him earlier, right? He is a good boy. They love him very much, and I am grateful that they are looking

[52] A Chinese phrase (酒肉朋友) to describe a type of friendship built upon 'drinking alcohol and eating meat together'.

> after him. I am not an unappreciative person, you know. But they want my wife to divorce me, take my son, and get married again. I guess they had this plan all along. But seeing me making little progress [in recovery], they became less and less patient [with me]. They have become really cold-hearted now. My parents got worried and visited us once. They behaved a little better afterwards. The neighbours have long noted this and started gossip, and their own sister scorns them and sometimes takes me to her home and to look after me there. So my in-laws won't just throw me out, even if they now only see me as a burden [to the family], and forget all the good I have contributed to the family. [*pause*] That won't change, unless I get better.'

After that home visit, Cao started to call me his 'big sister'. At first I felt rather uncomfortable, and kept calling him 'Cao'. I tried various ways to remind Cao of my role as a 'researcher' coming to learn about his experiences and viewpoints on stem cell therapy, clinical research and regulation. But, in my mind, I had an additional reason for my reservation because Cao calling me his sister was a dramatic change from his vigilant, or even cold, attitude towards me at our first meeting in the rehabilitation centre. During that focus group discussion, Cao did not participate much, but warily observed, and occasionally made blunt remarks on other patients' hope for stem cell therapy coming into fruition and better public policies. Other patients seemed unbothered by Cao's sour remarks, and often carried on their discussions without pause or responding to Cao. As the facilitator of that discussion, I noted these dynamics between Cao and the other patients, yet, at that time, I was relieved rather than concerned when his remarks did not interrupt the flow of group discussion.

Cao's coldness was brought up by his doctor, Dr Peng, in a subsequent interview I carried out. As a local host, Dr Peng also attended that focus group. In his early forties, Dr Peng was the chief doctor looking after over twenty in-patients with spinal cord injury in the rehabilitation centre. He was a warm person, and liked by the patients there, as shown in that focus group discussion and in my later interviews with Cao and a few other patients. Dr Peng mentioned Cao and his behaviours at that focus group discussion because he didn't want me to 'take Cao's remarks personally'. 'Cao is like that…a little cynical, short-tempered, and sometimes [*pause*] can be a little extreme,' he said, and then immediately added, 'but it's common among young male patients'.

Dr Peng told me that in clinical practice, they often observed similar emotional responses - anger, resentment, and depression - from this group of patients.[53] He suspected that spinal cord injury not only changed these young men's prospects for physical activities and work, but further threatened their likelihood of finding a partner (if they were single), or of maintaining their sense of 'being a man' in front of their partners. Dr Peng gave me an example,

> 'We don't know how to talk about, for instance, [*pause*] their sex life [with those young male patients], unless they bring this up to us. But this is an essential part [of their life] and usually causes tension between young couples. For the older patients, this problem is less important…they [the couples] may have been married for a long time and have had survived other bad luck in life. We see older patients adjust more smoothly in general, [but] need to stay vigilant about the young ones.'

Dr Peng's observation was confirmed by his colleagues - two other doctors and a physiotherapist - who I also interviewed. Their clinical observation helped me to better understand what Cao later revealed to me his life before and after the fall. It shed further light on why Cao wanted to call me his 'big sister'. No doubt, sensing my reluctance to accept the title of 'big sister,' Cao told me in one of our phone calls,

> 'I have always wished to have one [a big sister]. Someone who can look after and care for me…I am the elder one in my family and had to start to work to keep my [younger] brother at school. He is doing well now, studying psychology in a good university. I am very proud of him. But things have changed for me now, yet no one [from my family] is here for me….and I can't speak those things to others here either. I cannot bear being seen as weak and needy, and I know you don't [see me that way]…'

In that phone conversation, he also explained why he behaved the way he did at our first meeting,

> 'I learned my hard lesson from witnessing how my parents-in-law and friends changed their attitudes [towards me] after my accident. My boss constantly changes his mind about compensating me, and no one here helps me. In that [rehabilitation] centre, you saw we [the patients] got along well. But in reality, no one really wants you to recover better than oneself. So much so is just superficial, you know? So when you came with your research, of course I was interested, otherwise I wouldn't attend [the focus group]. But I just wanted to first see what you were *actually* up to.'

[53] Also see Hampton (2001) and Jiao et al. (2012)

In contrasting his life before and after his fall, and in comparing his family situation with other patients, Cao expressed most clearly his sadness, bitterness, and even suspicion and resentfulness towards the lifeworld he found himself in. Part of his lifeworld, as Cao clearly understood, was conditioned by the wider social-economic and political context, against which Cao had arduously fought to get his compensation, and to re-establish his manhood.

In summer 2016, I sat down again with Cao. After we talked about his family life and e-business, Cao took a pause, pulled out his phone from his pocket, opened something, and handed me his phone. On the screen, it was a photo of an intergluteal cleft injury - a small but deep cut in the buttock line. I was immediately startled, 'Goodness, is that you? What happened?' Cao calmly told me the following,

> 'Big sister, I couldn't send you the photo [via WeChat] which would scare you…I am so sick of my [former] boss and the local governments passing the buck! OK, if you didn't listen [to my demand], I must make louder noise! [so] Earlier this year I had a sit-in protest in front of the provincial government office building [to claim my compensation]. I no longer care about humiliation: first [I sat] in the square and then the guards dragged into their office [and left the injury visible on the photo]. They [the guards] could do nothing to me, but neither they care [about me]. In two days, many people just walked past me and ignored my existence.'

After a long pause, he continued: 'you always asked me to think about the positives: my [medical] conditions are not as bad as many [other patients], and I have a son who motivates me to work hard on this e-business. But you don't know this cruel world, sister, you have no idea…'

I was still trying to recover from my shock of seeing that photo, and for a moment or so I utterly did not know how to respond. Then, I remembered that I had planned to update him on recent news on stem cell clinical research. So I told him that the regulatory agencies just granted 30 hospitals permission to organise stem cell clinical research (NHFPC and CFDA, 2016). I paused and asked him, 'Do you still want to take part in stem cell clinical research as a research subject?' He sounded less eager than two years ago, but still determined,

> 'Yes, of course. It's a different matter altogether, if I am not like this [*pointing at his legs in the wheelchair*]. Even if [it is] a trial and the result is unknown, I

> can show my family that there is hope for me to walk again, even for one day…[*short pause*] Now I don't dare meet a business partner in person. All conversations are done on WeChat…I even thought about asking you to be the face of my business.…OK, OK, I know you don't want that. But think about it for me, OK? I wouldn't ask you, if people don't treat me like a loser. For sure if my e-business partners see me in this wheelchair, they will not be interested in signing me any deal…It's nice of you to think that my experiences can inspire other patients. But I don't want that either. I don't need that kind of attention. "Loser" or "pity," either way, that's how most people think when they eye on me. It is just how it is.'

He grinned, groaned, sighed and wet his eyes. I could do nothing but squeezed his hand, repeating, 'I am sorry.'

When we were saying goodbyes, I reminded him that I might write about his stories. 'Go ahead, big sister, I want everyone to know!' I saw him lifting up his body in the passenger seat, adjusting his position, smiling at me and being driven away. I looked at the package of wild *Goji* fruits which he left me to sample, and thought about his newest business plan of selling these wild *Goji*, which grow in the hills close to his parents, to health-conscious customers. I thought about his earlier comment that I 'did not know this cruel world,' and about Zou who also liked to tell me how little I knew about my own country.

I know neither Cao or Zou meant to embarrass me. They simply noted that my biography had little overlap with theirs, and what I had (thought that I) known about China alongside that trajectory was not the China they learned from their lives. But whenever I was reminded of not knowing China, I took a note to reflect on what I was taught about China on those occasions. This time, I jotted the following,

> "Cao's encounter with this 'cruel world' was closely linked with the inconvenience or even humiliation he has experienced since that fall from the roof. And as it seems to him, the most effective way to redeem what he had lost, in his now disabled body, was to 'get rich'. Stem cell therapy to him seems has a similar function.
>
> I have no doubt that one day Cao will make his dream of getting rich come true, without me being the face of his business nor with the help from stem cell therapy. But, how long he would still need that slice of hope presented by stem cell therapy to help him? To help him not necessary to stand up, but to reclaim

> his sense of worthiness and respect from his in-laws, his community, and, more crucially, from our society?"

I still wonder till this day.

Discussion: Tooling stem cell therapy

So far, I have introduced some of the patients and patient families who I met in this study. Among them, only two families had used 'experimental' stem cell therapy. The rest were more inclined to use stem cell therapy, or partake in 'legitimate' stem cell clinical trial, when 'it is ready'. Yet, they integrated this prospect of using stem cell therapy into their coping strategies, for problems not directly in the medical domain. In other words, they used stem cell therapy as a "tool" to address problems that were induced by their diseases or disabilities. In line with my conceptualisation of "toolised medicine," I propose using the concept of "tooling work" to depict these patients or patient families' mindful use of stem cell therapy, either in its 'experimental' or 'anticipatory' form.

The link between "toolised medicine" and "tooling work" resides in the concept of 'potentiality' that I introduced in the previous chapter. I first noted this difference between stem cell's biological capability and its medicinal potentiality in the clinician-researchers' defence of the existing regulations in China that categorised stem cell therapy as a 'medical technology'. Those clinician-researchers underscored that stem cell's biological materiality could not be straightforwardly 'translated' into medicinal potentiality by scientific knowledge gained in the laboratory. Instead, it needed to be worked out in, and through, clinical research and practice. Viewing stem cell therapy as a 'medical technology' that invites the exercise of clinical expertise in a concrete clinical situation of treating individual patients also permitted those clinician-researchers to acknowledge that the success of fulfilling stem cell's medicinal potentiality is relative and (potentially) can always be improved.

I suggest that these patients and patient families who I introduced in this chapter were also aware that stem cell therapy in its 'experimental' status did not hold certainty but, instead, provided potentiality to help them with their particular problems. Nevertheless,

they did not shy away from the 'experimental' status of stem cell therapy, rather, they carefully studied it and, in evolving situations, adjusted their decisions about using or not using 'experimental' stem cell therapy. In this way, they had already been using stem cell therapy as a "tool" to work on particular questions arising from their diseases or disabilities. In this discussion section, I will engage with literature that speaks to the experiences of my patient, and patient family, research participants. Of particular relevance[54] are Miyazaki's work on 'hope as a method' (2006), Mol and colleagues' work on 'care practice' (Mol et al., 2010), and social science studies on 'medicalisation'.

'Hope' is an important theme that arose many times in my conversations with patients and patient families. The practices around experimental stem cell therapy is commonly analysed as the exploitation of patients' (false) hope and criticised through the lens of political economy (Caplan and Levine, 2010; Petersen and Seear, 2011; Petersen et al., 2014). By contrast, I suggest how patients and patient families use hope in the context of experimental stem cell therapy deserves more scholarly attention. My observations suggest that the patients and patient families who I met did not invest their hope solely in stem cell therapy. Nor did they chase after hope as soon as they saw it in stem cell therapy. Rather, these patients and families carefully pondered over the use of 'experimental' stem cell therapy. In most cases, they integrated future use of 'ready' stem cell therapy into their daily management of diseases, disabilities, and their identities, family and social relations that were affected by these diseases or disabilities.

I thus consider these patients and patient families' current use of stem cell therapy - in either 'experimental' or 'anticipatory' form - resembles what Miyazaki (2006) saw in Suvavou people's use of petition writing, religious and gift-giving rituals, and business activities to keep alive their claim on the government for compensating them for the loss of their ancestral land. In inquiring how Suvavou people have used a variety of ways to replicate this hope that in turn sustains their self-knowledge (ibid.: 26),

[54] Medical anthropology, sociology and pharmaceutical studies in general (such as Whyte et al., 2002; Hardon and Sanabria, 2017; Lock et al., 2000; Burri and Dumit, 2007), and those viewing patients as users and experimenters and inquring subjectivity (Moreira, 2012; Hardon and Moyer, 2014; Cooper, 2012; Biehl et al., 2007) have all informed my thinking and analytical work. Here I focus on the most relevant ones.

Miyazaki suggested studying hope as ‘a methodological problem,’ and ‘reconsider[ing] hope as a common operative in all knowledge formation’ (ibid.: 9).

What is particularly useful in Miyazaki’s conceptualisation of ‘hope as a method’ is that what hope generates is knowledge that is reoriented towards the future. The patients and patient families I met in this study used hope in essentially the same manner. That is, they used hope to generate future-oriented knowledge about themselves, their family and social relations, and used the knowledge to help them construct their lives towards a ‘better’ future, which they saw as currently being constrained by their disease or disability. Yet, because this ‘better’ future is not solely defined in medical terms, this construction of a better future is a trial in itself, and the success of one’s working towards a ‘better’ future is relative and contextual.

This relative and contextual nature of an exercise of hope was clearly understood by those I met during the fieldwork. For instance, in making their final decision of using experimental cell therapy, Shen’s family took into consideration what they had learned from their ‘educational tour’ and communication with Dr Lang, that is, ‘It [cell therapy] doesn’t work for everyone, and everyone responds differently’. Possible failure in undertaking this medical journey did not prevent them from trying. Their acceptance of this particular aspect of ‘experimental' cell therapy was not, as critics of ‘stem cell tourism’ often suggest, an act of ‘desperation’. Instead, Shen’s family understood what Mol and colleagues suggested about the mixture of care and technology,

> ‘[Technologies] tend to have a variety of effects … [and] do not work or fail in and of themselves. Rather, they depend on care work. On people willing to adapt their tools to a specific situation while adapting the situation to the tools, on and on, endlessly tinkering.’ (Mol et al., 2010: 14-15)

Shen’s family appeared to have failed in their use of experimental cell therapy in treating Mr Shen’s ALS. Yet, as Mol and colleagues reminded us, failure in such experimentation should not be bracketed in our scholarly analysis, rather, ‘what follows from a failure’ deserves more scholarly attention. Mol and colleagues suggested what follows is ‘an ethics…an ethos of care: try again, try something a bit different, be attentive’ (Mol et al., 2010: 12-13).

The patients and patient families I met had cared for themselves or their family member along similar lines, that is, they kept looking for and trying out possible solutions to ease their pain and suffering that was induced by disease or disability. These patients and patient families' varied attempts in easing their pain and suffering are thus best understood as 'care practice' that should not, and need not, be explained by scholarly 'rationalist versions of the world' (Mol et al., 2010: 13).

Nevertheless, Mol and colleagues note the 'complexities and ambivalence' involved in care practices, and suggested that '"good enough" care may be a wiser goal than care that is "ever better"' (p13). In my fieldwork, I witnessed and was sometimes struck by how this ethos of 'keeping trying' in care practices might have ceased to do good and induced a burden or even suffering. This demanding feature of care is captured in a phrase that is often used by the patients and patient families I met: '*Jin renshi, ting tianming*' (尽人事, 听天命). Sociologist C. K. Yang introduced this Chinese idiom when explaining the Confucian concept of 'establishing fate' (Yang 1961: 272-274). Yang translated the idiom into English as '[to] exert the utmost of human abilities, and then resign the rest to the decree of Heaven,' and explained that 'in other words, man must plan and do his utmost, but must accept success or failure as the decree of fate' (ibid.: 273).

This dialectical interplay between exerting oneself and resigning to fate, I suggest, provides a way to comprehend patients and their families' persistent pursuit of medical treatments, including experimental therapy such stem cell, even if they are aware of these treatments' limits and risks. Recall when Mrs Xie stated that, 'Without hope, we are left with nothing,' she was explaining to me why, despite having doubts about the effect of experimental stem cell therapy, she continued her efforts in getting the therapy for her husband. To some extent, she was also rationalising this particular act to herself. Indeed, they practised hope and care, *as if* they were convinced that one must try everything that one knows of, and has access to, in order to improve their current situation; otherwise, it would get worse, and it would be their fault to let things get worse. Yet, the attribution of their life obstacles *as if* originating primarily from their medical conditions inclined them to look towards medicine for solutions. I use "as if" here, because in describing their experiences with diseases and disabilities, these patients and families often bracketed their experiences in the 'Chinese context,' and in

so doing, they demonstrated to me that they knew that those non-medical problems would not necessarily be a problem if they were in a different 'context'.

'Medicalisation' is a concept that helps social science researchers analyse 'a process by which non-medical problems become defined and treated as medical problems, usually in terms of illness and disorders' (Conrad, 2007: 4). I suggest what I observed in the fieldwork is like a reversed process of 'medicalisation'. That is, these patients attributed certain life obstacles that they encountered to their medical conditions and believed that alleviating these medical conditions would 'free' them from these constrained situations. This rationale is most evident when those living with type 1 diabetes and spinal cord injury used stem cell therapy in its anticipatory form as an aid in constructing their (future) bodies, family and social relations.

Critically, like the process of 'medicalisation,' this reversed medicalisation, as revealed in these patients' and patient families' use of stem cell therapy, informs about the "tool-like" feature of stem cell therapy and also the wider social-economic and political context. As my patients and patient families often pointed out, better policies and wider societal acceptance and support would help them to improve their current situations. For instance, for those living with type 1 diabetes, these social and political responses would be more direct and effective in helping them to live a 'normal' life, rather than new medicines. And they have been trying to do so.[55] Nevertheless, my research participants saw the 'Chinese context' that conditioned their individual, family and collective experiences as patients and patient families as unlikely to change in the foreseeable future. They, in turn, sought more actively 'promising' medicines such as stem cell therapy that they now could use, even if in an anticipatory mode, to overcome obstacles in life that they associated with their medical conditions. In other words, they bracketed the 'Chinese context' as if it is part of 'the decree of fate' that they could do little about; what they could do is to do everything else before 'standing ready to receive the ordination of fate' (Yang, 1961: 273). It is in this sense, I underscore that patients' "tooling work" is an act of agency and an illustration of vulnerability.

[55] For instance, type 1 diabetes patients and patient families have tried in consecutive years to submit their petition to the NPC through a few sympathetic NPC members, so far they have not received a positive response (M. Li, 2016).

The exercise of agency and vulnerability through one's "tooling work" was more intricately revealed to me during my participant observation in a biotherapy unit in a cancer hospital in southern China in early 2015. The next chapter details the experiences with experimental immunotherapy of those patients and healthcare professionals who I met in that spring.

CHAPTER FIVE. Immunotherapy: ordinary experimentation in an ambiguous situation

This chapter examines how hospitals once provided experimental immunotherapy to cancer patients in China in 2014 and 2015. Although an experimental therapy, those working and living with the experimental therapy in the ambiguous situation did so in a nearly ordinary manner. This peculiar situation was partly created by the Chinese health authorities' unequal treatment of the two experimental cell-based therapies. As mentioned earlier in the thesis, in 2009, following the regulation on medical technologies, the health authorities designated stem cell therapy and immunotherapy with the same status of 'category three medical technology'. In late 2011, Chinese health authorities intervened in the clinical practice of experimental stem cell therapy, but left alone clinical usage of immunotherapy until May 2016.

My participant observation in a biotherapy unit in a cancer hospital in south China, in early 2015, allowed me to study the impact of ambiguous regulation. I observed the participation of clinician-researchers, health care professionals, patients and their families in making and sustaining this ambiguous situation. I saw how their perception on the usage and value of keeping open the operational space, which enabled the practice and use of immunotherapy, was weighed against the conditional acceptance of inherent risk and uncertainty by individuals and institutions. Meanwhile, like those patients and families that I introduced in chapter four, attempts to achieve the potential medicinal, and associated, values of immunotherapy, involved individuals and institutions engaging in "tooling work". Through their joint "tooling work" they made experimental therapy ordinary and the ambiguous situation temporarily sustainable. I suggest that the collective experiences of my research participants largely corresponded to their changing political and social situation in China.

The organisation and daily practice of immunotherapy

This section introduces the institutional setting, the clinical setting and the clinical practice of immunotherapy that I observed in a public cancer hospital in southern China in early 2015. I elaborate, in particular, on the coordination between the laboratory, the

consultancy room, the treatment room and the inpatient ward. In these locations, doctors worked with cancer patients, and it was here that patients shared with me their experiences and evaluations of their treatment.

The institutional setting

The department where I conducted participant observation specialised in melanoma. Staff and patients also called the department the 'biotherapy unit'. Embedded in a cancer hospital, the department has its own in-patient ward and a team of specialists medics who take care of inpatients and outpatients. The hospital is affiliated with a local university that ranks among the top 20 in China, and is among the best cancer hospitals in China to treat patients with hard-to-diagnose and hard-to-treat conditions. In addition to treating patients, senior doctors there also hold teaching and research positions in that university.

In the department, daily work starts around 7.30am, with a handover briefing from night-shift staff, the head doctor's brief summary and comments. From 8am, a group of 10-12 doctors split into two teams led by the head doctor and the deputy head doctor respectively. The doctors review and devise future treatment plans for each inpatient. Each patient has one main doctor, and a doctor would look after about five inpatients at the same time.

Although the prevalence of melanoma is relatively low in China (Chen et al., 2016), a long list of patients wait for inpatient admission. The turn-over of the hospital beds is thus managed to keep inpatient stays to under two weeks. In addition to inpatients, the department has a flock of patients who suffer from cancers other than melanoma. These patients came to see Dr Jiang for immunotherapy, and had little contact with the other doctors.

For an experienced patient, their periodic visits runs in cycles. On their first visit a nurse took 50 ml blood. The blood sample was transported to the unit's laboratory which extracted a patient's blood immune cells and, over two weeks, transformed them into a patient's own specific immunotherapy. The patients could then return for second, third and fourth visits to receive immunotherapy administered through intravenous therapy.

Between these treatments, the patients took standard blood tests to let the doctors review the efficacy of the treatment on individual patient. Meanwhile, the patients were recommended to take a one-week rest after the first and the second treatments, and then a one-month rest between the third and the fourth treatments.

A cancer researcher (at the university affiliated to the hospital), who I knew from my previous work as a genetic researcher in a cancer genome project, introduced me to Dr Bao, the chief of the biotherapy programme. The cancer researcher mentioned that initially, he was put in charge to jointly oversee the biotherapy unit. Because he has dual-doctorates in cell biology and medicine and is also a licensed doctor, he could review patients' cases and see patients there. Nevertheless, after one year in post, he decided to resign his management position,

> 'It became a little too busy there [at the biotherapy unit], and in my view, things moved a little hastily. [*short pause*] I was asked to spend at least one day per week at the hospital. But I guess…hmm…I am more a science guy after all, and more into my cancer cell [research] [*laughter*] than developing treatment. So I resigned.'

Prior to meeting Dr Bao, I had seen him speak at several conferences where he said that the unit's work on breast cancer had produced promising results and been published in renowned science journals. Yet, since most cell-related conferences included topics related with stem cells, in 2014, the unit's achievement and continuous operation of immunotherapy also evoked interests from conference attendants for another reason - the different regulatory treatments of stem cell therapy and immunotherapy. Audiences often asked Dr Bao about his view on the ambiguous regulatory situation.

In his answer, Dr Bao stressed both his awareness of the problem and the institutional effort they had made in the hospital. That is, they strictly followed the guidance of the *List of Category Three Medical Technologies for Clinical Applications* (MOH, 2009b), so conducted research on novel therapies under the approval and guidance from the university's and the hospital's research and ethics committees and then only provided patients with these officially recognised types of immunotherapy.

The institutional support and safeguards Dr Bao listed were only available in top tiered hospitals in China and were established in response to the demand of multinational

pharmaceuticals that started to conduct clinical trials in China in the 1990s (Humphries et al., 2006), rather than for the biotherapy unit. When Dr Bao and his colleagues designed and opened the biotherapy unit around 2005, these pre-existing institutional policies and working committees came in handy.

Dr Bao's answer reminded me of a similar comment made by Dr Tang, a stem cell clinician-researcher and leader of a national stem cell society, at the society's annual conference,

> 'We are not doing anything wrong here [with our research], and we should be proud of what we have done for the patients! So please *go*, *go* to see the head of your departments and hospitals with the guideline from the SFDA and get your institutional approval! That is all we need!'

Before he gave this short speech during Q&A, Dr Tang had just ended his presentation with appreciative feedback from his patients who he treated with stem cell therapies. The photos of him with his smiling patients were projected on the big screen behind him during this speech. The regulation Dr Tang referred to was the *Guidance for Human Somatic Cell Therapy Research and Quality Control of the Products* that was issued by SFDA in 2003. It is one of the first guidance documents published by the authorities overseeing cell related research and product development, and still remains in force.

During this regulatory turbulence, those co-existing, and sometimes conflicting, regulations thus constituted varied ambiguous regulatory situations wherein particular research and clinical practices were proceeded without either regulatory approval or denial. Or, as Sleeboom-Faulkner (2016) suggests, they were practised in a large 'grey area'.

When Dr Bao and Dr Tang urged their audiences to win institutional approval from their superiors, their audiences did not respond in similar enthusiasm. In the middle of a regulatory impasse, granting clinician-researchers any kind of institutional support involved considerable managerial and executive risks. In reality, almost all hospitals that once provided stem cell therapies had closed down those programmes, and withdrew support for clinician-researchers to research on stem cells. A similar withdrawal of institutional support took place in 2016 when, amid the unfolding events

around Wei Zexi's death, the health authorities intervened in immunotherapy clinical practices.

The clinical setting and Dr Jiang

I met Dr Bao in the unit's laboratory that had recently relocated from the hospital in a two-storey office block in a residential community centre.

The relocation of the laboratory was part of the expansion of the immunotherapy programme. While the new laboratory, and researchers' and technicians' offices occupy the first floor, a large portion of the ground floor is converted into a treatment room that provides an option for patients to have their immunotherapy treatment in the community health centre. Considering that research and collaborative work around immunotherapy was organised and run independently from the clinical work, like Dr Bao himself, this outer location reflects well the adjunct relation between the immunotherapy programme and the melanoma department. This adjunctive positioning and function of immunotherapy was also manifested in Dr Jiang's coordination work and clinical practice around immunotherapy.

At my meeting with Dr Bao, I asked him for an opportunity to deepen my understanding of actual clinical practice through participant observation. After discussing what participant observation is and what I planned to do there, Dr Bao agreed to give my proposal some thought. Towards the end of a short tour around the laboratory, he gave me a telephone number and another note addressed to Dr Jiang, 'Here you go, text this number and arrange a visit with Dr Jiang. I will also tell him [about your research plan]. Once you are there, follow his arrangement.' I thanked Dr Bao, and contacted and met Dr Jiang soon after. Over the next six weeks, I shadowed Dr Jiang on the in-patient ward where he worked and saw immunotherapy patients.

Dr Jiang is in his late thirties, has a seven-year old son, and his wife also works in the hospital, in the department of breast and ovarian cancer. He is about six feet tall, has a flat-top hairstyle, and speaks softly. According to the hospital's website, Dr Jiang received postdoctoral training in the United States before returning to this hospital where he studied oncology with Dr Bao. As a promising junior oncologist, Dr Jiang was

assigned a special task to coordinate between the melanoma department and its cell laboratory in administering immunotherapy to the cancer patients. This task was in addition to his routine clinic work, and constituted mostly seeing and communicating with the patients: from the initial consultation and treatment to follow-up, evaluation and treatment.

The initial consultation constituted three parts: a basic introduction, practicalities and payment arrangements. First, Dr Jiang would ask about the new patient's cancer, treatment history and experiences, before introducing immunotherapy and the unit's experience with administering this novel therapy, which included talking about possible side effects such as temporary fever and the variable therapeutic effects on different patients. The second part covered a range of practical matters, including future visits for initial blood test, taking blood samples, and subsequent treatment. Eight intravenous injections over the course of three months was recommended as a complete initial treatment cycle: the first four treatments would be administered in constitutive weeks over a month, while the latter four would be given once a fortnight. In practice, most new patients I met there opted for 'trying out' the first four treatments, and using that month to assess the therapeutic effect and decide whether or not to continue. Follow-up treatments were also recommended in passing, but not elaborated on during this initial consultation.[56] The third part covered the patient's health insurance and payment methods. The price set for one treatment was about 10,000 yuan (about 1,000 pounds), thus a complete initial treatment cycle cost close to 100,000 yuan. Payment was always made prior to treatment and patients were advised to pay for at least two treatments at their first payment. Depending on their health insurance policy, a portion of the patient's treatment could be redeemed from their health insurers. Yet, being insured also complicated matters. For instance, the policies of local public health care insurers, dictated that eligibility to make a claim on reimbursement required that patients must be first admitted as inpatients, despite no medical reason for their admission. As local public health care insurers also set limits of maximum charges per admission, a maximum of four treatments were charged at once. Yet, this generic description about reimbursement only applied to those insured as citizen-employee. For patients insured

[56] Follow-up treatments were taken by experienced patients even more flexibly, as there was no strict doctor's order on when and how many treatments a patient needed after completing their initial treatment cycle.

as rural residents or as employees working for public institutions, the percentages of their reimbursements were different. Lastly, for patients without local public health insurance - those either from other cities in the same province, from other provinces or working as self-employed - the methods of payment and receiving reimbursement from their insurers was even more complicated. These varied health care insurance practices are well documented in the literature (Duckett, 2011; Meessen and Bloom, 2007; Lam and Johnston, 2012). China's health care reform starts to tackle the question of unequal access to public health care insurance with a focus on providing universal basic health care (Zhang et al., 2015; Yu, 2015). As a novel therapy, immunotherapy is not an essential drug and not listed in Central Government's insurable list, but is accepted by certain local governments (Bioogo, 2015).

In these complex cases, Dr Jiang would recommend that patients first check with their specific insurers before devising a payment plan with the unit. The detailed institutional rules created considerable work and paperwork for both the patients and Dr Jiang to complete before starting the treatment. As such, whereas the first and second parts of the initial consultation had rather standard content, the third part varied significantly from patient to patient and so was often a more detailed discussion.

Occasionally patients were silent or hesitant, most often during discussions about therapeutic effect, payment, or reimbursement. Yet, as I learned over time, those showing hesitation were patients who came to Dr Jiang either on the recommendation of other doctors from this, or other, hospitals, or were patients who had just heard of immunotherapy as a treatment option for their specific condition. Yet, the majority of new patients meeting Dr Jiang had made substantial efforts to study the status of immunotherapy in general and the particular treatment and expertise offered by this unit (often in comparison with treatment options provided elsewhere). They had also prepared their payments and worked out how to get reimbursements from their health insurers. Thus, the initial consultation could be as short as 15 minutes or even less - for example, when a patient came directly from a prior visit to the unit's chief and asked Dr Jiang one thing 'How can I pay and start [the treatment process]?' By contrast, the consultation could also be as long as half an hour. If more time was required for an initial consultation, Dr Jiang would advise the patient to 'Take the information home and give it a thought' because '[there is] no hurry for you to decide now.'

If, by the end of the consultation, a patient decided to take the treatment, Dr Jiang would give them a document titled '*Informed Consent on Immunotherapy'* which covered the first two parts of the consultation, that is, the status of the novel therapy, its known and remaining-to-be-seen effects and risks, and the arrangements for future treatment. Once a patient signed the informed consent form, Dr Jiang would start a pile of paperwork to prescribe the treatment, give his doctor's notes to the patients' employers and health care insurers, and so forth. In contrast to the overall worsened doctor-patient relation in China (Nie et al., 2017), the attentive way Dr Jiang worked with patients was frequently praised by those I came to know at the unit.

Despite his polite manners, Dr Jiang, nonetheless, was never forthcoming about his own views on the status or future of immunotherapy, neither to his patients nor to me. He would readily answer questions, but kept his answers as nondirective and neutral as possible. It appeared to me that Dr Jiang's gentleness, politeness and discretion, together with his interpersonal and organisational skills, were valued attributes in his job coordinating the work between the laboratory, the consultancy room, the treatment room and the inpatient ward. His careful work, I suggest, was critical for the maintenance of the unit's operation in an ambiguous situation.

The treatment and the patients

In late 2014, the media started to question the provision of experimental immunotherapy by hospitals directly to patients; these news stories spread through the social media. When I conducted my research in the cancer hospital in early 2015, I was curious to know how patients' views on immunotherapy, and their subsequent decision about treatment, were affected by these news stories. I asked this question in the first focus group discussion[57] that I had with the patients there. Overall, those patients seemed unconcerned by the news. As a breast cancer patient Mrs Qi elaborated,

[57] After consulting Dr Jiang, instead of organising focus group specifically for my study, I devised a contextualised procedure for group discussions. To best coordinate with patients' own schedules and having familiarised myself with patients, while patients received intravenous mediated immunotherapy in the treatment room, Dr Jiang would introduce me to the patients, and I would explain my research. Depending on the patients' willingness to participate in my research - I joined them in the treatment room and discussed their experiences with cancer and immunotherapy. Since intravenous therapy often lasted an hour, but varied among patients, the group discussions often lasted about forty minutes. Since I would stay till the last patient finished his or her treatment, those last patients in turn often shared their views

> 'Yes, I read *Nanfang Zhoumo*'s news report [on immunotherapy (Yuan and Li, 2014)]. *In fact* before I started [my treatment] here, I had heard that this therapy was still in an *experimental* stage. I did my thorough research [on immunotherapy] online, [and] talked with my knowledgeable friends, sought second opinions from some cancer experts, and visited the professors here, before I made up my mind. This is the best cancer hospital in the region, and most of the feedback I had received [during the research], especially from patients who had been treated here, was positive. So I decided to give it a go.
>
> It's almost two years now [since I started]. I know the therapeutic effect is hard to measure, but at least *I feel* it helps to improve my immune system. I catch less colds now and generally I feel better. It is even covered by the health care insurance and I only need to pay less than 1,000 yuan [around £100] per treatment. What more do you expect?'

As Mrs Qi stressed, she had done much homework prior to making her decision on 'giving [immunotherapy] a go' - a decision linked to her personal circumstances. Although *Nanfang Zhoumo* - one of the most reputable investigatory media in China - had questioned the legitimacy of experimental immunotherapy and its clinical operation, reports failed to persuade patients like Mrs Qi to reconsider their decision to use immunotherapy. After Mrs Qi gave her assessment, a few short follow-up comments from other patients indicated that it was the first time they had heard such a detailed description about the experimental status of the immunotherapy offered by the very unit that was treating them as they spoke. Nevertheless, Mrs Qi's recollection of her research did not stir much further interest, and her evaluation of the immunotherapy - 'I feel it helps [me]' - was quickly backed-up by nodding and additional examples given by some other patients there.

Mrs Qi's evaluation of immunotherapy included price and health insurance arrangements. Methods of payment and possible reimbursement from public health care insurers constituted a significant part of the initial consultation. I wondered how patients viewed the 'commercial' aspect of the operation of immunotherapy in (public) hospitals, that, in the case of experimental stem cell therapy was severely criticised by scientists and bioethicists, and investigative journalism. Indeed, despite the apparently prohibitive price for immunotherapy, cost itself seemed less important to those receiving the treatment at the unit. Instead, the patients often commented that the out-of-pocket payment of, on average, 1,000 yuan per treatment was acceptable, considering

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and experiences more in detail with me. In this manner, during my around three months there, I conducted two group discussions.

that they need to spend around 3,000 yuan (about £300) per month for routine cancer treatment, nutritional supplements, exercises and so forth. Even for patients, like Mr Chang, who came from other provinces and had to pay the full amount of treatment themselves, the price could seem 'reasonable'. As Mr Chang calculated,

> 'We only need a maximum of three or four treatment-cycles per year, and if you [the condition of one's cancer] are stable, you may well need only one or two [per year treatment-cycle]. [So] if you stretch the number [of the price] throughout the year, it is not much anyway.'

The majority of the cancer patients seeking immunotherapy, who I saw there, looked rather "normal" to me, if I had met them in different circumstances I would not have guessed that they had cancer. Mr Chang looked fit and sporty, dressed smart casual in a Nike cap. After the nurse gave the last patient intravenous therapy and left, Mr Chang speeded up his drips and completed the treatment in just under half an hour. He was not in a hurry, but he did so claiming 'My body is good enough [to take the drips faster]'.[58] While Mr Chang did exceptionally well in 'continuing living my life as before [cancer]' and accredited immunotherapy with keeping his spirit up and body well,

> 'A good attitude is key. No matter what happened - cancer, business failure or other sorts of accidents - one just needs to face it and beat it, isn't it? Like I am a long-time fan of mountain climbing, should I just give it up when I got cancer? Yes, it came cross my mind, but a second thought: no, I shouldn't let cancer determine who I am and what I can do. So once I got better, I resumed my training, and a couple of days ago, a couple mountain-buddies and I just climbed another one…Now we have this [immunotherapy] as an extra aid [in managing cancer]. I cannot speak for others, but I did find it helpful and [that is] why I keep coming [for the treatment]. So just make the best use of it, and well, I guess, life in general.'

Although Mr Chang lifted the spirit in the room, his circumstances niggled other patients in the room too. Almost immediately after Mr Chang completed his treatment and left, some patients informed me that Mr Chang was a businessman from the North, 'flies here for the treatment' and 'of course can live [the way] he wants'. I could almost detect envy in those comments, in particular towards Mr Chang's economic status. After all, as one patient concluded towards the end of this gossip about Mr Chang, 'Money is always a question' and other patients agreed. Nevertheless, the same patients later referred to Mr Chang's 'flying all the way just to get the treatment' as evidence

[58] This is a false impression yet reflects Chinese patients' general impression about the speedy effect of intravenous therapy, see Kan et al. (2015).

that immunotherapy must have certain therapeutic effects, and potentially gave new patients more confidence in this novel therapy.

Among those patients who I met at the unit, Mr Wu provided me most insight into not only the patient's experience with immunotherapy, but also the lifeworld of a cancer patient. Mr Wu demonstrated the importance of locating the experiences of patients with experimental therapy in the wider political and social-economic environment. He showed how patients learn to prepare themselves for constant change and to master their life skills towards being able to adjust.

Mr Wu: knitted hat, borderline case, and red peanut

Mr Wu, together with an older female patient Mrs Ma, were often the last ones to finish treatment. After so many hours in intravenous therapy the two knew each other well. Like Mr Wu, Mrs Ma was rather reserved in public and rested with her eyes closed most of the time during intravenous therapy. After the other patients completed their treatments and left, the two liked to chat with each other. When I was there, they accepted my accompanying them and shared their views with me. Mrs Ma understood mandarin but only spoke a local dialect which I only half understood. Fortunately for me, Mr Wu was there and helped me learn about Mrs Ma's long years' experiences with immunotherapy that dated back around 2010 when Mrs Ma had just retired as a nurse working in another hospital. Back then, 'It was research' and Mrs Ma was enrolled as a 'research subject' and 'hardly needed to pay anything.'

While others in the group eagerly shared their experiences and views on immunotherapy, Mr Wu hardly spoke or moved. He semi-closed his eyes and quietly sat in one corner of the treatment room. He also wore a knitted hat, so large that it reached his eyebrows. I learned later that the hat was made by his wife who is a school teacher and often came during her lunch break to deliver lunch for Mr Wu. In the semi-tropical climate, people rarely wear a sweater in winter. Yet, Mr Wu looked pale and cold despite layers of shirts and sweaters under his jacket. Overall, Mr Wu most closely resembled the image of cancer patients shown in the news and television shows in China.

After most of the patients had completed their treatment and left the room, Mr Wu started to talk with me. He asked for my views on the news report that was discussed earlier by the group. After some thought,[59] I said that I considered the news story was well investigated and the questions raised by the journalists about the experimental status of immunotherapy and its current, prevalent use in hospitals were worthy attention.

> Then I added: 'But I am more interested in learning about patients' views like yours, and that's why I am here doing my research.'
> He fell back to silence for a while, then took out his phone from his jacket and said: 'Hmm, nowadays there is too much information for one to catch up. The other day I read this one explaining the basics of immunotherapy. It's written by an expert, long but worth the time [to read] [*pause*] did you come across it? The one written by *Boluo* [the author's name]?'
> 'Ha, yes, in fact I did!' I smiled: 'It is a good one. Indeed well written and even humorous.'
> 'Exactly! It makes a good read [*smile*] I actually [*short pause*] like to know more about it [immunotherapy]. Like the others, I know that it is still in experiment. I too did my research. There was nothing the doctors can do [for me] after the chemotherapy, and I became rather weak after the chemo. It was then mentioned by my doctor as something I might try, and in fact long before that, I had heard about it. When one gets cancer, probably this is the first time you might want to do - to get all the information that may help you as much as you can - right? [*a transient, bitter smile, followed by a longer pause*] I guess it was about time, so I visited here and talked with Dr Jiang. I did some more research on the internet, and started [the treatment] not long ago,' he then closed his eyes, and before opening them again and, adding,
> 'Hmm, I feel it helps [me]".

This first impression of Mr Wu in his knitted hat, pale face and slow speech stayed with me, even weeks later when he sounded increasingly more confident in both his condition and immunotherapy.

The last time I saw him in the treatment room, he was there with his wife, Mrs Wu. He promptly told me the good news that he just received that morning, 'I got my latest [test] result today! The number [of white blood cell] is up again and I may soon be able to use my own blood!' It was around noon, and he and Mrs Ma were the last ones finishing their treatment. Mrs Ma and I were very happy for him, as he often talked

[59] I mentioned in chapter three that I abided by the research-ethics principle of not interfering in patients' treatments or influencing their views on experimental cell therapy. But occassions like this posed different ethical demands that required me to take into account the specificifities of the situation and proceed accordingly. See Guillemin and Gillam (2004) for a helpful distinction between procedural ethics and 'ethics in practice'.

about how the initial examination showed he was almost too weak to be eligible to have the treatment, and how, as a borderline case for eligibility, after discussing with his family, he had to convince Dr Jiang to start the treatment with him, but with a donor's blood. The donor was his daughter.

> 'I was lucky that my daughter was a match [in HLA] and she is willing to help me,' Mr Wu recited the story while his wife walked in with his lunch, '[but] she is a junior and about to have the entrance examination for high school. She is doing very well at school and I am very proud and really pleased to have such a good daughter [*a big smile turned into silence*] I feel bad, you know, every time [to prepare the treatment] they need to take 50ml of blood from her. It's a lot, [and] she is only 14, and [it felt] almost like a sacrifice…'

Mrs Wu, quietly nodded, but when Mr Wu talked about 'sacrifice' she grabbed his hand into her palms and interrupted him: 'No, no, *please*, don't say that! Our daughter wouldn't let you say that!'

> She turned to look at me, 'I tested too [for the HLA compatibility] but am not a match. How *badly* I wish I was! Then we needn't use our daughter's blood.'
> 'Of course, of course, you have to' I nodded, looked into Mrs Wu's nearly tearing eyes and reached my hand to hers, before turning to Mr Wu, 'So, the good news you just told me about the test…'
> 'Yes! That,' Mr Wu cheered up again, 'the number of my white cells has risen above 400 and I may soon be able to use *my own* blood for my treatment!'
> Mrs Wu's eyes lit up and exclaimed: 'What great news! Is that the result you got this morning?'
> 'Yes. I guess the red peanuts you bought this time helped!' Mr Wu smiled at his wife and then to Mrs Ma, 'You are right, Auntie Ma, sometimes those little things work the best.'
> Mrs Wu shyly joined her husband in thanking Mrs Ma, 'Yes, Auntie Ma, thanks for pointing out the farmer's market where I eventually found the right type [of the red peanut]. It is really good!'

We then all laughed and moved on to talking about various other nutrition, exercise and techniques they had explored or heard of since cancer occupied much of their lives.[60]

It was not the first time I heard about the red peanut - or more precisely, the skin of the red peanut - during patients' discussion about available options for treatments, remedies and supplements. Like Tai Chi which Mr Wu had also incorporated into his daily life

[60] There are other things Mr Wu worried about, including his job. As a civil servant, he considered that he should not worry as much as some other patients about being fired from private employers. But he felt himself increasingly becoming a liability to his colleagues and was concerned about possible institutional change in the new wave of political and bureaucratic reform. In chapter seven, I will deepen the discussion on how social-economic conditions affect patients' choices and decisions in pursuing health care in China.

since he was diagnosed with cancer, the red peanut skin was a recurrent form of therapy whose effect was said to have been documented in the Traditional Chinese Medicine and verified by many patients there. Sometimes patients would ask Dr Jiang about the effect of the red peanut, and even asked him to make prescriptions to get the red peanut from the hospitals' pharmacy. Dr Jiang in his impartial manner would tell the patients that he too has heard positive feedback from the patients, but there is no 'scientific proof' if that is what the patient wished him to verify. He seldom prescribed the red peanut, as 'you can get better ones in the farmer's market', but prescribed other supplements that were sold in the hospital's pharmacy.

The close-down of the 'ordinary' immunotherapy programme

I asked Dr Jiang about his views on the supplements that his patients asked him to prescribe to treat their cancers. Dr Jiang's answer was among the most explicit that he gave to me during my stay there,

> 'Nowadays, you can see those advertisements [on supplement to treat cancer] everywhere, on newspapers and TV, on the bus and in the tube, or well, of course, by word of mouth. Those supplements are approved [for marketing] by the authority [food and drug agency], so they must have some merit. If our hospital's pharmacy sells some of them, they [pharmacists] must have done their research and selected the reputable ones. And if a patient comes to me and say it works and wants me to prescribe, it may well work for him or her. I guess I am not in the position to contradict that…hmm…after all, they know their body and bodily responses [towards those supplements] the best, and it's their decision to make on how best to spend their money on their treatment.'

What he described was all too common in daily clinical practice. It even seemed sensible for doctors to respond to patients' requests in such a non-interfering manner. I returned to this theme of patient-doctor relationships after I had got to know the unit better. I asked Dr Jiang why some patients asked for adjustment for their own immunotherapy treatments and he often agreed.

He said, 'Those experienced patients know their bodily reaction the best [and] it probably works better to take their feedback into account.' Half minute later he added an afterthought, 'Of course, this is only for the old patients who have had the treatments for years and we follow them up and monitor the process'. It then occurred to me how

ordinary this novel immunotherapy had become in Dr Jiang's clinical practice and in his patients' lives.

Yet, the consequences of experimental immunotherapy becoming normalised manifested in clinical practices. After I returned after the spring festival holiday, I heard Dr Bao had worked through the entire holiday. He worked with other leading practitioners on a proposal to be submitted to China's health authorities on strengthening regulation and standardising the clinical practice of immunotherapy. Even though the patients who I had talked to were unconcerned by the negative publicity of immunotherapy in 2014, leading practitioners were more affected. So were the local governments. The municipal government notified all local hospitals to conduct reviews of their clinical practice and the effects of immunotherapies being provided. Doctors, like Dr Jiang, had to produce detailed documentation about each patient's treatment history, and review and evaluate their clinical practice. This policy change not only increased the workload for Dr Jiang, and all relevant personnel in the hospital, but also affected those patients who had become used to their routinised immunotherapy treatment. Rumours started to spread among patients that the government was considering removing immunotherapy from *the List of Essential Drugs* and would stop the reimbursement of immunotherapy treatment. Such policy change would significantly affect those patients' access to and use of immunotherapy. After all, 'Money is always a question'.

It was not the first time that local policy changes had impacted on immunotherapy. Patients told me that some municipalities had moved immunotherapy on and off local lists of essential drugs in the past two years. This time the augmented regulatory uncertainty in the following months led this biotherapy unit to closing down its immunotherapy programme in mid-2015. According to Dr Jiang, now only 'clinical research' is permitted in hospitals in China, 'just like stem cell'. I asked him what happened to those patients he used to treat. Dr Jiang did not answer.

In hindsight, this move to close down the immunotherapy unit was timely. When the news stories around Wei Zexi's death were headline national news and occupied the social media, the hospital was not involved in the latest round of media, public and regulatory scrutiny that hit many other cancer hospitals and immunotherapy companies.

Comprehending the ambiguous situation, revisiting toolised medicine

I mentioned in chapter two that I included immunotherapy in this study because of the differentiated regulatory treatment experienced by the two sister experimental therapies and their subsequent divergent clinical and socio-political lives in China. I also introduced how a series of events around Wei Zexi's death led the Chinese authorities' intervention in immunotherapy clinical practice. In this chapter, I have revisited the biotherapy unit where immunotherapy was routinely administered in early 2015 to cancer patients who seemingly understood the experimental nature of this novel therapy. I have introduced the negative media publicity surrounding immunotherapy, in 2014, and that unit's decision to close down its immunotherapy programme, in mid 2015.

Practitioners, who gave interviews to journalists, posted views on social media or conversed with me, were unsurprised by the downturn in immunotherapy practice. They had seen a similar process when their sister discipline - experimental stem cell therapy - evoked controversy which led to regulatory intervention. Immunotherapy practitioners had anticipated that one day the regulators would intervene in a similar manner to their practices as they had to stem cell therapy. Leading practitioners including the biotherapy's unit chief, had also taken proactive measures, asking regulators to strengthen the implementation of existing regulations. Yet, most practitioners chose to 'play edge ball' (*da cabianqiu*, 打擦边球), and continued providing immunotherapy in the 'grey area' once those provided experimental stem cell therapy manoeuvred (Sleeboom-Faulkner, 2016).

Social science researchers have developed concepts and theoretical approaches such as biocapital (Sunder Rajan, 2006), political economy of bioinnovation (Salter and Faulkner, 2011) and biomedicalization (Clarke et al., 2010) to describe and analyse various ways and forms wherein research, commercial and political interests and practices intersect, interact and mould one another. These concepts and approaches provide ready-made avenues to scrutinise the grey areas forged and sustained around cell therapy research and business activities in China.

Yet, similar pro-commercial research and clinical practices have been observed in other countries (Sipp, 2011; Berger et al., 2016) and varied grey areas have been formed and sustained through bionetworking activities between regions and countries (Patra and Sleeboom-Faulkner, 2009; Sleeboom-Faulkner and Patra, 2011; Rosemann and Chaisinthop, 2016). Those activities have lasted for over a decade and seemingly will not cease any time soon. Rather than joining the critics too readily, I consider it is worth querying: what if the grey area is internal to the making of new forms of medicines in the contemporary? If so, what the grey area can tell us about biomedicine, and vice versa?

Rather than driving the argument through concepts of biocapital and biopolitics, I want to consider the possibility that the formation, maintenance and eruption of these ambiguous situations also correspond to new forms of medicines that are developed in these situations. I will do so by taking a closer look at the practices and experiences of those developing and using experimental cell therapies.

I suggest that on the one hand, it is important to note that those developing and using immunotherapy to varied degrees understood that immune cells only hold potential in medicine. Furthermore, for patients, they understood that, to actualise these cells' medicinal potentiality, they need to participate in the process with their own work. In other words, in that biotherapy unit, doctors and patients deployed their "tooling work" in the making and using of "toolised medicine", and together, they helped sustain the ambiguous situation. On the other hand, I stress that those patients' and patient families' "tooling work" on immunotherapy revealed both their agency and their vulnerability that were conditioned by their social-economic situation in China. Their vulnerability were revealed most clearly when the department decided to close its immunotherapy programme in response to local policy changes, yet without consulting patients.

In this section, I adopt the lens of tooling work to look again at the clinical practices in the biotherapy unit. I extend the discussion, made in chapter four, on patients' and patient families' tooling work. Lastly, I position the events around Wei Zexi's death in this wider ambiguous situation constructed and maintained for biomedical innovation projects in China.

Toolised medicine: a second look at the biotherapy unit

The organisational work of immunotherapy, in particular the spatial separation and temporal continuation of the work done in the hospital and the laboratory, corresponds to the difference and distance of the cell (as biological material) and cell therapy. In other words, the coordination and collaboration between the hospital and the laboratory organises tooling cells into cell therapies. This spatial and temporal separation and continuation that is required by tooling work can be organised differently according to the purposes of tooling work and the arrangement made by coordinating parties (the prescriber, the developer or manufacture, the provider and the user of immunotherapy).

In that biotherapy unit, the organisational work in effect created a situation in which patients experienced still-in-study immunotherapy in a way that was close to having ordinary treatment. In Wei's experience, the organisational work, which he learned about afterwards, evoked doubt and criticisms of the promoter, the organiser and the operator of immunotherapy. I will now discuss how tooling work made patients' experiences with immunotherapy nearly ordinary, and return to Wei's case later.

In the biotherapy unit, patients have two direct contact moments with immunotherapy during one treatment cycle. At the beginning when a nurse extracts blood from a patient, and at the end when a patient receives immunotherapy through intravenous therapy. Between the two contact moments, their blood was developed into their individual immunotherapy in the laboratory. The ordinariness of these two contact moments and the laboratory work that is done somewhere else and between the two contact moments are critical in constructing patients' experiences with immunotherapy as an ordinary novel therapy in the clinical setting. Patient's first consultative visit to Dr Jiang at the biotherapy unit, prior to consenting to take immunotherapy there, was also an experience of ordinary novel therapy.

During their initial consultation, Dr Jiang made clear to the patients that the status of immunotherapy was still-under-study, a second-line therapy, and only offered potential (not certainty) to treat cancer. Dr Jiang adopted metaphors such as 'defence,' 'soldier,' 'weapon' to translate the techno-scientific-medical jargons of immunotherapy into plain language. Those metaphors were not Dr Jiang's invention. As Haraway (1993) points

out, they have long been used by researchers and doctors in immunological research and clinical practices, and have become exemplary cultural imaginaries about contemporary biomedicine in the United States. In recent years, as immunotherapies achieved 'breakthrough' status (Coontz, 2013; Regalado, 2016) and succeeded in curing cases of cancer (e.g. the Emily Whitehead case (Luk, 2017)), these metaphors took root in Chinese immunotherapy (Zhang and Lv, 2013; Wolchok, 2014).

Patients also need to comprehend and agree with the operational and financial arrangements. They need to commit to subsequent hospital visits and arrange their work and life accordingly. Support and collaborations from their employees, health care insurers, families, coworkers and friends were in many cases crucial for patients' incorporating immunotherapy into their management of cancer(s).

Blood samples and intravenous therapy were conducted in normal hospital setting and involved no sophisticated equipment. The environment was familiar to cancer patients and helped make immunotherapy mores comfortable and 'natural' than other cancer treatments patients had received. Compared with standard cancer treatments - surgery, radiotherapy and chemotherapy - patients considered having immunotherapy through intravenous therapy nearly painless. When compared with drugs that are known to have side effects, they thought immunotherapy was more 'natural'[61] and compatible with other remedies and therapeutic exercises they did outside of the hospital.

In that biotherapy unit and despite its outer location, the laboratory owned by and was supervised by the same hospital where the patient received health care. In his clinical practice with immunotherapy, a main task for Dr Jiang was to coordinate the care of patients in the clinic and the production of immunotherapy for those patients in the laboratory.

After patients gave a blood sample, their sample followed the organisational arrangement between two sites, the clinic and the laboratory, to be developed into cell-

[61] Several research participants (not only patients) commented to me that developing medicine from entities existing in nature, including the human body, is long established practice in Traditional Chinese Medicine and possibly makes cell therapy more readily accepted and populated among Chinese patients. Similar comparisons have been observed in other societies where traditional or indigenous medical practice values a more "natural" approach, see for example Rosemann and Chaisinthop (2016).

based products that the patient received as the immunotherapy treatment. Patients knew about this travel and the conversion of their blood (and immune cells with it) into immunotherapy. They had no direct experience with this arrangement other than a temporal suspension (a two week wait) during this cyclical procedure of immunotherapy. Patients also knew that the two sites were coordinated through Dr Jiang. Some experienced patients proactively partook in the design of their treatment plan by telling Dr Jiang their assessment of different immunotherapies and their preferences of using which type in the next treatment cycle.

Long-term doctor-patient relationships developed during the process of assembling immunotherapy together, the time required by laboratory work and the need to receive multiple treatments of immunotherapy. By comparison, doctor-patient relationship in China has generally worsened (Nie et al., 2017). The rather mundane, yet sustained, communication and interaction between patients and doctors that was required by tooling work helped to cultivate a friendly environment that contributed to the positive evaluation of immunotherapy experiences by most patients.

Patients and patient families' positive experiences with immunotherapy cannot be separated from their overall experience with the organisation and provision of health care services in that hospital and in that province and city. To a large degree, the mundane clinical interactions between health care professionals and patients and patient families, in the consultancy and treatment rooms, moulded the individual, family, and collective experiences of immunotherapy in the biotherapy unit. Similarly, patients' informed participation was essential to the operation of the immunotherapy programme in that biotherapy unit: a point that was fully acknowledged and incorporated in their clinical work by the health care professionals there. Patients contributed to the making of immunotherapy as much as the doctors. Clinical practices and interactions thus weaved the 'doctoring' by health care professionals' with the work of care and hope by patients' and patient families' and became 'shared doctoring': 'to seek what can be done to improve the way in which we live with our disease. And remember that failure is inevitable and death the only security we have' (Mol, 2008: 56).

Using experimental cell therapies in contemporary China: a reflection

Before elaborating on the ambiguous situation that I observed in that biotherapy unit wherein doctors and patients informedly practised and used experimental immunotherapy, I take a closer look at the events around Wei Zexi's death that I introduced in chapter two. Wei's case, I suggest, reveals the vulnerability of Chinese patients seeking health care services in contemporary China. Whereas the experiences of patients at the biotherapy unit revealed another kind of vulnerability linked with the toolised feature of biomedicine.

In Wei Zexi's recount of his and his family's experiences with immunotherapy, the doctor who Wei's father met at a prior visit misled Wei's family about the prospect of using immunotherapy to treat Wei (Wei, 2016). The doctor claimed that the therapy developed in collaboration with American scientists and would give Wei another 20 years to live. Wei's family went there with much hope, but the initial effect of Wei's treatment did not prevent his cancer from worsening. In his post on the internet forum *Zhihu*, Wei added that a friend who queried hospitals in the United States told him that the specific type of immunotherapy that he received in China was considered outdated by American hospitals. In contrast to the imported drug Keytruda (pembrolizurmab) he later purchased from Hong Kong, Wei deemed immunotherapy was a form of marketing constructed by the hospital and the search engine *Baidu* in order to deceive patients (ibid.).

It was this marketing strategy that disgusted Wei, and subsequently became one focus of the public outcry over Wei's death. Yet, this practise of marketing health services did not start with immunotherapy, instead there has been a gradual development in the marketisation of China's public health services since the 1980s, which accelerated with internet-based promotion (He et al., 2015). Wei (2016) named the internet searching company, *Baidu,* 'most evil', because they promoted that hospital's immunotherapy programme on their search results. It was not just the doctor or the hospital that had misled his family.

The intra-institutional arrangement, marketing and operation mechanisms that Wei exposed in his internet-forum post had long been known among healthcare professionals and biotech companies, as well as patients and regulators. Wei's passing-away and his question about 'the most evil' did more than bring together Chinese

patients through the internet. The public mobilised, demanding answers from the complicit parties and from the regulators on a couple of long standing social-economic and political problems. Problems such as the commercialisation and marketisation of healthcare services, privatisation of public hospitals, and dishonest clinical and business practices. These problems arose through China's public health reforms in the 1980s and 1990s that pushed the healthcare system into the marketplace and made public hospitals into market actors and Chinese patients into patient-consumers (Renshaw, 2014; Blumenthal and Hsiao, 2015).

The Wei's family's experiences thus evidenced and exposed well documented vulnerability of Chinese patients and represented suffering endured by Chinese people in China's ongoing political, social and economic transformation (Yip and Hsiao, 2015; Whyte, 2016; Liu et al., 2017). As the collective call for accountability on Wei's case gathered momentum, Wei's case also became an issue that demanded a political response from Chinese authorities. So the authorities reacted quickly and launched investigations into the hospital and *Baidu*, and made Wei's case a memorable event in order to 'quiet[en] social discussion in the short term' (J. Y. Zhang, 2017: 650). The authorities focused their investigation into the named 'evils' in Wei's case - that hospital and *Baidu* - and the organisational work of immunotherapy, yet left out more thorny questions rooted in the health care system and biomedical research enterprise. Even though the health authorities clarified that they had never approved any hospital to offer immunotherapy to the patients, they did not degrade immunotherapy nor investigate current practice in the industry. The validity and usefulness of immunotherapy was largely left as a techno-scientific-medical question for the scientific and medical experts to debate and decide. Nevertheless, regulatory responses to Wei's case led most hospitals and small biotech companies to close their immunotherapy programmes. I will discuss the effects of regulatory intervention in the last section, but now address a particular vulnerability of those patients who sought immunotherapy in the biotherapy unit.

As I explained earlier, the cancer patients I met in the biotherapy understood that today, immunotherapy is only an ancillary treatment and not yet able to cure cancer, although it may in the future. Nevertheless, this recognition did not reduce its attractiveness to those patients and their families. Rather, those patients partook in the making of

immunotherapy that helped to treat their cancers. In clinical practices, this reduced set of expectations, about the capacity of immunotherapy to provide revolutionary cancer treatment, somehow enabled patients to use it more actively. Viewing immunotherapy as an ancillary treatment whose therapeutic effect was individualised, allowed patients to judge it using the same criteria that they used in assessing the effectiveness of Tai Chi or red peanut skin. Patients could evaluate the success of any treatment and management of cancer by asking whether or not worked for their individual conditions. Local health care insurance policies further encouraged doctors and patients to integrate routinised immunotherapy treatments into long-term treatment and management plans for cancers.

In clinical practices, the trade-off between immunotherapy's novelty and its ordinariness seemed to increase its attractiveness to those patients who tooled this novel treatment for their cancer management and contributed to sustaining the immunotherapy programme. In other words, when the biotherapy unit ran its immunotherapy programme, the experimental status of immunotherapy denoted to doctors and patients the uncertainness and unknowns that are part of making immune cells into immunotherapy. Yet, it invited the active participation of patients' in the making of immunotherapy. "Toolised medicine" requires "tooling work" from all its users, including patients.

For the most part, I witnessed in the biotherapy unit, the agency of patients in their tooling work. It made those patients critical participants in the making of immunotherapy and the sustainability of the immunotherapy programme in the biotherapy unit. Yet, when the biotherapy unit closed its immunotherapy programme, the patients' tooling work was rendered irrelevant and their agency became their vulnerability. Dr Jiang never answered my questions regarding the whereabouts of his patients after the immunotherapy programme closed down. In the aftermath of Wei's death, journalists reported that immunotherapy patients were left unattended, and some of them pleaded to the authorities to let hospitals reopen the immunotherapy programmes (Wang, 2016).

In reply to the journalists in 2017, the Chinese authorities reaffirmed their position in supporting clinical research, but were vague about how and when such research would

be (permitted to be) translated into clinical usage (Wang, 2017b). Meanwhile, patients continued seeking alternatives to immunotherapy, including trying to get enrolled in clinical trials and purchasing new immune-based drugs wherever available (ibid.).

The patients I met in the biotherapy unit impressed me with their positivity and resilience in living with cancer and managing their lives around changing conditions. Facing sudden decisions made by their doctors and regulators in China, they might have found alternatives to the immunotherapies they once routinely used in that biotherapy unit, just like the patients in the news reports. For the Xie and Shen families, who I introduced in chapter four, their tooling work with experimental stem cell therapy also exhibited this particular vulnerability of patients. In other words, while toolised medicine makes patients' tooling work essential in making biological entity-based medicine, it also exposes patients to specific vulnerabilities that is conditioned by their tooling work.

In this study, almost all those patients and their families who I met not only used experimental cell therapies as new medicines, but also as part of their care work for family members. It is the calling of care and the demand of 'exerting one's utmost human abilities' that urged those patients and patient families to look for novel therapies to resolve medical and associated problems that they were enduring. Yet, the social-economic and political conditions that influenced their experiences with diseases, disabilities and health care practices were bracketed into the 'Chinese context' as part of 'the decree of fate'. The 'Chinese context', nevertheless, also conditioned the fate of immunotherapy in China.

Ordinary experimentation: complicity, ambiguity and contingency

The clinical situation where the biotherapy unit ran its immunotherapy programme resembles the practice of 'ordinary medicine' that Kaufman (2015) described in her study of health care practice in the United States. Kaufman (2015) developed the term to describe how once medicine that was once experimental and restricted, such as kidney and liver transplantations, became ordinary and even ethically mandatory for clinical use, including in situations when benefits were unclear to the patients, for instance those 80 years old and over. Kaufman identifies a key step in the transition of

an experimental therapy to become ordinary is when healthcare insurance programmes accept it, after it gains approval for marketisation (ibid.: 7).

Unlike kidney or liver transplantation, immunotherapy is an experimental treatment that has not received marketisation approval in China. Yet, government endorsements of immunotherapy research, and the existing regulation on medical technologies and local health care insurance policies, presented plausible reasons for hospitals to consider opening immunotherapy programmes and for patients to think about trying out this novel therapy. So, despite knowing that immunotherapy was still-under-study and its operation was questionable, patients, doctors and their families, institutions, professional societies and collaborators went ahead with it. Nevertheless, the same knowledge to various degrees unsettled those practising and using immunotherapy and cast doubts on their practices. No one was entirely satisfied with the status quo. For instance, Dr Jiang was reluctant to give full endorsement for immunotherapy, and Mr Wu continued monitoring news on immunotherapy and assessing the validity and effects of the therapies that he received.

Around these practices, a kind of local sociality was cultivated among those who participated in constructing and maintaining the clinical life of experimental immunotherapy. This local sociality bore a resemblance to what Steinmüller's (2010) study of Bashan village life in central China where he described 'community of complicity'. Steinmüller observed that certain activities such as *fengshui* and *li*, which are denounced by the Chinese state as backward and superstitious, were maintained in village life. Local villagers shared and practised these intimate knowledges but felt embarrassed when seen or asked questions by outsiders about these activities. The villagers' awareness of this intimate space and the tension between official representations and local sociality was revealed and concealed through their gestures of embarrassment, irony, and cynicism. Building on 'cultural intimacy' (Herzfeld, 2004), Steinmüller (2010) used the 'community of complicity' to describe the situation and to analyse China's state-formation, local sociality and the tension between state and society.

Yet, the word 'complicity' is a too strong and one-sided negative to capture the nuances in the organisational and clinical work and the nested emotions expressed by the doctors

and patients at the biotherapy unit. By different degrees, doctors and patients held ambiguous views on immunotherapy and their practices in the biotherapy unit, they also often publicly praised and celebrated the work done there for patients and patient families and for advancing the research and development of immunotherapy in China.

Furthermore, the boundary between the local and the official-outside was neither clear-cut, nor concealed, nor protected by those practising and using immunotherapy in the biotherapy unit. J. Y. Zhang (2017: 649) suggests that Chinese authorities exercised their '*post hoc* pragmatism' in handling Wei's case because their 'reactionary' regulatory intervention 'narrowly focused on addressing a particular criticism'. For those practising and using immunotherapy, and the local and national regulators observing these practices, Wei's case was less surprising for them than for the general public. Back in 2014, journalists had sought a response from the health authorities regarding the legality of public hospitals offering immunotherapy to cancer patients (Yuan and Li, 2014). They also reported that for years leading practitioners had anticipated that if immunotherapy continued to be practised in this grey area, a scandal like Wei's would happen (Wang, 2017a). They had alerted the national regulatory agencies about this ambiguous situation wherein immunotherapy was offered without full authorisation and asked for fuller implementation of the existing regulations (ibid.). In other words, prior to Wei's death drawing public's attention to the clinical and business practices around immunotherapy, the local and national officials were aware of those practices.

Thus, in contrast to local practices of *fengshui* and *li* in Bashan village, the local and the official-outside jointly managed this 'grey area' (Sleeboom-Faulkner, 2016), where clinical practices of experimental immunotherapy were sustained in certain times and places in China. To some extent, the events around Wei's death constitutes an 'existential test' (Boltanski, 2011) that exposed the contingency of this regulatory and clinical situation around immunotherapy. It originates from individual experiences yet resonates with other people and poses question on 'what is whatness' that reveal the difference between the 'world' and 'the reality' as announced by spokesperson of government (Boltanski, 2011: 107-108). Yet, revealing the world does not necessarily lead to rectifying the reality. It constitutes a 'radical critique' that may lead to emancipation (Boltanski, 2011: 108-110). In China, the political and legal system poses

serious constraints towards such emancipation, which reflects my interlocutors' tendency to bracket social and political problems that they encounter in daily life into the 'Chinese contexts'. So instead of exposing dubious operations right away, they often chose to make the best of the situation and in effect, helped to construct and maintain the grey area.

This grey area is conditionally maintained on the basis of what my interlocutors described as, 'no report, no investigation' (*min buju, guan bujiu*. 民不举，官不纠). My interlocutors used this phrase to describe not only the practices around experimental cell therapies in China, but also a range of social-political situations that they encountered in everyday life in China today. This phrase describes Chinese bureaucrats' general treatment of dubious operations that they are aware of, continue monitoring, yet, conditionally do not act upon, until serious complaints[62] are made against the operations and attract attention from the general public. To maintain the status quo, nevertheless, the conditional cooperation from all involved in this ambiguous situation, including those potentially being disadvantaged or exploited by the dubious operation, is essential. A serious enough complaint from a civilian(s) (*min*) may cause the officials to act and end the dubious operation.

In this ambiguous situation, the authorities are 'opening one eye and closing the other' (*zhengzhiyan, bizhiyan*, 睁只眼，闭只眼) to dubious operations. Yet, because authorities preserve the right to act once receiving a serious complaint, those involved and implicated in such ambiguous situations need to carefully observe the contingent regulatory situation (and prepare for prohibition or tighter regulation). It is thus important to note that authorities' non-action does not necessarily play out in favour of those seemingly taking the most advantage of the situation. For the maintenance of the ambiguous situation depends on the conditional cooperation from all involved and implicated parties. The conditional cooperation relies on every party to surpass the

[62] In China, direct appealing to the authorities remains an officially acknowledged and widely used form of petition or protest through which ordinary Chinese make individual and collective claims, seek justice and/or assistance from the governments at all levels. This petition-like activism is generically known in China as *shangfang* (上访), yet its effectiveness is constrained by the general and local political-social environments, and activists often devise locally effective ways to achieve their goals, see for instance, Steinhardt (2017), Li et al. (2012), Fu (2017). For example in chapter four, Cao's persistent pursuit for gaining compensation for his work accident from his private employee through appealing to the village, the township, the city, and eventually the provincial governments.

uneasiness generated by the shared situation. This ambiguous situation is inevitably contingent and no party has absolute control over it. Those taking the most advantage of the ambiguous situation are also likely to be those experiencing the most uncertainty and taking the most risk. When the ambiguous situation breaks down, they become most prone to ad hoc blame, loss and failure.

Chinese authorities' regulatory intervention into immunotherapy clinical practices after Wei's death illustrates the point when the officials decide to open both eyes. During the investigation of Wei's case, Chinese health authorities restated that immunotherapy had never been officially approved for clinical use (Jourdan, 2016) and subsequently banned clinical practice (Wang, 2017a). This regulatory action effectively transformed the public image of immunotherapy. The earlier widely available and, in a dozen of provinces, reimbursable immunotherapy was now denounced by national health authorities as unauthorised practices. Those who once practised immunotherapy with institutional support and even local government endorsement are now seen as mainly driven by self-interest and having operated illegitimately.

The representation of immunotherapy practitioners overlooked the aforementioned fact that leading practitioners had long worked on preventative measures to bring order into their shared enterprise. As I witnessed during my fieldwork, in late 2014, leading immunotherapy practitioners had started to work on a proposal asking the health authorities for clearer guidance and more stringent regulation on immunotherapy's clinical practice; and, in early 2015, they submitted their proposal to the health authorities. A similar, earlier effort from 2009 was documented by Wen et al. (2016). Vigilance and precaution thus preceded journalists' investigations into immunotherapy practices in 2014, and as I suggested before, was sharpened by what practitioners had witnessed in the downturn of experimental stem cell therapy. Nevertheless, despite their effort to strengthen both governmental and self regulation, in the aftermath of Wei's case and regulatory intervention, immunotherapy, too, fell into its winter. Like those who practised experimental stem cell therapy, immunotherapy practitioners and their institutions and collaborators took the most blame for creating the mess that now became subject of regulatory correction.

This rapid downturn of immunotherapy and the similar trajectory that stem cell therapy experienced in China thus, additionally, reveals the vulnerability of the practitioners and their institutions and networks. It further points to a critical implication of biomedicine being toolised in social, political contexts such as China. That is, when conceived as one tool in an expanding toolbox of future medicines, a particular biomedical product or entire programme is subject to selection, competition and elimination. In an organisational setting such as a hospital, the decision about whether or not to introduce, maintain, further develop, or kill a particular therapy programme is subject to professional, regulatory, and economic considerations. While who bears the cost of abandoning one programme or substituting one for another is seldom taken into account by those making critical decisions.

CHAPTER SIX. Living through the regulatory change as biotech entrepreneurs

This chapter focuses on the experiences of full-time[63] biotech entrepreneurs' during the regulatory impasse that I observed during my fieldwork. These biotech entrepreneurs either once worked, or continued to work, with hospitals in developing stem cell therapy and related industries in China. Prior to the regulatory change, they operated in a regulatory grey area, and they collectively referred to their business endeavours as a 'mess'. To rectify these 'wrong doings', Chinese health authorities initiated regulatory changes to stem cell clinical research and practices. These biotech entrepreneurs were among the most severely affected by the regulatory change. The decisive downturn and shrinking of stem cell therapy related industries in China put their business networks, companies, and livelihoods on the line. Yet, many saw business opportunities amid the various regulatory and market risks and, accordingly, devised their business strategies.

I observed that the experiences and perspectives of regulatory change for biotech entrepreneurs largely corresponded to their assessment of the industry's future, and their social-political standing as biotech entrepreneurs in contemporary China. Their counter-strategy to survive this regulatory change revealed that the composition of biotech entrepreneurship, and the power and working relations between biotech entrepreneurs and health authorities were undergoing a notable change in contemporary China.

Yet, the exit from stem cell industry by some companies while other companies expanded into other biotechnologies made visible a critical ramification of biomedicine becoming toolised. That is, because of its potential in other domains - on this occasion, the market - biomedicine is readily deployed as a tool to achieve these other values, yet, through (partially) actualising its medicinal potentiality. On this occasion, its developer - biotech entrepreneurs - also became its primary user. Acquiring this dual role of developer and user, biotech entrepreneurs' activities affect, in various ways, other users of toolised medicine, such as patients and clinician-researchers. I will discuss some of

[63] I distinguish full-time biotech entrepreneurs from part-time ones. Part-time ones have their primary job in, often, public institutions while working in the industry as co-founders, consultants, trustees or investors of certain companies. During the regulatory change, the option to step in or out of the business gave part-time entrepreneurs certain advantages in securing their (primary) job and livelihood, whereas full-time ones faced bleaker prospect of sustaining theirs.

these implications in this chapter, and take these discussions into the next chapter where I suggest and analyse when a nation-state (in China, more precisely, the party-state) acquired a primary usership of toolised medicine.

Yearning for regulation while preparing for exit

In chapter two, I mentioned that industry analysts such as Dr Bai described that the regulatory change brought a 'winter' to stem cell clinical research and related industries. When I started my fieldwork in January 2014, practitioners had lived in a regulatory impasse for about one year, since the MOH published the first draft of new regulations for consultation in March 2013 but then fell into silent. Given the regulatory uncertainty, the investors had also lowered their interests. Though according to some of my interlocutors working in pharmaceutical and investment industries, due to techno-scientific, manufacture and clinical uncertainties, investors had long been less interested in stem cell therapy as compared to immunotherapy, genetic testing or wearable diagnostics (see also Parson, 2008; Dodson and Levine, 2015). The regulatory impasse diminished interests from the private sector further and made biotech business survival during the regulatory impasse a hard-headed task for entrepreneurs.

In 2014, there were a handful of public companies that specialised in stem cell related business operating in China. The number increased in late 2014 when certain public companies in traditional industries - for instance textile, coal, and estate - bought biotech startups and extended their businesses into cell-based industries. There were a few sizeable biotech companies in different regions in China that were established before 2010. They accumulated notable resources prior to the regulatory change that enabled them to make necessary adjustments to survive the industry's winter. In particular, the importance of non-monetary resources, such as professional networks and government relations, heightened during the regulatory impasse; these biotech entrepreneurs further crafted their 'bionetworking' (Patra and Sleeboom-Faulkner, 2009), publicity and advocacy work.

The 'big players' - the chief executives of public and other sizeable companies - also frequently made public appearances in conferences and media to present their assessment of, and vision for, stem cell related industries. In those conferences and

interviews given to journalists, they often directly addressed their concerns and suggestions to the regulators on how to turn the disabling situation around and build a globally competitive, Chinese stem cell research-enterprise. For most of the time when I was in the field, they worked more closely with clinician-researchers and a few of them also passionately defended the existing regulation on medical technologies. But I also noted that, compared with laboratory-based scientists and clinician-researchers, most of these big players did not have a particular preference over whether to use a medical technology or drug model to regulate their industry. Or, as Dr Lv said, and I mentioned in chapter three, 'Whatever the regulation is, we can follow. What we want is simple: give me the regulation!' In late 2014, I started to hear more advocacy of business models that could be 'scaled up' that belittled the option of using stem cell therapy as a 'medical technology'. This change in their advocacy strategies mirrors the changing composition of biotech entrepreneurship and the power and working relationships between biotech entrepreneurs and health authorities - a point that I will return in the next section and elaborate in the next chapter.

The majority of the biotech companies were local, small in size and influence, and as Dr Bai recalled, most had already abandoned business that directly linked with stem cell clinical research and practices. Those biotech entrepreneurs quietly worked and lived in a manner well described by Dr Miao, the chief technology officer of a stem cell company, '[We] just got used to living and working with the unchanging changeable' (*yi bubian ying wanbian*, 以不变应万变). Considering himself primarily a scientist, Dr Miao was reluctant to talk about this side-business which he described as a way to produce 'blood' for sustaining the 'lifeline' of their main business that developed stem cell-based medicinal products. But because this main business had been constrained by the regulatory change, the side-business, in effect, preoccupied his work.

Towards the end of our interview, Dr Miao suddenly returned to the topic of the company's side-business. He sighed, 'It's kind of ironic, isn't it? As someone who truly believes in stem cell [therapy] and wants to join this revolution [of medicine], I now work like a supplier [*short pause*]. Well, a man has got to feed himself and his family, right?' I was struck by the sadness that I detected from his voice and thought of the similar tone I heard in Dr Bai's comment on the enterprise's winter. I was at a loss for words.

In late 2014, when the regulatory situation started to change for immunotherapy, I began to witness the withdrawing of practitioners from immunotherapy clinical practice and related business. I thought again of Dr Bai's description of the industry's winter and how, at one of our later meetings, he said that the downturn of stem cell clinical research and practices was 'such a pity'. I kept receiving news from my research participants about their decisions to close down their immunotherapy related business and I wondered where would they go. I noted myself becoming increasingly affected by this sense of mundane frustration, although like Dr Bai, my research participants did not talk about how they felt. They sounded detached from their business decisions and seemingly concentrated now on making a future in other fields. Nevertheless, as shown in some other cases that I introduce in the next section, those feelings and affects played a critical role in the survival strategies of other biotech entrepreneurs.

Biotech entrepreneurs and their survival strategies

While most small business owners such as Dr Miao kept silent or even secretive about their manoeuvres during the regulatory change, the executives and managers of public and large startup biotech companies - the 'big players' - devoted considerable effort in publicising their business visions and plans. Their publicity work gave me a window to understand the experiences of big players during the regulatory change.

Those big players often highlighted that strengthening the competitiveness of a Chinese stem cell research-enterprise was of national and local political, economic and social importance, and was in urgent need of support from national and local authorities. They also liked to introduce their business vision and plans under the rubric of 'strategic (re)positioning' (*zhanlue bushu*, 战略部署). Nevertheless, I contend that like small business owners, those big players also had survival as the primary goal of the business strategies they devised in response to the regulatory impasse.

Their sometimes lavish publicity work needs to be understood within a particular mode of survival. As they often said, 'risk and opportunity coexist' (*jiyu yu tiaozhan bingcun*, 机遇与挑战并存). When speaking about risks and opportunities, those biotech entrepreneurs did not limit their ambitions and visions to either stem cell therapy or China. Rather, other biotechnologies and foreign markets were frequently included in

their business plans. The connections between stem cell therapy and other biotechnologies, and between China and other nation-states, that they brought into discussions reflects the evolving landscape and practices of global biomedical industries. I, thus, use the biotech entrepreneurs' survival strategies to study the implications of this changing landscape on biomedicine and in China.

Public companies and their ambitious expansion

Public companies - those listed on stock markets - hold comparatively more resources than private companies, especially in terms of access to capital. The business and industry development model of 'high-tech' industries - driven by techno-scientific innovation and startup companies - is closely linked with the concept of the knowledge economy, as seen, for instance, in information and communication technologies and the success of Silicon Valley (Mazzucato, 2013). Worldwide, stem cell related industries are developed similarly to this model (French et al., 2014).

In China, entrepreneurial-minded scientists are pursuing this route, yet the existing big players gained their leading industry positions in different ways. So far, all public companies that have a business component in cell therapies and are listed in Chinese stock markets originated from more traditional industries. Among them, Zhongyuan Union (*zhongshan xiehe*, 中源协和) is the most known, and most vocal, about regulatory change. Sizeable startup companies accumulated most of their resources through the commercialisation of existing stem cell related technologies prior to the regulatory change. For instance, Beike Biotech (*Beike shengwu*, 北科生物, hereby Beike) is known internationally for its involvement in stem cell tourism, and BoyaLife Group (*Boya ganxibao jituan*, 博雅干细胞集团) specialises with umbilical cord blood banking.

In the evolving terrain and formation of biomedical industries in China, the recent past and future vision of these companies is illuminating. Zhongyuan Union and Beike are widely considered as industry leaders by practitioners and investors in China (Mu et al., 2015; Hong and Xu, 2015). During the regulatory change, the two companies acted like representatives of stem cell related industries and exerted considerable force in shaping

the future of Chinese stem cell research-enterprise through their publicity work (*yulun gongzuo,* 舆论工作) and government work (*zhengfu gongzuo*, 政府工作). I, thus, use these two companies to analyse how the big players responded to regulatory change and to learn from their experiences about biomedicine and China.

According to public record (Sina, n.d.), prior to dabbling into cord blood banking, Zhongyuan Union was a textile company named '*Wangchunhua*' and listed on Shanghai stock and exchange market since 1992. In 2008, it was renamed '*Zhongyuan Union Stem Cell Bioengineering Co*.' (*Zhongyuan Union* for short in English and *Zhongyuan Xiehe* in Chinese) and changed its registration location from Shanghai to Tianjin. In November 2014, it was renamed '*Zhongyuan Union Cell & Gene Engineering Corp., LTD*', and changed its name yet again in July 2017 into '*VCANBio Cell & Gene Engineering Corp., LTD*'. The executives of Zhongyuan Union and practitioners continue to refer the company, in Chinese, as *Zhongyuan Xiehe*.

This series of name changes records Zhongyuan Union's 'strategic (re)positioning' at different moments in the short history of China's stem cell related industries. The two more recent changes occurred during the regulatory change. Since 2013, Zhongyuan Union launched a series of mergers and acquisitions (M&A) deals in, and outside of, China. Its partial acquisition of Beike, in December 2014, attracted the most attention from practitioners, industry observers and investors. This deal had multiple implications for different parties.

I first heard the rumour about the Zhongyuan Union-Beike acquisition from Dr Bai as a 'side road news' (*xiaodao xiaoxi*, 小道消息) in mid-2014. Dr Bai first stressed: 'Don't tell [others that] I told you this.'

> I nodded, and he continued, 'It is a side road news, but more or less a done deal now. Zhongyuan Union is going to buy part of Beike's [ownership].'
> Knowing that Zhongyuan Union and Beike are both pioneers in stem cell related industries in China, I exclaimed, 'Really? Wow, that's going to be big news!'
> 'It's going to be interesting in the stock market', he grinned.

About six months later, Zhongyuan Union announced its 'strategic business move' in acquiring 13% ownership from Beike's founder and chairperson Hu Xiang (Zhongyuan Union, 2014). Its news release soon featured in finance news channels and was

discussed by traders in stock market internet forums[64] (Z. Wang, 2014; Zhongyuanxiehe Zixun, 2014).

As predicted by Dr Bai, stock market investors responded enthusiastically to this deal. A few months later, by chance, my landlady at the time told me how the stock market responded to this deal. I was about to move to another field site and my landlady invited me to a meal. On our walk to a local restaurant, we chatted about our lives and about my research.[65] When hearing about 'stem cell', my landlady tilted her face and exclaimed with a big smile,

> 'You know what? My husband trades in the stock market [*chaogu*, 炒股]. Not professionally, of course, [but] at home. He is very good at it and a few friends have entrusted him their money for years now…Stem cell, yeah, I remember one day he was excited, saying that a company performed particularly well. What's the name [of the company]? [*pause while thinking*] hmm, why can't I remember it now…well, it's a company…I think…in Tianjin.'
> 'Zhongyuan Union?' I asked.
> 'Yes, yes, that one! It just made a big deal, right? I remember that day, my husband was very happy and asked [me to cook] for his favourite dish', she laughed.

This M&A deal was, jokingly, commented on by practitioners and industry observers as a case demonstrating Zhongyuan Union's skills in 'playing the capital game' (*wan ziben*, 玩资本). I will return to this point and discuss this deal's implications on Beike in the next subsection.

Apart from acquiring partial ownership of Beike, Zhongyuan Union's deals with smaller biotech companies had nothing to do with stem cell research or product development. Those deals were deployed to help Zhongyuan Union reposition itself in a larger landscape of biomedical industries.

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[64] When I designed this study in 2013, only a handful public companies had cell related business in their portfolios. To manage the scope of my fieldwork, I did not systematically follow the fluctuation of those companies' stock price during the regulatory change. Instead, I followed closely business and finance news reports, and related discussions in social media and internet forums.

[65] During my fieldwork, I spent most of the time doing research outside, and often left early in the morning and came back late in the evening. So I did not have much chance to socialise with my landlords and landladies, and they usually did not know much detail about my research.

In early 2014, Zhongyuan Union announced a renewed business vision 'Driven by two hardcore technologies, and covering the entire chain of biotech industry' (Guo, 2015). Zhongyuan Union identified genetics and cell-based technology as its two hardcore technologies, and expanded its businesses into six sub-industries within the bio-pharmaceutical industry: cell bank, data bank, genetic and preclinical test, immunotherapy, pharmacy, anti-aging and cosmetic products (ibid.). To reflect this business upgrading, it changed its name to '*Zhongyuan Union Cell &Gene Engineering Corp., LTD*' in late 2014. In 2015, Zhongyuan Union embarked on its expanding outside of China. In 2016, it established two biotech companies in the United States - VcanBio USA and HebeCell - and a research centre named *VcanBio Centre for Translational Biotechnology* (Yang and Xiao, 2016). In 2017, it changed the company's English name into VcanBio Life Sciences (Sina., n.d.).

In publicising these deals, Zhongyuan Union rebranded itself and solidified its new image. It was no longer a company that specialised in cord blood banking, but a tradable Chinese company with a global vision and ambition in biomedicine and health markets. Zhongyuan Union's publicity work resembles Sunder Rajan's observations in *Biocaptial* about how leading genomics companies use forward-looking statements to cultivate market expectations for a postgenomics' promissory future (2006: 128-135). Yet, it is important to note that Zhongyuan Union's decisive march into immunotherapy and genetics diagnosis occurred during a regulatory impasse that had significantly reduced market interests on stem cell related business in China. In Zhongyuan Union's annual reports and consultancy companies' analyses, the regulatory uncertainty hovering over stem cell industries is listed as a primary risk that may affect the company's execution of its renewed vision and its market performance (Zhongyuan Union, 2015; Guo, 2015). This prediction was verified when events around Wei Zexi interrupted another M&A deal that Zhongyuan Union had announced prior to Wei's case becoming public, thereby affecting Zhongyuan Union's businesses in immunotherapy and its overall market evaluation (Xia, 2016; Li, 2017). Making business transitions into other industries and markets is a risk-taking endeavour. Unpredictable regulatory change increases the gambling element when undertaking such bold business moves, and makes the publicity work of companies akin to bluffing.

Startups and their patrons

While public companies are better positioned to survive this regulatory impasse by utilising capital through various channels, large biotech companies emphasised their startup identity and their local embodiment had national and global ambitions.

Since the regulatory change was initiated by MOH, and then stalled at the ministry-level negotiations between NHFPC and CFDA, biotech entrepreneurs relied increasingly on the support from local governments. Some powerful local governments introduced local policies to accommodate the development of stem cell related industries in their jurisdictions (shzj.gov, 2013; Luo and Huang, 2014).

Nonetheless, in the political system in China, local officials foremost need to respond to their superiors and ultimately, the party-state. Alongside this political system, as part of political and bureaucratic practice in post-Mao China, the Central government has used 'zoning technologies' to carve out 'special zones' wherein certain social-economic experiments are allowed and if they succeed, are replicated in other parts in China (Ong, 2004). Conducting 'experimentation under hierarchy' (Heilmann, 2008) is a risk-taking endeavour for local officials whose success and failure is subject to criteria that change with social-political contexts (O'Donnell, 2017). Launched by the current leadership in 2013, China's ongoing governmental-bureaucratic and social-economic reforms reportedly discouraged local initiatives (Teets et al., 2017). Thus, even though local initiatives on cell related industries were announced in various places in China, no concrete action was taken until the new regulations were published in August 2015 (Wang and Zhao, 2015; Yang, 2015; Luo and Huang, 2015).

During regulatory change biotech entrepreneurs worked closely with local governments to secure their businesses in certain localities. At the same time, they actively publicised their views on the regulatory change and suggestions on the new regulations to attract the attention of regulators. The dynamic and evolving relations and interactions between biotech entrepreneurs, local officials, health authorities and the Central government gradually moulded a Chinese stem cell research-enterprise that steered stem cell-based medicine towards economic and political gains. Here I take Beike, and its publicity and

government work, as a primary example of this process and also introduce other examples.

Publicity and government work

Beike was founded in Shenzhen in 2006. Shenzhen is a young city that rapidly developed from a fishing village into a megacity in the three decades since the Central Government named it as one of the first Special Economic Zones (SEZ) in 1978. Beike keeps its headquarters and international research and development base in Shenzhen (Beike Biotech, 2017).

Outside of China, the name of Beike is closely linked with stem cell tourism. Beike is particularly known, and criticised, for its use of internet based advertisement and patient testimonies to attract foreign patients to China to receive experimental stem cell therapies in its collaborating hospitals (Einhorn and Weintraub, 2007; Qiu, 2008). While Beike accumulated its case studies and profits, mounting criticisms of Chinese practitioners' unorthodox practices gradually pressured the MOH to intervene in such practices. As a target for correction, Beike is among the most adversely affected by this regulatory change.

Nevertheless, as noted in Sleeboom-Faulkner (2016), despite knowing Beike's controversial reputation outside of China, most Chinese practitioners viewed Beike positively. In China, Beike has a reputation for important stem cell research and product development. For instance, Dr Bai once contrasted Beike with others that were 'mainly after money', citing as evidence Beike's years of investment developing stem cell therapies and their contribution to Chinese stem cell research-enterprise. Most practitioners also praised Beike's chairperson Dr Hu Xiang for being a 'science guy' (*zuo kexue de ren*, 做科学的人), rather than a businessman.

Beike's executives speak highly about Shenzhen municipal government's 'financial and political support' (Beike Biotech, 2017). Likewise, the Shenzhen government recognises Beike's value as a leading biotech company that will further generate health and economic benefits for the locals and carry on the city's "miracle" (Chen, 2014).

Carrying on the 'Shenzhen miracle' is not only the municipal government's aspiration, but also of greater political significance to the Chinese party-state (O'Donnell et al., 2017). The success of China's social-economic reforms, in effect, justifies the party-state's legitimacy (Yang, 2006; Lieber, 2013; Sun and Guo, 2013a). The Central and local governments' investment into developing high tech industries and start-up companies, such as biomedical industries and Beike, carried expectations of returns not only economically, but also politically. Companies such as Beike understand the wider significance of making business successful and, accordingly, exhibit their achievements.

Beike has an informative website that details its footsteps and milestones (Beike Biotech, n.d.). This list of milestones is more than a chronology of the company's development. It documents the companies' achievements: patents, accreditations, successful collaborations and business deals, and visits by politicians and famous scientists. These milestones are selected and presented in a locally recognisable manner to demonstrate the company's capabilities and market potential. Accreditation by international organisations and visits of Nobel Laureates and politicians, for instance, are used as evidence of Beike receiving appraisal and support from professional organisations, science communities and governments.

These milestones not only help Beike to publicise its achievements, but also helped Beike seek support from local governments which became increasingly critical during the regulatory impasse. In other words, publicity work and government work is intricately linked in Beike's case. To achieve its expected result, publicity work thus requires careful design and performance like craftwork. A telling example is Beike's announcement of acquiring an immune-oncological product, *ALT-803,* from an American company.

Beike announced this deal at an event that it organised on cell therapy for the *3rd Biotech Expo and Innovation Forum,* in Shenzhen, in 2014. That year's *Biotech Expo and Innovation Forum* was organised under direct guidance from the municipal government. In a news release, the Shenzhen municipal government stated that having successfully nurtured the development of leading IT companies such as Tencent, it wanted to continue its legacy of honing high-technology industries such as biotechnology (sz.gov, 2014). With the direct funding and support of government, the

Expo became a citywide event and a festival for Chinese biotech industries. At the opening ceremony, the mayor of Shenzhen told his international audience that Shenzhen had started to build a 'Biotech Valley' with global attraction and influence (tech.China, 2014). Hosting Biotech Expo and announcing the government sponsored Biotech Valley project was, thus, the government's invitation to world talent in this field to start their enterprises in Shenzhen, like Beike and some other biotech companies had done.

A local official in charge of science and technology opened the *Cell Technology* event for Beike. Beike invited a number of leading practitioners as speakers for the event that attracted about two hundred people. There was only one speaker from the cell industry that had no existing connection with Beike: Dr Hing C. Wong. I had not heard of Dr Wong before, nor his company AltorBioScience. Many other attendees scratched their heads and asked one another about the speaker and company. The company, as Beike's chairperson Dr Hu Xiang stressed in his introduction, is an American biotech company specialising in immunotherapy, and the speaker is its chairperson. A Chinese American, Dr Wong gave the presentation on his company in Chinese. He showcased one particular immune-oncological product, *ALT-803,* that had recently received USFDA approval to conduct phase I/II trials on non-muscle-invasive bladder cancer. Despite its notable achievement, the relevance of AltorBioScience's appearance during this session remained obscure to the audience. It was at that the end of the session, however, that Dr Hu announced Beike's strategic collaboration with AltoBioScience, which granted Beike the right to co-develop *ALT-803* and the exclusive right to market the approved product in China.

Dr Hu's announcement first surprised and then excited the audience and transformed the conference venue into a news release room. While journalists and Beike's staff, documented the signing ceremony with professional cameras, many attendees took out their smartphones and shared the news together with photos on social media. The news was soon replicated in four different WeChat cell research and industry interest groups that I had joined.

After the event, Beike released its news release (PRNAsia, 2014). Government supported media, such as *STDaily*, *People's Daily* and *STCN*, and popular news centres, like *Phoenix New Media,* soon reported the story on their news channels. Three months

later, Beike's acquisition of the rights to develop and market *ALT-803* in China was mentioned in Zhongyuan Union's forward looking statement on its partial acquisition of Beike (Zhongyuan Union, 2014). It was cited as evidence of Beike's leading position in cell related industry in China.

Importantly for Beike, the positive responses from the media and the market strengthened Beike's image as a promising biotech company that it then listed as evidence of 'strength of Beike' on its website (Beike Life, n.d.). Soon after Chinese health authorities published the new regulations on stem cell clinical research, the Shenzhen government granted Beike the licence to build a regional cell bank in Shenzhen and, at the same time, acknowledged Beike's competitiveness, market potential and business vision (Yang, 2015).

When it came a time to keep low-key

I had another encounter with Dr Hu at the 15th annual conference of Chinese Society for Cell Biology (CSCB) when he appeared on a panel titled '*Special Dialogue on Co-development of Life Science Industry and Research'*. During his introductory speech, the chair of the panel mentioned that this event was organised under the request of the Shenzhen municipal government, which was a main sponsor for CSCB's annual conference that year. A local official confirmed this information in his opening address and added that the Shenzhen government would continue providing policy and administrative support for scientists, industrialists and investors who are interested in developing biotech industries in Shenzhen. After a group of scientists introduced their research, Dr Hu spoke to the event as an industry representative.

Dr Hu immediately apologised for the replacement of scheduled speaker,

> 'Sorry for the sudden change of speaker. Our CEO was supposed to come. But she received an urgent call from Beijing [regulators] to attend a consultation meeting on the draft regulation [on stem cell clinical research].'

It was early April 2015, and the draft regulations that Dr Hu mentioned had been published by Chinese health authorities about a month previously. Although Dr Hu mentioned these events casually, he instantly stirred interest from his co-panellists and the audience. Although Dr Hu, and some other industrialists, had long been active in

voicing their concerns on regulatory change and their wishes for new regulations on stem cell clinical research (Hu and Liu, 2015; Xiang, 2015a; Zhao and Wu, 2015), until now the regulators had not responded to their advocacy work, at least not publicly.

Rather, the regulators primarily relied on leading scientists and clinician-researchers and professional organisations in making the new regulations. The majority of scientists who I met during my study held negative views on the industrialists' advocacy work. As one of them told me, 'they [biotech entrepreneurs] are not helping with the situation, but creating noise and messing up the mind of the regulators'.

Given that Beike was first known for its involvement in stem cell tourism, the regulators' inclusion of Beike in its consultation meeting was significant. Nevertheless, Dr Hu did not elaborate on the news but proceeded to introduce Beike's new business models. In the last section of this chapter, I will return to Dr Hu's reflection on Beike's, and his own, transition and, in the next chapter, I discuss the significance of regulators accepting industrialists in the final stage of making the new regulations. Before that, the changing relation between biotech entrepreneurs and regulators needs to be examined.

Around the same time I heard Dr Hu's speech at the *Special Dialogue*, I had an interview with another well-known biotech entrepreneur, Dr Lian, who had also been vocal on matters related to industry policy and regulation making. I first contacted Dr Lian for an interview in autumn 2014, but, for various reasons, our agreed interview was deferred multiple times until this time. In between, we had stayed in contact on WeChat and occasionally exchanged views on new developments in stem cell research, industry and regulation. In late 2014, he invited me to visit his company.

Towards the end of our interview, Dr Lian handed me a hardcopy of a special issue published by *Economy & National Weekly* (Yunhui Wang, 2015) and said, 'This may be of interest to you [and it] covers most of what we just talked [about]'. I immediately noted the significance of the book-like special issue that he handed me from its title '*Special issue for the Two Sessions*' (*lianghui zhuankan*, 两会专刊) published by the official press agency of the Central Government. *Lianghui* is an acronym for the annual conferences of the NPC and CPPCC that are held in parallel in spring. They are the two most important political meetings in China wherein the party-government plans,

policies, laws and regulations are proposed, deliberated and voted by the participants. The subtitle of the special issue was '*Taking a Decisive Battle in Bio-energy*' (*juezhan shengming nengyuan*, 决战生命能源).

Flipping through the special issue, I noted that Dr Lian was a contributing author and among a few industrialists who wrote about their experiences and views on topics such as '*The Loss of Industry Planning*' and '*Nurturing Innovation Environment*'. 'Wow! This is huge!' I said to him. He gave me a smile, but said nothing. Some time later, we met in a conference and briefly talked about this special issue. I congratulated him again on being invited to co-author this special issue on biotech industries for an exclusive readership composed of China's top politicians, lawyers and policy makers. He nodded and smiled, but quickly changed the topic. I noted further that, as far as I know, he never mentioned in public the existence of the special issue, nor did he mention his involvement with this high level project. About a year later, the content of this special issue appeared on the internet.

The way Dr Lian played down this special issue and his personal involvement was in such a contrast to his outspoken public image. But I was familiar with this contrasting behaviour because I had seen this kind of discretion among other elite scientists who worked closely with the regulatory agencies. The way Dr Lian's manner changed prompted me to rethink about his and other biotech entrepreneurs' publicity and advocacy work. Biotech entrepreneurs could utilise the marketplace and local government relations to secure their survival and further development during the regulatory change. Yet, most of the time, they did not have access to the national regulators who were making the new regulations that would affect the future of their individual and collective ventures. Publicity work was thus one of a few things they could try to make their views heard by the regulators. Sometimes 'making noises' was necessary to get the regulators' attention, even if those biotech entrepreneurs knew that it would make them unpopular among certain groups such as elite scientists. While at other times, it was better for them to keep their views to themselves.

This event is informative about the changing status of biotech entrepreneurs and their working relations with the regulators in China. The gradual but decisive change of position and relations between biotech entrepreneurs and the regulators was not the

result of years of advocacy work by biotech entrepreneurs, but was instead a response to a more important change in the contemporary: the rise of the 'Chinese Dream' and the institutionalisation of 'innovation-led development' policy. I will discuss these changes and linkages in the next chapter.

When toolised medicine becomes a business plan: a reflection

The regulatory change to stem cell clinical research and practice adversely affected all biotech entrepreneurs who started their businesses prior to the regulatory change. During the regulatory impasse, while the chance of survival for small business owners became too slim for them to stay in business, more established companies took the regulatory change as an opportunity to put forward to regulators their business visions and to strengthen their leading position in biotech industries.

During the regulatory change, these biotech companies' varied business strategies also illustrate how biotechnologies are tooled into businesses ideas and models and subject to market evaluation. In the marketplace, as my interlocutors liked to remind themselves, 'risk and opportunity coexist'. While making decisions about which biotechnology to invest in and which to forgo, biotech entrepreneurs not only evaluated and promoted the utility of a biotechnology in a promissory manner, but also took precaution against foreseeable regulatory risk.

As a result, while the regulatory impasse took its toll on stem cell clinical research and related industries, biotech entrepreneurs started to shun away from stem cell clinical research and product development and to relocate their resources into areas such as immunotherapy and genetic testing. When possible, big players tried to nudge the regulatory change towards a direction that favoured their individual and collective enterprises. Nevertheless, unlike leading scientists (who, as technocrats, had direct access to regulators and politicians at a higher level), these biotech entrepreneurs had to use publicity work in the marketplace and government work at the local level to try to reach the final decision-makers on 'the top'.

In this process, biotechnologies, including stem cell-based biotechnologies, were devised as a tool and incorporated in these biotech entrepreneurs' business strategies,

publicity and advocacy work. When biotech entrepreneurs choose which biotechnologies to use for securing their survival and developing their industry, the biotechnologies were weighted against one another more for their value and risks in the marketplace and politics than for their medicinal potential. Yet, once a winning technology is chosen as a result of their accumulated individual decisions, those biotech companies are bound to change. While Chinese stem cell research-enterprise took shape, much of the burden and cost were borne by small business owners, clinician-researchers, and patients whose preferences and needs of developing or using stem cell therapy were rendered secondary. I focus here the effects on small business owners and startup companies, and, in the next chapter, will reflect on the effects and implications of the regulatory change on other groups.

The 'mess': old and new

Prior to and during the regulatory change, small stem cell companies were commonly perceived as mess-creators. They were distrusted as exploiting both stem cell science and patients, because they lacked sufficient resources to develop stem cell therapy properly but needed to make profits to ensure market survival. As in the case of Wei Zexi, those small companies were noted as primarily working with military, armed police and private hospitals in selling patients unproven and unauthorised stem cell therapies. They were further criticised for exploiting the regulatory loopholes and system flaws within health care system and medical institutions.

When Dr Bai first told me in March 2014 that, by late 2013, most small business owners had already forgone their projects that had direct links with stem cell clinical practices, I was sceptical of his claim. I wondered why the media and literature reported that the "mess" of stem cell therapy continued, when most programmes and businesses were closed? So I asked him,

> 'Where did they go?'
> He shrugged, 'Most stayed in related business. After all, as a whole, this is a large enterprise. Even if one cannot work on [stem cell] therapies, there are plenty things one can do.'

I nodded but marked on the margin of my notebook, 'To verify'. I later found that only a few small companies remained active in stem cell clinical research among which was

Dr Miao's company, which I introduced earlier. I learned that most former stem cell entrepreneurs and their employees switched to working with stem cell therapy's sister - immunotherapy. I gradually discovered a plausible reason why the mess hovering around stem cell therapy seemed to continue. It was a different kind of mess. Cell-based products were designed for health related, but non-medical, purposes, such as anti-aging, health-maintenance and cosmetic treatment. Compared with those investigating experimental stem cell therapy, the non-medical use of cell-based products was not publicly advertised and largely operated with discretion. I found far less news coverage on this topic, except a notable one published in 2012 (Lv, 2012). My clue to uncover these practices came from Dr Bai.

As if he detected my doubt, some months after our first meeting, Dr Bai invited me to visit a stem cell company that he thought would interest me. It was a pre-arranged meeting between Dr Bai and Mrs Fei, the company's founder and CEO. In preparation for the meeting, Dr Bai told me that he would introduce me as a researcher interested in stem cell research and practices in China - which is broadly true - yet advised me not to ask too sensitive questions regarding the regulatory change. We met Mrs Fei in her office, where I noted her company specialised in health maintenance (*yangsheng*, 养生).

At our meeting, Mrs Fei and Dr Bai discussed emerging cell therapies and her questions were focused on safety. She also updated Dr Bai on her research team's observational studies on her clients' treatment and her clients' own evaluation on using these cell-based products. She cited examples given by her clients, such as feeling energetic, looking younger and improved sexual performance.

Coming out of that meeting, I told Dr Bai about my surprise seeing a biotech company in an old residential building in the undeveloped suburb of a cosmopolitan city. Dr Bai first commended my good behaviour at the meeting - I spent most time listening and smiling - and then gave his impression of Mrs Fei, who he had known for a couple of years,

> 'It's part of the nature of her business that her high-end clients valued most their privacy. It's her discretion and meticulousness that wins her clients' trust. What you saw there is just a meeting venue for her to meet people like us, [while] her clients are treated elsewhere…As you saw yourself [at our meeting], as a former

> nurse, she is very thorough. Unlike many others, she does not chase the most fashionable [treatment]. She priorities safety and services in treating her clients. She has assembled her research team, and gives them plenty time and resources to develop and test new treatments…'

His description helped me understand why Mrs Fei invited Dr Bai for a private meeting, and why a researcher from a well-known research institute was scheduled after ours to meet with Mrs Fei. During my brief encounter with the researcher and his assistant, they mentioned that they were going to introduce some promising research results to Mrs Fei and discuss with her potential collaboration with their spin-off company.

In late 2014, a foreign science journalist and friend mentioned to me that once she visited a beauty and health maintenance centre that offers cell-based treatments almost exclusively to foreign customers who demand high-end services and protection of privacy. The umbrella company specialised in developing stem cell therapies for treating diseases, yet has been operating this side business for years in discretion.

Compared with using stem cell-based products for beauty or health maintained purposes, during my fieldwork, I heard people talk about using immunotherapy more often. The slogan 'We serve only the bosses!' was on a brochure a company executive gave me at my site visit. The company's campus was located near to a famous local mountain and about two hours' drive away from the city centre. It not only operated its own world-class laboratory, but also acted as a retreat where its high-end clients - mainly businessmen from the region and a few local politicians - would come to receive immunotherapy for maintaining and enhancing their health. Nevertheless, similar to the umbrella stem cell company that my journalist friend visited, that immunotherapy company's main mission was to develop cancer treatment. Its health maintenance services were operated discretely and not advertised publicly. Its founder - a returnee and patent-holder of the company's core immune-cell technologies - seemed slightly embarrassed when I asked about the results of their health maintenance treatment. The use of cell-based products for anti-aging, health-maintenance or cosmetic purposes is considered by almost all practitioners who I met as 'lacking any scientific evidence'. Yet, because there is no regulation on using cell-based products for non-medical purposes, the market is expanding (Mo and Yang, 2018). Its founder gave me a similar answer as that of Dr Miao: 'We need to produce our own "blood" to sustain the

“lifeline” our company’. In other words, they considered side-business as a source of income to support research and development activities.

It is important to note that using cell-based products for reasons other than treating diseases should not be dismissed altogether as nonscientific or advertising hype. Cell-based, anti-aging treatments are under development in research laboratories (Kaiser, 2016; Adee, 2017). I have also shown in proceeding chapters that, even in the clinical settings, patients and patient families may integrate other values and meanings into their use of cell therapies. Moreover, scholars such as Rosemann and Chaisinthop (2016) note similar operations exist in other countries. So these operations are not unique to Chinese cell industries, and they illustrate how the biological capabilities of cells can be retooled for non-medical purposes. Nevertheless, the regulatory change to stem cell clinical research in China, in effect, accelerated the development of the non-medical use of cell-based products by driving small business owners out of stem cell clinical research and product development and into greyer areas where one could still make a living. Moreover, as I described before, amid the regulatory and market uncertainty, even big players such as Zhongyuan Union and Beike distanced themselves from stem cell clinical research and product development, and diversified their business portfolios. Thus, biotech companies have also been retooled by this regulatory change.

The price to pay for survival

In the previous section, I introduced an M&A deal between Zhongyuan Union and Beike as part of Zhongyuan Union’s repositioning strategy. This deal is also informative about Beike’s experiences during this regulatory change and about biotech industries’ development in China in general.

I mentioned earlier that Beike’s business was among those most adversely affected by the regulatory change. Almost all practitioners and observers of stem cell industry, who I met, knew that Beike had been struggling to survive. But for the same reason that they viewed Beike as a serious stem cell company, practitioners seldom discussed Beike’s fall and harsh situation publicly. When Zhongyuan Union celebrated its partial acquisition of Beike, in social media and internet forums, many practitioners

nevertheless left messages such as ‘what a pity [for Beike]’, ‘he [Dr Hu] sold it cheap’ and ‘no wonder, Zhongyuan Union is a shark’.

This sentiment towards Dr Hu’s selling short his ownership of Beike to Zhongyuan Union was expressed also by Dr Bai shortly after he told me the side road news about the possible acquisition deal. After he commented on Zhongyuan Union’s stock price and grinned, Dr Bai fell silent for a few seconds. His silence occurred so suddenly that perplexed me. While I was trying to figure out how to respond, to my relief, Dr Bai broke his silence.

> He changed the subject to Beike: ‘Back then, Beike should have invested in cord blood [banking].’
> I thought about how, not so long ago, Dr Bai had also praised Beike for being serious about stem cell research. I felt slightly baffled now that he now implied Beike would have been better off not doing so. I also remembered that Beike had in fact entered cord blood banking business. So I tentatively asked Dr Bai: ‘But Beike has business in cord blood too, no? So you mean…?’
> He slightly nodded, then shook his head and explained,
>
> ‘Yes, it [Beike] did. But it was too late then. Beike specialised and made a name for itself early on in stem cell therapy, right? [But] it missed a critical business opportunity in cord blood [storage banking] in those early years too. [*long pause*] But who would know then the [business of] stem cell therapy was about to slump? [*short pause*] Then, when the therapy [related business] went south, Beike had to cut its business, lay off staff, [and] many talents left [Beike] under its restructuring… [and] when Beike finally turned to [cord blood] storage business for opportunity, the licences [for cord blood banking] had long been distributed [by the health authorities] among Zhongyuan Union and others.[66] [*short pause*] well, that storage business made Zhongyuan Union a fortune, didn’t it?’

Dr Bai’s voice fluctuated with sighs and frowns. I realised that he was not as excited about Zhongyuan Union’s deal with Beike as he first appeared to be. He not only felt pity about Beike’s selling short, but was also unimpressed by Zhongyuan Union’s success in this deal. Some other practitioners expressed their reservation about Zhongyuan Union more explicitly in jokes. They commented that Zhongyuan Union’s enlarged business ambition and plan to ‘cover the entire chain of biotech industry’ illustrated a popular saying in today’s China, ‘Rich man can play as one wants’ (*youqian jiu keyi zheme renxing*, 有钱就可以这么任性). Some were more critical and suspected that the main reason behind public companies’ purchasing startups was to

[66] See Chang (2017) for detail on the licensing and relative policies on cord blood banking in China.

increase their stock prices by 'fooling the little investors (*guming*, 股民)'.[67] Whereas working in the same enterprise and with the same regulatory uncertainty, practitioners and industry observers read those deals and accompanied publicity work with a grain of salt.

Nevertheless, my interlocutors seldom spoke with those outside of the industry about their criticisms of big players' business strategies. In public, most of them acknowledged Zhongyuan Union's leadership role in stem cell related industries and wished it succeed in expanding its business.

Despite their reservations about public companies using publicity to attract the attention of small investors and investment through the stock market, my interlocutors often acknowledged that this was part of the business and what need to be done. They cited reasons such as the nature of 'this cash burning (*shaoqian* 烧钱) business'. In this cash burning business, some considered that, it is less a choice of the big players than an inherent rule of the game. That is, those who aspire to be the industry leader must keep innovating and investing into research and development (R&D), and they must also keep seeking investment to ensure they stay in the business long enough to start to make profit from early investment into R&D. They added that the uncertain regulatory situation had made it nearly impossible to get investment from investment industries which are 'short-sighted' and focused on immediate return.

My interlocutors' understandings of 'the rules of the game' - business model and the influence from the investment industries - echoed what are also commonly believed and practised by biotech entrepreneurs in countries such as the United States (Booth, 2017; Lazonick and Tulum, 2011), the United Kingdom (Ginty et al., 2011) and Canada (March-Chordà and Yagüe-Perales, 2011). Their criticism of the ignorance of investment industries on the specificities of biotech industries is also voiced by social science researchers who caution against the weakness and flaws embedded in current biotech business and financialization models (Pisano, 2006; Hopkins et al., 2013; Lehoux et al., 2014). In addition, my interlocutors were acutely aware that investment

[67] The Chinese stock market has performed poorly in recent years. It is reported that 'big sharks' commonly relied on insider's news on trading and squashed money from small investors (Agence France-Press, 2016). Hertz's (1998) ethnography of the Shanghai stock market documents such inside trade and corruption problems.

industries are young, inexperienced and sensitive to policy changes in China (also see Chen et al., 2004; Qiu et al., 2014) and that, in times of regulatory and market uncertainty, entrepreneurs were not well positioned to bargain with potential investors, if any ever approached them.

Given their shared experiences of working in the same stem cell enterprise under accumulated regulatory and market uncertainty, most biotech entrepreneurs who I met were thus empathetic towards Zhongyuan Union's business strategies even though, they felt pity for those being disadvantaged during Zhongyuan Union's aggressive expansion and manipulation of the stock market. Overall, they wished leading companies such as Zhongyuan Union success in executing their business plans so that 'the shared cake could be made bigger' for everyone who survived the regulatory impasse.

Dr Hu, the chairperson of Beike, used the same rationale in adjusting his professional and business views during the regulatory impasse. In April 2015, Dr Hu told the audience at the aforementioned *Special Dialogue*,

> 'People *still* often ask me about my selling [partial] ownership to Zhongyuan Union. Well, we all know that Zhongyuan Union is a good company, [and] collaborating with them makes us both stronger. For myself, to be honest, many others don't believe this, but I don't care much about personal gain or loss [*smile, brief pause*]. I used to think that I am a scientist, a doctor [PhD holder], and never liked attending business networking events [*yingchou*, 应酬], especially business meals. I cannot even drink much [*titter*]! But now I have learned to go, to meet with [local] officials, big bosses of estate-, coal- and whatever industries. I would go and tell them that it is a golden opportunity for *them* to invest in *this* [biotech] industry [*forefinger pointing downwards*]. We [Beike] have technology, expertise, management and operational skills, [while] they have land and money, right? If we strike a deal, it will be a win-win situation. If not, it doesn't matter. I will go to [meet with] the next one. [When I] think about it, it's like I, *Dr Hu*, am working in estate industry now, [but] what I want to do is to build cell banks and factories that will bring the locals health, jobs and economic growth…'

Though Dr Hu laughed and stated that he didn't care about his personal transition and changes that needed to be brought to Beike, his tone gave away his sentiment towards alternating with his primary identity as 'Dr Hu, a science guy'. 'The scientist Dr Hu' was also the image that once helped to earn practitioners' respect and supported their beliefs that Beike was serious about stem cell research. But now Dr Hu chose 'not to

care' in order to do what needs to be done: to make new contacts, visit new places, and seek new business models that could keep Beike alive amid regulatory change.

When Dr Hu stepped down from the podium, I thought about something Mr Fang had recently told me, 'In this business [of stem cell], if you cannot afford such market and regulatory risk, then don't play'. When I met Mr Fang he was the founder and executive manager of a headhunting firm. Prior to starting, Mr Fang had worked at a stem cell startup company from 2010 to 2013. He told me,

> 'It was my first job after got my master degree [in bioengineering]. I liked it. It was exciting. The research, the treatment and product that we were developing, [and] the collaborations with doctors and interactions with patients. [*short pause*] We had some good times, but I cannot afford staying much longer when the business went south after the ban [was issued by MOH]. It is, after all, a cash-burning business. My [former] boss had so much trouble in finding new investment to help us change [business model]. Some [practitioners] say the industry is now reshuffling the cards. Sooner or later, we would become 'ashes after burn[ing much money] (*paohui*, 炮灰). Sorry [to my boss], but I don't want to get burned myself.'

In the next chapter, I will take a closer look at the cash-burning biotech industries. I suggested earlier that in China today, the heightened fever towards biotech industries is cultivated in a wider socio-political context. Nevertheless, the dreams to create the next unicorn company in the health sector or a Silicon-Valley biotech centre abound in the world (Pfotenhauer and Jasanoff, 2017; Bharadwaj and Glasner, 2009; Thompson, 2008). Similarly, the analogy used to compare developing biotechnologies and related business as game or play has been reported in other biotech fields such as marine biotech (Helmreich, 2007) and synthetic biology (Souleles and Scroggins, 2017). During this thesis, I have pointed out that China's new regulations on stem cell clinical research were made in response to both the contemporary social-political context in China and to the specificities of stem cell-based medicine, yet were also influenced by research and regulatory activities outside of China and stem cell research. I have suggested that the practices and use of unruly stem cell therapy in grey areas has been sustained because biomedicine has become toolised. I have devoted the proceeding chapters to recount how I came to learn about this tool-like feature of cell therapies and develop the concepts of toolised medicine and tooling work. In the next chapter, I put these two concepts into use to assess this recent regulatory change in China and discuss some of its observable effects.

CHAPTER SEVEN. The regulatory exercise as (re)tooling work

In this chapter, I will assess China's regulatory exercise using the lens of toolised medicine and tooling work. I suggest that regulatory change to stem cell clinical research and practices mirrored the wider integration of biomedicine into China's continuous nation-building project. Linking with preceding chapters, I underline how, during this regulatory change, stem cell-based medicine came to be valued by the regulated and the regulators for its potential in supporting the realisation of the Chinese Dream.

I will first introduce the new regulations and their intermediate nature. I will then discuss the rise of biotech industries in China in recent years and how, during regulatory change, a renewed Chinese stem cell research-enterprise is formed and consolidated. I will then use the lens of tooling work to assess the intermediate regulation and its effects.

The new regulations on stem cell clinical research are the first devised for biological entity-based medicine development in China and they have started to be used as a reference point for China's regulation of biopharmaceutical product development and marketisation. The effects of this regulatory change go beyond those being directly regulated and require continuous research. In the last section, I will discuss some of the current effects of the regulatory change. I will also broaden my reflections on the ethics of (bio)medicine.

The new intermediate regulations

On 20 August 2015, NHFPC and CFDA held a joint news conference and announced the publication of the *Management Measures on Stem Cell Clinical Research (Interim)* (NHFPC and CFDA, 2015c). The next day, the news was aired on CCTV premier morning news, and re-aired on the midday news (CCTV13, 2015a, 2015b). The regulation was reported as China's first regulation on stem cell clinical research. Its development was based on the principles of 'scientific, standard, transparent,

conforming to ethics, and adequately protecting the rights and interests of research participants' (*kexue*, *guifan*, *gongkai*, *fuhe runli*, *chongfen baohu shoushizhe quanyi*, 科学、规范、公开、符合伦理、充分保护受试者权益) (*my translation*). One third of the two-and-a-half minute news report showed an official from the NHFPC stating the significance of protecting research participants during stem cell clinical research, and explaining the institutional and procedural requirements set out in the regulation (ibid.). News stories reported by print and social media repeated both the emphasis on the regulation being 'the first' introduced by Chinese authorities on stem cell clinical research and the institutional and procedural requirements (H.Hu, 2015; Xiao, 2015).

A second regulation on quality control and preclinical research (NHFPC and CFDA, 2015d) was also published as a supplement to the regulation on clinical research. To a large extent, the publication of the new regulations received positive responses from stem cell practitioners in China. Among those I know from my study, it was welcomed more by laboratory-based scientists and leading biotech companies than clinician-researchers and small business owners. While a few clinician-researchers and biotech entrepreneurs publicly questioned the vagueness and impracticality of the new regulations, most only voiced their views anonymously in internet forums and social media, or said nothing about the new regulations.

The core of their concern was where the regulatory agencies expected the stem cell industry to go next and what roles biotech companies could play? The main confusion, discussed in a social medial group where I was a member, came from Articles 51 and 53 of the main new regulation (NHFPC and CFDA, 2015c),

> 'Stem cell clinical research completed under the guidance of this regulation must not be applied for clinical usage (Article 51).'
>
> 'This Management Measure is not applicable to…stem cell clinical trials that intend to apply for drug development. Following this guideline and completing the stem cell clinical research, if one intends to apply for drug-registry clinical trials, one can submit the research results as part of the application materials to be used as drug evaluation (Article 53).'

According to Article 51, achieving positive results would not lead to clinical application. According to Article 53, 'clinical research' does not equate with 'clinical trials' that aim to apply for 'drug' authorisation. In online discussions, some raised the

question, ‘What *exactly* would come out of stem cell “clinical research”?’ A member pointed out that Article 53 has a clause saying the results generated from clinical research can be used as evidence in applying for drug clinical trials. More members joined this discussion, trying to determine whether the new regulations signalled the regulators’ intention to regulate stem cell-based medicine like a drug in China, and whether or not stem cell clinical research is an optional or necessary step for one to apply for permission to conduct stem cell clinical trial.

These questions had been raised before when the two consultative versions were published in March 2013 and March 2015 (Meng, 2014; Bubuxiansheng, 2015). This finalised version did not clear the cloud hovering above stem cell clinical research, such that practitioners continued guessing about the ‘real intention’ of the regulators.

Some members questioned the regulators’ rationale and competence in understanding stem cell-based medicine and the high stakes involved in securing the Chinese market and competing at the global level. Yet, as suspected by Rosemann and Sleeboom-Faulkner (2016), and suggested by some of my participants, it is also likely that the Chinese health authorities tactically chose not to answer these questions that most concerned the practitioners.

I partly agree with their interpretation. Nevertheless, from the lens of “toolised medicine,” I contend that to assist Chinese practitioners and companies in competing at an intensified global biomedical industry is not the sole reason why the Chinese regulators chose to introduce an ‘interim’ regulation. They also did so because the rationale to develop stem cell-based medicine is premised on the potentiality of stem cells to make new medicine, even though, in practice, stem cells are ‘unruly’ (Haddad et al., 2013). In other words, while the answer on the best route to develop stem cells into stem cell-based medicine remains open, regulators in China have no optimal solution to regulate its research and product development. This is a challenge that regulators in other nation-states also face (von Tigerstrom, 2008; Zarzeczny and McNutt, 2017). Whereas their counterparts in Europe, Canada, Australia, South Korea and Japan have given tentative yet industry friendly answers, Chinese regulators were increasingly pressured to update their answer.

It is important to note that this is not the first attempt that the Chinese health authorities made to regulate stem cell therapies. This regulatory change is specific about how to regulate stem cell clinical research in China, yet it was also an attempt by the MOH to fix its failure in regulating stem cell therapy as medical technologies. As explained in chapter three, the MOH entrusted professional societies with the task of developing technological guidance documents for each category three medical technology, but did not implement those guidance documents. When Dr Wei praised the regulation on medical technologies as a 'real innovation', he meant the designation of medical technology fitted well with how cell therapies are used in clinical settings. He was let down by the regulators when they did not act on the draft technological documents, which thus left a loophole for practising cell therapies. He was further disappointed that the regulators now wanted to replace this 'really genius' regulation with an unworkable one.

The MOH introduced the regulation on medical technologies because it anticipated that new medical intervention such as cell therapies would be adopted by hospitals and that regulation and standardisation of clinical practices would be required. It was expected to curtail stem cell tourism and discipline the field (Chen, 2009). As shown in Beike's subsequent changes (Sleeboom-Faulkner, 2016), this regulation did achieve this aim to some extent. The messy expansion of cell therapies in Chinese hospitals, however, emerged during weak implementation of the regulation and oversight of practices. As the MOH was no longer able to regulate the clinical practices of stem cell therapies (which had received harsh international criticisms), it had to fix the mess with a new regulation. This explains why stem cell therapy was singled out from category three medical technologies for regulatory scrutiny. It further explains why, when the regulatory change was first announced, it had a clear direction to bring practices in China more into line with the internationally recognisable translational research model and to mandate clinical trials for developing stem cell therapy from initial laboratory-based research. The governmental structural change that ushered in this regulatory change also provided additional time for practitioners to debate whether this original plan was a good idea. Accordingly, the regulator was challenged with a new task of providing regulatory guidance for the development of stem cell-based medicine through clinical research in China. In section three, I will have a closer look at these changes.

Biotech industry as the next storm

Similar to the United States and Europe (Staffas et al., 2013), biotechnology is considered by the Chinese government as a new engine for economic growth and a matter of national competitiveness and security in the 21st century (Li et al., 2004; Ellis, 2018). Local governments have started to compete with one another to hone talents, biotech enterprises and investors in order to create the next unicorn companies in biotech industries, thus pursuing the lead set in the information and communication technology (IT) industries that produced 'legendary' enterprises (Deng, 2018). Successful stories of how Chinese entrepreneurs made a fortune in IT industries were enthusiastically reported in the media and talked about by biotech entrepreneurs and investors who I met in this study. Like the Shenzhen government, my interlocutors shared the same belief and enthusiasm towards the future of biotech industries.

In many aspects, the construction of stem cell research-enterprise in China that I am about to illustrate in this chapter, resembles the promissory work done in other countries which have been investigated by social science researchers. For instance, using the sociology of expectation and science and technology studies, scholars such as Brown and Morrison have critically investigated how science, policy making and market activities have co-constructed a promissory field of stem cell research in the United Kingdom (Brown et al., 2006; Morrison, 2017, 2012). Scholars have also provided more general critique on bioeconomy (Brown, 2003; Petersen and Krisjansen, 2015; Goven and Pavone, 2015; Birch, 2012). Rather than adopt a direct critique approach, I focus instead on analysing those who contribute to the construction of Chinese stem cell research-enterprise and I use their anticipatory work as a lens to study contemporary China and biomedicine.

In describing their views towards the future of biotech industries, my interlocutors liked to quote from Lei Jun, 'A pig could fly if it finds itself in the eye of a storm' (站在台风口，猪都能飞上天) (He, 2012). Lei Jun is the founder and CEO of smartphone company Xiaomi Tech. Lei founded Xiaomi in 2010 and entered the world market in 2015 (Dou, 2015). By July 2018, Xiaomi completed its initial public offering on the Hong Kong stock market (Lau and Zhu, 2018). In this phrase of 'standing at the wind',

the Chinese character 风 (*feng*) for wind is used for its figurative meanings - like a wind - and refers to two things: trend and venture capital. Using this pun, Lei attributed Xiaomi's instant success to the timely identification and execution of an optimum business opportunity where investment industries are ready to invest.

In talking about their ventures, my interlocutors liked to use this phrase and the 'flying pig' theory (*feizhu lilun*, 飞猪理论) it generated. The essence of the flying-pig theory is that entrepreneurs must be able to identify the strongest emerging opportunities in both technology innovation and investment industries and prepare oneself accordingly. They believed that they now stood in the eye of the storm. They enjoyed the humour and hopefulness in using this phrase, 'If a wind can make even a pig fly, how could an entrepreneur not succeed with one's venture in the right time?'

In addition to the general enthusiasm towards developing biotech industries in China, practitioners also liked to talk about the importance of strengthening a Chinese stem cell research-enterprise amid increasingly intensified global competition. While companies such as Zhongyuan Union stretched businesses into biotechnologies other than cell related ones, companies that were once specialised on other areas such as pharmaceuticals and genetics marched into cell related industries (WuXi AppTec, 2016; GE Healthcare and BGI, 2012). As their news releases show, these companies consider themselves to be Chinese biotech companies with global competitiveness and vision, and aspire to become global leaders in biotech industries. The vision these companies share is that biotechnologies are about to reshape how medicine, health services, agriculture and environment are currently understood, organised and managed. As visionary biotech companies, they must grab new business opportunities and move fast to position themselves at a leading position in this expanding globe research-enterprise.

These Chinese companies are not alone in envisioning this future for bioindustries. Successful American biotech companies such as Amgen have shown how startup biotech companies can grow into notable size and reshape the pharmaceutical industry (Owen and Hopkins, 2016). A success that politicians and industrialists in other countries, including the United Kingdom, Germany, France, Switzerland and Japan, are eager to replicate, yet find challenging (ibid.). Chinese biotech companies and investors

only recently appeared on the global stage but have received attention from industry analysts. For instance, Lawrence (2017: 414) notes that ever since the number of active biotech venture capital investors in Europe and the United States started to fall in 2014, China has been the only country that has seen an increase in investors. The investment interest came from both domestic and foreign venture capitalists who estimate that China will 'Eventually be the largest healthcare market in the world' (ibid.: 415). Their enthusiasm is further boosted by the observation that 'The big change in China over the past three years is a really big push [from the Chinese government] toward innovation' (quoting Gordon, in Lawrence 2017: 415).

These Chinese companies also share with established pharmaceutical companies the use of M&A deals in business expansion and strategic positioning, and an interest in investing in cell therapies. For instance, Micklus and Muntner show that, since 2014, M&A deals between biotech companies and big pharmaceuticals performed the best among different types of business deals (Micklus and Muntner, 2018). They also note that immune-oncology has attracted the most interest and volume of capital investment in the past years (ibid.) In 2016, cell therapy not only overperformed other biomedical sectors in attracting capital from the private sector, but also was the only one that attracted 'an increase in the number of financings' (Lawrence, 2017: 415).

Yet, as I discussed in chapter six, business strategies of Chinese biotech companies are also influenced by policy and regulatory change in China. While the regulatory change to stem cell clinical research and practices affected the existing industry landscape of stem cell related industries in China, industry leaders also tried to make their 'industry's perspectives' heard by the regulators. I mentioned that in the final stage of making the new regulations, regulators finally responded to the advocacy work of biotech entrepreneurs. Yet, I stressed that wider social-political change in today's China led regulators to reach out to biotech entrepreneurs for their inputs on finalising the new regulations. In the next section, I resume my analysis on this point and deepen my discussion on the changing status of biotech entrepreneurs and their working relations with the regulators in China. I start by introducing Dr Zhu, a part-time biotech entrepreneur who, like a few other professionals that I met, was comfortable with their multiple identities of stem cell scientist, doctor and founder and chairperson of a stem cell company.

Global science, Chinese enterprise

Dr Zhu is a pioneering stem cell researcher and entrepreneur who specialised in haematology and cord blood banking. He started his career in medicine and mostly considered himself as a doctor. Though he focused his research on preclinical studies, he has a clear aim to use the research results to guide development of specific products.

I first heard about Dr Zhu's work in my previous job at a genomics research institute. During my fieldwork, I saw him at almost every conference that I attended. Like Dr Wei, he was not a member of the Expert Committee but was familiar with the Expert Committee members and vocal about the regulatory change. He was more popular among clinician-researchers than Dr Wei. Science journalists often interviewed him for his expert opinion, not only because he appears more approachable, but also because he maintains dual research in the laboratory and the clinic.

In recent years, as shown in his publications and conference presentations, Dr Zhu focuses his research on developing methods to compare the safety, efficiency and viability of different types of stem cell in the preclinical setting. Dr Zhu's research attracted interest from both laboratory-based scientists and clinician-researchers. He was among the few people I met during fieldwork who was invited by both scientific and medical societies to attend their professional conferences as a keynote speaker. His conference presentations are among the most popular among attendees and his conference powerpoint slides were often photographed and uploaded on internet forums and discussed in the WeChat groups that I joined for this study.

After briefly conversing with him on a few other occasions, on a summer evening I eventually seized an opportunity to interview this busy man during a biotech industry conference in April 2014. Among various topics we discussed over 90 minutes, Dr Zhu's reflection on his career trajectory and the role of biotech entrepreneur left a lasting impression.

After our interview, I highlighted his monologue and noted in the margin that this might be of importance for my future fieldwork. The following excerpt is taken from that monologue which gradually became more important to me during my research.

> ‘I have been working in this field [of stem cell] for nearly thirty years. When they [a prestigious medical research institute] asked me to return to China [from Europe in the early 1990s] and join them, I thought: “Great! I can use what I learned for my people and country.” I soon realised there wasn’t much opportunity for me to do real translational research there. I didn’t see the point of working solely on the so called basic research either.
>
> I was trained first as a doctor and then started my science training in Europe. I really wanted to put our research into good use. So [in late 1990s] I decided to give the Director’s position [at that medical research institute] to others and started to build the [stem cell] industry. I’ve kept my lab and continued my research and training Ph.Ds there. We ask in our research questions such as which stem cell works best in clinical settings, through what procedure and in what circumstances, how to do quality control along the way. Those studies will not just sit on the shelf to boost one’s own [scientific] career. They are of clinical value and done first for patients.
>
> Many people had questioned why I got myself into the *business* side. In China, the academic culture is still very much against business. I know that, [*short pause*] behind my back, some say I am after money and I am no longer a *real* scientist. I kinda got used to that and no longer feel the urge to explain myself. But, as you probably know well, if one looks at the US, it is common for scientists to join relevant industries to create *social* wealth…
>
> It [working in the industry] was very hard at the beginning…the criticism and cynicism from my own colleagues, on top of exploring the business world. But I believed in what I am doing: we have such a wonderful thing - stem cell - to work with and for the patients, *how can you just let your research gather dust on your shelf*? I have faith also in the future of China’s stem cell [industry]. I just keep going.
>
> After more than twenty years, you can see people’s attitudes started to change, especially nowadays among the young people. Like yourself, young people understand better the importance of making science matter to the real world and are more positive about entrepreneurship. [*short pause*] It is also a different time now [compared to the 1990s]. Innovation is getting so much support from our leaders now, and no one would feel ashamed to say that I want to start a business with my science. It almost feels like [*pause, with a wry smile*] everyone is an entrepreneur now!’

In this monologue, Dr Zhu aptly linked his research experiences and career trajectory with his observations about academic culture and the wider, changing socio-economic and political context in China. As Dr Zhu noted, changes in the social status of entrepreneurs and, in particular, the endorsement of scientist-entrepreneurship, was directly influenced by China’s current leadership and their recent political and social-economic reforms. It was also an emulation of the ‘American’ way to make science ‘create social wealth’.

‘Big science’: emulating the Americans, doing it in a ‘two bombs, one satellite’ way

Senior practitioners such as Dr Zhu often contrasted the ‘situation in the US’ (*meiguo de qingkuang*, 美国的情况) to that in China. As I mentioned in chapter three, at conferences, Dr Xu liked to present a table of research and regulatory situations in Europe, the United Kingdom, Canada in comparison with China. To a lesser degree, Japan, South Korea and Taiwan are also included in those comparisons.

Chinese practitioners are not alone in these comparison exercises. In stem cell research and regenerative medicine, there is no shortage of comparison between nation-states whether about research funding and policy to specific laws or about regulations on the use of research materials, intellectual property and market authorisation (Taupitz, 2017; von Tigerstrom, 2015). Stem cell scientists, biotech companies and industry observers in countries such as the United States and the United Kingdom also deploy similar comparisons to lobby their governments to create favourable regulatory environments for stem cell research and industry development (Fowler, 2003; Harvey, 2011; Charo, 2015). More recently, Japan and South Korea’s regulatory innovation in stem cell research and regenerative medicine have caught worldwide attention (Reardon and Cyranoski, 2014; Faulkner, 2017; Hogle and Das, 2017). Given the global leadership of the United States in pharmaceutical and biomedical research and industry, its research policies and regulatory framework in biotech industries are commonly used by other countries as a benchmark to follow.

Although doctors such as Drs Zhu and Xu stressed that other nation-states are confronted by how to develop and regulate stem cell-based medicine, stem cell clinical research and practices in China portrayed the regulatory situations in other countries as better than the Chinese situation. The comparisons were used as a trope to advocate the development of a more enabling environment for research and industry development. It is in this sense, the ‘American way’ is idealised as an epitome.

This ‘American way’ affects the direction of research activities. It is associated with ideas and ideals of academic entrepreneurship (Grimaldi et al., 2011), high-tech industry, and knowledge economy (Salter, 2009; McMahon and Thorsteinsdóttir, 2013;

Das and Lam, 2016) that aim to turn successful research into business ventures, new commodities and industries, create jobs, social wealth and progress. The Patent and Trademark Act Amendments (known as the Bayh-Dole Act) is considered pivotal for American success and gaining a global leadership role in high-tech industries. By permitting research institutions to acquire and benefit from intellectual properties that are borne from publicly funded research, the Bayh-Dole Act provides scientists and research institutions with direct engagement with the marketplace. In evaluating the effects of the Bayh-Dole Act since it was passed in 1980, Loise and Steven (2010) concluded that 'data clearly show that it played a critical role in rejuvenating the entire U.S. economic system, transforming it from a manufacturing base to an innovation base'.

To develop a 'innovation-driven' economy and society is also the route set by the current leadership in China in the 21st century (Xinhua, 2013c; Xinhua, 2016b). Earlier in this chapter, and in chapter six, I introduced the zealousness towards biotech industries among the biotech entrepreneurs and city-level initiatives such as Shenzhen's 'Biotech Valley' project (Chen, 2014). In late 2014, I started to note that the commitment to developing biotech industries in China acquired a different tone and became something larger than upgrading local economies. I heard practitioners, especially leading scientists, advocating more often for another model to develop stem cell industries in China - the 'two bombs, one satellite project' (*liangdan yixing jihua*, 两弹一星计划).

This 'two bombs, one satellite project' was launched by Mao Zedong in 1956 to develop nuclear and space power in China. It was during the Cold War. The project's success made China a nuclear power and remains relevant to China's national security and international relations today. But I was baffled by its relevance to developing stem cell-based medicine and related industry in contemporary China. Until later I realised that those who advocated the 'two bombs, one satellite project' were interested in its organisational and management mechanism and work ethos, which was a Chinese model of 'big science' (Lewis and Xue, 2008). This meant gaining more direct and decisive support from the party-state and establishing a centralised planning and coordination system to advance cutting-edge stem cell research, facilitate efficient development of related industries, while also minimising duplicated work, hostile

competition and the waste of resources (Zhou, 2017). After nearly half a century, leading stem cell researchers considered that this big science model would give them the best chance to develop a globally competitive Chinese stem cell research enterprise. In asking for more support from the party-state, they also exhibited confidence in replicating the success of nuclear scientists and bringing equivalent success to contemporary China (ibid.).

Looking back, the regulatory change granted Chinese health authorities (and their trusted advisors) the time and space to direct stem cell research in China more clearly towards realising its political and economic potential. It thus, as I suggested before, resulted from joint tooling work of the regulators, leading practitioners and certain mediators. Nevertheless, I want to emphasise again that, what enabled the change of primary 'usership' (Faulkner, 2008b) and mode of R&D and marketisation during this regulatory change was the space that opened up during the actualisation of medicinal potential from the biological capabilities of stem cells. In other words, whereas this space makes it possible to develop stem cell-based medicine from different routes, during the regulatory change Chinese leading practitioners, regulators and their intermediaries reset the options into one. The new regulations set boundaries and rules for this renewed research-enterprise, while other modes of making and using stem cell therapies were officially denounced as illegitimate.[68]

This gradual formation and solidification of a renewed Chinese stem cell research-enterprise has also changed those who partook in making the new regulations and has far-reaching effects beyond the biomedical research and industries. This more profound change at the individual, institutional and societal levels in science, medicine, the marketplace and patients' care is set in motion by the new intermediate regulations, and its effects remain to be seen. To prepare my analysis on the current situation, I will take a closer look at the intermediate designation of the new regulations.

Tooling interim regulations

[68] The regulatory intervention in immunotherapy clinical practices and business activities after Wei's death is another example (see chapter five).

At the beginning of this chapter, I mentioned that the main interim regulation on stem cell clinical research (NHFPC and CFDA, 2015c) left many questions unresolved. The most critical question was what would come out of clinical research. I have underscored that the interim designation of this new regulation should not be interpreted as evidence of Chinese health authorities' inability to devise a regulation for this novel form of medicine. Rather, it is further evidence of the difficulties in regulating biological-entity based medicine. Three years have passed since its publication in August 2015. This temporal distance gives me an opportunity to assess its intermediate effects.

Currently, the confusion around the function of stem cell 'clinical research' persists but matters less to the practitioners, especially after the CFDA published a more specific guidance document, in December 2017, on developing cell-based therapeutic products (CFDA, 2017). CFDA's new guidance document - *Technical guidelines for research and evaluation of cell-based therapeutic products (Interim)* - points decisively at developing cell-based products like a drug. It emphases the safety and standardisation of manufacturing products, yet acknowledges the novelty of cell-based products and grants certain flexibility in conducting preclinical research and clinical trials.

CFDA's new guidance document was embraced by those practitioners who had long championed developing and regulating cell-based medicinal products in line with pharmaceuticals (L.Zhang, 2017). To some extent, it makes the interim regulation on stem cell clinical research (NHFPC and CFDA, 2015c), which is now fully implemented, outdated. Yet, the CFDA neither provide clarification on whether or not this new technical guidance will apply to all research and product development activities using cells, nor on the relationship between 'clinical research' and 'clinical trials'. CFDA's new guidance document on cell-based products is, thus, not a replacement of the regulation on stem cell clinical research. Rather, as revealed in health authorities' reply to NPC members' queries on immunotherapy policies (NHFPC, 2017), immunotherapy and the events around Wei Zexi's death played a key role in the CFDA's work on this new guidance document (also see Deng and Wei, 2018). Moreover, the document is also an interim regulation.

The publication of multiple, interim regulatory documents indicate that the regulators have chosen to adopt a 'drug-like' approach as a preferred mode of developing stem

cell-based medicine at the industrial level in China, but they have not foreclosed on using stem cell therapy as medical technology. It suggests that Chinese health authorities are taking time to conduct their regulatory trials to find out the workability and effectiveness of the current versions before devising final versions. Since this trial-and-error approach fits well with the Chinese government's experimentation practices in the reform era (Heilmann, 2008), so far practitioners have given it a warm reception.

Yet, the regulatory impasse suggests that to persuade Chinese regulators to undertake this trial-and-error exercise, the prospect of developing new medicines is not enough. Two meetings with an Expert Committee member prompted me to think about this question. At our first meeting in March 2014, Dr Ni mentioned that the Expert Committee had responded to the questions raised by CFDA officials and expected that the CFDA would take a more active role in finalising the new regulations. The CFDA became a ministry-level agency and, after a recent governmental reform, is no longer part of the NHFPC. Dr Ni mentioned that since the regulatory change was initiated by the MOH to discipline stem cell clinical practices, CFDA officials had been reluctant to join the clean-up. Although CFDA representatives sat at the discussion table, they had also indicated that the CFDA only oversees pharmaceutical, nutrition and food industries, while stem cell clinical research conducted in hospitals falls under the jurisdiction of the NHFPC (see also mentioned in Boshi, 2014).

Later in my fieldwork, several others told me that the techno-scientific and clinical uncertainties involved in developing stem cell therapies further discouraged CFDA officials, who had become extremely cautious in taking regulatory risks[69]. Because those practitioners acknowledged that regulation of stem cell therapy was a challenge, they often concluded that it was not a clear-cut case of regulators evading their responsibilities. For them, the subsequent regulatory impasse was understandable, yet annoying.

In late 2014, news leaked out that the Expert Committee had reached their consensus and submitted their final suggestion to the two regulatory agencies (Boshi, 2014). In our

[69] Their caution was connected to the death of their former chief Zheng Xiaoyu. Zheng was known as a determined reformer who brought China's pharmaceutical regulation in line with the international regulatory framework, but his corruption and death were also linked with his reform (Yang, 2007)

follow-up meeting, after confirming this significant achievement among Expert Committee members, Dr Ni said:

> 'They [the two agencies] shall no longer postpone decision-making. How would one know the effectiveness of the regulation unless they let it be tested out in practice? We should not be too scared of making mistakes! The most important thing is to manage the risk and learn from mistakes.'

Dr Ni was frustrated by the stalemate between CFDA and NHFPC, but also understood that CFDA officials needed to be convinced to take on the risk of regulating stem cell clinical research, and that assurance would probably need to come from a 'higher order'. As evidenced in the preamble of the second draft regulations, the State Council eventually intervened and ordered the two agencies to coordinate and work together on drafting the new regulations (NHFPC and CFDA, 2015a). After this critical breakthrough, regulators accelerated their actions and, four months later, published the new regulations (NHFPC and CFDA, 2015c, 2015d).

Thus, the designation of *interim regulation* also gives Chinese health authorities a critical protection when taking their regulatory trial to regulate (unruly) cell therapies. In order to convince regulators to take regulatory risks, they needed assurances from higher authorities that a mistake margin would be allowed and a reformist mode encouraged[70]. This dual function of designating regulations as interim also points at a more profound effect of the regulatory change to Chinese stem cell research and related industries. That is, it also started to form new subjects that are apt for the task of renewing Chinese stem cell research-enterprise.

Tooling biomedicine through regulation: a reflection

'This [the operation of experimental stem cell therapy] is a mirror of Chinese society.'

This quote came from Dr Cen, a science park manager, when he summarised our long discussion on my research project. I first met Dr Cen during my previous work in genomics and bioethics. Like some others who had known me from my previous

[70] See also documented in literatures on local officials' experimentation activities (O'Donnell, 2017; Teets et al., 2017; Teets, 2015; Altrock and Tan, 2018).

research, Dr Cen was not optimistic about the prospect of my study. He suspected the issue I was tackling was too complex and wished me luck.

In preceding chapters, I have introduced certain aspects of Chinese society that affected my interlocutor' views and experiences with cell therapies and the regulatory change. My interlocutors liked to call them the 'Chinese contexts', while I have tried to be more specific, referring to health care reform, science and medical education, business environment, political system and government structure. Yet, I have also repeatedly stressed that my interlocutors' views and experiences taught me as much about biomedicine as about contemporary Chinese society and politics. I have prioritised the former to develop the concepts of toolised medicine and tooling work. In the last section of this chapter, I discuss what I learned about contemporary China from this study.

In 2014 and 2015, it was hard not to notice how the Chinese Dream instills itself in almost all aspects in Chinese society (Editorial, 2013), how much Chinese leaders emphasised the importance of innovation to China's development in the 21st century (Xinhua, 2013c, 2014, 2015), and how President Xi Jinping concentrates power more than his predecessors since Mao Zedong (Lam, 2015; Editorial, 2014; Saich, 2017). The terms 'Chinese Dream', 'innovation-led development', and 'mass innovation & entrepreneurship' are 'officialese' (*guanhua*,官话) like the other authoritative discourse in China that is analysed by Hansen (2017). These slogan-like phrases sound empty, yet through 'the performance of *guanhua*', they exert real-life political effects wherein 'this choreography [of social reality] was achieved' (ibid.: 48).

During the regulatory impasse, these buzzwords were not only used by Chinese top leaders, but were effectively acquired by practitioners to adjust their research and business activities and to sharpen their criticism of the regulatory impasse and pressure the regulators to end it. While internalisation gradually changed practitioners, their effective use of officialese also contributed to the change of their power and working relations with the regulators. The resulting joint tooling work to steer stem cells towards maximising its economic and political potential, as I suggested before, has far-reaching effects beyond stem cell research and related industries.

New research enterprise, new subjects

During the regulatory impasse, two phrases - 'A different game in town now' and 'reshuffling the field' - were used by practitioners, especially small business owners, to describe the recomposition of their enterprise. The main aim of this reshuffling is to upgrade and scale-up Chinese stem cell therapy related industries. Or in my interlocutors' words, to build 'manufacturing factories' (*zhibei chejian*, 制备车间) and eliminate 'small workshops' (*xiao zuofang*, 小作坊). It explains why both clinician-researchers and laboratory-based scientists invited Dr Zhu to present his research on assessing the performance of different types of stem cells in preclinical settings. While the stem cell research-enterprise underwent reshuffling, it introduced new components, discarded some old parts but kept intact certain intermediate parts, such as those specialising in preclinical studies.

Even though the two phrases sometimes sounded like a joke, by comparing their situation as being in a 'game', my interlocutors conveyed their rather powerless experiences. Because in this game, the rules are not set by the players. While the big players manoeuvre to stay longer in the game, the majority of them are too small to even be counted as a player. So rather than enjoying the game, they felt like cards being reshuffled in a poker game (*xipai*, 洗牌), where the banker of the game is a coalition of regulators (and their trusted advisors) who all take the ultimate order from the party-state.

From the lens of toolised medicine and tooling work, my interlocutors noted a change of primary usership of stem cell based-medicine and related industries from patients and practitioners to the party-state. In the party-state's tooling work, stem cell's medicinal potential serves as a base for developing economic and political value, but its priority has sunk in the party-state's 'value practice' (Dussauge et al., 2015.).[71] One notable implication of this change of primary usership and the party-state's tooling work is that it effectively turned stem cell research and industry development into a political project, and started to form new subjects in contemporary China to work towards this goal.

[71] Dussauge et al. (2015: 6) propose a 'paramagnetic, practice-based definition of values' as 'things to be explained and explored' and advocate for studies on 'the making of values'.

Scientist-entrepreneurs as patriots

As mentioned earlier, in mid-2014, Dr Zhu was disappointed that 'the academic culture is still very much against business'. Among the most popular officialese that nudged a change of position among the academics are 'innovation-led development' and 'mass entrepreneurship and innovation'.

'Innovation-led development' affirms that innovation is valuable to the nation-state and, at the same time, requires innovation being responsive to the direction of the nation-state. In contemporary China, this development goal is set to actualise the Chinese Dream – a dream about 'great rejuvenation of the Chinese nation' that was first proposed by President Xi Jinping in 2012 (Xinhua, 2013b). 'Mass entrepreneurship and innovation' further orders every Chinese citizen to think as a potential entrepreneur and to help release the total innovative energy in Chinese society (Yan, 2014; Ye Wang, 2015; K. Li, 2016). Who would then, be better positioned than researchers working in areas with industrialisation potentials, such as biotechnology, to answer this call from one's country? Indeed, as Dr Zhu projected, 'everyone [working with stem cell research] is an entrepreneur now!'

Since then, the Chinese government has officially endorsed science entrepreneurship and big science. In 2015, Chinese legislators added a Bayh-Dole-like clause to China's existing law on technology and knowledge transfer (NPC, 2015). In 2018, the State Council further encouraged Chinese scientists and innovators to pursue global excellence and leadership in big science (Xinhua, 2018). Local government sponsored science-entrepreneurial activities abound (Xinhua, 2016d), including, since the release of the new regulations, stem cell research and industry development (Wang and Zhao, 2015; Luo and Huang, 2015).

With the endorsement from the Chinese government at all levels, scientists working in China today have ample opportunities to translate their research results into the marketplace. Yet, the Chinese government endorses through policies, laws and guidance documents a particular kind of science entrepreneurship. Not only is there the belief in the effectiveness and replicability of America's high-tech industry development model to bring success in China, but also there is a need to answer to China's highest political

agenda to rejuvenate the Chinese nation. This party-state sponsored science entrepreneurship thus not only encourages but also increasingly mandates Chinese scientists to take up their entrepreneur responsibility and contribute more directly to Chinese high-tech industries.

Notably, the 'two bombs, one satellite' exemplifies not only how big science can be organised and managed under the direct leadership of the party-state to achieve highest techno-scientific ambition, but also a 'spirit' (*jingshen*, 精神). Thus, the promotion of the 'two bombs, one satellite' way of doing science requires scientists not only do big science, but also internalise the big-science spirit. With increasingly explicit orders from China's top leaders (State Council, 2016a, 2016b, 2017; Xinhua, 2015, 2016b, 2018), notable institutional and personal changes have been enacted (Bai, 2015; Wan, 2018). In the field of stem cell research, leading scientists have aptly taken up this spirit and expressed their willingness to follow the examples of those working at the nuclear and satellite programmes. For instance, writing for CAS's special issue *World Science and Technology Power Construction,* the key architect of China's publicly funded stem cell research Dr Zhou Qi addressed the importance of integrating talent policy into the design of innovation pathway, and gave his view that the kind of scientists China's innovation projects need are those having dreams for science and love for the collective and nation-state[72] (Zhou, 2017: 439). During the regulatory change, linking their work with the grand Chinese Dream also added political credits to their proposal and pressured the regulators to end the regulatory impasse.

Scholars such as Yang (2014), Anderson (2012) and Laszczkowski and Reeves (2015) have shown how affect and affective work[73] links with (bio)power, politics and nation-state building. For instance, Yang (2014: 6) suggests 'affect as a felt quality that gives meanings and imaginative potential to political and economic transformations…affect triggers change, releases energy and imagination, and intensifies connectivity between objects, people and events.' I suggest that affect is also at work in moulding a new figure of scientist-entrepreneur in contemporary China. The significance of this

[72] My translation and summary of Dr Zhou's description of this figure of scientist. Original in Chinese: '忘记小我、实现大我、创新为民、敢为人先、有情怀的科学家'.

[73] The meaning and usefulness of affect remain contestable in social science (Martin, 2013; Skoggard and Waterston, 2015; Rutherford, 2016). Yet, I choose to use affect instead of feeling or emotion for its emphasis on and encompassment of intersubjectivity, collectivity and sometimes reflexiveness.

particular affective work on scientists can be seen in comparison with Chinese clinician-researchers' use of patriotic rhetoric in their defence of China's leading edge in stem cell clinical research during regulatory change.

In chapter three, I documented how Chinese stem cell clinician-researchers claimed this leading edge, and how they were vocal in raising concern on what they observed, 'While we are stuck [in the regulatory impasse], others are moving fast! We are about to lose the edge we have created for China!' Similar to the biotech entrepreneurs I introduced in chapter six, those clinician-researchers essentially used these patriotic narrations like their publicity and government work to demand attention and support from the regulators.

Currently, under Xi's strengthened leadership and direct guidance, science, technology and innovation projects are taking a decisive (re)turn to politics (Xinhua, 2013c, 2014, 2016b), and all scientists, engineers and innovators are called to internalise a patriotic spirit in their thinking, speaking and actions in science and high-tech industries. Those elite scientists' patriotic statements are their response to the party-state calling to make science nationalistic and making innovation valuable for actualising the Chinese Dream. To become a qualified scientist-entrepreneur in contemporary China, as Dr Zhou states in his article, one must embody the 'two bombs, one satellite' spirit and devote oneself to nation-building (Zhou, 2017: 493). This is, therefore, an effective exercise of affective work led by the party-state and taken up by research institutions and the science community in forming new subjects that value the use of science, technology and innovation in the fulfilment of a political dream.

Small businesses: watching the regulatory wind

Institutionalising this mode of big science, however, does not include everyone engaged in research and innovation activities. Whereas scientists are now encouraged to be more entrepreneurial, biotech entrepreneurs need to acquire a set of different skills to keep their places in this 'new game'.

When Dr Zhu commented 'everyone is an entrepreneur now', he did not mean everyone. He referred to those whose opinion mattered to him, his reputation and his

venture: other established researchers. This image of ‘a science guy’, as I mentioned in chapter six, was also associated with Dr Hu, the founder and chairperson of Beike. Whereas Dr Hu was praised for being more like a scientist than a businessman, Dr Zhu was questioned for being the other way around. Most of the clinician-researchers I met that used to practise experimental stem cell therapies - treating and charging patients for a fee for stem cell therapies that they developed in their hospital laboratories - often felt offended when seen as engaged in business activities. By contrast, small business owners made considerable efforts so that mainstream researchers would recognise them, and their products, as possessing scientific competence and validity. Engaging in side-business was necessary for creating profit that sustained R&D activities, but was an embarrassment for startup founders such as Dr Miao (see chapter six).

As mentioned earlier, there is a buzz around biotech industries. Those who I met in the fieldwork liked to quote Lei Jun and considered that they were standing ‘in the eye of a storm’. But they were also aware of the risk of ‘chasing the wind’ that was warned by other IT leaders such as Ma Yun. Soon after Lei’s quote became popular among young entrepreneurs, Ma created another catchy phrase to debunk Lei’s - ‘After the wind is gone, fall to death is also the pig’ (Custer, 2016). A few entrepreneurs admitted to me that they were more concerned about becoming ashes rather than a flying pig in emerging biotech industries in China. In addition to biotech’s cash-burning feature, mentioned in chapter six, those entrepreneurs’ experiences with China’s recent regulatory change taught them that regulatory intervention could easily change the wind.

In hindsight, Beike concentrating its business on stem cell therapy was recognised by both Beike and industry observers such as Dr Bai as ‘a mistake’. Beike not only missed the prime time to enter the business of cord blood banking, but also rendered its business model vulnerable to regulatory change. At the time, no one anticipated that a regulatory change to stem cell clinical research would happen. Thus, the rise and fall of Beike is not only a lesson for Dr Hu and Beike, but also for the practitioners and industry observers as a whole.

Having witnessed the fall of stem cell therapy and related industries, practitioners, industry observers and investors have started to pay particular attention to monitoring

'the direction of regulatory wind' (*zhengce fengxian*g, 政策风向) that affects the fortune of biotech industries in China. But being able to anticipate a possible change of regulatory wind does not guarantee successful preparation for such a change. Chinese authorities hardly consult in advance or make public their rationale of introducing, altering or determining certain regulations. In chapter five I explained how, despite knowing that immunotherapy was subject to regulatory change, leading practitioners pleaded to the regulators to provide more regulatory guidance, and the majority of practitioners could do nothing but carry on their work in the ambiguous situation. Additionally, the biotherapy unit which I studied decided to close its immunotherapy in mid-2015, but most immunotherapy programmes in China carried on until mid-2016 when the authorities banned the practice in the wake of a public outcry. In this ambiguous situation, whether or not, how and when to change one's practices needed to be carefully calculated against the odds that a regulatory change may occur and in what direction.

Those working in biotech industries and carefully monitoring the direction of the regulatory wind reflect the experiences of Chinese tanners working in Calcutta (Basu 1991). Basu studied small businessmen's gambling practices that at first seemed at odds with other entrepreneurial ethics such as hard work, frugality and careful planning. But her interlocutors explained to her that the two are 'both activities where one plays with fate' (ibid.: 249). The tanners considered gambling and entrepreneurship both 'involve luck and skill' and require 'taking risks in order to make gains', and that one's fate in both are 'beyond one's ultimate control' (ibid.: 284). Whereas Calcutta's Chinese tanners played mahjong with fate, the Chinese biotech entrepreneurs, I suggest, need to plan and conduct their high-tech businesses mindful of changing wind blown from technology, investment and policy. The small business owners thus not only need to prove their products' worth according to scientific criteria, but also to hone their 'gambling' skills in watching the regulatory wind while having their exit plans ready for escaping a deadly blow from regulatory change. Yet, the new wave of regulatory wind has also changed the regulators.

Regulators: caught in between

During my fieldwork, practitioners often complained among themselves and in conversation to me about regulators' inaction during the regulatory impasse. Outspoken practitioners such as Dr Wei also criticised regulators publicly, and published opinion pieces in magazines and newspapers to calling for regulators to act (Zhao and Wu, 2015; Hu and Liu, 2015). It seems regulators were also aware of practitioners' criticisms. Two events illustrate this situation.

At a biotherapy conference, titled '*High-End Dialogue*'[74], a clinician-researcher directed her question to Expert Committee members who sat at the panel,

> 'Could any of you academicians[75] tell us what is the status of regulation now? Our hospital wants to conduct [stem cell] clinical trials. We consulted the local health department, and were told we had to apply to the *national* health authority, and we did. But half a year has passed, we have heard nothing! [*yeahs and laughs from the audience*] Our patients are waiting, so are we and our collaborators from the US! What should we do? [*a short pause*] Look at the immunotherapy, it just goes ahead everywhere. No one asks them for any approval?!'

Her question immediately unleashed a wave of laughter, cheers, and chats among other attendees. Facing the aroused audience, the panellists quickly exchanged eye contacts among themselves, and nominated a senior member as their representative to address the question and who started the answer with a bitter smile,

> 'The fact is *we* have completed the draft [the revised version] and handed it to the authorities. Now it depends on how the officials decide. It was already some time ago [since we submitted the draft]. I now *call your action* to plea to your institutions, to the NHFPC and the CFDA, [and] to pressure *them* [the authorities] to move faster!'

A new wave of laughter and applause soon spread out around the conference room.

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[74] A high-end dialogue (*gaoduan duihua*, 高端对话) or its equivalence is commonly organised at national-level professional or industry conferences. During the regulatory change, the main topic of these special sessions was often set to address questions regarding regulation and the future of stem cell research and industries in China.

[75] Not every member of the Expert Committee was an academician. In China it is common to call someone holding an official or professional position with a higher rank, especially when it is unclear what rank one has. As a cultural practice, it is a way to show the speaker's respect and to give the addressee 'face'. It is slightly different from flattery. Because it also expresses the speaker's wish for the addressee to succeed in climbing their career ladder. This discrepancy between their real title and that being addressed can also be used by the speaker as a form of sarcasm. On this occasion, this clinician-researcher used 'academician' - the highest professional recognition a researcher can achieve - to direct her question to Expert Committee members.

At another national industry conference, after being repeatedly asked for an update on the regulatory deliberation, Mr Tao told the restive attendees, 'I cannot say much here, but the Expert Committee are working hard to reach an agreement on revising the draft.' He then turned to look at Dr Xu, who was co-chairing the session, 'Academician Xu, would you like to add something?' Dr Xu gave a succinct answer in his slightly raised voice, 'Only one point: it requires our policy-makers and regulators to work together to reach a final decision!'

Dr Xu's answer received immediate applause and laughter, and instantly lightened up the intense air that had accumulated during the session attended by about 200 people. I was amused by the sudden change of atmosphere, yet it also occurred to me that just before the session started, I spotted one of the regulators Mrs Yuan walking into the room and sitting in the back. As we exchanged brief greetings, she told me, 'I come here to learn about the community's opinion'. I instinctively tilted my head back towards where she sat, wondering how she felt being singled out like an inhibitor that hampered the development of stem cell enterprise in China.

Occasions like these two examples not only show that collegial bonds among practitioners were strengthened during the regulatory impasse, but also reveal changing dynamics among different groups of practitioners, and between practitioners and regulators. With the prolongation of the regulatory impasse, the subject and target of 'blame' started to shift towards the regulators - their inaction was costing China precious time to prepare for intensified global competition in stem cell research, product and industry development.

But it was not a task that the regulators alone could address. For example, a technocrat at another industry conference, who had a long working relationship with the health authorities, was invited to give an overview of China's bioindustry and industry policies. Before him, some speakers had been asked about regulatory change. When he started his, he told the audience,

> 'I know that many of you want to know when we will get the new regulation [on stem cell clinical research], and you have all been waiting in the past years. It is not pleasant [feeling] at all. It is understandable that you want it [the process getting] faster. Indeed, we all do. [*short pause*] But I would like to remind you that, for the regulators, to regulate complex uncertainties in stem cell [therapy]

> and its operation while at the same time to foster the growth of new domestic health market and Chinese biotech companies' competitiveness in the global health market is a sophisticated task. In particular because these goals are not compatible.'

This is why, despite the practitioners complained about regulators' inaction, leading practitioners did not advocate their vision for Chinese stem cell research-enterprise to the regulators. As mentioned earlier in this chapter, and in chapter six, they addressed their proposals directly to higher-level politicians and legislators. Similarly, though regulators such as Mrs Yuan stepped out of their offices to learn from the practitioners, they did not accelerate their regulatory action in 2015 solely because of the pressure that they sensed in those meetings. As mentioned earlier, NHFPC and CFDA were ordered by the State Council to jointly work on the new regulations.

In chapter six, I described how certain biotech entrepreneurs were invited to attend a consultation meeting in spring 2015. What the second event vividly captured is a changing working relation and power dynamics between those working in the biomedical industry and those regulating them. This changing relation, as the recomposition of biotech entrepreneurship that I described earlier, resulted from a higher-level directive. Whereas China's innovation agenda has lifted elite scientists' and biotech entrepreneurs' socio-political status, the State Council has also directed governments and regulators at all levels to transform their role towards being facilitators of innovation (K. Li, 2016; Ye Wang, 2015; Xinhua, 2016d).

Thus, during this regulatory change, both the practitioners and the regulators looked for the party-state to give directions and responded to the officialese coined by the top leaders. They have further participated in performing and internalising officialese to steer stem cell clinical research and product development towards answering the Chinese Dream and the innovation agenda.[76]

The invisible subject and the ethics of (bio)medicine

[76] Sleeboom-Faulkner et al. (2018) delineates how this regulatory change led Chinese health authorities' regulatory capacity building, and regulatory negotiation between ministries and region or municipal governments. My interest here is more on how those changes affected individuals, and vice versa.

When this renewed research-enterprise is formed to facilitate the development of industrial-level stem cell based-medicine and related industries, the other modes of research and development are rendered irrelevant. Among them, notably are clinician-researcher led, hospital-based clinical research and the development and use of autologous stem cell therapies to treat patients with their own stem cells. Those clinician-researchers, patients and patient families have also been changed by regulatory change, but the effects on them are less visible.

What clinician-researchers had studied and practised prior to the regulatory change was seldom acknowledged as science by laboratory-based scientists. Rather, sometimes their practices were blamed for damaging the reputation of Chinese science. Even though a particular science entrepreneurship is now officially endorsed by China's party-state, clinician-researchers find themselves at the margin of this new Chinese stem-cell research enterprise. After the publication of the new regulations on stem cell clinical research (NHFPC and CFDA, 2015c, 2015d), some clinician-researchers publicly criticised the regulators' preference for a drug model rather than medical technologies (biodiscover, 2015). Yet, most clinician-researchers have started to alter their roles, adjust their laboratories and change institutional settings to fulfil the requirements spelled out in the new regulation.

As clinician-researchers give up their primary role in developing stem cell therapies, and exit and abandon certain programmes, they leave behind those having been using or potentially want to use these in-development products. This is evidenced by the closing of immunotherapy programme in the biotherapy unit where I was based, and documented in cases such as Geron's ending of human embryonic stem cell clinical trials (Chapman and Scala, 2012). In both cases, the decisions were made not on techno-scientific and clinical data, but in response to changing regulatory and market risk profile. In chapter five, I suggested that this is one of the critical implications of biomedicine becoming toolised. I could have, following Chapman and Scala (2012)'s analysis of Geron's case, say serious ethical issues are at stake in developing biomedicine. But in this thesis, I have been refraining myself from engaging in discussions about the ethics of developing and using cell therapies. Similarly to concepts that are developed with the prefix of bio (Birch and Tyfield, 2013), there is much literature debating the ethics of stem cell therapies (see introductory chapter).

Nevertheless, after examining literatures around biocapital Helmreich (2008: 474-475), suggests that the word 'capital' has taken too much attention in the study of the economic with the biological, while 'capital itself…was unstable, was not so easily reproduced, or so generative, or omnipresent, after all?' I am wary of engaging too early or readily with ethical or political discussions. Having introduced my research participants' experiences with, and views on, cell therapies and regulatory change in China and having developed the concepts of toolised medicine and tooling work, I now reflect on certain ethical questions and briefly discuss how this study can respond.

At my first meeting with Dr Wei, he suggested that what I really should study is what novel therapy such as cell therapy should be really about and for. He told me that the only reason he agreed to spare his busy time meeting me was, 'to discuss real ethics imbued in clinical practice of cell therapy'. I became uncomfortable with his one-sided passion on this topic of ethics and had to clarify to him that my research interest lay in understanding the regulatory change and its effects and implications. Dr Wei maintained his position and stressed that this question of ethics should be at the core of the regulatory debate, and was surprised why it was not. His understanding and concerning with ethics was that the regulatory change reduces and attacks 'the ethics of medicine'. He considered this attack a symptom of China's diseased health care system and, as a doctor, felt he must defend the ethics of medicine. Even though this 'ethics' talk brought a rather awkward ending to our first meeting, we returned to discussions about the nature and effect of cell therapies, about the centrality of medical practice in administering cell therapies, about mutual understanding and trust between doctors and patients.

With the expansion and deepening of my fieldwork, in particular into patients' lifeworlds and actual clinical practice, I started to rethink Dr Wei's framing and questioning about ethics as questions about what cell therapy is and what it should be used for. For instance, the Shen's family's experimentation with stem cell therapy (chapter four) and the clinical practice of immunotherapy (chapter five) were telling about the necessity and importance of shared doctoring, care practice and hope in practising and using cell therapies. The combination of patients' individual conditions and malleability of cells made me rethink the dominant framing of scientific and ethical

standards and suggested to me that the ethics of medicine - not bioethics or research ethics - is in need of collective reflection and defence.

To rethink those issues does not mean I agree with Dr Wei's argument or interpretation of his practices. But I started to wonder how he would explain and feel about the popular portrait of him being a controversial clinician-researcher 'selling patients experimental cell therapies'. So, about half a year after we first met, I decided to ask him. After a nearly unnoticeable pause, he looked into my eyes and said,

> 'To be honest, I don't care what others think about me. I care about my patients and my responsibility as a doctor. And that is why I spent so much time talking to you and want you to re-structure your research and ask the question of "*what is the purpose of medicine?*" I think many [clinical researchers] have lost the sense of being a doctor, and our medical system is corrupted. We all took the Hippocratic oath when started our careers, and that is what I care about the most. I do not have time to think about *how I fee*l about others' criticism. Time will evidence that I am right [in practising cell therapies].'

I am not sure time will take the side of Dr Wei. Currently, in China, cell related research, product and industry development is taking a more drug-like model, rather than the one he passionately defended as medical practices. But Dr Wei's defence of medicine resembles Löwy's (2011) suggestion that, in studying biomedicine, social science researchers need to pay more attention to clinical practice.

Turning attention onto medicine further highlights the problems of using pharmaceutical research and regulatory framework as a benchmark in developing R&D, authorisation and marketisation regulations for biomedicine. When social science researchers studied pharmaceutical industries' research, marketisation and sales, regulatory and governance practices, they reported alarming results on the ethics and legality of certain practices (Sismondo and Greene, 2015; Abraham, 2008), including in practices around clinical trials (Will and Moreira, 2010; Jain, 2010; Fisher, 2009). The global reach and influence of pharmaceutical industries raises further concerns on justice, equality and power at the local, national and global levels, and in transnational travels (Petryna, 2009; Abraham, 2007; Boulet and Hanvoravongchai, 2003). Making biomedical product development and marketisation more compatible with existing international trade and marketisation arrangements could reproduce these questions that

have accompanied pharmaceutical industries since the 1970s. These are also questions about the ethics of medicine.

These normative questions go beyond what has caught most attention during the debates on experimental stem cell therapies. The experimental way of developing and using cell therapies appears as a transgression of the existing scientific and ethical standards that are institutionalised for pharmaceutical product development and marketisation. Putting aside those questions raised by social science researchers regarding pharmaceutical research and industries, scientists and biopharma industries have already acknowledged that contemporary biomedicine has challenged a static view of medicine and how to research, develop and regulate products (Kummar, 2017; Crommelin et al., 2010; Wagner and Kroetz, 2016).

Rabinow (2007: 2) suggests approaching 'the contemporary' as 'A moving ratio of modernity, moving through the recent past and near future in a (non-linear) space'. In this thesis, I have argued and depicted how biomedicine is different from standard pharmaceuticals. I distinguish the biological capabilities of a cell from its medicinal potentiality and contend that this distance between biological capabilities and medicinal potentiality makes biological entity-based medicine become toolised. I have documented and stressed that cells can be conceptualised and used as tools not only by researchers, but also by patient and patient families (chapters four and five), and tooling work includes not only scientific research, business strategies and political imaginations, but also doctoring, care practices and the work of hope (chapters three to five).

Whereas techno-scientific and clinical uncertainty cannot be eliminated from tooling a biological entity into a medicinal product, discussions on the relative value of these products should not be limited to an exclusive group of those developing, investing and regulating the in-the-development products. The events around Wei Zexi's death reveal that as everyone is a potential user of toolised medicine, public debate on how to organise the practices of toolised medicine, and how to integrate that into existing health care systems, is possible and necessary. In China, due to institutional constraints, such public debates often occur in the cyber space or *post hoc*. Yet, the validity and value of public debate is undeniable and has recently caught the attention of elite

scientists and regulators in China. Given that biomedicine is a global research-enterprise, whether or not and how to develop, practise and use tool-like new medicines awaits global debate. Questions such as where best to invest in not only biomedicine but also medicine and health care, should take a higher priority.

Toolised medicine and tooling work, thus I hope, will help reorient social inquiry more towards understanding biomedicine in its clinical life and contemporary forms and movements. After properly deciphering what biomedicine is and can be, as social science researchers, we may be better prepared for the task of critique and social imagination.

CHAPTER EIGHT. CONCLUSION

In this thesis, I introduced and developed the concepts of "toolised medicine" and "tooling work". Using the example of cell therapy, I argue that contemporary biomedicine has become "toolised," and its "tool-like" feature resides in the distance and difference between a biological entity's biological capability and its varied potentialities in and beyond medicine. This difference between biological capability and medicinal potentiality creates a space for a user to integrate what value, in addition to medicine, into their use of toolised medicine, and at the same time requires its user to carry out their tooling work to help fulfil various particular potentials. I consider "toolised medicine" and "tooling work" are 'mid-range' concepts (Amit et al., 2015: 3),

> '[Mid-range concepts] are "good to think with" because they are neither too narrowly defined nor too sweeping. They can be used to think through ethnographic situations, but they are not particular to one kind of ethnographic circumstance. They are, in short, of the "not too hot, not too cold" version of conceptual articulation.'

"Toolised medicine" and "Tooling work" are derived from my anthropological research into a recent regulatory change to stem cell clinical research and practice in China, and are best illustrated through anthropological writing. The preceding chapters demonstrate that the concepts of toolised medicine and tooling work can help analyse diverse situations.

I have no intention to replace 'thick' concepts, such as 'biocapital' and 'political economy' of biomedicine, with toolised medicine and tooling work. These thick concepts provide critical scholarly orientation for social science researchers' investigations into biomedicine, and its economic and political ramifications. Nevertheless, I agree with Helmreich (2008) and Birch and Tyfield (2013) that the proliferation of 'bio-' concepts, may constrain our scholarly understanding of both biomedicine and the contemporary life in which we live. Unfortunately, precisely because of their handiness, these concepts tend to be too readily used in current scholarly work as reference points to explain almost every economic or political aspect of biomedicine.

My fieldwork investigated China's unfolding regulatory intervention in the 'grey area' (Sleeboom-Faulkner, 2016) where 'unruly' stem cell therapy (Haddad et al., 2013) took root and grew. During my fieldwork, I noted that this recent regulatory change had introduced considerable uncertainty to stem cell clinical research and practice, and to the marketplace. The ordinary Chinese people I met in this study – researchers, doctors, patients, biotech entrepreneurs, industry analysts, and investors - seemingly got along and, in some cases, made use of uncertain, contradictory, or ambiguous situations to continue their pursuit of developing, or using, cell therapy. Their experiences did not fit well with the logic, or simply reflect the effects of biocaptial or political economy of biomedicine.

To grapple with the perspectives and actions of those ordinary Chinese people in living through this regulatory change in China, I followed Landecker (2007)'s appeal to examine how a biological entity is conceptualised and used as 'technology,' and responded to Löwy (2011)'s calling to look at how 'bio' and 'medicine' is connected through clinical research and practice. Landecker and Löwy argue that addressing these questions would help grapple with biomedicine's unfolding social and political lives. In this study, I have, therefore, traced, documented, and analysed how these unruly cell therapies and grey phenomena were understood and utilised by various people and their families, institutions and associations during this regulatory change in China. Along the way I developed the two 'mid-range' concepts: "toolised medicine" and "tooling work".

I would like to clarify again that attending to unorthodox practices and use of experimental cell therapies does not equate to endorsing them. Sharing the concern and dismay of others (Lysaght et al., 2017), I am saddened when I read in the news about patients hurt in these processes. I also respect those who have devoted decades of work in strengthening the regulatory and governance framework and clarifying the regulatory pathways in China. I, like most of those I met in this study, see the necessity and merit of new regulations being introduced, implemented and put into good use in China.

My fieldwork observations together with my survey of literature and documented debates in the field of stem cell research and biomedicine, nevertheless, made me concerned that standards, principles and regulations have grabbed almost all of the attention. Yet, the subject of these efforts - biomedicine - is insufficiently understood.

Scholars such as Wallach (2015) point out that governing emerging technologies has a 'pacing problem' because of 'the growing gap between the time technologies are deployed and the time effective means are enacted to ensure public safety' (p60). Social science researchers have also called for an earlier engagement with scientists, engineers and innovators in conceiving, designing and developing new technologies and products (Webster, 2016; Guston et al., 2014). I align myself with this early-stage intervention and want to take a step further by recognising, revealing and stressing that what biomedicine is and can be is an open question. Once the question is reset, other questions arise about who can and should be invited to partake in this open inquiry and who can make critical decisions that accumulatively shape our shared future. Moreover, the question about how to make this open inquiry and decision-making work at a global level has become essential and urgent. My thesis is my calling for this reorientation of our collective attention.

Furthermore, I need to stress again that this is not a case study of Chinese stem cell clinical research and regulation. Because similar and sometimes identical practices and arguments have been documented by scientists, social science researchers, biotech entrepreneurs, industry analysts and politicians in other countries. Instead, I hope my study serves as a case for advancing social science inquiry into biomedicine in its contemporary form, mode and assemblages as Rabinow (2007) suggests. Contemporary here, as defined by Rabinow, is 'a moving ratio of modernity, moving through the recent past and near future in a (non-linear) space' (ibid.: 2, emphasis deleted). In the study of the contemporary, a case is not predefined, but part and parcel of one's research on the contemporary (Rabinow and Stavrianakis, 2016: 425). To advance our collective grappling with the contemporary, Rabinow and Stavrianakis further underscore the need of collaboration in inquiry and in identifying and studying interconnected cases (ibid.: 410). My thesis is thus also my response to this calling of studying the contemporary.

In the introduction to the thesis, I explained how, in recent years, stem cell research has made notable achievements towards making 'regenerative medicine'. Nevertheless, its diversified research practices have challenged the 'translational research' model (a model which remains a main reference point for discussions about biomedical research and regulation). Against this setting, during the first decade of the 21st century, some

Chinese clinician-researchers and biotech companies started to offer 'unproven and unauthorised', and thus, 'experimental' stem cell therapy to Chinese and foreign patients. Their clinical practice and business activities raised serious doubts among scientific and bioethics communities, both in China and internationally, who denounced those practices as transgressions of scientific and ethical standards and further called for the Chinese government to introduce regulatory intervention. Regulatory changes to stem cell clinical research in China provided a starting point for my research into biomedicine that led to my conceptualisation of "toolised medicine" and "tooling work"

Chapter two described the context of my research. It contained a literature review of relevant social science studies of stem cell research, clinical practice, business activities and regulatory situation in China in the last two decades. It gave an overview of my fieldwork, and introduced three interlinked aspects of the regulatory situation that were critical to understand the views and actions of my research participants. I also reflected on how I gradually learned from my research participants, in particular patients and clinician-researchers, and realised that, by studying regulatory change in China, a window opened for me to study biomedicine.

Chapters three to seven are ethnography-based analytical chapters that introduced and developed the concepts of "toolised medicine" and "tooling work". From chapter three to chapter six, I revisited different groups of my research participants who I met at various venues and times during the fieldwork. In sequence, I focused on clinician-researchers, patients and patient families, health care professionals, and biotech entrepreneurs. I introduced and analysed their views on and experiences with cell-based therapy and the regulatory change that constituted part of their health care, work and life conditions. By bringing their various views and experiences together, I illustrated how toolised medicine was perceived and could be used in reality. These analyses led to my contention, in chapter seven, that China's recent regulatory change to stem cell clinical research and practice can also be viewed and assessed as a tooling process.

In chapter three, I described the struggle for recognition by clinician-researchers, which centred on the validity and value of their clinical work that, in their view, had helped China to gain a leading edge in stem cell clinical research. Their struggle was reflected in their views on, and responses towards, the regulatory change: they forcefully

defended the existing regulation that designated certain types of cell therapy as ‘category three medical technologies’. Yet, laboratory-based scientists largely dismissed the claims of clinician-researchers, and asked for the replacement of the existing regulation on medical technologies with one that would bring China’s regulation on stem cell clinical research in line with the internationally acknowledged translational research model. In tracing those clinician-researchers’ collective struggle, I noted their differentiation between stem cell’s biological capability and its potential usage in medicine. This difference between biological capability and medicinal potentiality is, to some extent, acknowledged in the translational research model as a ‘gap’ that needs to be bridged between the ‘bench’ and the ‘bedside’. Yet, its practical and regulatory implications, and significance to social science studies of biomedicine has not been discussed properly. In this gap, I located my conceptualisation of “toolised medicine”.

In chapter four, I revisited some patients and patient families who were willing and able to use experimental stem cell therapy in order to resolve both the medical, and non-medical, problems that they were facing. These patients and patient families had learned from their doctors and the media that stem cell’s medicinal potentiality had yet to be attained, and thus all had doubts and hesitations about using ‘experimental’ stem cell therapy as a treatment. Yet, this yet-to-be-attained potentiality of stem cell therapy in treating their diseases did not dissuade these patients and patient families from using experimental stem cell therapy to address their medical and non-medical problems. Rather, my interlocutors effectively turned the prospect of using stem cell therapy to alleviate their suffering as a tool to better manage their health, family relations and life in general. To turn experimental stem cell therapy into a tool in managing their health and life, my interlocutors carried out concrete work of hope and care for themselves and one another. I subsequently used the term “tooling work” to capture and analyse this explorative way of using stem cell therapy. I explained that when patients and patient families use “toolised medicine”, their own work of hope and care is part and parcel of the “tooling work” that helps to attain the biological entity’s potentiality in medicine and in other domains. Nevertheless, I cautioned against romanticising patients’ “tooling work” as an act of agency, because it is often, simultaneously, an illustration of vulnerability.

In chapter five, I introduced my participant observation in a cancer hospital in spring 2015. I observed how immunotherapy was provided by doctors and used by cancer patients as an experimental therapy, however, this happened in a nearly ordinary manner. This ordinariness included working and living with experimental therapy in an ambiguous regulatory situation. Having being listed as a 'category three medical technology' in 2009, immunotherapy was incorporated as a novel, yet, auxiliary treatment into cancer patients' treatment in public hospitals across China, and in some provinces it was included in local public health insurance schemes. Nevertheless, because Chinese health authorities had not permitted clinical use of immunotherapy, those who practised and used immunotherapy did so in a grey area.

Like those patients and families that I introduced in chapter four, the patients and health care practitioners I met in the biotherapy unit were aware of the experimental nature of immunotherapy and the ambiguous regulatory and clinical situation. As later highlighted in the events around Wei Zexi's death, it was not ideal to live and work with this ambiguous situation. Patients and health care professionals in the biotherapy unit, who seemed settled in this ambiguous situation, paradoxically, sustained the experimental life of immunotherapy and the ambiguous situation. Agency and vulnerability - the two components essential to "tooling work" - revealed themselves clearly in the aftermath of events around Wei Zexi's death. Responding to public outcry, Chinese health authorities decisively issued a ban on immunotherapy and ended the ambiguous regulatory situation. Meanwhile, those who made and used immunotherapy, as an ordinary, experimental therapy, were silently left behind.

Considering how experimental stem cell therapy was once practised and then brought under regulatory scrutiny in China, it is clear that the two 'sister' cell-based therapies had, essentially, identical regulatory experiences, yet, were experiencing it in disjunctive times. Noting that my interlocutors considered the ambiguous situation as part of the 'Chinese context,' I acknowledge that, certain political, social-economic conditions of contemporary China had helped to make experimental cell therapy ordinary. Yet, I stressed that biomedicine's toolised feature is of equal importance to understand the unfolding, significance, and ramifications of China's regulatory changes to cell-based therapy. The distance between cell's biological capability and its medicinal potentiality opens up space to accommodate varied views of what cell

therapy is and what it is for. In this space a different kind of tooling work was conducted by the regulated and the regulators during the regulatory change, which finalised China's new regulations on stem cell clinical research and directed the future of Chinese stem cell-based medicine and industry.

In chapters six and seven, I thus moved my concept work of toolised medicine and tooling work to the business and the political arenas that best illuminate this mutual selection and accommodation of toolised medicine and contemporary China.

In chapter six, I focused on biotech entrepreneurs' counter-strategies that they developed during the regulatory impasse. Despite apparent differences in format and conducted venues, I suggested that all counter-strategies were, foremost, survival strategies. Amid varied regulatory and market risks, biotech entrepreneurs also saw and chased after business opportunities that were presented by biomedicine. In their collective plea to the regulators to end this regulatory impasse, biotech entrepreneurs stressed cell therapy's value for public health, economy, national security and competitiveness: a set of criteria that had gained increasing political potency in contemporary China. In other words, during this regulatory change and the industry's winter, biotech entrepreneurs used biomedicine as a tool in devising their survival strategies. They further used as guidance their educated guess about the foreseeable economic and social-political future of biomedicine in China to advance their individual and collective enterprises. I stressed that, as developers and users of toolised medicine, the tooling work of biotech entrepreneurs had consequences on other users such as the patients.

In chapter seven, I discussed the effects of different users' tooling work on one another. I examined how leading practitioners gradually reached a consensus to develop a globally competitive Chinese stem cell research-enterprise during the regulatory impasse - a vision that they collectively forwarded to the regulators. Viewed from the lens of toolised medicine and tooling work, I suggested, while biomedicine is effectively made into a tool to aid China's nation-building in the 21st century, the regulatory change provided the leading practitioners, regulators and various mediators an opportunity and venue to exercise their joint tooling work to prioritise actualising stem cell's potentialities in economic and political domains rather than treating

individual patients. This in-the-making future of Chinese stem cell research-enterprise not only revealed and changed the composition of biotech entrepreneurship, but also the power and working relation between biotech entrepreneurs and health authorities in contemporary China. Regulatory change has ramifications. The move towards a Chinese stem cell-based medicine and industry has started to affect how the other users and user-groups would be able to use stem cell-based medicine in the future.

In conclusion, in this thesis, I have delineated and analysed the "tool-like" conceptualisation and use of cell therapy by different users. I have identified and demonstrated that this "tool-like" feature of cell therapy resides in and derives from the difference and distance between a cell's biological capability and its medicinal and non-medicinal potentialities. I have demonstrated that, as agile, mid-range concepts, "toolised medicine" and "tooling work" offer a nuanced understanding of cell therapy and are apt to analyse contemporary, unfolding, clinical, economic and social-political lives of cell therapy. Since this difference and distance between biological capability and medicinal potentiality corresponds to the difference and distance between bioscience and medicine, I consider comprehending this "tool-like" feature of cell therapy sheds new light on our understanding of biomedicine in general; in particular, of new medicines using biological entities as their core conceptual and material components. Future research can thus explore both specific diagnostic and therapeutic approaches that use biomaterials such as genes and tissues, and collectively reflect on the scientific, social, commercial and political implications of biomedicine becoming toolised.

More specifically, I consider social science researchers who are interested in studying biomedicine or biomedical research and regulation can take up "toolised medicine" and "tooling work" in their work in three ways. First, I suggest toolised medicine and tooling work are useful in attending and speaking to the uncertainty, ambiguity, and fluidity of conceptualising, developing, practising and using biomedicine. Second, I suggest that, by paying attention to ambiguous and fluid views and practices, toolised medicine and tooling work can help preserve these ethnographic situations wherein multiple versions of biomedicine coexist in the same, or different, times and places. Third, accumulated multiple versions of biomedicine will counteract the tendency by researchers to interpret unorthodox views and practices around experimental biomedical

interventions mainly as manifestations of capital or politics, or as a deviation from scientific rationale or ethical principle. Instead, I hope social science analyses can go beyond denouncing such phenomena as ‘irrational’ and the people involved as ‘questionable’. I hope they can learn from these alternative views and practices in order to enrich scholarly considerations of biomedicine and, sharpen the critical gaze at the contemporary so as to co-construct the future with those we care about. I hope my work on toolised medicine will serve as a tool to help reorient scholarly work towards this direction.

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APPENDIXES

Table 1

Table 1 Comparison of main differences occurred in the regulation documents

	Initial draft, March 2013	**Management Measures, August 2015**
Title	a. Management Measures on Stem Cell Clinical Trials Research (Interim, consultation version), i.e. *MM-2013a* b. Management Measures on Stem Cell Clinical Trials Bases (Interim, consultation version), i.e. *MM-2013b* c. Guideline on Quality Control of Stem Cell Manufacture and Preclinical Trials (Interim, consultation version), i.e., *G-2013*	a. Management Measures on Stem Cell Clinical Research (Interim), i.e., *MM-2015* b. Guideline on Quality Control of Stem Cell Manufacture and Preclinical Trials (Interim)*, i.e., *G-2015*
Regulation Agencies	MOH and SFDA as a joint force, since SFDA was part of MOH	NHFPC and CFDA as separate regulatory authorities and will be in charge of different activities. The coordination plan and workflow remain unclear.
Scope of Regulation		
Management style	Hands-on, even meticulous in developing criteria for how many cases are required for each phase in clinical trials.	Hands-off, while keeping regulatory tools such as registration and monitoring of clinical research, and punishing violations.
Accountability	Distributed among central and provincial Health and Food-and-Drug agencies, clinical trial sponsors, clinical trial bases and clinical trials researchers.	Identifying medical institutions hosting clinical research as the sole entity that holds responsibility for stem-cell clinical research and related activities.
Expert Committee(s)	Central Expert Committee to be set up by the MOH and the SFDA to review applications of clinical trials bases and clinical trials.	MM-2015, Section 6 (Articles 38~43) delineates the Duties and Responsibilities of Expert Committee*s*. Expert Committees to be set up at the central, provincial and institutional levels. The functions of these expert committees have broadened from developing policy advice to provide training and education to researchers.

Table 1 Comparison of main differences occurred in the regulation documents *cont.*

	Initial draft, March 2013	**Management Measures, August 2015**
Conceptualisation of stem cell(s)	- MM-2013a, Article 2 & G-2013, Preface: 'stem cells are a group of cells that have various differentiation potentials and remain self-renewal ability in non-differentiation status.' - G-2013, Preface continues: '…stem cells that are used for cell therapies include adult stem cells, embryonic stem cells and induced pluripotent stem cells (iPSC)…'	G-2015, Preface: 'Stem cells are a group of cells that have various differentiation potentials and remain self-renewal ability in non-differentiation status. … Stem cells that are used for cell therapies include adult stem cells, embryonic stem cells and induced pluripotent stem cells (iPSC)…'
Supporting Measures		
Punishment	MM-2013a, Section 6 (Articles 32 ~ 35) & MM-2013b, Section 5 (Articles 14 ~17): in violation of MM-2013a or MM-2013b, the clinical trials sponsors, bases and researchers will be filed criminal and/or civil charges.	MM-2015, Section 7 (Articles 49~50, 52): in violation of MM-2015, NHFPC and CFDA will stop, condemn and record such activities as violation of research integrity; for severe violations, medical institutes and researchers will be punished according to *Drug Administration Law of P.R.C* and *Administrative Measures for Medical Institutions*.
Risk assessment and management	Only mentioned in MM-2013a in the review process (Section 2: Application and Filing Records)	Risk assessment and management is highlighted in MM-2015, Article 13 to be integrated as protection mechanism for research participants: '…for research with higher risk, special monitoring and management should be put into place, and insurance should be purchased through a third party to provide compensation for research related harm or death.'

*: *MM-2013b* disappeared from the regulation package published in August 2014. *G-2013* survived two-year's deliberation without much change in texts, and was issued as *G-2015*, eleven days after the publication of *MM-2015*. Some content developed in *MM-2013b* is integrated into *MM-2015*, especially in Section 2: Eligibility and Responsibility of Institutions.

Figure 1

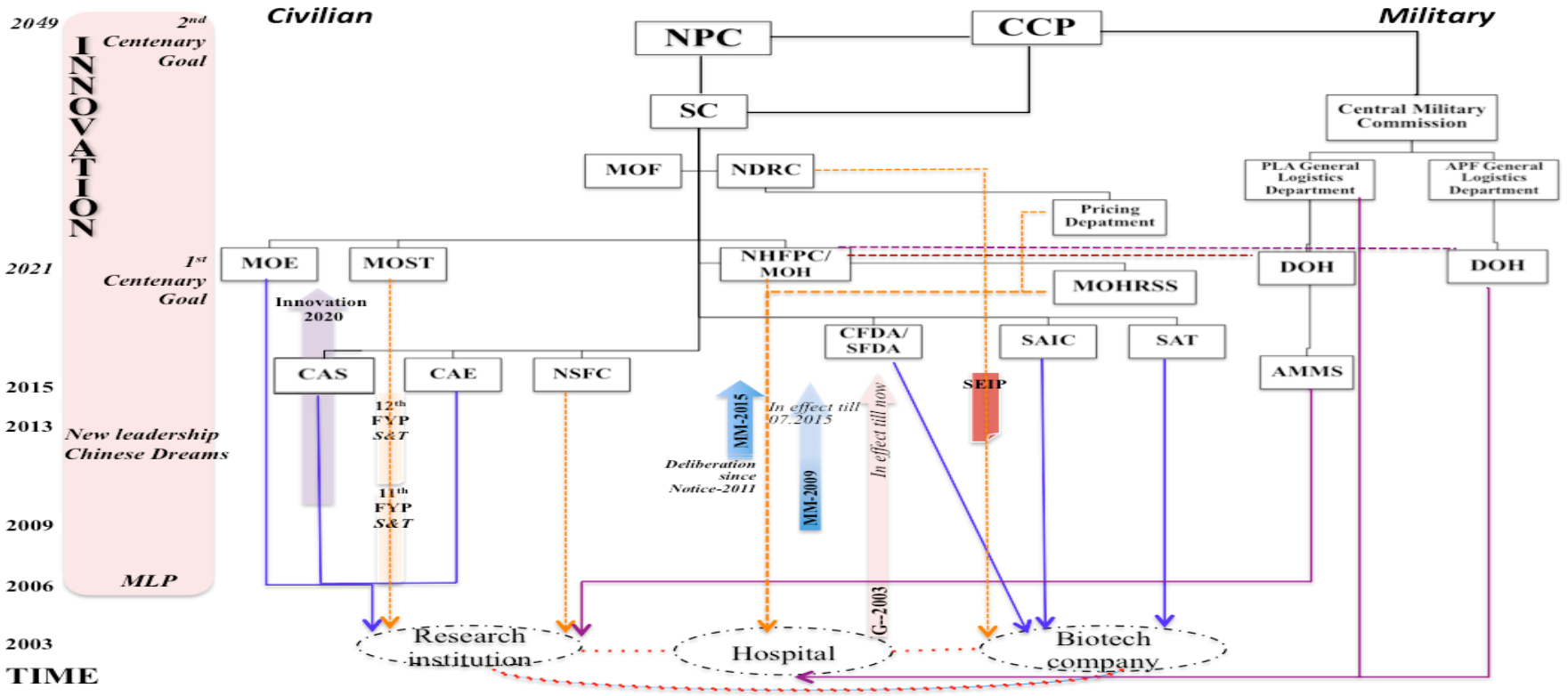

Figure 1. Illustration of the wider regulatory situation amid which the health authorities navigated in finalising the new regulation on stem cell clinical research

MM-2015 refers to Management Measures on Stem Cell Clinical Research (Interim) (NHFPC and CFDA, 2015c), *MM-2009* refers to Management Measures on Clinical Application of Medical Technologies (MOH, 2009a), *G-2003* refers to Guidance for Human Somatic Cell Therapy Research and Quality Control of the Products (SFDA, 2003). *Notice-2011* refers to Notice on Self-Examination and Self-Rectifying of Stem Cell Clinical Research and Application (MOH, 2011). Other abbreviations see Abbreviations of Organisations and Programmes (p.i).