

**PERSPECTIVES**

# Stem cell translational medicine: The Tianjin model revisited

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**Abstract**

Stem cells hold great promise for cell therapy to treat a wide spectrum of intractable diseases. Despite enthusiasm for stem cell therapy, the clinical and translational research of stem cells overall has been a slow and cumbersome process. This article uses the “technological system” as a framework to analyze the Tianjin model of stem cell translational medicine. It shows how heterogeneous elements interact with one another and relate to scientific, technological, social, economic, and political variables in order to fulfill the system goal of producing cell therapy in China. Then the strengths and weaknesses of the Tianjin model are compared with translational programs in other countries and the implications for the cell therapy industry are discussed.

**KEYWORDS**

cell therapy, China, stem cells, technological system, translational medicine

**Significance statement**

This article uses the Tianjin model of stem cell translational medicine as a case to show the complexities in bringing scientific discoveries to clinical settings. The Tianjin model represents a microcosm of stem cell research in China and offers rich experience for the development of translational medicine.

## 1 | INTRODUCTION

Stem cells hold great promise for cell therapy to treat a wide spectrum of intractable diseases and to improve human health. Many countries have invested heavily in the stem cell field to translate basic and clinical research to stem cell therapies and clinical practice. In the past decade, stem cell clinical trials have been rapidly evolving and carried out worldwide using various stem cell types, such as mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and human embryonic stem cells.<sup>1</sup> As of February 2021, more than 8000 clinical trials on stem cells have been registered at ClinicalTrials.gov; most of these are in phase 1 or 2, with only approximately 10% in phase 3. MSCs have generated interest among scientists and have become

popular cell types for stem cell clinical trials. More than 900 of the registered clinical trials used MSCs on a wide range of diseases and injuries. MSCs are also debated in the scientific literature with regard to their meaning and so their defining biomarkers.<sup>2-4</sup> Despite enthusiasm in stem cell therapy, the clinical and translational research of stem cells overall has been slow and cumbersome due to translational gaps and innovation challenges.<sup>5,6</sup> Only a small number of stem cell-based products have demonstrated sufficient scientific evidence and clinical benefits to be approved for the market worldwide. Most of these products are based on MSCs and are mainly produced in North America and Europe; none are from China.<sup>7</sup>

Early on, China made stem cell research a priority in its science and technology policies. It launched various programs to fund stem

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cell research and attract talent back home from overseas.<sup>8</sup> In recent years, both local and national stem cell policies and programs have advocated for stem cell translational research and industry.<sup>9</sup> Tianjin, a city in North China, has expended considerable effort in building a “stem-cell city” based on its local advantages in hematology, stem cell research, and applications at the Institute of Hematology and Blood Diseases Hospital (IH) of the Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC).<sup>10</sup> After working in France for nearly 10 years, Professor Zhongchao Han, a specialist in hematology and stem cells, returned to China to work at the IH in 1997. Han then began to design and develop the Tianjin model of stem cell translational medicine. Professor Tao Cheng, a renowned researcher in the biology of hematopoietic stem cell biology and regenerative medicine, returned to the IH from the University of Pittsburgh (Pittsburgh, Pennsylvania) in 2007. Cheng took over Han's duties to continue stem cell translational medicine in Tianjin.

I performed a case study of the Tianjin model of stem cell translational medicine in 2008.<sup>11,12</sup> Using data from my fieldwork in Tianjin and other Chinese cities and secondary sources from 2006 to now, this article aims to revisit the Tianjin model and to discuss the strengths and weaknesses of the Tianjin model in the national and global contexts. Adopting the “technological system”<sup>12,13</sup> as an analytical framework, it shows that stem cell translational medicine is a technological system that contains complicated and problem-solving components: various organizations (such as research institutes, hospitals, enterprises), physical artifacts (such as laboratory equipment, raw materials, storage infrastructure), and nonphysical artifacts (such as industry standards and specifications, business model, regulatory strategy, workforce development). These disparate elements interact with one another and relate to scientific, technological, social, economic, and political variables. Thus, fulfilling the common system goals of producing innovative, safe, effective, and affordable regenerative medicine products requires no less than reordering the material world.

System builders play a crucial role as “heterogeneous engineers”<sup>14</sup> in the invention, development, and consolidation of technological systems. To build a successful technological system, system builders need a systematic approach to relate everything to a single central vision. They use organizing principles to integrate heterogeneous factors and components, and they coordinate a team of diverse professional backgrounds. These are people who are consistently committed to solving a blend of scientific, technological, financial, business, political problems that hinder the growth of the technological system.<sup>13</sup> The next sections show how Zhongchao Han and Tao Cheng, two such system builders, constructed the technological system of stem cell translational medicine in Tianjin.

## 2 | METHODS

This article draws upon data from my ethnographic research on the governance of stem cell translational medicine in Tianjin in October to December 2008 and follow-up studies of the Tianjin model in June to July 2018 and August 2020. Tao Cheng offered the access that

allowed my study in Tianjin to go forward. He introduced me to the heads and main figures of various departments and sectors in the Tianjin stem cell translational medicine network. I interviewed these people, having numerous personal communications with some of them and with Tao Cheng, either face to face or through phone calls, emails, and WeChat (the most popular mobile communication tool in China in recent years). I visited research labs, hospitals, cord blood banks, companies, national platforms, and other facilities within the network, collecting both internal and published documents. This article has also been informed by my research on the governance of stem cell translational medicine in China since September 2006. I have conducted interviews with stakeholders, including scientists, clinicians, entrepreneurs, patients, and policymakers. I have followed the evolution of stem cell policies and the development of stem cell research in China through participant observations at seminars, workshops, and conferences that I attended, and through multiple forms of secondary data, including publicly available news, reports, policy documents, and scientific publications. Interview transcripts and observation notes were subject to thematic analysis<sup>15</sup> to understand the Tianjin model and its embedded social, economic, and political environment.

## 3 | FINDINGS

### 3.1 | The Tianjin model

The core component of the Tianjin model is IH, which was founded by clinical hematologist Jiadong Deng in 1957. IH is the national center of excellence in hematology research and education, and the top-ranked specialty hospital for clinical care and scientific impact in hematology in China. In 1986, Wenwei Yan and her team performed the first autologous hematopoietic stem cell transplantation (HSCT) in patients with acute leukemia in China.<sup>16</sup> HSCT laid the cornerstone of stem cell biology and regenerative medicine in IH. The State Key Laboratory of Experimental Hematology (SKLEH), which specializes in hematology, hematological cancers, and stem cell biology, was formally established in 1991 by the Ministry of Science and Technology, People's Republic of China, and is housed at IH.<sup>16</sup> Zhongchao Han acted as the director of IH (1997-2004) and SKLEH (1998-2008) and is the first system builder of the Tianjin model.

Han had the vision to transform the results of good scientific research to technological products and social benefits. He devoted his career to translating stem cell knowledge gained from laboratories to stem cell products and industrialization. Han and his team have conducted innovative research in this field, winning several local and national science and technology progress awards.<sup>16</sup> In the early days, they worked on blood stem cells and tried autologous transplantation of peripheral blood stem cells in the treatment of patients with severe lower-limb ischemia.<sup>17-19</sup> Han proposed that perinatal tissues, including cord blood, umbilical cord, and placentas, are important natural sources of MSCs.<sup>20</sup> In 2002, under Han's leadership, IH and the investors built one of the largest stem cell bank in the world, the Tianjin

cord blood stem cell bank, and established a standardized process for banking human umbilical cord-derived mesenchymal stromal cells for therapeutic uses.<sup>21</sup> Following MSC safety studies for clinical applications, they conducted clinical studies on umbilical cord-derived MSCs to treat diseases, such as mild graft vs host disease (GVHD)<sup>22</sup> and refractory hematologic malignancy.<sup>23</sup> Most recently, Han and his team have been pioneers in building placenta-derived stem cell banks and have carried out translational research, product development, and application.<sup>24-26</sup>

As a system builder, Han has made great efforts to set up the essential components for the ecosystem in early 2000. IH, in collaboration with Shanghai Wangchunhua Group (now Vcanbio Cell & Gene Engineering Co., Ltd.), in 2001 founded the Tianjin Union Stem Cell & Gene Engineering Co., Ltd., which runs the cord blood stem cell bank. The following year, IH collaborated with Tianjin Economic and Technological Development Zone and set up the IH-affiliated TEDA Research Center for Life Science and Technology. The National Center of Stem Cell Engineering and Technology was approved by the Ministry of Science and Technology in 2002; Tianjin AmCellGene Engineering Co., Ltd was established as the legal entity of the National Engineering Research Center of Cell Products, which was approved by the National Development and Reform Commission in 2004. The Tianjin model integrated research institutes, specialized hospitals, stem cell banks, enterprises, and national centers for stem cell technology and products.<sup>10,11</sup> It became the earliest and largest stem cell industry cluster in China.

### 3.2 | The Tianjin model revisited

Tao Cheng, the current director of IH and SKLEH, continues to expand and optimize the Tianjin model. Within the CAMS and PUMC system, Cheng established the Center for Stem Cell Medicine at CAMS in 2009 to facilitate the collaboration of basic science, clinical research, and the commercialization of stem cells. To promote talent cultivation, Cheng founded the Department of Stem Cell and Regenerative Medicine and created the “stem cell and regenerative medicine” discipline under clinical medicine at PUMC in 2012.<sup>16</sup> The new department recruits undergraduate students with clinical backgrounds to study for their master's and doctoral degrees. These programs invite experts from multiple disciplines, including basic medicine, clinical medicine, quality control, cell manufacture, industry, and bioethics, to teach courses in the department. In 2019, the Regenerative Medicine Clinic was created to serve patients and to lead the development of hospital-based regenerative medicine discipline. To strengthen international cooperation, exchange, and influence, Cheng has initiated international cooperation with foreign research institutes, invited top-level scholars in the fields of hematology and stem cell to visit IH, and organized a series of international conferences and forums on stem cell and hematology in Tianjin.<sup>16</sup>

Limitations of personnel, expertise, space, and funds of IH prompted Cheng to seek external resources, as well. He realized that quality-related biological research and standard formulations are key

to promote the benign development of stem cell products and industry. But China has no national quality-control standards for the production of stem cell products, which has been a barrier in stem cell translational medicine. In 2020, IH signed a cooperation agreement with the Tianjin Institute of Materia Medica affiliated Joint Innovation Biotechnology Inc. to jointly establish a Research Center for Cell Product Quality Control, in order to promote the development, quality control, and applications of cell products (interview, August 19, 2020).

Given that cell therapy is one of the most promising fields in the biomedical industry, the People's Government of Tianjin Binhai New Area planned the Cell Valley project to accelerate technological innovation in the cell industry. IH takes the lead in constructing the Cell Valley, which will consist of four areas: core industry, achievement transformation, academic exchange, and supporting services. Its infrastructure is currently under construction. The concept and development logic of Cell Valley is similar to Silicon Valley, a global center for high technology and innovation in Northern California, USA, which brings in all the essential components, such as innovative enterprises, top talents, venture capital, research projects, and preferential policies. The design of Cell Valley refers to the U.S. cell manufacturing roadmaps to 2025 and 2030 (interview, February 22, 2021).

### 3.3 | Heterogeneous and interacting variables

Bridging translational gaps between bench and bedside is difficult and has been likened to crossing the “valley of death”.<sup>27</sup> Four key aspects—active program leadership; substantive and productive interdisciplinary collaborations; innovative research resources; and training, education, and community engagement—were identified as crucial in advancing clinical and translational research.<sup>28</sup> Two system builders of the Tianjin model, Han and Cheng, are hands-on leaders who have worked hard to transform IH from an academic research institute and hospital into an active hub in the integrated network of clinical and translational research. They used systematic approaches to resolve the challenges in the full chain of stem cell therapy and industry.

Han is a scientist-entrepreneur who designed and developed the Tianjin model. He was instrumental in IH forming partnerships with industry; constructed national infrastructures for stem cell technology and industrialization; established companies to run stem-cell-related business; and set up commercial stem cell banks of cord blood, umbilical cord, and placenta. Cheng is more like a scientific conductor who endeavored to rejuvenate the previous Tianjin model of stem cell translational medicine through integrating and expanding various resources. He ignited interdisciplinary and multisite collaborations with domestic and foreign institutes; set up education and training programs to cultivate young researchers; and participated in building the Cell Valley to give full play to the original advantages and to assemble more resources. Although IH was the first to promote stem cell industry in China and has laid a good foundation, the Tianjin model has not yet led to clinical products not seen elsewhere in

China's stem cell sectors. In the following, this article analyzes a range of heterogeneous and interacting scientific, technological, social, economic, and political variables contributing to the Tianjin model's current situation.

As the largest port city in North China, Tianjin is often where new overseas technology and culture land. In the late 1990s, Tianjin acted with foresight to bring in Han to develop stem cell research and industry with the hope of securing a leading position in the field. Han's central vision was to promote the stem cell industry, which united the main forces in the early stem cell field of China. Tianjin model's strengths embrace the IH's solid foundation in stem cell research and banking, and national platforms for stem cell technology and cell products. Part of its weaknesses comes from Tianjin's culture and social environment; its conservative political culture and lack of funds are the most salient features. Tianjin borders Beijing, China's capital city and political center. It is relatively conservative and less risk tolerant compared with cities like Shenzhen, which lies in the Pearl River Delta and is a technological and institutional innovation demonstration zone. Tianjin's government-supported funds are limited, and private capital is not active, while other life science centers in cities such as Shanghai and Shenzhen could attract more public and private funds (interviews, August 19, 2020; January 31, 2021; February 22, 2021).

Despite the great expectations for stem cells, delivering stem cell therapies faces overwhelming obstacles. Among these obstacles are the scientific novelties and complexities of stem cells. Each cell type has its own strengths and weaknesses in the development of stem cell therapies. Although they are promising cell types for clinical translation, MSCs have yet to overcome various scientific and technical issues in the development of future MSC-based therapies, such as the origin of MSC tissue sources, MSC donor-related variability, and isolation procedures.<sup>2</sup> Cell therapy, including stem cell therapy and chimeric antigen receptor T-cell therapy, has enormous potential to address unmet medical needs and represents considerable market opportunities. It is also a transformative and disruptive technology that confronts unprecedented innovation challenges. For example, the business models and necessary infrastructures for the cell therapy industry are distinct from those of the pharmaceutical, biotechnology, and medical device industries, and are not yet in place. Therefore, the 3Rs (regulation, reimbursement, and realization of value) of cell therapy are vital elements for the success of a technological system of stem cell therapies.<sup>29</sup>

Regulations have been a major challenge, sometimes becoming a hindrance for stem cell translational medicine.<sup>30</sup> This problem was salient in the Chinese context. China's controversial, inconsistent, and protracted regulations on stem cell therapies have long impeded the progress of this field.<sup>31</sup> Only in 2017, did the National Medical Products Administration (NMPA, former China Food and Drug Administration, CFDA) stipulate the "cells-as-drugs" approach for cell therapy.<sup>32</sup> Han and his team's application for umbilical cord-derived MSC clinical trials on GVHD in 2006 was suspended due to pending regulations and a lack of experience in reviewing stem cell therapies. After approximately 12 years' delay, many new studies and corresponding adjustment of proposals, the investigational new drug—an umbilical

cord-derived MSC product to treat refractory GVHD—was finally approved in 2020 by the NMPA for clinical trials.

Moreover, scientists dominate in decision-making in the process of the development planning of stem cell technology, and in the establishment and evaluation of major technological innovation projects in China; the absence of entrepreneurs and engineers in the process has impeded China's stem cell innovation.<sup>33</sup> The Tianjin model also faces these problems. Meanwhile, Tianjin faces stiff competition from its Chinese and international counterparts, as other institutions and regions have also amassed all kinds of resources to stimulate translational programs to produce cell therapy.

## 4 | DISCUSSION

To address stem cell innovation challenges and enhance global competitiveness in the stem cell and regenerative medicine industry, some countries have issued favorable policies and initiated translational programs. In addition to the conventional "cells-as-drugs" approach, which was first adopted by the United States in 2007, several expedited regulations for cell and regenerative medical products have been instituted in the United States, Japan, and the European Union, known as the Breakthrough Therapy Designation (2012), the Sakigake Designation (Pharmaceuticals and Medical Devices Agency, 2015), and PRIME (PRiority Medicines) (European Medicines Agency, 2016), respectively. Each regulatory agency has its original framework but also adopts others' regulatory strategies.<sup>34</sup> The translational programs include, for example, the Cell and Gene Therapy Catapult (CGTC) in the United Kingdom<sup>6,35</sup> and the iPSC research network in Japan.<sup>36</sup> This section comparatively analyzes the advantages and disadvantages of the CGTC program, the iPSC research network, and the Tianjin Model in their respective settings, then discusses the implications for the cell therapy industry.

With strong government support, the CGTC was established in 2012 in the UK as a center of excellence to cross the translational gap between scientific research and the commercialization of cell therapy. As an innovation accelerator agency and an intermediary agency, the CGTC has advantages to coordinate various activities and expertise to overcome business, manufacturing and supply chain, clinical, and regulatory barriers so as to speed the development, delivery, and commercialization of cell therapy, and to secure the UK's global leadership in this important industry.<sup>6,35</sup> Among the disadvantages of the CGTC program is that it has also generated competing values and priorities among the stakeholders. For example, the commercialization of biological material has given rise to a debate concerning public good vs private ownership.<sup>6</sup>

Capitalizing on its strength in iPSCs, Japan has focused on supporting the development and commercialization of iPSC-based regenerative medicine products (RMPs). With generous research funding from the government, the iPSC research network was established in the early 2010s to foster collaboration among academia, industry, and government agencies, and to expand clinical research infrastructure. To accelerate the commercialization of RMPs,

Japan has also revised regulatory policies, including conditional, time-limited approval for RMPs, and alternative schemes to provide RMPs under early-stage, small-scale human clinical research.<sup>36</sup> The iPSC initiative and flexible and expedited regulations are conducive to Japan's leadership in the global cell therapy market. The disadvantages include that the safety and efficacy of RMPs are not yet assured, the clinical application of RMPs may burden the Japanese health insurance system,<sup>37</sup> and international collaboration using clinical-grade iPSCs is challenging.<sup>36</sup>

Consistent with global development trends, recent years have witnessed the emphasis of translational research and the revival of the cell therapy industry in China.<sup>9</sup> China's regulatory strategies for cell therapy are generally similar to but slower than those of other developed countries. Parallel to the "cells-as-drugs" approach for cell therapy, the CFDA and the National Health and Family Planning Commission (NHFP) issued regulations on stem cell clinical research in 2015 as an alternative and flexible approach. This allows investigators from the designated stem cell clinical research institutes to apply for stem cell clinical research. Once investigators gather sufficient scientific evidence and clinical benefits from these clinical studies, they can use these data to apply for clinical trials through the "cells-as-drugs" approach.<sup>38,39</sup> The Measures for the Administration of Drug Registration (revised 2020) develop the accelerated and conditional review and approval procedures for breakthrough therapy and priority medicines.<sup>40</sup>

Similar to the UK's CGCT program and Japan's iPSC research network, the Tianjin model has also capitalized on IH's core advantages in the field of stem cell and established a translational research network to bridge multiple translational barriers. But the development of the Tianjin model is more restricted by local and national factors such as policy, economy, society, and expertise, which makes it lag behind other programs in the commercialization of cell therapy at present. To further develop and consolidate the Tianjin stem cell technological system to produce cell therapy, system builders need to function as "heterogeneous engineers." They can then take the lead in associating entities ranging from professions with a variety of expertise and related organizations, to physical and nonphysical artifacts, and assemble them in appropriate ways, in order to tackle scientific, technological, social, economic, and political problems.

On the whole, the global field of stem cells has been subject to the institutionalization of commercialization pressure.<sup>41</sup> The main purpose of establishing the translational programs in each country is to promote the commercialization of cell therapy. Nevertheless, these translational programs have pros and cons. They could facilitate collaborations across diversified disciplines, expertise, institutions, and artifacts to foster knowledge translation, generate value, and speed product development. At the same time, they could also create conflicts of interest among various stakeholders, such as researchers, industry partners, patients, and the public. Therefore, the issues of commercialization need to be addressed in a timely and constructive manner to realize the maximum benefits of translational programs.

## 5 | CONCLUSION

This article presents a case study of the Tianjin model of stem cell translational medicine from the perspective of a technological system.

The system builders have implemented a variety of initiatives to invent and develop the technological system, and they have gathered momentum for its growth and consolidation. As a large, novel, and daunting technological system, however, it met with a mass of interactions with an array of scientific, social, economic, and political variables. The Tianjin model embodies similar advantages and disadvantages with translational programs in other countries. The Tianjin experience could serve as a valuable and instructive reference for other institutions in stem cell translational medicine.

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## CONFLICT OF INTEREST

The author declared no potential conflicts of interest.

## AUTHOR CONTRIBUTION

H.C.: conception and design, collection and/or assembly of data, data analysis and interpretation, manuscript writing, financial support, final approval of manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## REFERENCES

1. Trounson A, McDonald C. Stem cell therapies in clinical trials: progress and challenges. *Cell Stem Cell*. 2015;17(1):11-22.
2. Kabat M, Bobkov I, Kumar S, Grumet M. Trends in mesenchymal stem cell clinical trials 2004-2018: is efficacy optimal in a narrow dose range? *Stem Cells Transl Med*. 2020;9(1):17-27.
3. Caplan AI. Mesenchymal stem cells: time to change the name! *Stem Cells Transl Med*. 2017;6(6):1445-1451.
4. Mastrolia I, Foppiani EM, Murgia A, et al. Challenges in clinical development of mesenchymal stromal/stem cells: concise review. *Stem Cells Transl Med*. 2019;8(11):1135-1148.
5. Gardner J, Webster A. The social management of biomedical novelty: facilitating translation in regenerative medicine. *Soc Sci Med*. 2016; 156:90-97.
6. Gardner J, Webster A. Accelerating innovation in the creation of bio-value: the Cell and Gene Therapy Catapult. *Sci Technol Human Values*. 2017;42(5):925-946.
7. Cuende N, Rasko JEJ, Koh MBC, et al. Cell, tissue and gene products with marketing authorization in 2018 worldwide. *Cytotherapy*. 2018; 20(11):1401-1413.
8. Yuan W, Sipp D, Wang ZZ, et al. Stem cell science on the rise in China. *Cell Stem Cell*. 2012;10(1):12-15.
9. Xiang N, Wang G, Li X. Status quo, policy review and prospect of stem cell clinical trials in China. *Chin J Cell Stem Cell*. 2020;10(5): 303-309.

10. Chen H. Stem cell governance in China: from bench to bedside? *New Genet Soc.* 2009;28(3):267-282.
11. Chen H. Cord-blood banking in China: public and private tensions. *East Asian Sci Technol Soc Int J.* 2011;5:329-339.
12. Hughes TP. The evolution of large technological systems. In: Bijker WE, Hughes TP, Pinch T, eds. *The Social Construction of Technological Systems: New Directions in the Sociology and History of Technology* (Anniversary Edition). Cambridge, MA: The MIT Press; 2012: 45-76.
13. Hughes TP. The electrification of America: the system builders. *Technol Cult.* 1979;20(1):124-161.
14. Law J. Technology and heterogeneous engineering: the case of Portuguese expansion. In: Bijker WE, Hughes TP, Pinch T, eds. *The Social Construction of Technological Systems: New Directions in the Sociology and History of Technology* (Anniversary Edition). Cambridge, MA: The MIT Press; 2012:105-128.
15. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol.* 2006;3(2):77-101.
16. Institute of Hematology and Blood Diseases Hospital (IH), ed. *The 60th Anniversary Album of the Institute of Hematology and Blood Diseases Hospital (IH) of the Chinese Academy of Medical Sciences and Peking Union Medical College (1957-2017)*; 2017.
17. Huang P, Li S, Han M, et al. Autologous transplantation of granulocyte colony-stimulating factor-mobilized peripheral blood mononuclear cells improves critical limb ischemia in diabetes. *Diabetes Care.* 2005;28(9):2155-2160.
18. Huang P, Li S, Han M, et al. Autologous transplantation of peripheral blood stem cells as an effective therapeutic approach for severe arteriosclerosis obliterans of lower extremities. *Thromb Haemost.* 2004;91(3):606-609.
19. Huang P, Yang X, Li S, et al. Randomised comparison of G-CSF-mobilized peripheral blood mononuclear cells versus bone marrow-mononuclear cells for the treatment of patients with lower limb arteriosclerosis obliterans. *Thromb Haemost.* 2007;98(6):1335-1342.
20. Han Z, ed. *Perinatal Stem Cell*. Beijing: Science Press; 2020.
21. Gong W, Han Z, Zhao H, et al. Banking human umbilical cord-derived mesenchymal stromal cells for clinical use. *Cell Transplant.* 2012;21: 207-216.
22. Wu Y, Cao Y, Li X, et al. Cotransplantation of haploidentical hematopoietic and umbilical cord mesenchymal stem cells for severe aplastic anemia: successful engraftment and mild GVHD. *Stem Cell Res.* 2014; 12(1):132-138.
23. Wu Y, Wang Z, Cao Y, et al. Cotransplantation of haploidentical hematopoietic and umbilical cord mesenchymal stem cells with a myeloablative regimen for refractory/relapsed hematologic malignancy. *Ann Hematol.* 2013;92(12):1675-1684.
24. Du W, Li X, Chi Y, et al. VCAM-1+ placenta chorionic villi-derived mesenchymal stem cells display potent pro-angiogenic activity. *Stem Cell Res Ther.* 2016;7:49. <https://doi.org/10.1186/s13287-016-0297-0>
25. Jiang R, Han Z, Zhuo G, et al. Transplantation of placenta-derived mesenchymal stem cells in type 2 diabetes: a pilot study. *Front Med.* 2011;5:94-100.
26. Liang L, Li Z, Ma T, et al. Transplantation of human placenta-derived mesenchymal stem cells alleviates critical limb ischemia in diabetic nude rats. *Cell Transplant.* 2017;26:45-61.
27. Butler D. Translational research: crossing the valley of death. *Nature.* 2008;453(7197):840-842.
28. Institute of Medicine. *The CTSA Program at NIH: Opportunities for Advancing Clinical and Translational Research*. Washington, DC: The National Academies Press; 2013.
29. Caplan AI, Mason C, Reeve B. The 3Rs of cell therapy. *Stem Cells Transl Med.* 2017;6(1):17-21.
30. Abbott A. Behind the scenes of the world's first commercial stem-cell therapy. *Nature.* 2015. <https://doi.org/10.1038/nature.2015.17022>.
31. Chen H. Reflection on the governance of clinical stem cell research and applications in China. *Regen Med.* 2017;12(6):593-597.
32. National Medical Products Administration (NMPA). *Technical Guidelines for Research and Evaluation of Cell Therapy Products (Trial)*. 2017. <https://www.nmpa.gov.cn/ylqx/ylqxggtg/ylqxzhdyz/20171222145101557.html>. Accessed February 27, 2021.
33. Zhang L. How stem cell innovation cross the "valley of death". *Chin Med Biotechnol.* 2015;10(5):385-391.
34. Nagai S. Flexible and expedited regulatory review processes for innovative medicines and regenerative medical products in the US, the EU, and Japan. *Int J Mol Sci.* 2019;20:3801.
35. Thompson K, Foster EP. The cell therapy catapult: growing a U.K. cell therapy industry generating health and wealth. *Stem Cells Dev.* 2013;22:35-39.
36. Azuma K, Yamanaka S. Recent policies that support clinical application of induced pluripotent stem cell-based regenerative therapies. *Regenerat Ther.* 2016;1(4):36-47.
37. Sipp D. Conditional approval: Japan lowers the bar for regenerative medicine products. *Cell Stem Cell.* 2015;16(4):353-356.
38. China Food and Drug Administration (CFDA) and National Health and Family Planning Commission (NHFPC). *Regulation for Stem Cell Clinical Research (Trial)*. 2015. <https://www.nmpa.gov.cn/yaopin/ypfgwj/ypfgbmgzh/20150720120001607.html>. Accessed February 27, 2021.
39. China Food and Drug Administration (CFDA) and National Health and Family Planning Commission (NHFPC). *Guidelines for Quality Control and Preclinical Study of Stem Cell Preparations (Trial)*. 2015. <https://www.nmpa.gov.cn/xxgk/fgwj/gzwj/gzwjyp/20150731120001226.html>. Accessed February 27, 2021.
40. State Administration of Market Supervision and Administration. *Measures for the Administration of Drug Registration*. 2020. [http://www.gov.cn/gongbao/content/2020/content\\_5512563.htm](http://www.gov.cn/gongbao/content/2020/content_5512563.htm). Accessed February 27, 2021.
41. Burningham S, Ollenberger A, Caulfield T. Commercialization and stemcell research: a review of emerging issues. *Stem Cells Dev.* 2013;22:80-84.

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