

Chapter 2

The Legal Framework of Stem Cell Science and Medicine in China: An Overview

Travel to another country for stem cell treatment, “stem cell tourism”, has boomed in recent years. China became one of the best destinations for stem cell therapy. According to some studies, the main incentive and motivation of stem cell tourism is a belief in the potential efficacy of the provided treatment and a faint hope that the treatment might help.¹ In practice, many claimed stem cell therapies are unverified medical treatments.² Without the safety and efficacy clinical trials in humans, some clinics and hospitals in China charge patients thousands of dollars for stem cell therapy.³ To explore stem cell therapy, scientists or clinics are operating in the dark in China because HESC policies are uncertain. Two different approaches are adopted in stem cell research and therapy: certain researchers insist on following the procedures and requirements for drug approval, and other doctors and companies exaggerate the effects of stem cell therapy to treat patients.⁴

One reason for such problematic matters is the disparities on HESC regulation among nations. Another reason is that China’s regulatory turns a blind eye to the unauthorised stem cell therapy. HESC research and advanced clinical stem cell therapy in China are still seriously unregulated. Moreover, where moral exclusion is concluded in the patent system, HESC researches are not properly supervised in China. Even if immoral research cannot be patented, immoral research can still be carried out. Given that the scientific and economic potential of HESC, the strategies adapted by China aim to develop an effective competition in the scientific, commercial and clinical application of HESC research worldwide.⁵ Driven by the

¹Master Z., Zarzeczny A., Rachul C. and Caulfield T., ‘What’s missing? Discussing Stem Cell Translational Research in Educational Information on Stem Cell “Tourism”’ (2013) 41 *Journal of Law, Medicine & Ethics* 254–268.

²Kiatpongsan and Sipp (2009).

³Murray F. and Spar D. ‘Bit Player or Powerhouse? China and Stem-Cell Research’ (2006) 355 *New England Journal of Medicine* 1191–1194.

⁴*ibid.*

⁵Salter (2009).

market pursuit of high technology interventions, the number of clinics and hospitals in China offered stem cell therapy to patients is rapidly increasing. Under the political environment of socialism with Chinese characteristics, China seems to offer a liberal and favourable environment for HESC research and its application. However, the culture response, business practice and regulation mode of HESC research are yet unclear. This chapter will first explore HESC research environment, including HESC research funding in China and HESC industry in China. Then the legal framework of HESC research, which mainly refers to the Patent law of People's Republic of China (P.R.C), the Guideline for patent examination of P.R.C and the Ethical Guideline for HESC Research, will be examined. Likewise, some exemplary cases concerning whether the inventions are related to HESC were excluded from the patent based on Article 5 of patent law and the issue of whether adult stem cells have a practical applicability under Article 22 of patent law are discussed hereto.

2.1 HESC Research Environment in China

Compared to the EUROPE, China's policy on HESC-related research and applications is relatively liberal and supported by Chinese culture and values. Since the Chinese people have reached a consensus that abortion is legal, in China, embryos are not typically treated as people.⁶ Generally, human embryo use is not considered immoral by the Chinese.⁷ In an interview by Dominique S McMahon, one Chinese expert stated, 'When we draft our Guideline, we always need to think about our culture as well. For Chinese people, we have not so strong religious ideas about the [embryo]... This is not a person, we don't think so... so we accept'.⁸ And the majority finds 'the Chinese people incapable, unsuitable or uninterested' in participating in a public debate on moral issues related to HESC.⁹ Therefore, China seems to enjoy a considerable advantage in conducting HESC research and protecting the intellectual property right of relevant inventions.¹⁰ Moreover, the general public's acceptance of HESC research is a great benefit to the application of stem cell therapy in clinic and the development of the stem cell industry.

⁶Fu and Zhao (2011).

⁷Liu lidong, 'analysis of the possibility apply for patent of HESC' (2013) 30 Hospital management forum 9–11.

⁸McMahor et al. (2010).

⁹Faulkner (2010).

¹⁰ibid.

2.1.1 HESC Research Funding in China

The major funding of HESC research in China is obtained from governmental organisations, ranging from the Ministry of Science and Technology, the National Natural Science Foundation to the Chinese Academy of Sciences. The 973 programmes¹¹ and the major scientific research project programme¹² are the two main sources of HESC research funding. The supporting priorities depend on the China national Five Year plan for National Economic and Social Development. During the eleventh Five-Year Plan, 29 stem cell research projects were funded by the 973 programmes and the major scientific research project programmes.¹³ The money from these programmes exceeded 832 million RMB. Over 50 research centres throughout the country obtained sponsorship from these programmes.

Generally speaking, the funding strategy was successful, particularly in the following three areas. First, the research field of funded programmes is within the popular areas of world stem cell research.¹⁴ Of the funded programmes, there are five programmes which refer to the regulatory network of stem cells, seven are involved with the IPS and HESC and ten are concerned with embryo differentiation and transplant. The remaining programmes mainly focus on tumour stem cells and the stem cell research platform.¹⁵ Second, China's stem cell research consisted of experts, most of whom have either obtained an overseas university degree or have spent some time training overseas.¹⁶ The China Global Expert Recruitment programme is highly attractive with a variety of financial and research incentives.¹⁷ Third, some results of the funded programme considered to be pioneering research worldwide. For example, Chinese scientists were the first to verify the totipotent of ips cell,¹⁸ as well as the first to find a way of generating the induced pluripotent cell.¹⁹

¹¹The 973 programs, also called the national basic research program, were established in June 1997 in order to promote creativity and the sustainable development of China. Stem cell research is one supporting priority project by the 973 programs.

¹²The major scientific research project mainly sponsor four areas: Protein research, research on quantum control, Nanotechnology research and research on development and reproduction.

¹³Chen et al. (2011).

¹⁴The hot research area in the world stem cell research is the embryo differentiation and transplant, ips, HESC, tumor stem cell, neural stem cell, regulatory network of stem cell, stem cell used in heart disease treatment and core blood stem cell. See *ibid*.

¹⁵*ibid*.

¹⁶*ibid*.

¹⁷*ibid*.

¹⁸Zhao et al. (2009).

¹⁹Esteban et al. (2009).

2.1.2 HESC Industry in China

The HESC research development to some extent depends on economic progress. Although the Chinese economy has grown in recent years, there is still a tremendous gap between China and Western countries. With regard to HESC research, the fundamental facilities in some laboratories such as those in Beijing or Shanghai are considered world class.²⁰ The environmental facilities and equipment of some laboratories are even envied by the world leading experts.²¹ For average, Chinese laboratory facilities still lag behind those in developed countries. However, the stem cell industry in China, both with regard to technology and business models is in a rapid development phrase and this bodes well for future prosperity.

Focusing on therapy, stem cell research in China is in the rapid process of being transferred from basic scientific research to practicable diagnostic procedures. Shen Zhen Beike (Beike) is one such company that has won world renown for its stem cell therapy. From the laboratory to hospital application, Beike's highly reputable therapy is attracting patients from all over the world to undergo treatment in China. With the benefit of the first special economic zone of China, Beike combined laboratories and hospitals to establish treatment centres.²² As the president of Beike Hu Xiang said, '[i]nitially, we only cooperated with laboratories and hospitals which offered a good standard of equipment, excellent environment and a high level team'.²³ In order to promote the interaction, 'Beike creatively launched a stem cell public technical service platform and constructed a stem cell clinical research network'.²⁴ So far, Beike has announced the world's largest clinical application security evaluation of allogeneic human umbilical cord blood-derived stem cells, as well as publishing the research data of effective treatment in systemic lupus erythematosus, hereditary ataxia and muscular dystrophy wait.²⁵

Hoping to grasp the opportunities brought by stem cell research, the city of Tianjin set up China's first stem cell industry alliance that included 22 biotech companies and research institutions such as the National Industrial base of Stem Cell Technology and the National Centre of Stem Cell Engineering and Technology.²⁶ The alliance aims to cure complicated diseases, create new stem cell technology, establish a public service platform and accelerate the transfer of

²⁰ibid.

²¹Xv (2007).

²²The city Shen Zhen was benefit of the "opening and reform" policy by the Chinese leader Deng Xiaoping. As the first "special economic zone", Shenzhen attracted many foreign investments as well as tax deductions. See Song (2011).

²³Yue Yong, 'Beike biotech: win the respect and appraise by the stem cell frontier technology' (The Chinese economic, June 2nd 2011) http://district.ce.cn/zg/201106/02/t20110602_22458434.shtml accessed November 20 2015.

²⁴ibid.

²⁵The Beike Biotech website. <http://beikebiotech.com/> accessed November 20 2015.

²⁶ibid.

scientific results to clinical products.²⁷ However, from the viewpoint of some academics, ‘the issue of healthcare system and physician–patient relationship, the intellectual property and other commercial conflicts of interest produce obstacles for translational medicine’.²⁸

Even in the capital market, it is possible to find companies whose main business relies on the stem cell industry. As the only one in the Shanghai and Shenzhen market, Zhongyuan Union Stem Cell Bio-engineering Corporation successfully operates three famous stem cell enterprises: Union Stem Cell Genetic Co. Ltd, Union East China Stem Cell Gene Engineering Co. Ltd. and HeZe biotechnology Co. Ltd.²⁹ The company holds certain important patents such as umbilical cord tissue derived mesenchymal seeded separation method, human umbilical cord mesenchymal stem cell the antifibrotic injection and its preparation method, human adipose adult stem cell acquisition method and construction of the stem cell bank.³⁰ From the above, we can conclude that Chinese companies have already entered the downstream market of the stem cell industry.

2.2 The Legal Framework of HESC Research in China

It has been argued that developing countries profit from the legal and bioethical vacuum.³¹ In particular, with regard to international collaboration which has increased in the areas of HESC research, China is determined to grasp the promise of regenerative medicine. Although China has established the moral based HESC regulation framework, the implementation of these regulations in research and clinic has not been carried out well.³² Not only were poorly educated people unable to understand the relevant regulations, but also some medical staff and researchers have not been properly trained.³³ Thus, the application of HESC research in practice, to some extent, still faces many moral, political and material risks under the current legal framework in China.³⁴

²⁷Li (2010).

²⁸Chen (2009).

²⁹ibid.

³⁰Ruan (2011).

³¹*Supra* note 27; see also *Supra* note 21.

³²Hennig (2006).

³³ibid.

³⁴Moral risks refer to ‘The violation of cultural values’; political risks is related to ‘the political economy of bioethics and public debate’; material risks is involved with ‘the distribution of material resources and wealth’. See Faulkner (2010).

2.2.1 The Patent Law of China and Its Guideline for Patent Examination

Like the EUROPE patent convention, the patent law of the People's Republic of China does not contain a moral exclusion either. Article 5 of the patent law states 'no patent right should be granted for any invention-creation that is contrary to the laws of the State or social morality or that is detrimental to public interest'.³⁵ According to the explanation by the Commission of legislative affairs,³⁶ the social morality standard depends on its acceptability by the public. If the invention is accepted by the public as well as being allowed by the moral standard, it may be granted a patent.³⁷ For example, artificial human organs for non-medical purposes and human-animal hybrid embryo are non-patentable due to the consideration of morality. Furthermore, the Guideline for patent examination (Guideline) indicates the following:

The connotation of the laws, administrative regulations, social morality and public interest is quite broad, which may vary with time and from region to region. Sometimes certain restrictions may be added or removed because of enactment and implementation of a new law or administrative regulation or amendment to or abolishment of a preceding law or administrative regulation. Therefore, the examiner shall pay special attention to this point in conducting examination according to Article 5.³⁸

The Guideline also provides the definition of social morality which refers to 'ethical or moral norms and rules generally recognized as justifiable and accepted by the public'.³⁹ It reemphasised the fact that social morality is based on 'certain cultural background, continuously changes with time and social progress, and varies from region to region'.⁴⁰

In addition, the Guideline touches on some specific regulations related to HESC. First, Article 3.1.2 in part II chapter 1 of the Guideline states that the use of human embryos for industrial or commercial purposes is contrary to social morality and therefore should be excluded from patenting. Second, Article 4.3.2.1 in part II chapter 1 lists 'methods of fertilization, contraception, increasing the number of sperm, adosculation, or embryonic transfer for the purpose of treatment' falls under 'methods of treatment' and therefore its subject matter should be excluded from

³⁵The Article 5 of patent law, People's Republic of China, promulgated by the Standing Committee, National People's Congress December 27 2008, <http://www.wipo.int/wipolex/en/details.jsp?id=6511> accessed August 1 2015.

³⁶The commission of legislative affairs is affiliated to the National People's Congress of the People's Republic of China. The explanation of patent law of China aims to provide the explanations by the authority.

³⁷ibid.

³⁸Part II Chapter 1 of Guideline for patent examination by the State Intellectual Property Office of China.

³⁹ibid.

⁴⁰ibid.

patent protection under Article 25.⁴¹ Third, Article 9.1.1.1 in Part II chapter ten of the Guideline states that ‘both an embryonic stem cell of human beings and a preparation method thereof shall not be granted the patent right in accordance with the provisions of Article 5.1’.⁴² Fourth, Article 9.1.1.2 points out ‘the human body, at the various stages of its formation and development, including a germ cell, an oosperm, an embryo and an entire human body shall not be granted the patent right in accordance with the provisions of Article 5.1’.⁴³ Fifth, Article 9.1.2.3 reads ‘an embryonic stem cell of an animal, an animal at the various stages of its formation and development, such as a germ cell, an oosperm, an embryo and so on, belong to the category of the animal variety... they are unpatentable in accordance with the provisions of Article 25 1(4).’⁴⁴

From the above we may conclude that neither inventions related to “use human embryo for industrial or commercial use” nor creations referred to “HESC and a preparing method” are allowed to be patented under the Patent laws of China. But, in terms of the differentiation, use and preservation of HESC, both patent law and its guideline do not provide any prohibitive provisions.

2.2.2 *The Ethical Guideline for HESC Research*

In order to promote the development of HESC research in China, the Ministry of Science and Technology jointly with the Ministry of Health released the Ethical Guideline for HESC research (Ethical Guideline) in December 2003.⁴⁵ The Ethical Guideline directly defined the justified source of HESC and regulated how to conduct research legally. Meanwhile, the Ethical Guideline declared that it is illegal to perform any productive cloning research and any embryo sale.⁴⁶ This was the first time to issue a guideline to clarify the illegitimate issues of reproductive cloning research. Undeniably, the Ethical Guideline has been of great significance to the rapid and healthy development of HESC research.

However, the Ethical Guideline contains some serious flaws and has received much criticism.⁴⁷ For example, Article 5 of the Ethical Guideline claimed HESC could be only obtained from: ‘(1) embryos that are left unused after in vitro fertilisation procedures; (2) foetus cells from spontaneous abortion or voluntary abortion; (3) embryos created by means of somatic cell nuclear transfer technique;

⁴¹ibid.

⁴²ibid.

⁴³ibid.

⁴⁴ibid.

⁴⁵The Ethical Guideline for HESC research, 2003 <http://www.cncbd.org.cn/News/Detail/3376> accessed February 2 2015.

⁴⁶ibid.

⁴⁷Xian Jing Xiao, ‘The ethical guideline lacks morality’ (China Science Daily, July 23 2004).

(4) voluntarily donated germ cells.⁴⁸ Obviously, the creation of a human embryo utilising sperm and egg is not allowed for research purposes. However, the Ethical Guideline ignored the main source of HESC—already existing embryonic stem cell lines. In Western countries such as Germany, the UK and the US, already existing embryonic stem cell lines are a very popular source of HESC.

Another argument is focused on the Article 6: ‘use embryos from In Vitro Fertilisation, somatic nuclear transfer, a single replication technology or genetic modification blastocysts obtained in vitro, only embryos for a maximum of 14 days could be used in research’.⁴⁹ This article is similar to the Article 36, clause 4 of the Human Fertilisation and Embryology Bill.⁵⁰ The 14 days restriction is also regulated in many other countries such as Germany and Japan.⁵¹ It seems reasonable because we use the restriction that is popular in other countries. The problem is the restriction cannot be applied well to the situation in China. The reason is that, unlike in western countries, abortion is considered legal in China. Therefore, considering moral and culture difference, it may be pragmatically meaningful for the regulators to rethink whether the 14 days restriction should be adopted in China.⁵² Moreover, the Ethical Guideline should justify the necessity for ‘transplanting’ the regulations of Western countries.

In addition, one fatal problem pointed out by the ethicists is that the Ethical Guideline lacks the relevant moral definition as well as the relevant moral objection. From article 5 to article 10, the regulation places its focus on the code of conduct instead of moral behaviour.⁵³ Thus, the Ethical Guideline is lacking in moral connotation and appears monotonous and mechanical. In fact, it is necessary to express moral connotation and moral reasons in an appropriate form in order to let people deeply understand and accept the Ethical Guideline. In addition, it is noticeable that article 9 states ‘the Ethical Committee should consist of the biologists, the doctors, the lawyers and the socialists. The responsibility of committee is to examine, supervise and provide consultation to HESC research.’⁵⁴ The clause did not mention the ethicists, who should play a critical role in the Ethical Committee. It is no exaggeration to say that whether the Ethical Committee can reach its aim depends largely on the participation of the ethicists.⁵⁵

⁴⁸The Ethical Guideline for HESC research (2003).

⁴⁹*ibid.*

⁵⁰The Human Fertilisation and Embryology Bill 2008.

⁵¹Sven Pompe, Michael Bader and Christof Tannert, ‘Stem cell research: the state of the art’ (2005) 6 EMBO Rep 297.

⁵²Ren Zong Qiu, ‘The review of the ethical guideline of HESC research’ (2004) 4 Medical and philosophy 275.

⁵³*Supra* note 48.

⁵⁴*ibid.*

⁵⁵*ibid.*

2.3 Case Studies

Most disputes over HESC are gathered in patent granting beyond the article 5 of the patent law: ‘no patent right should be granted for any invention-creation that is contrary to the laws of the State or social morality’.⁵⁶

2.3.1 *Whether Article 5 of the Patent Law Excludes Inventions Related to HESC?*

As shown by the following analysis, HESC differentiation and culturing methods are both prohibited by patent law in China. In addition, preparations of pre-implantation embryo for therapeutic cloning use are not patentable. However, in judicial practice, inventions related to existing HESC lines do not contrary to morality under the Article 5 of Patent Law.⁵⁷

Case Advanced Cell Technology Related to the Differentiation of HESC and its Culture Method: Lacking the Explanation of “Embryo” and “Industrial or Commercial Purpose”

Advanced Cell Technology’s⁵⁸ patent application on January 24, 2005 covers methods for improved cell-based therapies for retinal degeneration and for differentiating HESC.⁵⁹ Its publication date was May 23, 2007. Initially, the claims covered the differentiation of HESC into retinal pigment epithelial cells used to treat retinal degeneration.⁶⁰ Under Article 5, the patent could not be granted unless it deleted that claim.⁶¹

A similar situation also occurred in the context of Beijing University’s patent application on May 17, 2006 related to a method for culturing HESC in a special culturing medium.⁶² The patent application deleted claims involving HESC culturing before the patent was granted.⁶³ Likewise, the authorisation of a patent application covering methods of preparing feeder-cell-free, xeno-free HESC and

⁵⁶*Supra* note 35.

⁵⁷*ibid.*

⁵⁸Advanced Cell Technology, Inc., is a biotechnology company that specializes in the development of cellular therapies for the treatment of diseases and conditions that impact tens of millions of people worldwide. The company applies stem cell-based technologies (both for adult and “embryo-safe” HESCs).

⁵⁹CN 1968608 A (Improved modalities for the treatment of degenerative diseases of the retina.).

⁶⁰*ibid.*

⁶¹*ibid.*

⁶²CN 1844374 A (Culture method for HESC and special culture medium thereof.).

⁶³*ibid.*

stem-cell cultures specified the elimination of the HESC culturing methods that had been included in the applicant's public specification.⁶⁴

It is well established in this case that patent could not be granted to the differentiation of HESC and its culture method. However, neither "embryo" nor "industrial or commercial purpose" were defined in this case.⁶⁵ Although the Chinese patent office encountered the same problems as the European office,⁶⁶ it neither provided any explicit explanation nor offered any judging approach.

Case Shanghai Genon Biological Product Related to the Preparation of Pre-implantation Embryo for Therapeutic Cloning Use: HESC with the Possibility of Developing into Human Being is within the Scope of Human Embryo

Shanghai Genon Biological Product Co. Ltd.'s (Genon) November 2, 1999, patent application referred to the preparation of pre-implantation embryos for therapeutic cloning use.⁶⁷ The publication date of the patent application was July 11, 2001. In 2003, the China's Intellectual Property Office (IPO) rejected the application pursuant to Article 5. The decision was made for the following reasons: First, the method used in the invention involves mixing a donor nuclear cell and non-mammal cytoplasm derived from donor oocytes. The reconstructed cell is stimulated and transplanted into non-human mammals.⁶⁸ Finally, the cell is developed into early embryos. The IPO held that because the cell contains complete genetic information, the early embryo should be identified as a human embryo. The preparation method of an early embryo is equivalent to human cloning. Therefore, the invention falls within the moral exclusion of Article 5.⁶⁹ Second, the IPO held that the invention was for industrial and commercial purposes and therefore, it

⁶⁴CN 100549163C (Methods of preparing feeder cells-free, xeno-free HESCs and stem cell cultures prepared using same); CN 1748025A (Methods of preparing feeder cells-free, xeno-free HESCs and stem cell cultures prepared using same.).

⁶⁵*Supra* note 35.

⁶⁶Brian Salter, 'Governing stem cell science in China and India: emerging economics and the global politics of innovation' (2008) 27 *New Genetics & Society* 145–154 (stating that with its accession to the World Trade Organization (WTO) in 2001, China agreed to conform to the requirements of the Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement. Since then China has cooperated frequently with the World Intellectual Property Organization (WIPO) and the European Patent Office (EPO) on personnel training and promoted IPR teaching and research in over 70 universities; see also Tang huadong and Wang dapeng, 'the analysis of the patentability of HESC' (2013) 5 *Intellectual Property* 52–54.

⁶⁷Shanghai Genon Biological Product Co. Ltd. become the high and new technology enterprise in Shanghai, Little Giant Breeding enterprise, important enterprise of feed industry in Shanghai and the main unit which drafts out the national standard of "Spray dried globin protein powder for feed." The company has taken large number of special government projects such as industrialization project of high and new technologies from National Development and Reform Commission, National Spark Plan, innovation fund for medium and small enterprise, domestic cooperation projects in Shanghai, "develop agriculture by science and technology projects" in Shanghai and "four news" technology projects in Shanghai.

⁶⁸See the 5972 re-examination decision by the patent review committee.

⁶⁹*ibid.*

violated Article 5.⁷⁰ Third, as stated in the patent claim, the resulting embryo would be a human-animal hybrid, which is forbidden by the patent-examination Guideline.⁷¹

In 2004, Genon appealed to the Patent Review Committee making the following arguments: First, although the embryo includes human genetic information, it is a human-animal hybrid, not a human embryo. Thus, the invention is not related to the industrial or commercial use of a human embryo.⁷² Second, the embryo created by this method has no possibility of becoming human because claims 1–10 of the application contain no human-cloning steps.⁷³ Third, the invention represents one aspect of human organ transplantation technology.⁷⁴ Therefore, the invention is properly classified as therapeutic cloning. Neither its aim nor its method involves human cloning. In conclusion, the invention is not against the law, social morality or the public interest.⁷⁵

The committee reexamined the patent application and concluded that the invention is unlawful based on Article 5 for two reasons.⁷⁶ First, the nuclei donor's genetic information has a decisive impact on the cell's overall performance. Genon's patent application contains human nuclei materials that possess the characteristics of human cells.⁷⁷ As claimed in the patent application, the invention is primarily used for the purpose of tissue or organ transplantation. If so, the invention could not exclude the possibility of developing into a human being. However, the committee did not ignore the possibility that the embryonic cells would exhibit the characteristics of an animal.⁷⁸ In that situation, the method still violates public morality because it changes the genetic identity of a human germ line. Second, the claim does not exclude the possibility of the early embryos developing into humans. Genon did not provide any evidence to prove that the embryos could not develop into human beings.⁷⁹

It has been speculated that HESC comes with the possibility of developing into human being are against public morality under Article 5 of patent law. The argument in this case seems to provide the interpretation of human embryo. However, there are many extant ambiguous aspects, especially how broadly or narrowly to construe the possibility of developing into human being.

⁷⁰ibid.

⁷¹ibid.

⁷²ibid.

⁷³ibid.

⁷⁴ibid.

⁷⁵ibid. See also Liu lidong, 'Analysis of the possibility apply for patent of HESC' (2013) 30 Hospital Management Forum 9–11.

⁷⁶ibid.

⁷⁷ibid.

⁷⁸ibid.

⁷⁹ibid.

Case the Regents of the University of California related to the Oligodendrocytes Derived from Already Established HES Cell Lines for Remyelination and Treatment of Spinal Cord Injury: it is Improper to Trace the Origin of the World's First HESC Lines

The next patent application that we consider was filed by the Regents of the University of California in 2003 and covered oligodendrocytes derived from HESC for remyelination and the treatment of spinal-cord injuries.⁸⁰ The IPO held that this invention violated Articles 5 and 22 of the Patent Law of China.⁸¹ The committee believed that the patent specification and claims in their entirety related to HESC obtained from human embryos, thus violating social morality through the use of human embryos for industrial or commercial purposes. In addition, the pluripotent cell derived from non-embryo tissue required bone marrow or other human or animal tissues through a surgical method for non-therapeutic purposes. Thus, the invention could not satisfy the utility standard set forth in Article 22.

The applicant appealed to the Patent Review Committee on the following two grounds: First, the HESC aspect of the invention had been removed from the patent specification, and the cell lines used in the invention belong to established, mature, already-commercialised HESC lines. Second, the application's claims explicitly excluded direct decomposition from the human-embryo or HESC-related technology solution. In addition, the application had deleted all industrial or commercial uses of human embryos.⁸²

With respect to Article 5, the applicant argued that the origin of HESC should not be traced in perpetuity. The starting material of the application consisted of established HESC lines capable of unlimited in vitro proliferation. In the prior art, there are many ways to obtain mature and stable HESC lines. Moreover, it is improper to trace the origin of the world's first HESC lines. Using established

⁸⁰See the 42698 re-examination decision of the patent review committee.

⁸¹Patent Law of China (promulgated by the Standing Comm. of the Seventh Nat'l People's Cong., Sept. 4, 1992, effective January 1, 1993) the Article 5 <http://www.chinatradeoffice.com/about/laws2.html#2> accessed September 1 2015 (providing that "No patent right shall be granted for any invention-creation that is contrary to the laws of the State or social morality or that is detrimental to public interest."); Patent Law of the People's Republic of China (promulgated by the Standing Comm. of the Seventh Nat'l People's Cong., Sept. 4, 1992, effective January 1, 1993) the Article 22 <http://www.chinatradeoffice.com/about/laws2.html#2> accessed September 1 2014 (providing that "Any invention or utility model for which patent right may be granted must possess novelty, inventiveness and practical applicability. 'Novelty' means that, before the date of filing, no identical invention or utility model has been publicly disclosed in publications in the country or abroad or has been publicly used or made known to the public by any other means in the country, nor has any other person filed previously with the patent office an application which described the identical invention or utility model and was published after the said date of filing. 'Inventiveness' means that, as compared with the technology existing before the date of filing the invention has prominent substantive features and represents a notable progress and that the utility model has substantive features and represents progress. 'Practical Applicability' means that the invention or utility model can be made or used and can produce effective results.").

⁸²ibid.

HESC lines could decrease human-embryo abuse and in turn, limit the use of HESC to mature strains. Therefore, the application does not violate Article 5's social-morality provision.⁸³

Recognising that it is inappropriate to trace the origin of HESC lines, using established stem cell lines is allowed by the morality provisions in the patent law. However, in the following decision 24343 made by the Patent Review Committee, the Committee held that although HESC could be obtained from commercial channel, the source of HESC still lay on the destruction of the human embryo.⁸⁴ More definitively, the culture of HESC featured problems like being time-consuming, difficulty to operation, and easy to contaminate. As a result, established cell lines are not the steady and long-term source of HESC. Subsequently, the argument that HESC could get rid of the destructing human embryo is unrealistic.⁸⁵

The uncertain decision made by the Patent Office is due to the misunderstanding of the moral provision.⁸⁶ The moral standard as well as the relevant definition should be clarified and developed as soon as possible.

2.3.2 Whether Adult Stem Cell Has the Practical Applicability Under Article 22 of Patent Law?

There are no specific clauses either in the patent law or the guideline for patent examination towards the practical applicability of adult stem cell. According to the article 22 of patent law, 'practical applicability means that the invention or utility model can be made or used and can produce effective results'.⁸⁷ If you apply a patent for the product, the invention must be able to manufacture in industry. Or if the patent application is referred to the method, the invention must be able to utilise in industry. In the section 4.3 of guideline for patent examination, 'methods of surgery for non-treatment purposes do not have practical applicability because these methods are practiced on the living human or animal body and cannot be used industrially'.⁸⁸ In practice, this provision is widely used in examining adult stem cell patent application. Because the preparation method for adult stem cell includes

⁸³ibid.

⁸⁴The 24343 re-examination decision of the patent review committee.

⁸⁵See NIH fact sheet on human pluripotent stem cell research Guideline, <http://stemcells.nih.gov/news/newsarchives/stemfactsheet.asp> accessed October 28 2013.

⁸⁶*Supra* note 57 (observing that the lack of consensus in the supplication of the morality provision suggests that there is a fundamental misunderstanding regarding the nature of the provision. The closer this analysis has gone to achieving an operative understanding of the provision, the greater recourse to commentators has been required in order bridge the gaps in practice.).

⁸⁷The Article 22 of patent law of the People's Republic of China.

⁸⁸Section 3.2.4 in Part II of Guideline for patent examination by state intellectual property office of the People's Republic of China.

the surgical procedure, the adult stem cell inventions for non-treatment purposes do not have practical applicability.

The Natural Killer T cell by Kirin Brewery Company: Lacking Practical Applicability due to the Step Involved with Human Body

The patent application by the Kirin Brewery company in 2001 claimed the culture method of natural killer T Cells as well as the relevant Reagent.⁸⁹ The method includes the mononuclear cell from the peripheral blood and the steps using granulocyte colony stimulate stem cells in the peripheral.⁹⁰

The substantive examination department of the State IPO objected the patent application on the grounds of Article 22 of the patent law. The IPO held that according to the description in the specification of the patent application, the invention must have the step of collecting peripheral blood from human body and injecting granulocyte colony stimulating factor.⁹¹ This step is involved human body as objectives therefore cannot be used in the industry. As a result, the invention lacking practical applicability does not comply with Article 22 of patent law. Accordingly, the relevant Reagent that does not have practical applicability cannot be patented either.⁹²

The Culture and Growth Method by Da An Gene Co. Ltd. of Sun Yat-Sen University: Lacks Practical Applicability Because it Contains the Surgical Method

The patent application by the Da An Gene Company in 2003 claimed the culture and proliferation method of stem cell derived from adipose tissue.⁹³ The claimed method comprising:

- (1) [T]he collection of healthy human adipose tissue from the 3–18 years old boy and the preparation of conditions to produce the culture medium;
- (2) the isolation and purification of stem cells provided by a human adult adipose tissue;
- (3) the further purification of the products from claim 1 and 2;
- (4) the purification of stem cells obtained from step 3 and directed differentiation of the cultured stem cells.⁹⁴

The substantive examination department of the State IPO rejected the application on the grounds of Article 22 of the patent law. The legitimate reason is: although the pluripotent stem cell culture method cannot be identified as the “surgical method for non-therapeutic purposes” under guideline for patent examination.⁹⁵ But the claim contains the step of fetch samples from the human body that belongs

⁸⁹The CN1444648A patent application.

⁹⁰ibid.

⁹¹ibid.

⁹²ibid.

⁹³The CN1597936A patent application.

⁹⁴ibid.

⁹⁵Section 3.2.4 in Part II of Guideline for patent examination by state intellectual property office of the People’s Republic of China.

to the typical surgery for non-therapeutic purposes. Therefore, the patent application lacks practical applicability because it contains the surgical method.

2.4 Conclusion

This chapter has examined the regulation of HESC research in China. As the above passage observed, public debate on HESC research might be considered a political risk due to its potential in undermining HESC research. Due to the lack of the public debate on HESC research, the legal framework of China on HESC is still far from perfect. Neither China's patent law nor the Ethical Guideline by the Ethic Committee provided any prohibitive provisions towards the differentiation, use and preservation of HESC. Although the Ethical Guideline forbid to transfer the embryo into the uterus, due to the lack of relevant moral definition and moral ground for objection reasons, the line between moral research and immoral research is blurred. In addition, there are mainly two disputes in patent law: one is whether the Article 5 of patent law is the legitimate reason to exclude HESC research to be patented; the other is whether adult stem cell has the practical applicability under the Article 22 of patent law. Practically, many cases testified that moral objection in Article 5 is allowed for patent exclusion. Patent application involved with adult stem cell is insufficient in practical applicability and therefore could not be patented. However, China has appeared to be a powerhouse in HESC transfer. Despite that the government concerns with the safety and quality of transferring stem cell research from laboratories into the clinics, stem cell therapy is booming in clinics and hospitals. Lacking transparent legal framework and proper supervision, hospitals and companies could easily carry out stem cell therapy in patients and collaborate with each other on any level.

Referring to patent law in China, there are two core issues. One focus is on whether the inventions related to HESC are excluded from patents based on Article 5 of patent law—'no patent right should be granted for any invention-creation that is contrary to the laws of the State or social morality'.⁹⁶ Based on case analysis, the author found that most patent applications involving HESC have been refused due to moral reasons. But, many such applications have been granted after they have deleted the human element in their claims.⁹⁷ The other core issue contemplates whether adult stem cells have the practical applicability under Article 22 of patent law—'practical applicability which means that the invention or utility model can be made or used and can produce effective results'.⁹⁸ In practice, such patent application lacks a practical applicability due to the fact that it comprises the surgical method. Moreover, regarding the differentiation, use and preservation of HESC,

⁹⁶The Article 5 of patent law of the People's Republic of China.

⁹⁷Tang and Wang (2013).

⁹⁸The Article 22 of patent law of the People's Republic of China.

both patent law and its guideline do not provide any prohibitive provisions. The moral exclusion could not clearly demarcate the line between moral research and immoral research.

In general, based on the previous analysis, the author proposed that China should establish specific legal documents on HESC research instead of putting moral exclusion in the patent law. The specific legal document should clear the lines between allowed research and prohibited research. Moreover, in terms of HESC research transfer, state legislation is more proper than the ethical guideline considering the different execution.



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