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How to promote the accessibility of technology in the era of hESC patents—A comparative analysis of the systems of the US and China

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SUMMARY

We have entered the era of human embryonic stem cell (hESC) patents and the focus of discussion has shifted to how to rebalance interests. A potential way is to limit hESC patents and seek more effective utilization forms, such as ethical limitation, compulsory licensing, antimonopoly law regulation, experimental exception, and open licensing. This paper compares the restrictive measures in two major hESC markets, the United States and China, and explores the possibility of a balanced interests system.

INTRODUCTION

Since the first attempt was made in 2010 to use human embryonic stem cells (hESCs) to repair spinal cord injuries, a dozen clinical trials have used cells derived from hESCs to treat diseases such as Parkinson's disease and diabetes (David, 2018). Early results suggest that some approaches have proven to be effective, which supports the alluring prospects of hESC technology. Currently, induced pluripotent stem cells (iPSCs) cannot replace hESCs, as further scientific research has shown that iPSCs have defects such as carcinogenicity and gene mutations caused by foreign gene integration (Okita et al., 2007). With the further development of technology, hESCs have become an invaluable treasure with unlimited potential, triggering a new round of scientific and technological competition. Many countries provide policy and financial support for hESC research and even elevate it to the national level (Chen and Li, 2021). Although this research remains controversial, hESC-related technologies have been granted patents in many countries and regions. Compared with the previous period where there were no or few patent authorizations, it is no doubt that the world has entered into the era of hESC patents.

The private attributes of intellectual property justify the legal monopoly of patentees. However, excessive emphasis on private attributes may lead to fierce conflicts between intellectual property and public policy objectives in fields such as culture, medical care, health, and education (Wu, 2003). The realization of these public policy objectives is fundamental to human development. Therefore, it is necessary to reconcile the human rights attributes with the private attributes of intellectual property rights. Since the promulgation of the *Universal Declaration of Human Rights*, major international human rights conventions have endowed intellectual property rights with human rights attributes. These rights include two aspects: protecting the intellectual achievements of creators and sharing the benefits of intellectual creation with the public (Chapman, 2001). At present, the interests of patentees can be guaranteed by patent authorization. Therefore, the focus of discussion has shifted to how to share the benefits with the public, that is, improving the accessibility of corresponding technologies (Zhang et al., 2022). In this regard, the potential way is to limit the private rights of hESCs and seek more effective forms of transaction or utilization to rebalance interests (Bergman and Graff, 2007). This article aimed to explore the restrictive methods in the era of hESC patents. In terms of the selection of research objects, since North America and the Asia-Pacific region remain the most important stem cell markets globally, this paper takes the United States and China as representatives to compare their restrictive measures for hESCs and explores the possibility of designing a balanced interests system to promote the accessibility of hESC technologies and realize the dual value of intellectual property rights.

POTENTIAL PATHWAYS FOR LIMITING hESC PATENTS

The patentability of hESCs has become an indisputable fact and a global trend. To enhance the social benefits brought by intellectual property sharing and scientific and technological progress, it is necessary to strike a balance between the interests of the patentee and the public. In this regard, it is more feasible to explore the limitation of hESC patents under the framework of the existing system than to set up a new system that involves a long process and high risks. Since countries around the world have not yet reached an agreement on the patentability of hESCs, discussions are still mainly focused on the first stage of patentability standards, and few scholars have explored the second stage of restrictive methods after the global authorization of hESC patents. Under the current patent laws of the United States

and China, possible paths include ethical limitation, compulsory licensing, antimonopoly regulation, experimental use exception, and open licensing.

The limitation model of hESC patents in the United States

The United States has always advocated strong protection of patent rights. This is reflected in the absence of specific ethics clauses and patent type restrictions on the subject of patentability and in the lack of restrictions on patent rights in US patent law. In terms of function, most hESC patents are fundamental patents. These patents are usually used as critical tools for research. However, under US patent law, the scope of the experimental use exception has been continuously narrowed in judicial precedents. It is very limited and applies only to entertainment, curiosity, or pure knowledge exploration (733 F.2d 858, 861, Fed. Cir. 1984), but not to research and development for commercial purposes (216 F.3d 1343, 1349, Fed. Cir. 2000), which include research and development activities related to business in academic research institutions (307 F.3d 1351, Fed. Cir. 2002). Therefore, there is almost no possibility of an experimental use exemption in the United States. At the same time, the United States lacks systems for open licensing and platforms for sharing patent information (Bergman and Graff, 2007). Therefore, the United States currently has limited ways to restrict hESC patents and mainly relies on three tools: ethical limitation, compulsory licensing, and antimonopoly law regulation.

Potential limitations of ethics and morality

However, the absence of a specific "moral clause" in US patent law does not mean that ethics do not have an impact on the US patent system. In the field of biotechnology, the limitations of ethics and morality are mainly reflected in the revision of the US patent law in 2011, namely, the "America Invents Act" (AIA), which is the largest revision of US patent law since 1952. According to the AIA, "no patent may issue on a claim directed to or encompassing a human organism." However, since the AIA does not define the concept of "human organism," improperly expanded interpretations of this concept may hinder the patent authorization of inventions related to embryonic stem cells (Sonya et al., 2015). Therefore, the patentability of hESC products or methods in the United States is still subject to ethical and moral restrictions, which may become the trump card to restrict the patentability of hESCs.

Deterrence of compulsory licensing

US patent law (35 U.S.C.A.) does not specifically provide for a compulsory licensing system for patent abuse or public interest. When the US patent law was revised in 1952, there was a bill in Congress to incorporate the provisions of the compulsory licensing of patents into the patent law, but it was ultimately deleted. In spite of this, the US compulsory licensing system for patents is relatively complete. Although being scattered in many laws and regulations, the rules are specific and detailed, and many cases have appeared in practice. In the field of hESCs, there are mainly two related systems: government use and march-in rights under the Bayh-Dole Act.

(1) The use of the patent by the government and its contractors

According to 28 U.S.C. § 1498, the United States allows the federal government and its contractors to use patented technology without the consent of the patentee under the condition of "reasonable and complete compensation." Furthermore, § 1498(a) provides the government with a broad, almost unrestricted compulsory license: (1) there are no limitations on the field of invention, which means that as long as a patent is recognized under US patent law, it can become the object of government use; (2) the negotiation process for the government to obtain a license from the patentee is exempted, which means the government and its contractors can use or manufacture the invention patent without the permission of the patentee and without notification; and (3) the clause stipulates a wide range of persons that are eligible for government use, including "contractors, subcontractors, any individual, partnership, company, or those whose actions are authorized or agreed upon by the government." The application and manufacturing of invention patents by these persons are for the sake of the United States. Moreover, in specific cases, the court has not only lowered the threshold for government "authorization or consent," arguing that consent is not necessarily open and specific (359 F. Supp. 467, at 470, 1973), but has also held that bidders who have not officially become contractors for government contracts also enjoy the exemption (806 F.2d 1057, 1060, 1986). In special circumstances related to public health, industrial competition and development, etc., compulsory licenses may be issued as long as reasonable and complete compensation is given to the patentee. Due to the broadness of the US government use, patents related to hESCs can also become eligible objects (Amy et al., 2016).

(2) March-in under the Bayh-Dole Act

The Bayh-Dole Act was proposed by the US Senators Birch Bayh and Robert Dole and was amended in 1984 for inclusion in Chapter 18 of the US Code (U. Code 35), titled *Patent Rights for Inventions Made by Federal Independence*. Before the Bayh-Dole Act, the government owned the patent rights generated by the scientific research projects it funded, and the transfer approval process of these patent rights was so complicated that less than 5% of the patented technologies could be commercialized. The

Bayh-Dole Act facilitated tripartite cooperation among the government, scientific research institutions, and industry through reasonable institutional arrangements. The Bayh-Dole Act allowed scientific research institutions such as universities that received federal funding to own the patent rights of technologies produced in their own research projects and to authorize these patents to others for commercial development, thus revitalizing the technology development and application of the industry. However, the Bayh-Dole Act stipulates that the government can require the funded unit that retains the power to grant a third party a license to implement the invention under certain circumstances, or the federal government can directly grant a license to the third party to implement the invention, which is called march-in authority. The original intention of march-in authority was to ensure that federally funded inventions could be commercialized as soon as possible under "good faith." It allowed the government as a funder to effectively ignore the exclusivity of patents granted by the Act, either on its own motion or at the request of a third party, and to grant additional licenses to other "reasonable applicants." For example, when the government determines that a patented technology should be released as soon as possible to benefit the people (for example, a special drug to overcome the Ebola virus), march-in authority enables it to ignore the interests of the original patentee and to issue nonexclusive licenses and control prices. Since President Obama lifted the restrictions on federal funding for stem cell research in 2009, the United States has successively funded many studies related to hESCs. According to the Bayh-Dole Act, the US government reserves the right to intervene in these funding projects, and rational use of this right helps to promote the accessibility of corresponding technologies.

Regulation under the antimonopoly law

From the perspective of the laws involved, the United States has generally gone through three stages in its regulation of patent right abuse. The first stage mainly relied on patent law for restriction; the second stage resorted to the antimonopoly law for adjustment; and the third stage (the current stage) utilizes the combined effects of the antimonopoly law and patent law for adjustment (Yang and Wang, 2009). As far as existing cases are concerned, measures such as compulsory licensing have been used by authorities as a remedy against cartels and monopolistic practices. For example, in the US v. National Lead Co. (332 U.S. 319, 1947), the defendant established a cartel in the form of a "patent pool" and was finally sentenced to compulsory licensing of patents. In the case of US v. Aluminum Co. (91 F. Supp. 333, at 408–11, S.D.N.Y., 1950), the defendant abused its dominant position to suppress research and development through grantback clauses in licensing and was ultimately remedied by voluntary free licenses. Compulsory licensing can sometimes serve as a condition of agreement to a merger, which may lead to patent abuse. For example, the US v. 3D Company and DTM Company (2001 WL 964343, D.D.C.), the US v. Miller Industries and other companies (2000 WL 33141220, D.D.C.), and the US v. Halliburton Company and Dresser Industries (1999 WL 1705506, D.D.C.) initiated by the Antitrust Bureau of the Ministry of Justice all ended in compulsory licensing as a condition for agreement to a merger; that is, after the merger, the patents determined by the court had to be granted to competitors. Therefore, the abuse of patents is very likely to lead to open licensing of patents under the current US antimonopoly law and patent law. hESC patents, as an extremely valuable fundamental type of patent, are likely to cause patent abuse in future research and development by the patentee, such as monopoly agreements or the concentration of operators. In this context, it will be feasible to promote the opening of corresponding patents through the regulation of antimonopoly law.

China's restriction models for hESC patents

China officially entered into the era of hESC patents through the revision of the China's Guidelines for Patent Examination (CGPE), but discussion of hESC patents in China is still limited to the standard of patentability. Much less attention is given to the restrictions of patent rights, which, to some extent, is related to the inadequacy of hESC patent authorization in China. Many scholars have not realized that we have entered into the new era and lack a developed vision. Under China's current patent law, the possible paths of restriction are similar to those in Europe, which are mainly reflected in four aspects: limitation of ethics, restriction of compulsory licensing, regulation of antimonopoly law, and exception of experimental use and the incentive of an open licensing system.

Limitation of ethics and morality

In China, the Article 5 of Patent Law of the People's Republic of China (CPL) is an "ethics and moral clause" that rules out the patentability of inventions that violate the law or social morality or harm the public interest. For further clarification, the CGPE (pre-revised version before September 2019) stipulated that "the application of human embryos for industrial or commercial purposes is a violation of social morality," that "hESCs and their preparation methods are not patentable subjects," and that "germ cells, fertilized eggs, embryos, and individuals are all considered as various stages of human formation and development and thus are not patentable." The above-mentioned legislations have limited the patent authorization of hESC-related inventions to an extremely narrow space. However, after the revision of the CGPE came into effect on November 1, 2019, the above stance has undergone a significant shift. hESCs

and their preparation methods were allowed to be the subject of patents (Chen and Li, 2021). Moreover, the invention of using hESCs from human embryos that have not undergone *in vivo* development and have been within 14 days will not be considered as a break in ethical ethics, which means it does not violate Article 5 of the CPL (Xie et al., 2020). However, despite significant changes in the CGPE, Article 5 of the CPL, which is legally superior to it, remains valid. In this context, an application for an invention that directly destroys human embryos to obtain stem cells will still be rejected for violating Article 5 of the CPL. In other words, Article 5 of the CPL will continue to act as a "moral gatekeeper" in the application of hESC patents.

Restriction on compulsory licensing

The regulation of patent compulsory licensing has a long history in China since the first promulgation of the CPL in 1984. However, China has not granted any patent compulsory license thus far, which limits the discussion on patent compulsory licensing in China to the theoretical level. In view of the tremendous prospects of hESC application in medicine, discussion of the compulsory licensing of hESC patents is forward-looking. Currently, the vast majority of hESC patents in China are fundamental patents, such as embryonic stem cells and their preparation methods, cultivation methods, and directional differentiation methods, which face great market and social demand. Under certain conditions, the Patent Administration Department of the State Council may issue compulsory licenses to the corresponding patents in response to applications from other units and individuals or on its own, mainly based on the following five situations. First, there is insufficient implementation. When the patentee fails to implement or fully implement the hESC patent within a reasonable period of time and fails to meet the needs of the domestic market, such as patents related to specific embryonic stem cells and other fundamental patents, units and individuals with the ability to implement such patents can apply to the Patent Administration Department of the State Council for a compulsory license. The second is monopolistic behavior. When the patentee abuses the hESC patent and constitutes a monopoly, other subjects can apply for a compulsory license. The third is cross-compulsory licensing. When other individuals or units can make further inventions and creations on the basis of hESC patents and obtain major technical patents with higher economic value, they can apply for a compulsory license of the previous patent. The fourth issue is public interest. hESC patents have broad prospects in medical and health fields. When the corresponding patents are of great importance to the public interest, such as the treatment of infectious diseases and public health needs, the Patent Administration Department of the State Council can issue a compulsory license. The fifth issue is public health. This regulation is mainly to achieve the public health goals set in the *Doha Declaration*. For drugs that have obtained an hESC patent, the corresponding patented drugs can be exported to countries that meet the requirements under the condition of achieving public health purposes.

Regulation of antimonopoly law

To clarify the relationship between intellectual property and monopoly and regulate monopoly behaviors in intellectual property, the Anti-Monopoly Commission of the State Council promulgated the *Anti-Monopoly Guidelines of the Anti-Monopoly Commission of the State Council for Intellectual Property Rights* in January 2019. Two types of behaviors involving the abuse of market dominance of intellectual property rights are clearly stipulated, namely, "licensing intellectual property rights at unfairly high prices" and "refusal to license." When determining unfairly high prices, previous license records, the calculation method of license fees, and the value contribution of intellectual property rights to related products can be taken into account. When license fees and blanket licenses are charged beyond the geographical scope of intellectual property rights or the scope of covered products, they will most likely be deemed "unfairly high." "Refusal to license" is determined on the premise that the patentee has market dominance while comprehensively considering the following factors: the previous commitments made by the patentee (such as the statement in the standard essential patent), whether other operators must obtain intellectual property licenses to enter the relevant market, the impact of refusal on the license, and whether the corresponding refusal will harm the interests of consumers or the public interest of society. In view of the cutting-edge research on hESC and the existing relevant fundamental patents in China, the patentee is likely to be identified as an operator with a dominant market position. When the patentee refuses to license such patents, other business operators can then apply for a compulsory license for the corresponding patent on the grounds that the exercise of the patentee's rights constitutes a monopoly in accordance with the provisions of Article 53, Paragraph 2 of the CPL, which in turn may ensure reasonable pricing and licensing by hESC patentees.

Experimental use exception

Currently, most hESC patents in China are fundamental patents. These patents are likely to be used as tools for research on hESC, and their use is based on the requirement of "scientific research and experimentation" stipulated in Article 4 of Paragraph 1 of Article 75 of the CPL. "Exclusive use of relevant patents for scientific research and experiments" does not constitute infringement, which is deemed an experimental use exception. Based on the systematic interpretation of the CPL, Article 11 stipulates that no one may exploit an authorized patent "for production

and business purposes" without permission. Article 75 stipulates the exception for experimental use, which means that experimental use in China includes purpose of production and operation use. This conclusion can also be drawn through reverse inference. If the experimental use is not based on production and business purposes, the corresponding use cannot even be deemed an infringement according to Article 11 of the CPL. Therefore, the scope of experimental use in China is more relaxed than that in the United States, and experimental use by Chinese universities and scientific research institutes for purpose of production and operation is legal (Fan and Meng, 2011). Overall, China's experimental use can limit the scope of hESC patent rights to a certain extent and provide institutional guarantees for the development of hESC research in China (Chen et al., 2020).

Implementation of the open licensing system

China added a "patent open licensing system" to the 2020 revision of the CPL to promote the sharing of patents led by the government. This system aims to provide policy incentives and institutional guarantees and is premised on the voluntariness of the patentee. After the patentee voluntarily opens the license, the patent right will be restricted, that is, the patentee cannot perform monopolistic or exclusive licensing and cannot deny general permission requests from other entities. Currently, China's patent open licensing system is being piloted in several key provincial-level administrative regions. As of June 23, 2022, 13 provincial-level administrative regions in China had launched patent open licensing pilots. These mainly take three forms: the introduction of specific implementation plans for local patent open licensing, the establishment of an information platform for patent open licensing, and the introduction of special fund support policies for patent transformation. China's relevant policies have also played an active role. Some provincial-level administrative regions have provided supporting policy incentives worth up to 2 million yuan. As of October 2022, three provincial administrative regions had established information licensing platforms, and a total of 323 patents had been launched online. Although there is no open licensing of hESC patents yet, China's patent open licensing system may provide a new way to access such patents.

CONCLUSION

Although the patentability of hESC inventions remains controversial, many countries have granted patents for related inventions (Viola, 2019). The acquisition and use of hESC patents has become a global issue, and the exploration of possible solutions is undoubtedly of practical significance. By analyzing the relevant systems of the United States and China, it can be found that both countries have retained potential accesses to hESC patents. Ethical restrictions, compulsory licensing, and antimonopoly law regulation are their common means. In this regard, ethical reviews play a crucial role in obtaining patent authority in China, while the market regulations in the United States are stricter than those in China. Furthermore, it should be noted that China is actively exploring new potential ways. At present, many Chinese scholars are calling for the expansion of the scope of experimental use to better enhance the accessibility of corresponding patents, and the Chinese government is actively promoting the patent open licensing system, hoping to promote the efficiency of patent use and conversion.

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AUTHOR CONTRIBUTIONS

W.L. made substantial revisions and improvements. W.Z. and J.C. organized the literature and wrote the articles. H.Z. made amendments and supplements to the US patent law.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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