

Forum

Ethical and Policy Considerations for Human Embryo and Stem Cell Research in China

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China's stem cell research policies are based on a cultural understanding that grants special protection to human embryos but does not assign them equivalent moral or legal status as fully developed humans. We discuss ethical considerations for embryo research and policy changes as China moves toward adopting internationally recognized rules.

Over the last few decades, stem cell research has advanced considerably, gradually progressing from bench to bedside. However, ethics and policies related to stem cell and embryonic research remain under debate worldwide. In particular, human embryonic stem cell (hESC) research is controversial ethically and politically mainly because the process of isolating stem cells normally necessitates the use and destruction of human embryos. Likewise, the possibility of applying advanced genome editing technologies to heritable germline editing in human embryos has sparked international debate (Pei et al., 2017). Moreover, an embryo is considered to have a moral status identical to that of a fully developed human by some people, most of whom hold relevant religious beliefs. However, this viewpoint is not shared universally. For instance, in Europe, because of the diversity of society and culture as well as the debated legal status of the human embryo, a pan-European consensus on the ethical acceptability of hESC research does not exist (Elstner et al., 2009). In the US, this ethical debate has led to a constantly changing and uncertain environment for stem cell research policies at the federal level in the past two decades (Levine, 2011).

China has had a distinctive culture for thousands of years, and Western religious culture has not exerted a strong influence on Chinese people. Consequently, China has tailored its own policies and regulatory approaches toward research using embryos and derived stem cells. We primarily

explore the ethical issues and public debates over stem cell research, particularly hESC research, along with the associated policies and regulations, as well as their implications for clinical translation of stem cell technologies in China.

Ethical Issues and Public Debates

To understand the ethical issues and public debate associated with stem cell research in China, the complex attitudes of the public about embryos must be understood first. Confucian, Taoist, and Buddhist teachings have substantially affected the societal and ethical framework and norms of China. In contrast to Western religious beliefs, none of these teachings consider a human embryo sacred from the moment of conception. Consequently, the majority of Chinese people do not regard the embryo as a human being. This is exemplified by the prevalence of artificial termination of pregnancy in China: the country registers approximately 13 million medical terminations annually, compared with 20 million births (BBC News, 2009). Moreover, several Chinese people oppose artificial termination of pregnancy mainly because of its negative effects on women's physical and mental health rather than concerns regarding the moral status of embryos (Hardee et al., 2004).

However, it does not mean that the Chinese do not have strong respect for the embryo. Instead, Chinese people do respect the human embryo; they consider the early-stage embryo to be some type of biological life with some inherent moral

status, warranting special respect and protection (Nie, 2005). Chinese people thus may be considered to have a somewhat pragmatic moral position concerning the embryo: although they believe that an embryo has a certain inherent moral status, they would be tolerant of the destruction and use of human embryos, particularly when it is in the interest of humankind. Hence, Chinese people support research on human embryos and hESCs, particularly when it is aimed at achieving treatments for diseases.

Information derived from media reports in China also sheds light on how Chinese people perceive research using embryos and derived stem cells. The use of "embryonic stem cell" as a search term in China's largest newspaper database (<https://kns.cnki.net/kns/brief/result.aspx?dbprefix=CCND>) revealed that 1,087 related news reports have been published between 2000 and 2019. However, when "ethics" was added to the search term, only 121 (11.2%) reports remained—implying that most of the relevant reports did not concern ethical issues related to hESCs. Further detailed analysis of the content of the 121 ethics-related news reports revealed that most of these reports were on the ethical debates regarding stem cell research abroad. Taken together, these results signify that ethical issues related to stem cell research are not a primary concern for the Chinese media and that the destruction or use of human embryos such as that in hESC research has not provoked a backlash in China.



Legal Status of a Human Embryo

In addition to its moral status, the legal status of a human embryo may affect embryonic and stem cell research policies and regulations in a jurisdiction. Under Chinese law, a human embryo is not considered to be a person, and no legal principle states it must be treated as such. Humans only become part of the community of law at birth. Nevertheless, this does not mean that a human embryo has no legal protection whatsoever. In the noteworthy 2014 Frozen Human Embryo case in China (<http://www.dffyw.com/sifashijian/ws/201409/37076.html>), which concerned the question of whether frozen embryos could be inherited by a deceased couple's parents, the first instance court, Yixing Court, ruled that the embryos generated by *in vitro* fertilization carried the potential to develop into a human being; as a "special thing" containing future life features, the embryos could not be transferred or voluntarily inherited as common personal property. The appeal court, Intermediate People's Court of Wuxi City of Jiangsu Province, considered the human embryo something between a person and an object (*Intermediate People's Court of Wuxi, 2014*); it should have higher moral status than inanimate objects, and deserve special respect and protection. At last, the appeal court revised the decision of the first instance and ruled that the parents of the deceased couple shared the rights to custody and disposal of the frozen embryos. As can be seen, the judicial decision revealed that although Chinese courts do not consider the embryo to be a human being, they regard the embryo as a matter deserving special respect and protection, a position that is consistent with the aforementioned Chinese morality. Evidently, the view that a human embryo is sacred from the moment of fertilization is incompatible with the moral and legal status of the embryo in China.

Moreover, in the past, the *Guidelines for Patent Examination* of the China National Intellectual Property Administration (hereafter, CNIPA Guidelines) had excluded the patent eligibility of "hESCs per se and the preparation methods of them," because the CNIPA considered the destruction of an embryo to be immoral (*Peng, 2016*). However, in September 2019, the CNIPA Guidelines were revised to allow and grant patents to inventions in which

stem cells are isolated or obtained from a human embryo fertilized *in vitro* after no more than 14 days (*CNIPA, 2019*; <http://www.sipo.gov.cn/zfgg/1142481.htm>). Specifically, the CNIPA does not consider the destruction of early-stage human embryos to be a violation of ethics, which is consistent with ethical attitudes of Chinese people and the legal status of the embryo in China.

Policy and Regulation on Stem Cell Research

On the basis of the moral culture and an embryo's legal status, China has tailored numerous policies to promote the development of stem cell research. For example, in the 13th Five-Year Plan (for the period of 2016–2020), stem cell research and regenerative medicine are considered the key research and development (R&D) programs of national importance (*State Council of China, 2016*). Moreover, China has been making considerable efforts to attract overseas talent to return (*Sleeboom-Faulkner and Patra, 2008*) and has been actively establishing stem cell research infrastructure in the country; this is exemplified by the establishment of the National Stem Cell Resources Center in 2007 (<http://www.bjscb.cn/dms/>).

With regard to regulating stem cell research, China mainly relies on the *Measures for Ethical Review of Biomedical Research Involving Human Subjects* (hereafter, Measures for Ethical Review) (*National Health and Family Planning Commission, 2016*) and *Ethical Guidelines for Human Embryonic Stem Cell Research* (hereafter, Ethical Guidelines) (*Ministry of Health and Ministry of Science and Technology, 2003*). The Measures for Ethical Review prescribes general bioethical principles for biomedical research but without any specific guidance for stem cell research.

For hESC research regulation specifically, China primarily relies on the Ethical Guidelines rather than law. However, the Ethical Guidelines consist of 12 short articles, only 6 (Articles 4–9) of which target the actual research procedure (see *Table 1*). The Ethical Guidelines closely follow the principles used widely in other jurisdictions. For example, Article 4 specifies that any research on reproductive cloning is prohibited, but research for disease treatment and prevention is permitted. Article 5 requires that research-use

hESC lines be obtained through *in vitro* fertilization, somatic cell nuclear transfer, or parthenogenesis. Article 6 prohibits implantation of any research-use embryos into human or animal wombs, prohibits the fusion of human and animal gametes, and provides a 14-day criterion for *in vitro* research, which stipulates that the *in vitro* culture period for the created embryos should be less than 14 days, beginning from the fertilization or nuclear transfer stage. Article 7 bans the commodification of human gametes, zygotes, embryos, and fetal tissues.

Moreover, the Ethical Guidelines require institutions engaged in hESC research to establish ethics committees and formulate corresponding detailed measures and regulatory rules in compliance with the Ethical Guidelines. To a large extent, this provision has made the regulation of hESC research in China the purview of individual research institutions. Notably, no penalty is mentioned in the Ethical Guidelines, which, to some extent, renders the document a dead letter. Therefore, from this document, in terms of the types of hESC research allowed and the degree of regulation and oversight involved, the Chinese regulatory approach is relatively permissive.

The hESC research regulation approach adopted by China, involving the use of the aforementioned guidelines without any active monitoring or sanctions, may lead to the formation of a self-serving, market consumer model for stem cell products, particularly when the amount of private investment in this field increases. Given this, the Ethical Guidelines—criticized for their inability to provide any assistance to regulatory bodies in hESC research regulation—has been condemned as inadequate for clarifying how administrative instruments should be operated (*Zhang, 2012*). Thus, China's current regulation for hESC research warrants further improvement and being more prescriptive.

Future Directions and Recommendations

In November 2018, the "gene-edited babies" incident occurred in China. One year later, in December 2019, He Jiankui and two other defendants who conducted these activities were convicted of illegal medical practice by the Shenzhen Nanshan District People's Court. He Jiankui

Table 1. Key Ethical Considerations Included in the Ethical Guidelines for Human Embryonic Stem Cell Research

	Content	Details
Article 4	prohibition of human cloning	any research on human reproductive cloning is prohibited
Article 5	means of deriving human embryonic stem cells (hESCs)	hESCs used for research purposes can be derived only by the following means with voluntary agreement: 1) spared gametes or embryos after <i>in vitro</i> fertilization (IVF) 2) fetal cells from accidental spontaneous or voluntary abortions 3) embryos obtained through somatic cell nuclear transfer technology or parthenogenetic split embryos 4) voluntarily donated gametes
Article 6	prohibited research	researchers must abide by the following rules during their research: 1) the <i>in vitro</i> culture period of embryos obtained from IVF, human somatic cell nuclear transfer, parthenogenesis, or genetic modification techniques may not exceed 14 days starting from the day when fertilization or nuclear transfer is performed 2) the implantation of embryos created through the previously described means into the reproductive organs of humans or any other species is prohibited 3) the mixing of human gametes with gametes of any other species is prohibited
Article 7	prohibition of commercialization	the buying and selling of human gametes, fertilized eggs, embryos, and fetal tissues is prohibited
Article 8	informed consent and protection of privacy	the principle of informed consent and informed choice shall be upheld, informed consent forms shall be signed, and participants' privacy shall be protected in all research activities related to hESCs; informed consent and informed choice refer to researchers using accurate, clear, and understandable language to inform participants of the expected objectives, potential consequences, and risks of the experiment and obtaining their consent by using a signed informed consent form
Article 9	institutional ethics committee	research institutions engaged in hESC research shall establish an ethical committee consisting of research and administrative experts in relevant fields—including biology, medicine, law, and sociology—who are responsible for providing scientific and ethical review, consultation, and supervision of research activities related to hESCs

was sentenced to 3 years in prison and fined RMB 3 million. This judicial decision indicated that China adopts a strict attitude toward biotechnological research that seriously violates social ethics. Undoubtedly, the judgment will play a positive role in guiding research in life science and technology in China; to an extent, it sounds the legal alarm for scientists who ignore the fundamental principles of bioethics. He Jiankui was convicted of the crime of illegal medical practice because no clear criminal law directly prohibits the gene editing of babies; thus, China's legislation urgently requires improvement.

Since this incident, the Chinese authorities have sought to establish an early warning and monitoring system for science and technology (S&T) safety and ethics. The government has acted positively in not only supervision but also legislation. Specifically, a plan has been approved to establish the National Science and Technology Ethics Committee, which can advise the government on governance in S&T ethics. Notably, numerous pieces of legislation, including the Biosecurity Law, an amendment to

the Criminal Law, are in active development and will likely be introduced into law, and work has been conducted to ensure the healthy development of research and development.

In May 2020, the Civil Code was passed. It stipulates that those engaged in medical and scientific research related to human genes and embryos shall abide by all laws, administrative regulations, and relevant national regulations, and they shall not harm the health of a person, violate ethics or morality, or harm public interest. Moreover, in July, an amendment to the Criminal Law (exposure draft) was published. It explicitly prohibits human reproductive cloning and any clinical application of human germline genome editing. This was the first time that a criminal law has prohibited research in the field of biotechnology in China. This fully demonstrates that the Chinese authorities have paid unprecedented attention to the ethics of biotechnological research, including stem cell and embryonic research.

Overall, these actions are expected to improve China's embryonic and stem cell research regulations in the near future. However, the Chinese political and regula-

tory approach is explicitly based on the specific morality of the Chinese people and the development of the industry; therefore, a restrictive policy on general embryonic and stem cell research may never be established in China—in contrast to countries such as Germany, which has enacted strong protective laws regarding human embryos and has restricted stem cell research considerably. Unsurprisingly, the supportive measures and permissive regulatory approach to stem cell research will continue in China.

The Chinese legal system requires improvement in stem cell and embryonic research. For example, in the aforementioned amendment to the Criminal Law, only human cloning and the clinical application of human germline genome editing were prohibited. However, similar scientific research activities, such as the use of stem-cell-based entities (e.g., animal-human chimera embryos or artificial embryos) for reproductive purposes, also seriously violate social ethics and should be considered for prohibition in criminal law. Relevant legislation in China, including the Criminal Law, should provide sufficient legislative space for future

technological development and ethical control.

The relevant regulatory agencies of the Chinese government must further revise the Ethical Guidelines. As the field evolves, the guidelines must be regularly revisited and revised in line with technological development. For example, relevant terms and the sources of stem cells, such as embryonic stem cells, must be redefined to provide practical guidance for scientific researchers in research and development and applied research. Moreover, the Ethical Guidelines should be placed higher in the legal hierarchy, punishment measures should be increased, and corresponding legal responsibilities should be stipulated.

Chinese legislators, managers, and researchers should strengthen internal and international dialog in terms of ethics and regulatory policies in stem cell research, particularly in relation to embryonic stem cells, because this field is extremely controversial globally and technological development is rapid. Moreover, Chinese scholars and scientists can participate more in the formulation of relevant international ethical guidelines, such as those of the International Society for Stem Cell Research. In turn, the relevant regulatory bodies in China may learn more from the dialog and participation.

The aforementioned efforts will help to ensure that embryonic and stem cell research in China is conducted ethically. In particular, these recommendations will help China's regulatory policies become more prescriptive and transparent and help the international scientific community and the Chinese public understand the activities of researchers in China. These efforts will promote the healthy development of related research in China.

Conclusion

A key issue that may influence the evolution of policies and regulatory approaches toward stem cell research is the social

and ethical considerations in specific jurisdictions. In China, although embryos are considered to deserve certain special respect and protection, they are not recognized as humans. Accordingly, Chinese people are more likely to tolerate embryo use and destruction; consequently, in China, research on embryos and derived stem cells is supported by the public. This has allowed the Chinese government to invest a large amount of research funds to support such research as well as promote the concept of embryo protection in its regulation.

Regarding stem cell and embryonic research regulation, China has moved toward adopting internationally recognized principles and rules; however, its current regulation still warrants further improvement. In the future, the governance of ethical issues will become an integral component of the innovation system in the field of biotechnological S&T in China. Notably, on the basis of its specific culture and practical needs, China may continue tailoring its research policies and regulatory approaches—with improvement in the embryonic and stem cell research regulations—enabling a more prescriptive, diligent, and informed process.

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WEB RESOURCES

National Stem Cell Resources Center, <http://www.bjscb.cn/dms/>

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