Human Embryos and Gene-editing Research and regulation in China

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Outline

- Policy and National Regulation
- Publications and Funding
- Suggestions from CAS and Society

Policy, National Regulation Related to Human Genetic Research

1998 — Interim Measures for the Administration of Human Genetic Resources(MOH/MOST)

2003 — Ethics Guidelines of Human Embryonic Stem Cell Research （MOH/MOST）

2007 — Regulation on Ethical Review of Biomedical Research Involving Human Subjects (MOH)

2009 — Regulations on Clinical Use of Medical Technologies （MOH）

2010 — Guidelines for Ethical Review of Drug Clinical Trials (CFDA)

2012 — Notification on Self-Evaluation and Self-Correction regarding Clinical Stem Cell Research and Applications （MOH/CFDA）

2015 — Regulations on Stem Cell Clinical Research *(Trial)* （NHFPC/CFDA）

* The Ministry of Health (MOH), The Ministry of Science and Technology (MOST)
China Food and Drug Administration (CFDA), National Health and Family Planning Commission(NHFPC)

Policy, National Regulation Related to Human Genetic Research

- **The first regulation for the administration of human genetic resources was published in 1998 by then-MOH and MOST.**

- **The Updated Regulations on the Administration of Human Genetic Resources *(draft)* was published based on the first policy in 2012 by MOST.**

Policy, National Regulation Related to Human Genetic Research


中华人民共和国科学技术部
Ministry of Science and Technology of the People's Republic of China

www.most.gov.cn

科学技术部、卫生部关于印发《人胚胎干细胞研究伦理指导原则》的通知

国科发生字〔2003〕460号

各省、自治区、直辖市、科技厅（委）、卫生厅（局），新疆生产建设兵团科委、卫生局，国务院各有关部门科技司，各有关单位：

为保证生物医学领域人胚胎干细胞的研究活动遵守我国的有关规定，尊重国际公认的生命伦理准则，并促进人胚胎干细胞研究的健康发展，科学技术部和卫生部联合制定了《人胚胎干细胞研究伦理指导原则》。现印发给你们，请认真贯彻执行。

二00三年十二月二十四日

附件：

人胚胎干细胞研究伦理指导原则

第一条　为了使我国生物医学领域人胚胎干细胞研究符合生命伦理规范，保证国际公认的生命伦理准则和我国的相关规定得到尊重和遵守，促进人胚胎干细胞研究的健康发展，制定本指导原则。

第二条　本指导原则所称的人胚胎干细胞包括人胚胎来源的干细胞、生殖细胞起源的干细胞和通过核移植所获得的干细胞。

第三条　凡在中华人民共和国境内从事涉及人胚胎干细胞的研究活动，必须遵守本指导原则。

第四条　禁止进行生殖性克隆人的任何研究。

第五条　用于研究的人胚胎干细胞只能通过下列方式获得：

- **Ethics Guidelines of Human Embryonic Stem Cell Research, 2003, MOH and MOST**

-- To prescribe **the basic principles** that should be followed in carrying out **human embryonic stem cell research**, including scope of research activity, research content of embryonic stem cell that should be allowed and forbidden to carry out, “Informed consent” and so on.


医政司

卫生部关于印发《医疗技术临床应用管理办法》的通知

卫医政发〔2009〕18号

各省、自治区、直辖市卫生厅局，新疆生产建设兵团卫生局：

为加强医疗技术临床应用管理，建立医疗技术准入和管理制度，促进医学科学发展和医疗技术进步，提高医疗质量，保障医疗安全，我部组织制定了《医疗技术临床应用管理办法》。现印发给你们，请遵照执行。

二〇〇九年三月二日

（信息公开形式：主动公开）

- **Regulations on Clinical Use of Medical Technologies, 2009, MOH**

-- To establish **medical technology access and management system**, **stem cell transplant technology** was grouped into **category III** medical technology, which included technologies considered as risky, ethically controversial and in need of clinical verification.

Policy, National Regulation Related to Human Genetic Research

➢ Regulation on Ethical Review of Biomedical Research Involving Human Subjects (Interim)

-- Enacted by then-MOH in 2007

-- April 30th, 2014, the NHFPC published a revised version on its website to elicit comments from the public.

-- It aims to:

1) Improving and strengthening ethics review and inspection system;

2) Improving ethics review principles, protocols and other measures.

Policy, National Regulation Related to Human Genetic Research

➢ SFDA/CFDA's Regulations on Pharmaceutical Industry (ethical review related, some highlight)

-- Chinese Good Clinical Practice (2003)

-- Guidelines for Ethical Review of Drug Clinical Trials (2010)


CFDA 国家食品药品监督管理总局
China Food and Drug Administration

关于印发药物临床试验伦理审查工作指导原则的通知

国食药监注[2010]436号

2010年11月02日 发布

各省、自治区、直辖市食品药品监督管理局（药品监督管理局），总后卫生部药品监督管理局：

为加强药物临床试验的质量管理和受试者的保护，规范和指导伦理委员会的药物临床试验伦理审查工作，提高药物临床试验伦理审查工作质量，根据《药品注册管理办法》和《药物临床试验质量管理规范》的有关规定，国家局组织制定了《药物临床试验伦理审查工作指导原则》，现予印发。请你局指导本辖区内药物临床试验机构学习，参照执行。

-- ……

-- Guidance on Multi-sited International Drug Clinical Trials (Interim) (2015)

Policy, National Regulation Related to Human Genetic Research


国家卫生计生委科技教育司

关于印发干细胞临床研究管理办法（试行）的通知

国卫科教发〔2015〕48号

各省、自治区、直辖市卫生计生委、食品药品监管局，新疆生产建设兵团卫生局、食品药品监管局，国家卫生计生委直属有关单位，食品药品监管总局直属有关单位：

为规范并促进我国干细胞临床研究，国家卫生计生委与食品药品监管总局共同组织制定了《干细胞临床研究管理办法（试行）》（可从国家卫生计生委、食品药品监管总局网站下载）。现印发给你们，请遵照执行。

国家卫生计生委 食品药品监管总局
2015年7月20日

干细胞临床研究管理办法（试行）

第一章 总 则

第一条 为规范和促进干细胞临床研究，依照《中华人民共和国药品管理法》、《医疗机构管理条例》等法律法规，制定本办法。

第二条 本办法适用于在医疗机构开展的干细胞临床研究。

干细胞临床研究指应用人自体或异体来源的干细胞经体外操作后输入（或植入）人体，用于疾

- **Regulations on Stem Cell Clinical Research (NOT Trial), 2015, NHFPC and CFDA**

-- The **main responsibilities** of stem cell clinical trial research unit, ethics committee, expert committee and national and provincial health administration and food and drug regulatory authorities; clearly stipulated **the declaration and record** of stem cells, clinical research, rights and interests protection of donor and subject, report, supervision and punishment.


国家卫生计生委科技教育司

关于印发干细胞制剂质量控制及临床前研究指导原则（试行）的通知

国卫办科教发〔2015〕46号

各省、自治区、直辖市卫生计生委、食品药品监管局，新疆生产建设兵团卫生局、食品药品监管局，国家卫生计生委直属有关单位，食品药品监管总局直属有关单位：

为加强我国干细胞制剂和临床研究质量管理，国家卫生计生委与食品药品监管总局根据《干细胞临床研究管理办法（试行）》，共同组织制定了《干细胞制剂质量控制及临床前研究指导原则（试行）》（可从国家卫生计生委或食品药品监管总局网站下载）。现印发给你们，请遵照执行。

国家卫生计生委办公厅
食品药品监管总局办公厅
2015年7月31日

干细胞制剂质量控制及临床前研究指导原则
（试行）

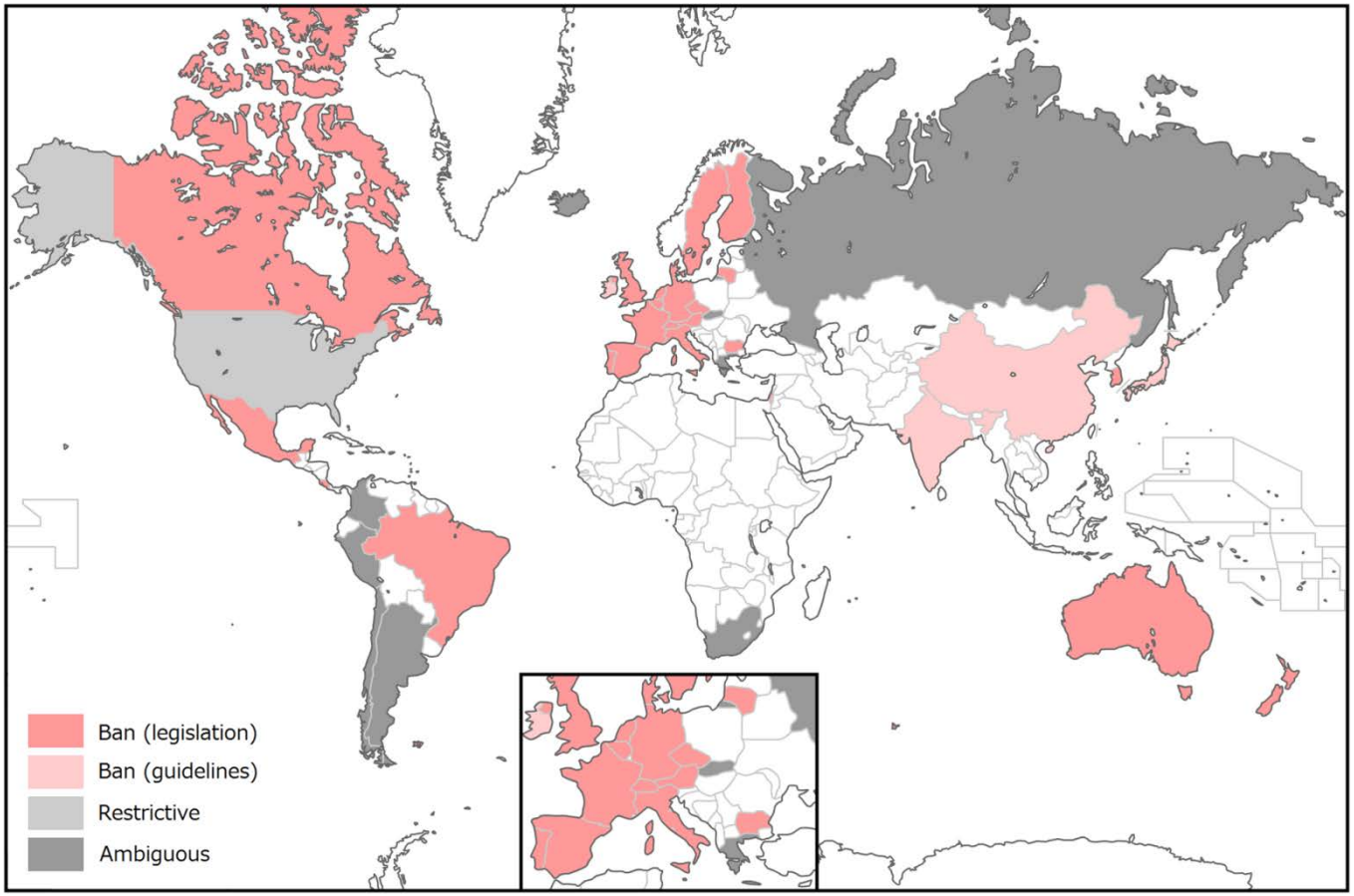
一、前言
二、干细胞制剂的质量控制
（一）干细胞的采集、分离及干细胞（系）的建立
（二）干细胞制剂的制备
（三）干细胞制剂的检验
（四）干细胞制剂的质量研究
三、干细胞制剂的临床前研究
（一）安全性评价
（二）有效性评价
名词解释

- **Guidelines of Stem Cell Preparations Quality Control and Preclinical Research(Trial), 2015, NHFPC and CFDA**

-- For **stem cell products quality control** (collection, separation, and establishment of stem cell lines; preparation, inspection, and quality research of stem cell products) and **preclinical research** (the research and evaluation of stem cell product safety and effectiveness in preclinical stage).

Policy, National Regulation Related to Human Genetic Research

- **An international regulatory landscape regarding human germline gene modification**



Source: Araki M, Ishii T. *Reproductive Biology and Endocrinology*, 2014, 12(1): 108.

Policy, National Regulation Related to Human Genetic Research

China

Using human egg plasma and nuclear transfer technology for the purpose of reproduction, and manipulation of the genes in human gametes, zygotes or embryos for the purpose of reproduction are prohibited.

The UK

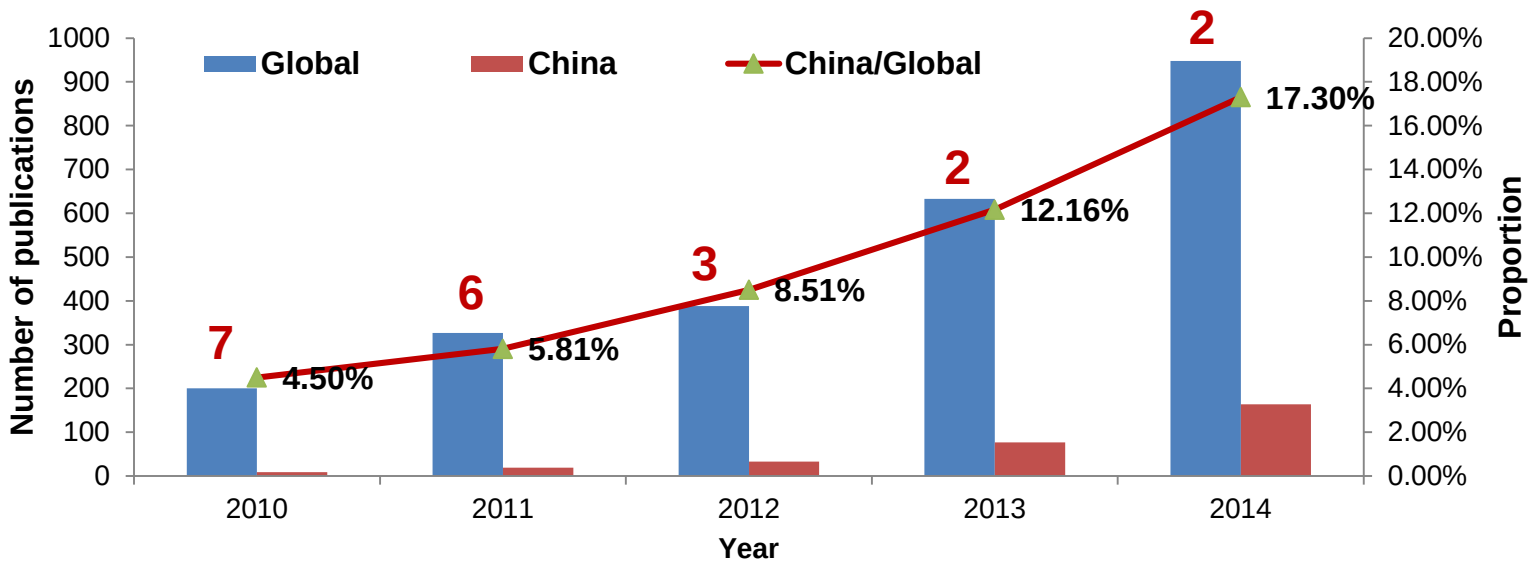
Reproduction is prohibited when using gametes or embryos other than a permitted egg or sperm or embryo: (a) from the ovaries of a woman or testes of a man (b) nuclear or mitochondrial DNA has not been altered (c) no cell has been added to it other than by division of the embryo's own cells.

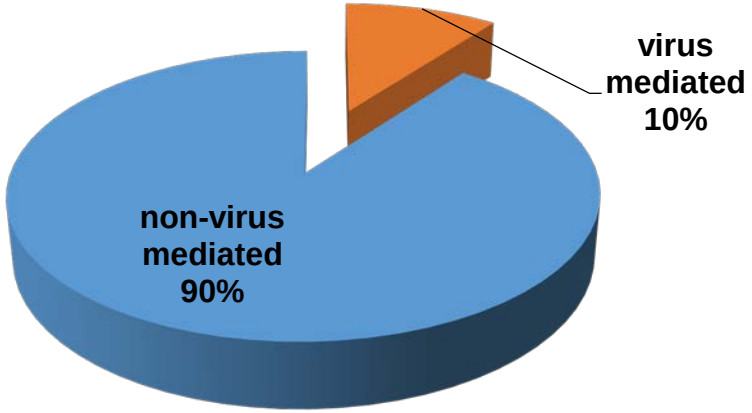
The USA

At present, clinical trial proposals for germline alterations will not be accepted by the Recombinant DNA Advisory Committee (RAC) of the National Institutes of Health (NIH). The Food and Drug Administration also regulates the clinical study.

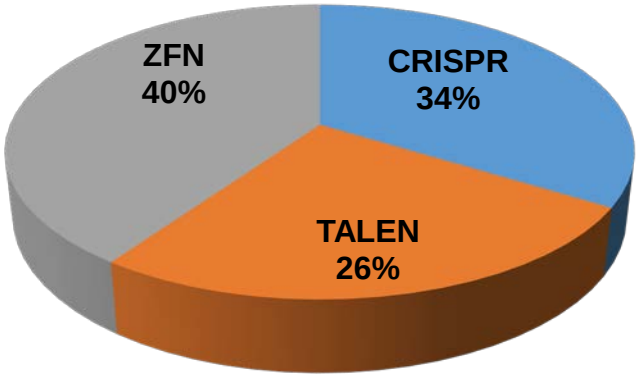
Source: Araki M, Ishii T. *Reproductive Biology and Endocrinology*, 2014, 12(1): 108.

Publications in the field of genome editing





Virus mediated gene editing publications
Proportion in China in 2005~2014

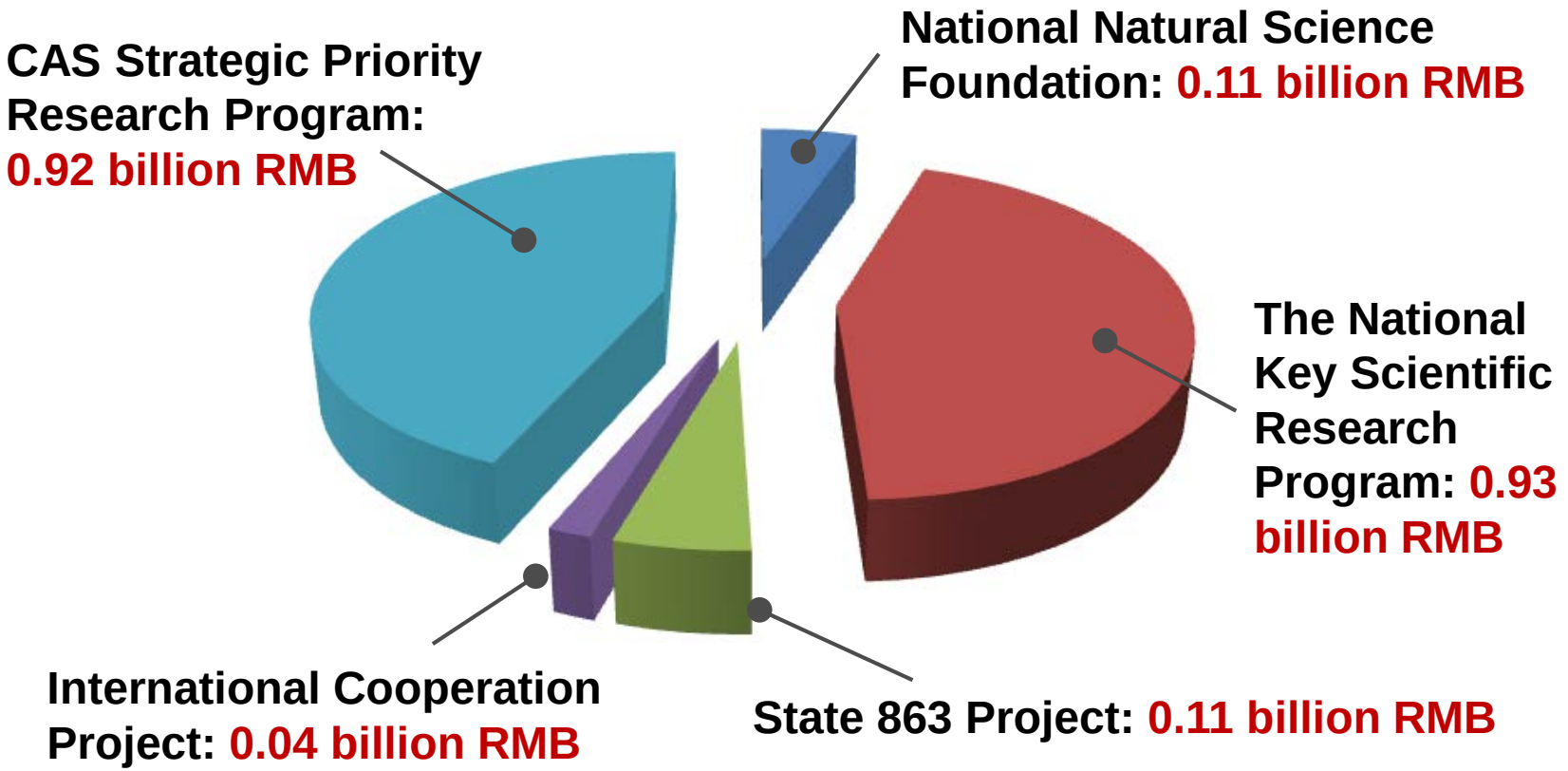


ZFN, CRISPR and TALEN publications
Proportion of China in 2005~2014

Source: ISI Web of Science

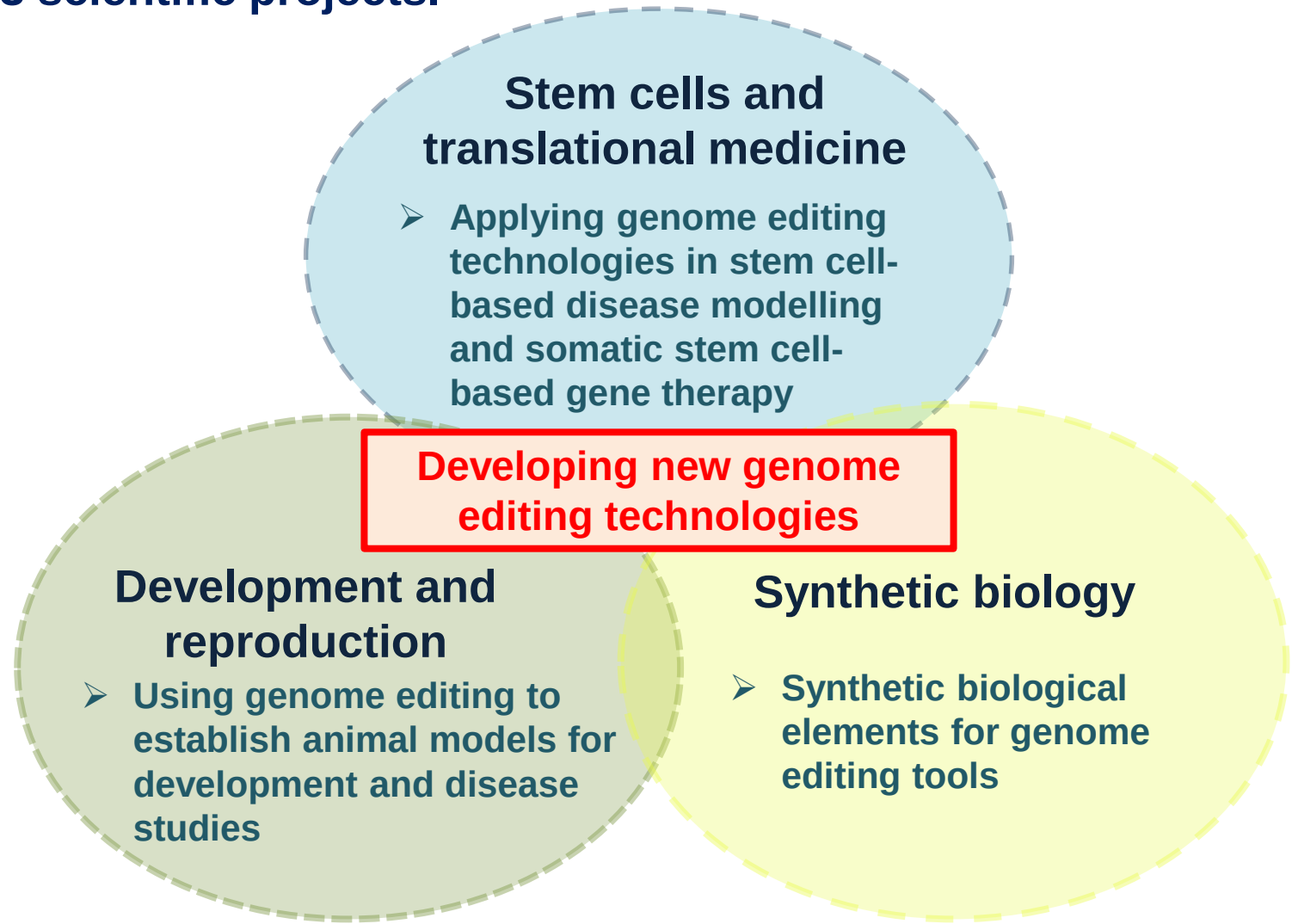
Funding related to human embryos and gene editing

- According to incomplete statistics, the research funding for stem cell fundamental research is **2 billion RMB (about 300 million USD)** in the previous five years.



Overall arrangement on genome editing in next five years (-2020)

- **The future R&D plans related to genome editing will be funded by 3 scientific projects.**



Funding of stem cell research in next five years (- 2020)

- In the next five years, there will be **2.7 billion RMB (400 million USD)** funding for stem cell research in China, **10%** for gene editing.

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中华人民共和国科学技术部
Ministry of Science and Technology of the People´s Republic of China

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【字体：大 中 小】

干细胞与转化医学重点专项实施方案征求意见

日期：2015年02月26日　　来源：科技部

根据国务院《关于深化中央财政科技计划（专项、基金等）管理改革的方案》总体要求，科技部将会同有关部门，启动国家重点研发计划“干细胞与转化医学”重点专项试点工作。

目前，“干细胞与转化医学”重点专项已进入实施方案编制阶段。实施方案主要包括重点专项实施的重要性、发展趋势、现有基础、总体目标、主要任务等。现就重点专项实施方案（征求意见稿，见附件）向社会征求意见和建议，请发电子邮件至gxbyj@most.cn，反馈截止日期为2015年3月5日。

Suggestions from CAS and Society

"Both the Chinese scientists and government are aware of the pros and cons human gene editing. CAS scientists have organized panel discussion meetings and coordinated with related government agencies for regulatory policies on this issue. We would like to work together with international communities for the proper regulation and application of such technology. "

-- Chunli Bai

President of the Chinese Academy of Sciences

Suggestions from CAS and Society

CRISPR germline engineering—the community speaks

Katrine S Bosley, Michael Botchan, Annelien Bredenoord, Dana Carroll, R Alta Charo, Emmanuelle Charpentier, Ron Cohen, Jacob Corn, Jennifer Doudna, Guoping Feng, Henry T Greely, Rosario Isasi, Weihzi Ji, Jin-Soo Kim, Bartha Knoppers, Edward Lanphier, Jinsong Li, Robin Lovell-Badge, G Steven Martin, Jonathan Moreno, Luigi Naldini, Martin Pera, Anthony Perry, J. Craig Venter, Feng Zhang & Qi Zhou

***Nature Biotechnology* asks key members of the international community to comment on the ethical issues raised by the prospect of CRISPR-Cas9 engineering of the human germline.**

With rumors circulating of CRISPR-Cas9-mediated human germline engineering, are we at a new Asilomar moment? In a letter to *Science* in March entitled "A prudent path forward for genomic engineering and germline gene modification," 18 signers indicated "A framework for open discourse on the use of CRISPR-Cas9 technology to manipulate the human genome is urgently needed." They wrote of "unparalleled potential for modifying human and nonhuman genomes," to cure genetic diseases in humans and to "reshape the biosphere." But they warned of consequent "unknown risks to human health and well-being."

Nature Biotechnology contacted 50 leaders of the global community including researchers, ethicists and business people to comment on ethical issues raised by CRISPR engineer-

rent efforts into solving the technical problems and testing the safety and efficacy of germline engineering treatment with animal experiments, but we can leave the door open for germline modification for future application in curing some severe diseases.

Is it possible to have an Asilomar-type resolution today, given the questions swirling around CRISPR germline engineering, the international nature of research, and ease of use of technology and rise of 'garage' biology outside of traditional centers?

Zhou: I think an Asilomar-type conference involving [AU:OK?]scientists in different countries is a useful way to draw some consensually agreed guidelines to address this question.

The ethical challenges are the same, however. Do we allow such biomedical approaches to be used to achieve genetic enhancement of future generations? Human therapeutic cloning does not directly involve germline changes. For human reproductive cloning, I think the scientific community and governments all over the world have already reached a consensus that it should be banned completely.

Qi Zhou

Suggestions from CAS and Society

- Assigned by China government, CAS has organized several meetings to discuss about human genomic editing and the proper use of human embryos in scientific research, participants including Chinese leading stem cell biologists, the major funding agencies and other related government agencies.
- Chinese Society for Stem Cell Biology has already communicated with ISSCR and other societies about the human gene editing.
- Government agency is collecting suggestions and comments for genome editing for the guidance of regulatory policies.

Thanks