Ethical reflection on the Creation of Human Genetic Database

Ethical reflection on the Creation of Human Genetic Database: Based on a National Survey on Chinese Genetic Scientists

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Abstract

Chinese health authorities have not set up a very clear legal framework or ethical guideline on genetic research involving a huge number of human genetic samples. A nationwide mail survey was conducted to identify whether Chinese research communities identified the fundamental ethical issues. This paper provides in-depth analysis about the attitudes of target groups towards ownership, commercial conflict of interest, international cooperation and ethical review mechanism that may be used to inform national guidelines related to genetic databases in China.

Key words: genetic database; ownership; ethical review; China

1. Introduction

In the 1990s, China as the only developing country joining the international Human Genome Research Project. The so-called "1% Project" wais successful and attracted great attention of not only the biomedical community but also among the highest policy makers in China. In 1998, to catch up with the latest developments in this highly competitive field, China's Ministry of Science and Technology (MoST) established two National Human Genome Research Centers which are located in Beijing and Shanghai. These two national centers, together with many other genetic bases at provincial level, have announced the establishment of several special disease-related databases.[1] For instance, Chinese geneticists have constructed the database for Genomic Polymorphism of Chinese 56 Ethnic Groups (GPCEG).[2]

The international debates indicate that national databases established to collect, process, use, and store human genetic samples have raised a lot of ethical, legal, and social issues in many countries.[3] UK and Iceland have discussed those complex issues and then set up ethical guidelines and/or regulation in the course of creating a national database. Undoubtedly, the regulation of this field has become an important political topic for parliaments and regulatory bodies. Unlike the UK BioBank or Icelandic Health Care Database, Chinese health authorities have not set up a clear legal frameworks or ethical guidelines on those genetic research involving huge human genetic samples.

Until now, little knowledge is available over the attitudes and perceptions of Chinese biomedical communities regarding the creation of genetic databases. A nationwide mail survey was conducted in National Human Genome Research Center (Beijing and Shanghai) and several other provincial genetic bases.[4] The objectives of the survey were to know whether the Chinese research communities identified the fundamental ethical issues that have been heatedly discussed over years in the international level? What are their opinions and attitudes about ethical issues arising with developing genetic databases in China? What proper interventions and strategies do the research community think are best to avoid the ethical constraints? We hope our research will be critical for establishing national ethical guidelines on genetic databases and the tentative results may contribute to the international discussion on the significant and sensitive issues.

In the survey, a total of 300 respondents returned back the valid questionnaires, with a response rate of 77%. The respondents included 166 males and 134 females. 52% were aged between 31and 50. 38% had studied or worked abroad. 36% of them held Ph.D.s. 74% used human genetic samples directly in their work. 53% claimed that they have been involved in databases more than one year. 14% said they had reviewed protocols related with genetic data collection and usage. As part of our final finding, this paper provides analysis about the attitudes of target groups towards ownership, commercialization, international cooperation and ethical review mechanisms that may be used to inform national guidelines related to genetic databases in China.

2. Ownership

In the Icelandic Health Care Database, the licensee shall not be counted as the owner of the biological samples, but has rights over them, with the limitations laid down by law.[5] The Estonian Genome Project Foundation has the right of ownership of the tissue

[1] www. chgb.org.cn

[2] Ghen X, Zhang Y, Wang JM, Huang Y, *et al.* GPCEG-A database for genomic polymorphism of Chinese ethnic groups. *Yi Chuan Xue Bao.* 2003 Jun;30(6):509-14.

[3] Austin MA, Harding SE, McElroy CE. Monitoring ethical, legal, and social issues in developing population genetic databases. *Genet Med.* 2003 Nov-Dec;5(6):451-7.

[4] Xinqing Zhang, Human Genetic Databases in China: Ethical Issues and Scientist's Attitudes Science [in Chinese] 2007 56(2) in press

[5] Ministry of Health and Social Security, Act on Biobanks No. 110/2000, (2000), http://www.stjr.is/interpro/htr/htr.nsf/pages/Act-biobanks, (date accessed : 16 April 2002), 10.

samples.[6] In China, any institution or individual who holds important pedigrees and genetic resources in the specified regions shall immediately report to the relevant departments, and no institution or individual may sample, collect, trade, export human genetic resources, which has been regulated by Interim Measures for the Administration of Human Genetic Resources issued by MoST and Ministry of Health (MoH) in 1998. Although the Interim Measures did not say directly about the ownership of the genetic samples, in most cases this reporting and registration system on important pedigrees and genetic resources indicates that those samples are controlled by the governments at different levels and belong to the central public institutions, rather that a kind of public goods or a property of the donors themselves.

The following scenario will help us to identify the sampling population's attitudes about the ownership of the collected genetic samples/data. Suppose there is a big genetic sample collecting project related to hypertension, sponsored by Chinese MoST and carried out by a prestigious Chinese public institute along with a top public hospital. The question is that: Who should be the owner of the samples. The result of this multi-choice questionnaire indicates: 41% of respondents agreed that the central government should be the owner; 37% argued that the samples/data is global public goods; 20% thought they should be shared by the hospitals and institutions which collect and store those samples; 8% said those samples belong to donors themselves. The result shows that the sampling population held a diversity of opinion regarding ownership.

In this scenario, almost half of the respondents thought those genetic samples/data should belong to the central government. Partly it is because the current genetic databases are state-owned. However, the practical issue is who has the right to represent the central government? It goes without saying, MoST and MoH will play a key role in sponsoring and monitoring of genetic databases. The Chinese qualified hospitals and institutions could have the right to store and utilize samples they collected, with the limitations laid down by Interim Measures, which claims that the Chinese institution who collected samples shall have the priority to access information about the human genetic resources, any transfer of important pedigrees and genetic resources and the relevant data to other institutions shall be prohibited without permission. Even though these did not say that the institution are the owners of the genetic material, researchers may eventually acquire intellectual property rights or commercialized products, according to the Interim Measures.

Still, about two thirds of the Chinese respondents regarded the samples/data as global public goods. The Interim Measures also claim that no foreign collaborating institution that has access to the above mentioned information may publicize, publish, and apply for patent rights or disclose it by any other means without permission. Therefore, in a symbolic sense, the collective human genetic sample is the heritage of humanity as mentioned in UNESCO and HUGO statements. In reality, many question whether these genetic samples are global public goods.[7]

3. Commercialization and conflict of interest

Although there is little critique about the development of genetic databases in China, still many worry about how to balance protection and utilization of Chinese genetic resources. For one thing, in such a socialist country as China, a fundamental assumption is that only state-owned databases might maximize rare Chinese genetic resources. For the other hand, in such an economic transition period, the expansion in the construction of genetic repositories could not be sustainable without the positive participation of private sectors. We are living in an interesting time. There are a lot of ethical and political issues which are worth discussing, such as: Should a national genetic database be a public or private one? Who will look after the benefits of Chinese donors in any commercial agreements?

There are different opinions about the sensitive issue of commercialization in China. Some worry that commercialization would bring bad effects on the development of Chinese genetic databases. Others argued that private genetic databases should be encouraged because it will contribute to solve the problem of financial shortcoming. Stakeholders such as investigators, Ethical Review Committees (ERCs) members, and policy makers should be aware of the tension between encouragement and discouragement of private databases. In the survey, we pose a question: do you think our central government should set limitation for the commercial investment in the establishment of genetic databases? 38% gave a positive answer, 49% said no, and 13% could not make a choice.

It goes without saying that commercialization may raise the problem of conflicts of interest. A conflict of interest is a situation, rather than an action. It is not necessarily illegal or immoral. In addition, China could not close the door to the private investment in this highly competitive field. The key issue is how to avoid the bad consequences of conflict of interest. One of the main areas of conflict of interest in the field of research rooted the relationships between scientists and pharmaceutical companies, which may give researchers

[6] ESTONIAN GENOME FOUNDATION, "Gene Donor Consent Form," http://www.geenivaramu.ee/mp3/Geenidoonorinousolek-ingl.doc (date accessed: 10 May 2002), 3.

[7] Knoppers BM, Fecteau C. Human genomic databases: a global public good? *Eur J Health Law*. 2003 Mar;10(1):27-41.

and their institutions a variety of financial benefits. [8] Commercial interests should be disclosed to the ERCs and to sample donors via consent forms. Disclosure of financial conflict of interest is a proper measure. It helps the donors and ERCs to make a sound judgment.

How do our Chinese scientists think about disclosure of financial arrangement? Supposing a public research hospital sponsored by a private pharmaceutical company collects data related to hypertension, 59% thought it is necessary for the researcher to tell the donor that it is sponsored by a private sector, while 37% thought it is unnecessary. 4% had no idea. The result indicates a significant proportion of respondents do not take financial conflict of interest for granted. In fact, until now "conflict of interest" has not appeared in any dictionary or encyclopedia in China. It is incumbent upon researchers to explain to the potential donors and/or their family about the commercial arrangements regarding the development of products with commercial application derived from the research as well as the commercialization of the bank itself. However, mere disclosure of commercial interests does not solve the problem entirely. Since conflicts of interest need to be managed properly, there may be a need for other mechanisms for regulation.

4. Benefits sharing in international cooperation

Scientists in different countries often collaborate on research involving the collection of human genetic samples. Seeing the following scenario, a developed country posed to provide technology and to train Chinese local researchers. The question is should China's government support such kind of international cooperation? 37% discouraged that kind of cooperation; 40% encouraged it; while 23% had no idea. The result shows that the sampling population did not develop a clear approach on the proper mechanism for sharing benefits in international cooperation. Interim Measures do not close the door on international cooperation. It requires that the rights and obligations of each party should be explicated in order to fully and effectively protect their own respective intellectual property rights. For instance, the right of utilizing, transferring and sharing scientific findings from the collaboration shall be specified in the collaborative contract or agreement signed by both parties.

In consideration of the principle of justice, benefits should be distributed fairly in the process of international cooperation. The unsolved problem is: How to make an equitable use of genetic data? [9] For example, one donated his/her genetic samples, in general he/she may not take part in any profit-sharing process, especially in those genetic research using public funds. In a sense it is unfair when donors consent to sampling but not to the ownership and not eventually commercial benefits. The Human Genome Organization states that even in the absence of profits, immediate health benefits as determined by community needs could be provided that "profit-making entities dedicate a percentage (e.g. 1% - 3%) of their annual net profit to health care infrastructure and/or humanitarian efforts.

Actually, benefits could be the prompt diffusion of research results, collaboration with members of the scientific community, attribution of licenses when the invention resulting from the research is patented, for example. If a research project yields profits, the distribution of benefits could include access to future treatments resulting from the research or donation of a part of the profits to a local humanitarian organization or financial support for research or contribution to health technology infrastructures.

Compared to the increasing growth of creation of genetic databases, no clear guidelines or regulation are available to benefit sharing mechanism. Chinese policy makers should develop a kind of genetic sample transfer agreement which specifies collaborators' rights and responsibilities with respect to the collection of samples. The key point is that, before both sides agree on the MTA, it is a precondition to set up several basic ethical criteria for sharing benefits among different stakeholders. Unfortunately, the Interim Measures did not provide such clear criteria, which only prohibits those protocols where the proportioning of ownership and share of intellectual property right is unfair or unclear.

5. Attitude about ethical review capacity

It is of importance to review protocols involving human genetic sample collection and usage. In China, however, many ERCs have no extensive policies and procedures regarding human genetic research In addition, procedures and requirements of those responsible ERCs differ from place to place, between protocols and may reflect inconsistent treatment of different types of genetic research. However, we know little about Chinese scientists and ERC members' attitudes about ethical review from current literature.

This survey attempted to identify how Chinese scientists, policy makers and Ethical Review Committees (ERCs) think about the value of ethical review. In this multi choice questionnaire, 86% of the respondents said it is to protect the rights and benefits of the subjects in genetic sample collection and usage. The majority of the respondents had a good consensus on the fundamental role of ethical review. In the survey, 67% said that the ethical review mechanism is to protect and exploit Chinese genetic resources reasonably. The result reflects a sense of nationalism. In order to fulfill the national interests, in a sense China has taken somewhat strict measures to safeguard Chinese genetic resources which has been reflected in the Interim Measures in

[8] Ren-zong Qiu Conflict of interests in research ethics: a Chinese perspective *The Journal of Clinical Ethics* Spring 2004 Vol. 15 No. 1.

[9] Sulston J. Beyond release: the equitable use of genomic information. *Lancet*. 2003 Aug 2;362(9381):400-2.

1998. The administrative department of both MoST and MoH are jointly in charge of the administration of human genetic resources of China to carry out routine duties on international collaborative projects. State-owned Institutions apply to the relevant administrative departments for examination and approval prior to entering into an official contract. The province-owned institutions apply to the local administrative department for approval. The underlying assumption of this claim is that there are significant difference between human genetic research and other types of research.

It is necessary to develop the review capacity in China. Appropriate measures should be taken to improve the ethical quality of China's human genetic databases. In the survey, 55% reported that the data storage process should be standardized for fear of wasting resource. 54% appealed for the sharing of benefits in international cooperation. 39% argued to take measures to protect the welfare of donors. 38% said it is important to clarify the ownership of samples and data; 21% agreed that China should take steps to encourage the free flow of genetic information.

6. Recommendation

The survey provides a complex picture of respondents' perceptions and attitudes in general. There were obvious disagreements over the issues such as ownership and commercialization. Because of the actual ethical and regulatory problems identified and addressed in China, proper measures should be taken to build up ethical review capacity. Without national guidelines of sample collection and usage, we will not protect the welfare of the research participants. It is time to establish national ethical guidelines and regulations concerning genetic databases in China. China should develop her own guidelines to address her own ethical concerns, rather than just copy international guidelines, such as the HUGO Statement on Genetic Databases. The ethical issues in the creation of UK BioBank and Iceland Health Sector Database are not the same, the regulation and guidelines are different. The proposed guidelines should be built into the current ERC system, so that it becomes a useful tool to promote the Chinese capacity of ethical review on genetic research involving databases with identifiable information.

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Stem Cell Research: Science, Ethics and the Popular Media

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Abstract

Few advances in the history of science and technology have generated as much ethical controversy and captured as much public attention as research on human stem cells. This paper distinguishes two parallel research programs involving stems cells: embryonic and adult stem cell research programs, then surveys the ethical arguments advanced for and against human embryonic stem cell research. The popular media has tended to exaggerate the therapeutic potential of embryonic stem cells. Adult stem cell therapies are already available for different kinds of cancer and a host of autoimmune diseases such us lupus, multiple sclerosis, Crohn's disease and rheumatoid arthritis. Furthermore, recent research has shown that human adult stem cells have more plasticity than previously thought. Taking this into consideration, and using the principle of subsidiarity which states that if the same results can be obtained by two types of research, one should undertake the research that is least offensive or problematic, I argue that a moratorium on human embryonic stem cell research should be considered. In the meantime, I suggest that research on human adult stem cells and both animal embryonic and animal adult stem cells should continue.

Introduction

The successful derivation of human embryonic stem cells in 1998 (Thompson et al 1998) triggered an intense debate over the morality of destroying human embryos for therapeutic purposes, a debate that continues up to the present day. After describing the science behind stem cell research and distinguishing between adult stem cells and embryonic cells, I will survey the arguments advanced for and against human embryonic stem cell research. I must point out at the outset that it is not my intention here to take sides in this debate. My main aim is to show that embryonic stem cell research raises serious ethical and social questions that should not be dismissed lightly.

The biology of stem cells

Before discussing the ethical issues surrounding stem cell technology, a basic understanding of the underlying science is called for. Stem cells are the essential building blocks of multicellular organisms that are capable of differentiating into all the adult tissues of the body under the right environmental conditions. In addition, they have the unique capacity for self-renewal.