Ethical Governance of Biological and Biomedical Research: Chinese-European Co-operation

2nd WORKSHOP REPORT

Ethical governance of reproductive and stem cell research and stem cell banks

CAS-MPG Partner Institute for Computational Biology
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Introduction – Regenerative Medicine: The rise of the art in Europe, China and between

In European countries, and in China, over the last decade, stem cell research has become emblematic of both the hopes and fears that are associated with advanced bioscience. On the one hand, it is hoped that some of the most debilitating diseases and disorders – e.g. neurodegenerative disorders, spinal cord damage, diabetes, eye diseases, multiple sclerosis, immune disorders and blood diseases – can some day be treated if not cured. On the other hand, the development of effective regenerative treatment that relies on stem cell research requires the ethically controversial sourcing and manipulation of human cells to generate stem cell lines, which can then be transplanted into sufferers of degenerative diseases. Such self-renewing stem cell lines can be sourced from six-day old *in vitro* fertilised human blastocysts, aborted human foetal tissues, umbilical cord blood, bone marrow, brain and other somatic sources as well. The challenge for stem cell researchers is how to generate and perpetuate these stem cell lines into the large stem cell populations that are necessary for regenerative therapy in an ethically acceptable and accountable way.

Stem cells, then, are sourced from embryos, foetuses or adults; are manipulated and cultivated in laboratories; with the hope that they can then be transplanted back into human patients in the treatment of degenerative diseases. Each of these stages of research and treatment (sourcing, manipulation and transplantation) embodies ethical challenges, and it is the goal of this second BIONET workshop on stem cell research to address these challenges in a Chinese and European context, with a special focus on collaborative Sino-European research in this field.

In Europe, there have been a diversity of responses to the ethical challenges raised by stem cell research in different countries. The procurement of human embryonic stem (hES) cells, somatic cell nuclear transfer (or "research cloning", popularly known as 'therapeutic cloning'), creating hybrid human-animal embryos for research purposes and distinctions between 'research grade' and 'clinical grade' stem cell lines in human treatment have been the subjects of some of the key scientific and ethical debates. Some countries allow for the *in vitro* creation of human embryos for the purpose of procuring hES cell lines, others allow for the procurement of hES cells only from so-called 'surplus embryos' (unused by a couple following infertility treatment) while still other countries prohibit procurement from human embryos.

In July 2007, a Joint committee on the Human Tissue and Embryos (Draft) Bill in the United Kingdom explicitly proposed that "an inter-species embryo may only be created, kept and used under licence, subject to the 14-day rule and may not be placed either in a woman or in an animal". In most other European countries, the creation of hybrid / cybrid embryos for research or other purposes is prohibited.

On the therapeutic side, few (if any) clinical trials have to date been officially approved for stem cell therapies. Some clinics, for example in the Netherlands, have offered patients 'experimental' therapies for multiple sclerosis but this remains controversial in many European countries for two reasons. First, there are concerns that the procedures have not been tested rigorously through clinical trials and second, there are safety, quality and ethical concerns as regards where and how stem cell lines used in the treatments have been procured and manipulated. Moreover, there have also been concerns about 'therapy tourism', namely that European citizens are traveling within Europe or to Asia in order to undergo often costly though 'unproven' and perhaps risky regenerative medicine treatment.

In recent years, scientific observers and policy makers have been highlighting China as an emerging hub for stem cell research (together with South Korea and Singapore). Research centres in Beijing, Shanghai, Changsha, Tianjin and Guangzhou have reportedly carried out stem cell research for several years in the fields of neural stem cells, cord blood stem cells as well as hES cells. The Chinese government has identified stem cell research as a key strategic field, and provides direct funding through the Ministry of Science and Technology as well as the Chinese Academy of Sciences and the National Natural Science Foundation. In China, there is a diversified focus on laboratory research aiming to improve procedures for deriving and cultivating stem cell lines and also clinical research into potential stem cell applications in neurodegenerative diseases, muscular dystrophy as well as other diseases.

Alongside with these developments, a number of guidelines and regulations have also been debated and passed in China to address some of the many ethical challenges surrounding this research. These have included "Ethical Principles and Governance of Human Embryonic Stem Cell Research", submitted by the Ethics Committee of the Ministry of Health (ECMOH) on 15 September 2001, to the Ministry of Health. The Ethics Committee of the Chinese National Human Genome Center at Shanghai submitted on 20 August 2002, "Ethical Guiding Principles for Research on Human Embryonic Stem Cells (2003-460)" were passed on 24 December 2003 by the Ministry of Science and Technology and the Ministry of Health. Finally new regulations from the Ministry of Science and Technology on scientific misconduct (2006) as well as from the Ministry of Health on the ethical review of biomedical research involving human subjects (2007). Notwithstanding this increasing regulatory activity with a focus on stem cell research, just as has been the case in Europe, a number of concerns have been raised in China about the implementation of regulations, especially enforcement and compliance regarding the provision of 'unproven' stem cell treatments. Also, some Chinese commentators have suggested that the regulations on scientific misconduct from 2006 were much needed, as they raised questions about whether the current system of scientific peer review was sufficient to ensure good quality results and to deter misconduct.

Moreover, it is obvious that the systems of governance differ sometimes significantly and are embedded in different social environments and science cultures, between China and European countries. In view of the growing intensity, frequency and established routine of Sino-European collaborative research and the accompanying demand to develop an

overarching system of ethical governance of biomedical research across the regions, it becomes imperative to work together towards adequate understanding of the different systems and joint strategies towards best practice.

The background of the Second BIONET workshop

It is with these many ethical and governance-related challenges surrounding stem cell research and stem cell banks in mind, that 60 Chinese and European experts convened in Shanghai on 9-12 October to assess the state of the art, discuss and exchange views on issues of ethical oversight and governance in stem cell research. Choosing a diversity of discussion methods, and an on-site visit of a famous clinic with a specialty in tissue and organ transplantation medicine, so as to create multiple perspectives and starting points for deliberation, the Shanghai workshop continued the discussions, interactive methodology and working process that had started at the first BIONET workshop in Beijing in April 2007 (see report at www.bionet-china.org). This second workshop entered new related areas of concern, working towards the completion of the empirical, conceptual and policy-related scope of the BIONET consortium's agenda.

To achieve this goal, the main issues, concerns, ethical ideas and possible solutions had to be introduced from different professional and national perspectives, with a diversity of individual experts' insights. Participants discussed the experience in different established governance and ethics systems, and in the policymaking process. The common goal was, jointly, to explore ways of improving regulation, governance and practice, according to shared ethical and scientific standards as well as allowing legitimate differences to be integrated fruitfully.

From the European side, there was particular interest in determining the best forms of governance of European research activities in China, based upon a more accurate understanding of the situation on the ground. From the Chinese side, there were specific interests in learning more about European standards and creating a momentum to support related developments in China, but also getting a clearer picture of the actual ethical and legal situation of Chinese and European researchers working under the jurisdiction the other region, respectively.

The long-term plan of the BIONET is to provide a solid basis to develop advice for the governance of Sino-European research projects in the life sciences, in the form of evidence based best-practice guidance. In the process, BIONET is supporting and continues to support network building, towards a

sustainable quality infrastructure for consultation and co-operation on matters related to the ethics of life sciences research between Europe and China. The process of preparation for this second workshop had already been built upon advanced networking and cooperation, within China and Europe, and across the continents. In particular, the research conducted by BIONET junior researchers, in China and European countries, has begun to bear encouraging progress, with valuable contributions to our agenda.

The workshop was also intended to inform BIONET partners about the requirements, the limitations and challenges in access to information about bioethical governance, the diverging opinions and experiences about moral or ethical values and procedures or cultures, and about practical obstacles for understanding. These explorations and learning activities were informed by an empirical approach towards the issues, as a basis for the long-term purpose of mapping of bioethical governance, and the preparation of policy advice. The outcomes from the first and the second workshop will be crucial for the preparation of the larger BIONET symposium in 2008 and, with workshops number four and five, in the second symposium in 2009.

Finally, this second workshop intensified the collaborative efforts and the internal consultations among consortium members in and in connection with the formal sessions of the Steering Committee and the Expert Group.

Workshop Setting

The second BIONET workshop, held in Shanghai in October 9-12, 2007, with 60 participants, provided an opportunity for European and Chinese BIONET members, together with invited experts, to enter the second round of 'mapping' the regulatory frameworks and practices concerning informed consent, good governance and best practice in research and clinical contexts, with a focus on regenerative medicine and stem cell banks.

The workshop's discussions and presentations lasted 3 days, with an additional day for a site visit at the Shanghai Renjing hospital. Participants discussed particular concerns of different groups, related to regenerative medicine, in particular stem cell research and stem cell banking: bench scientists and medical researchers, patients and research subjects, biomedical research institutions (hospitals and research units), policy-makers, legal experts, educators, and experts in ethics and culture.

Participants explored the formal legal and regulatory structure, and their conceptual basis, namely that of the sciences, the related ethics and governance regimes on either side. The

focus of the workshop was on enabling participants to relate these frameworks to practical problems and cases in clinical and research settings, rather than pursuing the exchange of normative positions. The workshop consisted of presentations, group discussions, case discussions and site visits, covering different cultural contexts.

The participants from 9 cities in China and 7 countries in Europe convened for the second BIONET workshop in the Shanghai Institute for Advanced Studies (SIAS) Shanghai. Delegates came from the academia, clinical and research professions, and also from different ministries, administrations, and from the leading Chinese journal specializing in medical ethics (Yixue yu zhexue / Medicine and Philosophy, published in Dalian). European delegates from the UK Medical Research Council's CURE project (China-UK Research Ethics) participated as active observers. In terms of gender and age, participation was fairly distributed. According to the general plan, the conference programme was methodically structured in seven sessions.

It started with introductions of the scientific state of the art and outlines of major legislation, followed by explorations of the key regulatory and ethical issues in stem cell research. After this, examples of major research projects and applications were addressed with a special interest in clinical studies and the situation of therapy applications. BIONET researchers shared their findings. Issues arising under conditions of international collaboration were pinpointed, including linguistic, cultural and legal themes, and conceptual discussions, leading over to the final 7th session, which was entirely dedicated to taking forward the BIONET agenda. The site visit provided a unique occasion for in situ inspection of governance in an emerging state. During the workshop, three extended case discussions provided opportunity to explore selected exemplary problems with typical intricacies for international research, to be considered for in depth analyses.

The pre-conference day had been reserved for meetings of the BIONET Core Management Group, the first meeting of the BIONET Steering Committee, and the Expert Group. Steering Committee and Expert Group had more meetings arranged during the workshop.

Governance in stem cell research/therapy

In both Europe and China, stem cell research has emerged as a key strategic field attracting considerable investment in recent years. It is especially the promise of therapies and treatments for degenerative diseases that has led this drive to understand and therapeutically harness the biological properties of stem cells. One of the key topics at the Shanghai workshop was that of governance. What were the components of an effective system of ethical governance? It had been pointed out in various BIONET's discussions that understanding among participants of workshops and conferences is complicated by the fact that there is no clearly defined term for 'governance' in Chinese, which is further complicated by differing English definition of this emerging area of study. The related issues of understanding and successful communications that depend on proper translation of key terminology and concepts was also emphasized by Prof. Paul Unschuld (through a

lecture delivered on his behalf by Dr. Ole Doering). He suggested three scenarios which must be looked at carefully when translating ethical texts: situations where 1) language has / has not followed social development, 2) language has / has not followed social development but may be misleading and 3) language has followed social development but human error in translation jeopardizes cross-cultural communication. This was especially crucial beyond mere terminological matters, when fundamental ethical ideas, laws, ethical guidelines or regulations were translated from Chinese to English or English to Chinese (or any other languages).

When it came to the translation of 'governance', it was suggested that both *zhèng fǔ* (政府) which means 'government' and *zhì lǐ* (治理) which means 'to govern, administer or control' convey a certain top-down directedness where decrees, ordinances, orders, laws, statutes and regulations are passed and adherence is ensured through some form of coercion. Prof. Zhai Xiaomei used the term *guǎn zhì* (管治) to describe good governance (*liáng hǎo de guǎn zhì* 良好的管治) while another translation often used in mainland China for 'governance' is *guǎn lǐ* (管理). In these terms the common character *guǎn* (管) means 'to take care (of), control, manage, be in charge of, look after' while *zhì* (治) means 'to rule, govern, manage, control' and *lǐ* (理) means 'reason, logic, science, inner principle or structure'. It was suggested that a good governance system required good regulations (with ethically justifiable norms that are operable), implementation capacity (which required education and training), mechanisms of oversight, incentives and disincentives, a regulatory body and sufficient resources to fund all of these.

Prof. Nikolas Rose explained that in English 'governance' is considered to be a non-hierarchical term as it worked through systems of mutual collaboration, coordination and negotiation among and between not just state organizations (such as ministries, municipalities or judiciaries), but also a whole range of non-governmental institutions, organizations and bodies (science institutions, clinics, lawyers, academic journals, patient groups, etc.). Thus it depends upon co-operation between the different agents, and a system of sharing of tasks and responsibilities, organised in a manner that allows flexibility and adaptability. It did not only include written regulations and rules, but also informal working practices, peer oversight and the like. Hence, governance was considered more applicable in "complex circumstances of modern organisational life, [where] it is often difficult to fix responsibility", as put by Dr. Nick Bunnin in his presentation on levels of concern in the ethical governance of stem cell research. Accordingly, in order to understand the respective governance structure properly, it is necessary to describe the different levels of relevant law, the individual situation and the state of responsibility and compliance in detail. In the context of stem cell research, when governance is unclear, there can result an undesirable impact on practice. For example,

the combined effect of reported international research scandals and gaps or inconsistencies in the global mechanisms for governance and ethical oversight, according to Prof. Cong Yali, together with the permissive government policies in this area, has led to an impression in the minds of many researchers that there are in fact no serious limits for any scientific research.

Prof. Herbert Gottweiss provided an example from the perspective of a political scientist, analysing the complexities of governance in a case when it has been shown not to work. His presentation analysed the multifarious nature of the 'Hwang scandal' in South Korea, as a national, international and science community affair. In his presentation, Prof. Gottweiss showed how the Hwang scandal emerged first as an ethical case about how Woo Suk Hwang procured the thousands of eggs he required in his attempts at therapeutic cloning only to then turn into a case of scientific misconduct involving the use of fraudulent data. In this case, the data upon which Hwang's internationally renowned research was based turned out to be ethically tainted and scientifically fraudulent. According to Prof. Gottweiss, this scientific and ethical misconduct came about through a complex network of international collaborators, scientists, fertility clinics, hospitals, reputed international journals, government officials and corporate sponsors all of whom supported Hwang's research. This overview provided an outline of the structures on the 'map' of good governance, illustrating both, the importance of transparent responsibilities and good co-operation in a research community. As a result, he argued, "research integrity is increasingly a matter of network integrity" and therefore that "science culture matters" since ethical governance is not just about how guidelines and regulations are implemented and followed, rather it involves a complex system where research practice is guided by respect for the rule of law, transparency, scientific and ethical accountability, human rights and freedom from corruption.

Among foreign observers, there has been concern and uncertainty about the noted lacking of comprehensive governance by law regarding stem cell research in China. In a presentation on bioethics legislation in China, Dr. Liu Yinliang of the China University of Political Science and Law introduced the current state of the development of regulations. He explained how there are important differences between several instruments, such as laws, regulations, measures, ethical guidelines and technical norms. There are differences in scope and enforceability as well as in the respective objectives. Laws (*fǎ* 法) are passed by the standing committee of the People's Congress or its standing committee and are fully enforceable by the responsible institution specified in the law. Regulations (*tiáo lì* 条例) are approved by the State Council and are also enforceable. Technical norms or standards (*jì shù guī fàn* 技术规范) which are intended to ensure safety and effectiveness, and ethical principles (*lún lǐ yuán zé* 伦理原则) which are intended to maintain 'social order', on the other hand are only enforceable if they are specifically

authorized in the text of a law or regulation. Finally, there are also measures (*guǎn lǐ bàn fǎ* 管理辦法) which are directed at the administration and management of certain research and therapeutic practices and which are binding for those institutions, which are licensed to carry out these practices. According to Dr. Liu, there has been a 'legislative boom' in China over the past few decades. This trend corresponds with the general direction of the policy of opening and transforming China, and to employ standardisation measures as a policy instrument to foster China's international role as a global player. In terms of the ethical regulation of reproductive and regenerative medicine, this has meant that "almost every bioethical aspect regarding biomedical manipulations, including those involving hESCs, has been put into place to protect the rights of human subjects and public morality… however, it is noticed that there are fewer laws and regulations, and more technical norms or ethical guidelines which generally do not enforce legal liabilities (civil or criminal) and damages".

In general term, this discussion showed that the situation can be described as Europe having a mixed governance system including hard and soft law components; whereas China, in the area of the life sciences, shows a tendency to soft law. At the same time, it was noted that 'soft' does not imply 'weak' here. The weakness of a legal system in terms of oversight and compliance is not in line with, but rather contradicts the rationale of soft law. On this background, it was suggested that China is going to consider to introduce more components of hard law in this area, in the near future.

Prof. Qiu Renzong suggested that the time had come to update the existing "Ethical Guiding Principles for Research on Human Embryonic Stem Cells (2003-460)" which were jointly promulgated on 24 December 2003 by the Ministry of Science and Technology and the Ministry of Health. In contrast to assisted reproductive technologies which were regulated by a measure, technical norms and ethical principles which required that institutions providing them were licensed and therefore subject to ethical review, Prof. Qiu pointed out that in China, currently stem cell research was only the subject of ethical principles which were not enforceable: there were no requirements regarding the qualifications of stem cell researchers, no oversight mechanisms and no agency responsible for overseeing the upholding of the guidelines. As such, "current policies seem to be maximising scientific freedom and minimising ethical/regulatory constraints", he suggested, perhaps as a way to achieve "the ambition to be a power in bioscience and biotechnology". In particular, suggested Qiu, China needs to introduce a comprehensive monitoring system and fill the gaps in the legislation, especially to clarify the responsibility of actors. Prof. Zhai Xiaomei argued that the idea that the "development of biomedical research and biotechnology without constraint will allow China to more rapidly catch up with efforts in developed nations" was "both wrong and dangerous". Wrong because it assumes that ethical accountability impedes scientific progress and dangerous "because Chinese science and technology could lose its essential

integrity and public support both at home and abroad – the scandals over Hwang Woo-suk in South Korea and Chen Jin (referring to the 'Motorola-chip scandal at Jiaotong Univsity) in China convincingly illustrate this point."

Prof. Fan Minsheng of the Shanghai Medical Ethics Association, and the local co-organisor of this workshop, offered a historical explanation, which was that in the past Chinese students travelled overseas to be trained as scientists before returning home to China. These students, he suggested, were trained as postgraduate, without the curriculum including topics of science reflection in conceptual or societal context. This may have contributed to a perception of science as 'neutral' techniques, and not necessarily involving issues of medical humanities or ethics. It was only recently with a focus on medical ethics in China that the ethical context of scientific practice had come into focus. He gave the example of an application for a licence to establish a fertility clinic that was recently rejected by a hospital ethics committee that he was a member of. The application had been of very high quality and "indicated that the hospital had equipped research rooms, proper facilities, researchers, an organized ethical review committee to support the research except as well as the competent medical experience. Yet, since the objective of the application was research instead of reproduction, the application was rejected".

In the discussion, Prof. Lu Guangxiu wondered, how to practically deal with cases where law (hard or soft) might have been violated. How to proceed, if one side does not know exactly about the legal situation of the other? Would it be, e.g., a Chinese partner's responsibility in a co-operation with German stem cell researchers, to make sure they do not violate German law in China, and how was one to know when this might be the case?

Prof. Liu suggested that, "it is necessary for China to take a further step in the field of bioethics legislation, to add the necessary provisions to the laws or regulations". However, it was also noted that this had become an increasingly laborious and slow process since it overlapped the areas of different Ministries and also since formulating laws and regulations involved consultations with numerous experts from the legal, bioethical, social and medical fields. Participants at the workshop did not seem to think that any such laws or regulations when it came to stem cell research were imminent at this stage. It was speculated that the Chinese government might have deliberately resorted to the currently weak state of law to see how science and ethics would develop internationally, and to intervene at a suitable stage so as to secure the widest feasible range of options. As a direct consequence of the current state of affairs, it was very difficult to get a clear idea about how many and which institutions were carrying out stem cell research apart from the main centres of stem cell research which were in Beijing, Shanghai, Changsha and Tianjin. This observation reconfirms the need to systematically include the study of the relevant social scientific and humanities' issues, so as to be more readily prepared to approach the work of cross-cultural comparison.

Europe has developed different laws and legal cultures, on national and community levels. Accordingly, in Europe, there has been a diverse set of governance responses to the ethical challenges raised by stem cell research in different countries. BIONET junior researcher Thomas Streitfellner introduced a mapping study of governance situations

related to the possibility to conduct embryo research. He showed, how European countries could be classed into those that 1) prohibit research involving destruction of human embryos and even the production of 'spare' embryos, those that 2) allow creation and research on 'spare embryos' donated by couples in IVF clinics, those that 3) allow the creation of embryos for research through Somatic Cell Nuclear Transfer (SCNT), and those that 4) allow research only on imported hESC colonies. More recently, a fifth category has emerged, those countries allowing, or intending to allow the creation of chimeras or cybrids for research purposes. He also indicated that, in total, "European regulation is getting more permissive over time" as, for example, whereas only three countries had a legislative framework authorizing stem cell research in 2001, by 2007 this had increased to 14 and what is more, four countries had explicitly legalized research involving SCNT. According to Streitfellner, some of the key factors contributing to national systems of hESC research governance were: political interests, religious belief systems, public support, economic strength, funding structures/bureaucracy, networking amongst scientists and collaboration with other disciplines (e.g. social scientists), and different ways to deal with cultural and historical heritage and special constitutional requirements that would limit the options to manipulating human life.

In the specific case of the United Kingdom, which is considered to have a permissive stem cell research regulatory environment, Prof. Martin Johnson showed how the British system of ethical oversight around stem cell research had emerged over 20 years from the work initiated by the Warnock Committee in 1984. The Warnock Committee, guided by the perspective of a natural scientist, "set out the central principle of a gradualist approach to the developing moral status of the embryo that accorded it a special legal status such that human embryo research is permitted *only under licence from a regulator* and is limited to a maximum of 14-days *in vitro*". Johnson pointed out that this concept of the 'legal embryo', not a biological construction. It would be just a legal, and otherwise "completely arbitrary" concept. The licensing of stem cell research is therefore overseen by the Human Fertilisation and Embryology Authority, which was established in 1991 following the HFE Act which was passed in 1990 calling for its creation. The Department of Health initiated a consultation of this Act in 2005, which has recently culminated in a Draft Human Tissue and Embryos Act (May 2007). Prof. Johnson pointed out, that, as required by due procedure of consultation of experts and the public, the process of the drafting of these Acts and Bills, had been long and laborious. This slow regulatory process (a point also emphasised in China) was in sharp contrast to the rapid advances of the science itself, so much so that new laws and regulations were always at the risk of being outdated by the time they were passed. In discussions, Prof. Jack Price pointed out that in the UK, stem cells are regulated through their sources (often connected to fertility treatment) and not their biological properties as a result of this process. Nevertheless,

Prof. Johnson argued that in the long run, it is in stem cell scientists' interests to have their field as tightly regulated as it is in the UK, a point made by Prof. Zhai in a Chinese context as well.

Continuing the theme in the European context, Dr. Christian Woopen, a member of the German National Ethics Council, in a presentation about key regulatory and ethical issues in Europe, showed how regulatory diversity in Europe created challenges for European Union policies on and funding of hESC research. From the background of the manifold European debates, Dr. Woopen posed three important questions for BIONET, regarding Sino-European collaborations: "To what extent is moral consensus necessary and achievable? How to find policies under circumstances of moral diversity in fundamental questions? Does it make sense to harmonize laws in a globalizing world?" These were all governance related challenges. This led to a discussion among participants about whether there can or should there be a single regulatory system in a world, which is both global and local – with much moral and ethical diversity, or, if there should be a global regulatory framework, and what would then be its respective prescriptive status? If there is a unity of science, there seems also to be a diversity of law, regulation and morality. And while scientific progress can be fast, regulatory processes are often slow leading to the question of whether scientific progress itself will make current ethical concerns redundant while introducing a new set of concerns – not how tissue is derived, but what we should do with it. What is more, the question of ethical governance in stem cell research is further complicated by how to cope with conflicting hopes, expectations and interests of researchers, clinicians, parents of children suffering from disease, biotech companies, politicians, national ambitions, etc.

The situation in restrictive countries, such as in Germany, and permissive countries, such as in the UK or China, creates a tension and a potential conflict of authority, tantamount to the question, whether someone under German jurisdiction, who takes part in a research project with Chinese or UK partner labs, which involves the destruction of human embryos, can be charged of accessory to a crime. This workshop was not prepared to solve this dilemma, but identified it as a priority matter for clarification. Such challenges require not only legal but also in depth bioethical investigation.

Sourcing – the moral status of biological materials

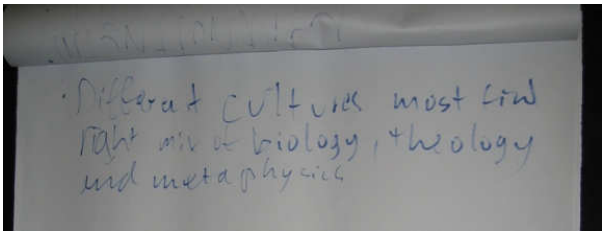
One of the key areas of difference to emerge from discussions at the BIONET workshop was around the question of sourcing. In Europe, the most controversial ethical debate about stem cell research has concerned the moral status of the human embryo – the source of human embryonic stem cell colonies, currently considered to be the most promising in the treatment of disease. This debate has concerned attempts to agree on a precise moment when full moral status – which entails full legal respect of human dignity and human rights – is accorded to what appears from a certain scientific view as a special kind of biological material, even when considering only the legal, not the scientific concept of the embryo. Should it be from the moment of fertilization, nidation, perception of 'primitive streak' or birth? Does it suffice to define it in biological terms? It was mentioned in the discussion that, from an accurate biological point of view, the widely

accepted notion of the beginning of the human's life at the moment of the fusion of the genetic material of egg and sperm is biologically not convincing.

In the United Kingdom, the Warnock Committee, as mentioned earlier, adopted a gradualist view where there is a "gradation in the respect accorded to a foetus as it develops from zygote to early embryo to its birth" – from 'special status' to 'full moral status'. In Germany, as Dr. Woopen pointed out, full moral status was accorded by the Embryo Protection Act to "*any fertilized human oocyte* after that point in time at which the pronuclei have fused, *any later stage of its development* and to *any totipotent parts* which could, under the proper circumstances, be able to develop into an individual being". This law reflects Germany's effort contain the liberty of any actor, including the state or scientists, to interfere with the integrity or the very existence of any human being; the latter is notably understood as remaining beyond the grasp of definition.
Recently, there has been a tendency to re-interpret the human ontogenesis from a gradualist standpoint and in terms of the 'potentiality' to develop into an entity with 'full' worthiness to be protected. Prof. Christoph Rehmann-Sutter took up this topic of potentiality in his talk on "Genomic metaphysics and Strategies of Legitimacy in Stem Cell Politics". Rehmann-Sutter suggested that in this argument it is "the potency of E to become a person (future) which confers a right to be protected (present)". He argued that this statement relied on a metaphysical metaphor, with the metaphoric assumption of a 'genetic program', which is regularly associated with an ontological privileging of DNA as the primary organizer molecule and active substance, and therefore a conclusion that "destroying the program will also eliminate the ethically relevant 'potency' of the embryo". Such 'program genomics', argued he, was at odds with 'system genomics', which did not privilege DNA but rather saw genetic information as something continuously produced during development in the course of interactions between DNA, cells and the environment. Rehmann-Sutter described these two approaches as examples of different 'cultural narratives' and concluded that the moral status of the embryo cannot be determined independently of a metaphysical concept. Fundamentally, Rehmann-Sutter proposed the concept of a reflected ethics and theory of

science, which pays attention to the systemic and contextual questions of bioethical issues.

In China, Prof. Qiu Renzong suggested that the Traditional Confucian position is still regarded as valid by many in society, according to which "a person begins with birth and ends with death… and is an entity which has the capacity for social relationship". At the same time, he argued, a "human embryo is a human biological life, a precursor of person, not merely 'stuff' like placenta… so it deserves due respect: if there is no sufficient reason, it should not be permitted to manipulate or destroy it". Prof. Tu Ling of the Hunan Institute of Reproduction and Stem Cell Engineering agreed, arguing that the embryo is not just a 'mere' cell as it contains the potential for adult development and should therefore be accorded "a certain degree of respect". According to Prof. Tu, the majority of scientists and people agree with this view.

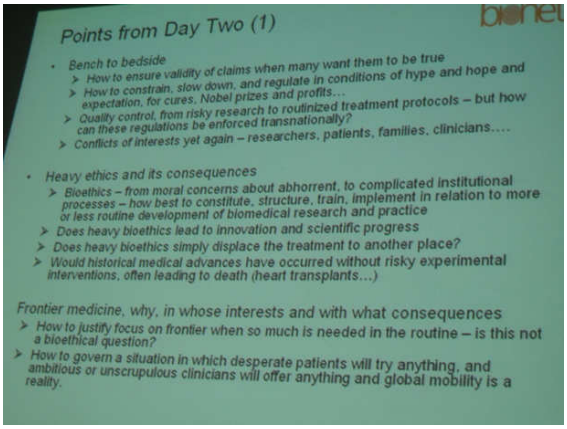


In discussions, it was suggested that underpinning such pragmatic compromise with metaphysics is a constant historical companion to the development of science in different social and cultural contexts. Earlier examples of this phenomenon could be seen in the debates about the moment of origin or location of the soul, for example in Aristotelean, Christian, Jewish or Islamic writings, and as they still can be encountered in religious arguments in bioethics around the globe. And as Prof. Martin Johnson put it, "each culture must find the right mix of biology, theology and metaphysics to satisfy it – to fit with its cultural narrative". 'Drawing the line' it seemed paradoxically, was both arbitrary and essential if socio-political or moral roadblocks were to be avoided. Moreover, identifying such metaphysical underpinnings can support the cohesion of science in society and the meta-reflection of science. Empirical evidence showed that these debates cannot be resolved by appeal to nature or to a universal moral philosophy (e.g. potentiality or dignity) as these do not close controversy. And so, when it came to the question of the moral status of the human embryo, it did not appear that a material global consensus was realistic, not to mention a European consensus. This observation reconfirms the purpose of bioethics, to support reasoned argument, make diversity fruitful and seek sustainable rules for such a discourse. This perspective includes the option to further develop the approach to bioethical issues; for example, the prevalence of 'status of an entity' approaches could be challenged by 'virtue', 'interpersonal responsibility' oriented or 'justified maxim' approaches, as they are traditionally rendered in Confucian or Kantian ethics.

From home to clinic to laboratory to bedside – informed consent in the sourcing of stem cells

As already noted, potentially self-renewing stem cells can be sourced from six-day old *in vitro* fertilised human blastocysts, aborted human foetal tissues, umbilical cord blood, bone marrow, brain as well as other somatic sources. That is to say, stem cell lines are

derived from biological samples, which are taken from human embryos, foetuses, newborns or adults. This of course raises questions of informed consent as well as propriety – how to respect the potential donors and whom do these biological samples belong? Consequently who should consent to their being 'immortalised', donated for research and/or donated for therapeutic purposes? How to frame and qualify such consent regarding incalculable future developments and benefit sharing? This also raises the issue of commercialisation; even though the commercial use of gametes and embryos is forbidden by law, in China and other countries, the notorious problems of under-regulation and compliance remain. This question is closely related to distinctions and definitions of what constitutes 'biological waste' as opposed to a 'biological sample'. Here comes in another, even more fundamental question of anthropology. The meaning of being a human, the attitudes towards the body and 'body parts' could not be discussed in depth at this workshop. Chinese participants explained, however, that 'filial piety' (xiao) should be strongly considered as an inculturated obstacle for volatile use of body matter.



One of the most ethically controversial areas of hESC research concerns the donation of eggs and embryos for research by recipients of fertility treatment. This research relies on a steady supply of 'spare' eggs and embryos and as a result the links between fertility treatment and stem cell research are intimate and it is common to find stem cell research facilities in close proximity to IVF clinics. This proximity can also create conflict of interest, as there may be undue pressure on clinicians to stimulate 'extra' eggs or to create 'extra' embryos for research rather than reproductive purposes. This potential conflict of interest was explored through a case discussion from Switzerland where the law on IVF allows clinicians to fertilize only as many oocytes as can be transferred to the uterus of the women within one cycle (i.e. usually 2 or 3 depending on the age of the woman). Yet this law was in contrast to recent developments in fertility treatment techniques which favoured longer ex vivo cultivation and transfer of a single viable embryo after 5 days. As had been commented by a director of an IVF clinic: "In my clinic, I would reach two ethically important goals at once: improving the pregnancy success rate of my patients and providing embryos for research in our stem cell group. The 0.5 Mio SFR technical investment for clean air facilities in our fertilization laboratory can be useful for both." In the case discussion that followed it was underlined that mechanisms for keeping patient and research interests were crucial – there should be clear institutional oversight mechanisms, and it was suggested to reconsider a 'cordon sanitaire' between research and treatment locations. Prof. Fan Minsheng's case (see above) which saw the rejection of an application to establish an IVF clinic in Shanghai because the objectives had been research-related was an example of such ethical oversight. The specific Swiss law was also discussed as it was asked

whether the main objective of such a law was to protect the embryo or to ensure the best possible fertility treatment.

In her presentation on socio-ethical considerations around acquiring eggs and embryos for hESC research, Prof. Erica Haimes emphasised how important and instructive for ethics it was to include donors' experiences into any ethical deliberations. She showed how a couples' deliberations over just what are considered 'spare embryos' were very different from the definitions of clinicians or embryologists, owing to the respective 'stories' from each particular experience and outlook on life. For patients, discussions about whether to donate or not were predominated by 'baby talk' as there was a social process of negotiation whereby an embryo became 'our embryo'. In this process there were doubts about whether even so-called 'poor quality' embryos could be labelled as 'spare'. There were constant calculations on the part of the couple who were being asked to make decisions about what to do with their 'spare embryos'. The language of 'waste' was a consistent theme in such calculations, and sometimes deemed inappropriate. Some might consider allowing spare embryos to perish as 'wasteful', while others might see the inevitable destruction of spare embryos through hESC research as 'wasteful'. And so Prof. Haimes suggested that there was more than just a clinic-laboratory-bedside relation at stake, rather relationships and interactions should be seen to span the more complex social home-clinic-laboratory-bedside relations, involving family members and friends, fertility experts, fertility counsellors, embryologists, stem cell researchers, and more. Prof. Haimes suggested that it was through donor experiences that we might be able to identify some of the social and ethical costs of hESC research.

In a Chinese context, Prof. Tu Ling argued that "it is the patients who must decide the fate of their embryos" in a presentation on how the informed consent process was organised and carried out at the Hunan Institute of Reproduction and Stem Cell Engineering. Through a highly elaborated informed consent procedure, fertility patients in Changsha must decide whether they want to "voluntarily contribute poor quality embryos" as well as "surplus frozen embryos" after the successful delivery of a healthy baby following treatment for scientific research. One important difference in the kind of social scientific research being carried out on the patient perspective in stem cell research is that while in Europe there is often focus on qualitative research methods where patients are interviewed and their testimonies analysed, in China there is a focus on quantifiable survey research. For example, Prof. Tu cited a random analysis of 414 signed informed consent forms which showed that in 62% of the cases patients had indicated that they would donate frozen 'spare embryos' for research as an indicator of patient attitudes to stem cell research.

In both Europe and China, it was stressed that crucial to informed consent procedures is organising a trustful communication culture and in particular taking the time to explain sometimes very complex information about stem cell research and also ensuring that there is no undue coercion. Donation must be strictly voluntary and must not influence fertility treatment in any way. Informed consent should be obtained by a third party and not by the treating doctor or researching scientist. Also donation should not be commercialised so as to ensure that no inducements are present. In fact, all relevant Chinese regulations expressly forbid any coercion or commercial incentives to achieve the donation of eggs or embryos. And finally, the principles of patient benefit and minimisation of harm must always come first, a point that is all the more important bearing the close connections between fertility treatment and stem cell research.

When it came to donating eggs, the question of inducement was important in both China and Europe. In both the United Kingdom and China, for example, in exchange for donating eggs to research couples were given reduced IVF treatment fees. Some argued that this was undue inducement since harvesting eggs from infertility patients required invasive procedures as well as the use of drugs with potentially serious side effects. These risks made it all the more important to ensure that informed consent procedures were complete and fully comprehended by patients. One of the key ethical debates in hESC research has also been about whether or not it is wasteful of human eggs (e.g. Hwang's subsequently scandalised research had used over 2,000 eggs). As will be discussed later, this ethical problem has been a key driver behind efforts to allow human-animal cybrid research.

A second area in which informed consent was discussed at the workshop was around umbilical cord blood. One of the case discussions at the workshop centred on an example of how umbilical cord blood had transformed from being considered as 'biological waste', left over after childbirth, which was at the disposal of hospitals to being considered a 'biological sample' with considerable value. Until recently it had been common practice for laboratories to pay hospitals a certain service fee in exchange for cord blood samples which they then could use for research (and not therapeutic) purposes. This was done without the knowledge or informed consent of the mother or father of the child. However, ever since the technical management norms (*jì shù guǎn lǐ guī fàn* 技术管理规范) for the collection of non-autologous hematopoietic stem cells were promulgated by the Ministry of Health in 2006 it has become the prescribed standard that "collecting cord blood requires the mother's consent before delivery and it must be explained to donors why it is collected, the potential harm to the mother or baby, measures to prevent and tackle risks, benefits of collecting and preservation, as well as other things related to medical science and ethics, which include that mothers have the right to decline without any discrimination".

The case discussions raised questions about the status of this 'biological waste' with some participants suggesting that all patients have a right to expect that any biological leftover that results from a stay in hospital will be disposed of unless informed consent had been given. In this view what was done with remaining biological matter was

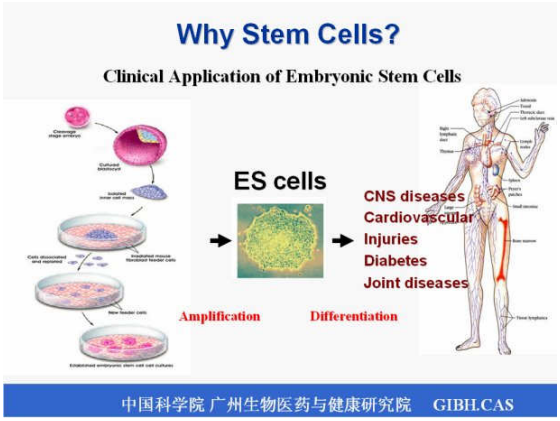
considered to be a question that the 'producer' or 'source' of this substance should decide. These were new regulations in China and as a result before they could be implemented, doctors in delivery hospitals as well as patients should be made aware of the potential value of cord blood. Some participants suggested that not many people in China were aware of its value. It was also stressed that informed consent procedures should be followed well before the final stages of pregnancy, since this was an anticipated situation that could be prepared thoroughly in advance. It was argued that informed consent before the collection of cord blood should always be obtained regardless of whether the purpose of the collection was for a cord blood bank, therapeutic use or research on derivation techniques.

A final case in which informed consent in the sourcing of stem cells came up in the presentation of Prof. Zhu Jianhong from Shanghai's Huashan Hospital who has done extensive therapeutic trials with neural stem cells from adult patients. In these cases patients were often not competent due to brain damage or neural disorder and as a result informed consent for the retrieval and use of stem cells for autologous use was to be obtained from a proxy or legal family representative. In this case informed consent was also a legal question as it relied on definitions of capacity to consent.

Manipulation and cultivation – the quest to understand and harness pluripotency

Stem cells are considered a promising avenue in the search for cures and treatments for degenerative disease because of their particular biological properties. Especially human embryonic stem cells are often described as possessing the innate capacity to become any cell in the human body. Ideally, if understood, this self-renewing and pluripotential generative capacity of stem cells could be harnessed to repair damaged cells (e.g. in cases of degenerative disease or brain injuries) and/or to produce certain tissues (e.g. heart valves, livers). Pluripotentiality is the 'holy grail' of stem cell research. Yet, if one thing is clear from hitherto stem cell research, it is that understanding mechanisms of action is extremely complicated and still very basic science; it is time consuming, expensive and requires a large and steady supply of biological materials from consenting human subjects. What is more, with human embryonic stem cells considered the most promising sources of viable therapeutic stem cell lines, scientists face numerous ethical challenges in securing access to research material. Moreover, the rationales for obtaining support and research funds sometimes challenge scientists' sober-mindedness, inviting hype and speculation. As a result, workshop participants were given examples of different ways in which such ethical challenges are being tackled in the laboratories.

Prof. Pei Duanqing of the Guangzhou Institute of Biomedicine and Health had trained in the United States of America but decided to return to China not least because of what is considered a more restrictive stem cell research climate in the US. In his presentation at the BIONET workshop, Prof. Pei showed how the key challenges in stem cell research are understanding how stem cells amplify self-renewal and how they differentiate into, for example, liver, brain or heart cells. Because "once you understand you can



manipulate". And partly as a response to difficulties in obtaining eggs and embryos, his lab had begun focussing on discovering whether differentiated cells can be coaxed 'back' into becoming pluripotent cells – induced pluripotential cells (iPCs). In this way pluripotentiality could be engineered out of differentiated cells using transcription factors and knowledge of epigenetics, allowing scientists to bypass the ethically sensitive task of procuring embryonic stem cells and egg cells.

Another strategy to circumvent ethical controversies surrounding the procuring of human eggs and embryos for research has been that of using SNCT to create human-animal hybrids or cybrids where an animal egg is emptied of its nucleus and is in turn enucleated from a human somatic cell. This strategy has been especially pursued in the United Kingdom. According to Prof. Martin Johnson, there were three major changes being proposed in the Draft Act on Human Tissues and Embryos from May 2007: 1) the Bill makes a clear legal distinction between "Research Embryos" and "Embryos for use in treatment" and introduces the legal concept of the "permitted embryo", 2) the Bill expands the purposes for which Research Licences may be granted to include, a) increasing knowledge about serious disease or other serious medical conditions, and b) developing treatments for serious disease or other serious medical conditions, and finally 3) the Bill proposes that a distinct legal category of embryos called "Interspecies embryos" (animal-human embryo chimaeras, animal-human embryo hybrids & cybrids) is created. Interspecies embryos can only be used for research purposes and are subject to the 14 day rule, i.e. they must be destroyed no later than 14 days after fertilisation. One of the driving factors behind these developments has been an argument by scientists that the creation of cybrids would minimise the 'waste' of human eggs and embryos by allowing vital mechanism of action research to be carried out on these cybrids.

In China, the creation of hybrid embryos has been very controversial following the publication of work by Prof. Sheng Huizhen of the Second Medical (now Jiaotong) University in Shanghai in 2003. Prof. Sheng, who did not participate in this workshop, reported that she and her team had successfully transferred a human skin cell nucleus into a denucleated rabbit egg, created about 400 human/animal embryos and then derived stem cells from them. The work had been rejected by a few journals such as *Science* but was eventually published in *Cell Research* in August 2003, an English language journal edited by Chinese, but belonging to *Nature*. The publication of this research led to an ethical debate internationally leading some to condemn such work on chimeras as unethical. Others have discredited the results suggesting that there may have been fraudulent use of data as had happened in the Hwang case, though without any evidence to back up such claims in public to date.

Prof. Pei Xuetao defended Prof. Sheng's publication, arguing that, whereas other researchers had just done similar work in secret, she had proven great efforts to meet ethical standards and seek peer discussion. From a scientist's perspective, Sheng had followed best intentions, but had not been able to anticipate the ensuing ethical quandary.

This international attention to the developments in China happened to coincide with the final drafting of the Ministry of Health and Ministry of Science and Technology's jointly promulgated ethical guiding principles (*lún lǐ zhǐ dǎo yuán zé* 伦理指导原则) on human embryonic stem cell research which banned hybrid research in stating that "it is prohibited to hybridize human germ cells with the germ cells of any other species". The Ethical Guidelines for Human Embryonic Stem Cell Research which had been issued by the Ethics Committee of the Chinese National Human Genome Center at Shanghai two years before in 2001 had explicitly stated that "use of the 'human-animal' cell fusion technique is permissible in basic research with non-clinical application" although it had also stated that "joining a human gamete with an animal gamete is not permitted". In his presentation at the BIONET workshop, Prof. Qiu Renzong argued in favour of human/animal cybrid research "because the use of human eggs in cell nuclear transfer research is inefficient" as well as animal/human chimera research "because of the scientific benefits and potential social benefits (human disease model, research in stem cell motion, regulation, differentiation, xenotransplantation research, etc.) and no noticeable harm is caused to any stakeholder". The debate on hybrid research it seems is as yet unsettled in both China and Europe as was evident from discussions that followed with some arguing against all chimera research and others for limitations on certain forms of chimera/hybrid research.

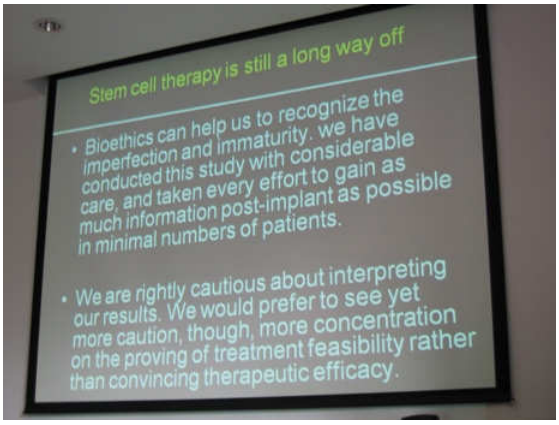
In his presentation, Prof. Jack Price recapped some of what is known about pluripotentiality – that it "somehow resides in the enucleated cell [which] gives a mechanism to generate pluripotential cells (stem cells, if you will) with any genetic makeup" via SCNT. Yet, Prof. Price also pointed out that "the attempt to generate patient-specific lines and disease specific lines has [as yet] not proven possible". For this reason mouse research into induced pluripotential cells (like that carried out by Pei Duanqing and his colleagues) has become very interesting especially since there is "no nuclear transfer; no chimerism, no complicated reprogramming – just easy technology using simple laboratory vectors". It may well be that scientific developments will make current ethical concerns redundant, although not necessarily in the near future as work on iPCs has to date been carried out in mice and not on human biological materials. Instead, Prof. Price suggested, citing Nishikawa that we may well be entering "a new era of human biology in which any type of cell can be prepared from somatic cells of a particular genetic background", which raises an entire host of new ethical challenges.

Further to research on understanding the self-renewing and differentiating properties of stem cells, there is also a growing body of research into possible modes of action of stem cells in the treatment of disease. It has been common to suggest that one of the principle modes of action of stem cells in treating disease will be through tissue regeneration – hence the term 'regenerative medicine' and the focus on pluripotentiality. However, Prof. Jack Price pointed out that "ironically we are discovering that pluripotentiality is less

significant than we had previously conceived in the clinical application of stem cells" as there may well be alternative modes of action that are more important, for example, induced plasticity mechanisms, anti-inflammatory mechanisms and immunomodulatory mechanisms. Not enough is known at this stage about modes of action in disease treatment, which raises a number of questions for research priorities, clinical trials and stem cell treatments as discussed below.

"Tomorrow's medicine today!" – the dangers of desperation and 'experimental therapy'

In his presentation on "Stem cell biology for brain regenerative medicine after brain injuty", Prof. Zhu Jianhong, who has done pioneer experimental research using autologous adult neural stem cells to treat open brain trauma, underlined that "stem cell therapy is still a long way off" and that we must be cautious as we proceed. The safety of human patients must come first, especially since "we don't understand the biology enough". Nevertheless, as any random internet search will tell you, stem cell therapy is a reality and it is being offered to patients throughout the world who suffer from very serious diseases, often at high costs. This reality was the topic of heated debates and discussions at the workshop.



Most importantly, what emerged from the discussions and presentations was that when it came to regenerative medicine or stem cell therapies, there were two very different worlds. The first was that presented by Prof. Pei Xuetao, Prof. Zhu Jianhong and Prof. Jack Price, where experimental therapy is subject to strict clinical protocols, ethical review and informed consent procedures and where safety of the patient is the priority; ideally embedded in a comprehensive system of ethical and social checks and balances. The key principle in this kind of experimental research is that of caution. From Prof.s Zhu and Price's presentations emerged one of the key ethical challenges for current clinical testing of stem cell therapies – namely how to proceed when not much is known about the biological mode of action of stem cells as they are used to treat degenerative diseases or brain trauma. What is more, as Prof. Rehmann-Sutter pointed out in discussions, in history, many of the most important medical advances have required 'experimentation' on human lives with inevitable casualties but also with significant benefits for future patients. This is sometimes used as a strategic argument against ethical concerns. So, how to balance caution, a 'pre-clinical' requirement to know modes of action, patient safety and clinical experimentation, and learn from the sometimes lamentable historical precedence, at the same time? Prof. Price argued:

> The general point concerning mechanism is this. You may not at the outset have a defined clinical mechanism for the therapy, by the end of the study you will certainly know more but you still might not have a very refined mechanistic understanding. Why don't regulatory authorities demand this? Why don't they demand you understand the mechanism before you go to the clinic? Because it is too high a hurdle and too imprecise a hurdle, and we would end up denying safe, efficacious medicines to sufferers who need them. You might think you know how a medicine works, but you might be wrong and a thorough scientific proof might take twenty years. The process is more trustworthy —experience tells us that if a medicine is demonstrably safe and efficacious then we have a basis on which to proceed with care.

What is most important is ensuring that any stem cells destined to be transplanted into humans are of 'clinical grade' which means that there must be a quality controlled process for generating a final therapeutic from defined starting materials and that each batch of cells used must be the same. Any move into human testing, as Prof. Zhu argued, must start with a small group of patients to demonstrate safety. Only then should testing begin on a larger group of patients. Here, the interests of best science and ethics appear to coincide.

In a presentation on "Stem Cell and Tissue Engineering Research in China", Prof. Pei Xuetao of the Beijing Institute of Transfusion Medicine, gave a broad overview of Chinese state investment into this field of biomedical research. He suggested that this research was becoming crucial as China's population continued to age with a growing proportion being over 65 years of age. This demographic change meant that the prevalence of degenerative and cardiovascular diseases was also on the rise affecting millions of people. Notwithstanding the limited role medicine can play in mending the largely environmental and lifestyle-related causes of such diseases, medicine hopes to make a significant contribution to the improvement of this field. Funding into stem cell research was growing via the 973 and 863 programmes. BIONET junior researcher Joy Zhang also showed how the Chinese R&D system was broad covering Ministries of Science and Technology, Health, Education and Finance as well as many funding agencies, the most important of which was the Chinese Academy of Sciences. There was a clear emphasis on developing clinical applications out of basic research into stem cells. As noted by Prof. Qiu, "since 1999, China's spending on research and development (R&D) has increased by more than 20 per cent each year. In December 2006 China had moved ahead of Japan for the first time, to become the world's second highest R&D investor after the US". Such state sponsored development of clinical applications from stem cells are of course subject to state regulations and requirements which includes a requirement to acquire a licence from the SFDA for any clinical trials.

Notwithstanding these important efforts to develop clinical applications from stem cell research, one of the other key topics of debate at the workshop was that of a 'murky world' of stem cell therapy. In a case from the Netherlands prepared by BIONET junior researcher Thomas Streitfellner and in a presentation by Dr. Ayo Wahlberg, it was shown how stem cell tourism had emerged as a new field of health tourism as patients with debilitating and untreatable diseases were willing to travel far and to pay much for unproven or experimental stem cell therapies. The provision of such stem cell therapy across national borders was largely unregulated and it happened throughout the world from Europe and America to China and India, taking advantage of different levels and

policies of regulation. The case discussion concerned a clinic in the Netherlands offering unproven stem cell therapy to sufferers of Multiple Sclerosis, which had attracted many patients from the United Kingdom; another case was discussed where patients were lured into Belgium to receive a premature "therapy" that had been forbidden in the neighbouring Netherlands. In China, Prof. Qiu mentioned that many clinics were offering stem cell therapy to unknowing patients, often making unfounded claims about its effectiveness and charging as much as 20,000 RMB for treatment. It was suggested that in China there was a direct link to the commercialisation of healthcare and the provision of expensive and unproven stem cell therapies. Prof. Zhai provided a case example:

> A biotechnology company 'invented' neural stem cell therapy to treat neural diseases such as Parkinsonism, spinal injury etc. They work with several hospitals which recruit patients and they provide neural stem cell treatment. After they advertised, a great number of patients went to these hospitals to seek the treatment of their desperate diseases from China and abroad. Each course consists of 4-6 injections and costs 12,000 RMB (€ 1,200). The company has never sought the approval from the Ministry of Health and has not been reviewed by an IRB.

The point being that stem cell therapy is currently on offer globally to those who can afford it and who can be persuaded that it is a hope for them, which raised an entire host of ethical problems which were discussed.

The first ethical challenge was how to safeguard patients who were often in very desperate situations and willing to take on almost any form of treatment. In China, 'experimental' stem cell therapies did not require approval from the SFDA but did require institutional ethical review board approval. And since the standards of ethical review boards varied from hospital to hospital, there was scope for situations where certain hospitals offered stem cell therapies "exaggerating benefits with little mention of risks and actually cheated desperate patients", as argued by Prof. Zhai. Informed consent procedures in such cases were at best poor and at worst manipulative and misleading.

The other key ethical challenge was how to ensure safety since it was very clear that in the vast majority of cases stem cell therapies did not consist of 'clinical grade' stem cells but more likely were of 'research grade' or even worse. The main reason for this was that quality control was very expensive. Citing Halme Kessler, Dr. Wahlberg suggested that one reason for this was that "unlike pharmaceutical products, many stem-cell-based products originate in academic laboratories where researchers are unfamiliar with the applicable regulations". Controlling quality means ensuring the purity (safety), type and potency (efficacy) of stem-cell-based products which in turn requires that good practice standards must be observed in the selection of donors, retrieval of tissues, testing, processing, storage and delivery of finished tissues, as suggested in a UK Code of Practice.

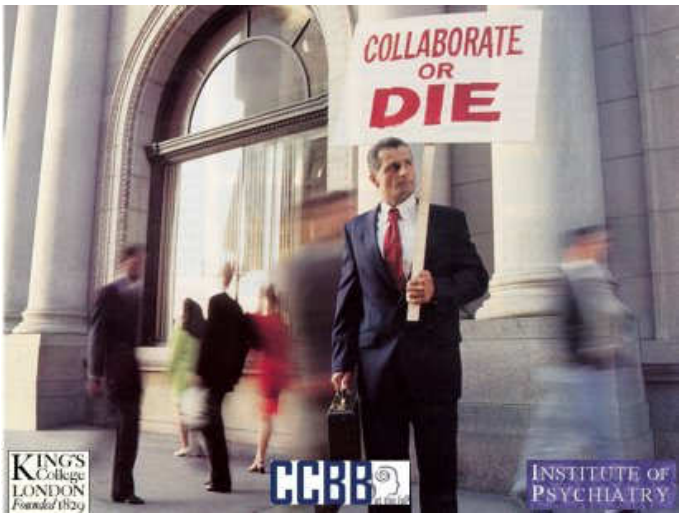
In short, the availability of stem cell treatment – of "tomorrow's medicine today" – raised numerous challenges including: the obvious absurdity of the promotional slogan, how to protect consumers/patients, especially across borders; how to ensure validity of claims when many who are just despaired want them to be true, how to constrain, slow down, and regulate in conditions of hype, hope and expectation, for cures, Nobel prizes and

profits, how to enforce quality control (from risky research to routinized treatment protocols) especially transnationally and finally how to minimise conflicts of interests between researchers, patients, families and clinicians. Such questions, in effect, aim far beyond the scope of medicine, science and ethics. They relate to the larger issues of good and effective governance, within national, regional and global communities.

A final ethical discussion around regenerative medicine concerned health priorities. It was clear that the degenerative diseases which could potentially be treated through stem cell therapy were growing in prevalence throughout the world. Nevertheless when resources are limited there will always be a debate about whether and how much state investment and private capital should be directed at certain medical fields. Such investment was not always lead by health concerns but was also influenced by commercial interests, the prestige of scientists who wanted to be at the 'frontier' as well as national interests to be a leading force in bioscience. So there is an epidemiological and public health-related ethical question which concerns research priorities as well as relevance of the research to the studied population.

Summarising Issues for Collaborative Research on BIONET's Agenda

As Dr. Sleeboom-Faulkner explained, 'having guidelines' is different in China, compared with European countries. Therefore, it is important, not only to describe and compare the law, but put particular scrutiny on the relevant cultural and social context, together with the specific characteristics of the respective practice.



Throughout the discussions it was repeatedly observed that crucial factual information about the actual projects and cooperations in stem cell research, in both regions and with inter-regional participation and the proper means to access such information, are still missing. A reliable database for reference and perhaps facilitation of such projects would be highly desirable. This is owing to the nature of emerging and transforming fields of research and science, but also to insufficient and non-transparent governance. In particular, no institution is in charge and accountable for the required governance tasks.

Dr. Woopen proposed to introduce a model project of a Sino-European certificate that involves clinical research and certifies quality, when actual licensing is not feasible. Prof.

Hennig suggested setting up an agency that would organise a clear system of registration and standardisation, for oversight and advice of Sino-European activities.

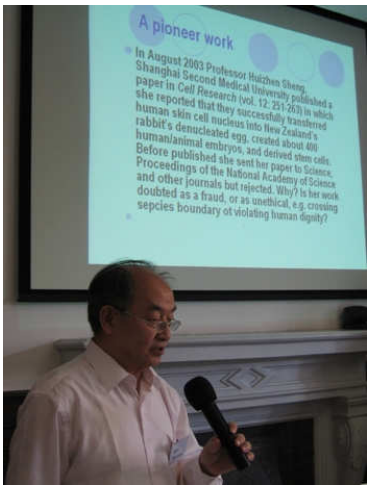
On the increasingly important legal side of Sino-European collaborations, it would be helpful to find out specifically, what kinds of protocols are in place to deal with scientific, legal, diplomatic questions interaction are in place or should be installed, when collaboration is required in order to facilitate implementation of law or prosecution, in bilateral and multilateral constellations. This applies in particular in areas where 'research or therapy tourism' occurs.

The workshop made it clear through numerous examples that in the areas of governance and regulation regarding stem cell research there are significant differences between Europe and China, some of which even raise questions of comparability of the systems.

An important task in approaching shared standards on the practical levels of science and ethics is to face the challenge of understanding. The process of communication, translation between different conceptual or native languages, especially when it comes to sensitive or normative matters requires careful study and the relevant skills, which have to be acquired and trained in specially designed educational programmes.

At present, not many real cases of actual co-operative research projects involving European and Chinese partners are known to be in place. The growing interest in such research, however, is obvious. Hence, greater attention of the science community and policy makers to these questions is as urgent as it is timely.

Chinese participants in particular expressed their desire to be given a 'map' of the diversified internal European regulatory landscape. The emerging sector of 'biobanks' was quoted as a most imminent example.



From a view of the history and philosophy of science and ethics, Dr. Bunnin introduced a broader vision of a systematic research programme in bioethics for China, since this area of study is rather immature and should not depend solely on Western models. Such a programme would encourage China to develop her own intellectual and institutional resources towards a timely and culturally embedded bioethics.

Prof. Qiu argued that now would be the proper time to develop a joint Sino-European focus, circumscribing the common concerns and identifying an agenda for action. He estimates that some 20% of all life science research in China could be fraudulent. When Europeans come to China, substantial funds should be earmarked for training on topics such as research interests and responsibility, how to deal with vulnerable populations, benefit sharing, and applied ethics.

Prof. Cong Yali expressed concern, how to support Chinese researchers who have expressed their need for better information and training regarding bioethics, for example stem cell issues? It was recognised that there was a great need of general education among the public in Europe and in China, but that further efforts for the benefit of scientists and ethicists is crucial recognising the role of these professions in society. A joint effort from both sides would be helpful in order to develop common minimal standards, technical and ethical, in co-operative projects in stem cell research and clinical application.

Programme

Ethical governance of reproductive and stem cell research and stem cell banks

Organised by:
CAS-MPG Partner Institute for Computational Biology in cooperation with the Shanghai Medical Ethics Association

Shanghai
9 – 11 October 2007

VENUE

Shanghai Institute for Advanced Studies (SIAS)
Building 11
319 Yue Yang Road
200031 Shanghai
http://www.sias.ac.cn/p2.html

Monday, October 8
Arrivals and registrations

10.00 - 12.00	Meeting of BIONET Core Management Group
14.00 - 16.00	First meeting of BIONET Steering Committee
16.00-18.00	*Expert Group*
18.30	Informal dinner and Steering Committee working dinner

Tuesday, October 9

Morning Sessions 8.30 – 13.00

CHAIRS

8.30 – 9.00 Opening and Introductions of the programme

Lu, Rose

Session 1 Stem Cell Research: State of the Art

9.00 - 9.20	PEI Duanqing (Guangzhou)
9.20 - 9.40	Martin JOHNSON (Cambridge)
9.40-10.00	Jack PRICE (London)

10.00-10.40	Discussion
10.40 – 11.10	Coffee / tea break

Session 2 Stem Cell Research and Regenerative Medicine – key regulatory and ethical issues

11.10 – 11.30	TU Ling (Changsha)
11.30 – 11.50	Christiane WOOPEN (Cologne): "Stem cell research and regenerative medicine - Key regulatory and ethical issues"
11.50 – 12.10	LIU Bin (Beijing): "Advances in stem cell research (hES) and ethical problems"
12.10 – 12.30	Erica Haimes (Newcastle): "Key issues in acquiring eggs and embryos for hESC research in Europe"
12.30 – 13.00	Discussion
13.00 – 14.00	Lunch break

Afternoon Sessions 14.00- 17.15

Session 3 Stem Cell Research: Governance and Regulations Cong, Doering

14.00 – 14.20	PEI Xuetao (Beijing)
14.20 – 14.40	Herbert GOTTWEIS (Vienna): "Stem Cell Governance in International Comparison: Trends and Developments"
14.40 – 15.00	LIU Yinliang (Beijing)
15.00 – 15.30	Discussion
15.30 – 16.00	Coffee / tea break
16.00 – 16.30	Case discussions in 2 working groups
16.30 – 17.00	Report from groups and discussion
17.00 – 17.15	Summary and conclusion of the day
18.00-20.30	Welcome Dinner

Wednesday, October 10

Morning Sessions 8.30 – 12.00

Session 4 Stem Cell Research: Projects and Applications Sleeboom-F, Zhai

8.30 – 8.50	ZHU Jianhong (Shanghai)
8.50 – 9.10	Ayo WAHLBERG (London): "The ethical status of 'experimental therapies'"

9.10 – 10.00	Discussion
10.00 – 10.30	Coffee / tea break
10.30 – 11.30	Case discussions in 2 working groups
11.30 – 12.00	Reports from groups and discussion

Lunch break 12.00 – 14.00

Afternoon Sessions 14.00- 17.15

Session 5 Stem Cell Research: Ethical Issues Qiu, Unschuld

14.00 – 14.20	FAN Minsheng (Shanghai)
14.20 – 14.40	Nick BUNNIN (Oxford): "Stem Cell Research and Regenerative Medicine – Levels of Bioethical Concern"
14.40 – 15.00	QIU Renzong (Beijing): "The historical, social and philosophical background of Chinese policies regarding human embryonic stem cell research"
15.00 – 15.20	Christoph REHMANN-SUTTER (Basel)
15.20 – 15.50	Discussion
15.50 – 16.20	Coffee / tea break
16.20 – 16.50	Case discussions in 2 working groups
16.50 – 17.20	Report from groups and discussion
17.20 – 17.30	Summary and conclusion of the day
18.00 – 20.00	Dinner

Thursday, October 11

Morning Sessions 8.30 – 12.00

Session 6 Issues in International Research Collaboration Hennig, Yang

8.30 – 8.50	Introducing the Issues ZHAI Xiaomei: "Challenges that require governance and regulatory responses – China"
8.50 – 9.10	Paul UNSCHULD (Berlin) "Translating Ethical Key Texts"
9.10 – 9.30	ZHUO Xiaoqin (Beijing) "An International Research Cooperation Case"
9.30 – 9.40	Commentary Wolfgang HENNIG (perspective of *science*)
9.40 – 9.50	Commentary FAN Minsheng (perspective of *ethics*)

9.50 – 10.00	Commentary Nikolas ROSE (perspective of *governance and regulation*)
10.00 – 10.45	Discussion
10.45 – 11.15	Coffee / tea break
11.15 – 12.00	Reporting research findings (BIONET researchers)
11.15 – 11.35	Joy ZHANG (London) "Societal and Cultural Factors in Stem Cell Research: China"
11.35 – 11.55	Thomas STREITFELLNER (Vienna) "Societal and Cultural Factors in Stem Cell Research: Europe"
12.00 – 14.00	Lunch break

Afternoon Sessions 14.00- 17.30

Session 7 Taking forward the BIONET Agenda Liu Bin, Rose

14.00 – 14.40	Chinese and European Views on Expectations Towards Governance of Research Collaborations Discussion
14.40 – 15.30	Working session: Suggestions for amendments "Which topics, issues, perspectives should be added?"
15.30 – 16.00	Coffee / tea break
16.00 – 17.00	Structured discussion (With guiding questions set towards the BIONET agenda) Recommendations in preparation of the Changsha conference Recommendations for the Expert Group
17.00 – 17.30	Summary and conclusion of the workshop

Friday, October 12

9.30 – 12.00	Site visit to Renjin Hospital, Shanghai Jiaotong University Medical School, Pudong site, Shanghai
Afternoon	Shanghai tour, with dinner

Participants

Name	Institute	City
PEI Xuetao	Beijing Institute of Transfusion Medicine	Beijing
PEI Duanqing	Institute of Biomedicine and Health	Guangzhou
WANG Yanguang	Chinese Academy of Social Sciences	Beijing
LIU Yinliang	China University of Political Science and Law	Beijing
PENG Ruipeng	Central China University of Science and Technology	Wuhan
FAN Minsheng	Shanghai University of Traditional Medicine	Shanghai
LIU Bin	Peking University Health Science Centre	Beijing
ZHU Jianhong	Huashan Hospital	Shanghai
CHEN Haidan		Wuhan
Wolfgang HENNIG	CAS-MPG Partner Institute for Computational Biology	Shanghai
LU Guangxiu	Central South University	Changsha
TU Ling	Central South University	Changsha
HE Ginny	Central South University	Changsha
CHENG Lamei	Central South University	Changsha
QIU Renzong	Chinese Academy of Social Sciences	Beijing
CONG Yali	Peking University Health Science Centre	Beijing
ZHAI Xiaomei	Peking Union Medical College	Beijing
YANG Huanming	Beijing Genomics Institute	Beijing
SU Yeyang	Beijing Genomics Institute	Beijing
ZHAO Mingjie	Journal of Medicine and Philosophy in China	Beijing
Martin JOHNSON	University of Cambridge	Cambridge, UK
Christine WOOPEN	University of Cologne	Cologne, Germany
Erica HAIMES	University of Newcastle	Newcastle, UK
Nikolas ROSE	London School of Economics	London, UK
Herbert GOTTWEIS	University of Vienna	Vienna, Austria
Ole DOERING	German Institute of Global and Area Studies	Hamburg, Germany
Margaret SLEEBOOM-FAULKNER	University of Sussex	Sussex, UK
Jack PRICE	King's College London	London, UK
Ayo WAHLBERG	London School of Economics	London, UK

Christoph REHMANN-SUTTER	University of Basel	Basel, Switzerland
Renata SALECL	University of Ljubljana	Ljubljana, Slovenia
Nicholas BUNNIN	University of Oxford	Oxford, UK
Alicja LASKA-FORMEJSTER	University of Lodz	Lodz, Poland
Paul UNSCHULD		Berlin, Germany
Thomas STREITFELLNER	University of Vienna	Vienna, Austria
Joy ZHANG	London School of Economics	London, UK
Michael BARR	University of Newcastle	Newcastle, UK
Achim ROSEMANN	Leiden University	Leiden, Netherlands
Athar HUSSEIN	London School of Economics	London/Beijing
Catherine ELLIOT	Medical Research Council (CURE)	London, UK
Amanda DICKINS	King's College London (CURE)	London, UK
David WARRELL	University of Oxford (CURE)	Oxford, UK

Media Release

October 11, 2007

Ethics of European-Chinese biomedical research collaborations

The European-Chinese co-operative consortium, BIONET, dedicated to the Ethical Governance of Biological and Biomedical Research announces its second workshop, taking place 9 – 11 October 2007 in Shanghai, on the topic of „ethical governance of reproductive and stem cell research and stem cell banks", at the CAS-MPG Partner Institute for Computational Biology in cooperation with the Shanghai Medical Ethics Association, in Shanghai.

Background
In recent years, many scientific observers highlight China as an emerging hub for stem cell research. The Chinese government has identified stem cell research as a key strategic field, and provides direct funding through the Ministry of Science and Technology as well as the Chinese Academy of Sciences. In China, there is both focus on laboratory research aiming to improve procedures for deriving and cultivating stem cell lines and also clinical research into potential stem cell applications in neurodegenerative diseases, muscular dystrophy as well as other diseases. In tandem with these developments, a number of guidelines and regulations have also been passed in China to address some of the many ethical challenges surrounding this research.

Notwithstanding this increasing regulatory focus on stem cell research, just as has been the case in Europe, a number of concerns have been raised in China about the enforcement of regulations, especially regarding the provision of 'unproven' stem cell treatments. Also, some Chinese commentators have suggested that the regulations on scientific misconduct from 2006 were much needed, as they raised questions about whether the current system of scientific peer review was sufficient to ensure good quality results and to deter misconduct.

It is with these many ethical challenges surrounding stem cell research in mind, that 50 Chinese and European experts will meet in Shanghai on 9-11 October to discuss and exchange views on issues of ethical oversight and governance in stem cell research.

Short description of BIONET
BIONET is a network of European and Chinese researchers which will work to undertake research, training, workshops and conferences, together with the production of relevant materials and documentation, on the ethical governance of research in the life sciences and biomedicine within and between China and European countries. The project will run

from October 2006 to September 2009. Website: www.bionet-china.org

Objectives
BIONET workshops have a number of objectives:

- To provide a platform for scholars with different cultural and academic backgrounds to improve understanding
- To provide capacity building for a range of professionals across China who are involved in research, research ethics and decision making in these areas, including members of ethics review boards
- To explore differences in approaches, and current themes around, ethical review and regulation, particularly around informed consent
- To enhance understanding of the strengths and weaknesses of different approaches to the regulation of biomedical research and practice
- To gather evidence of problems, cases and practices in the ethical governance of research in this area, as they are experienced on the ground by different professional groups in different regions in relation to different issues.
- To define lines of future studies in the clinics of doctor/patient relationships, and on other issues which may arise
- To facilitate the development of evidence based social scientific research on ethics, and awareness of the need to research the experience and views of patients and research subjects.
- To learn from each other about the ethical governance of stem cell research.
- To visit places where real research activities are taking place so as to improve knowledge and mutual understanding.

Participants
About 50 participants from China and Europe have taken part in the BIONET workshop on stem cell research. These include stem cell researchers, bioethicists, lawyers, social scientists as well as government representatives.

Interviews can be requested and information is available through Dr. Ayo Wahlberg at the secretariat of the Expert Group at the BIOS centre, London School of Econom ics in Europe and through Prof. Wolfgang Hennig, CAS-MPG Partner Institute for Computational Biology.

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新闻稿

2007， 10 月 11

中欧生物研究合作的伦理

2007 年 10 月 9-10 日，BIONET（中欧合作：生物医学研究的伦理管理）第二次研讨会在上海举行，这次讨论的主题是“干细胞研究及其临床应用中的伦理、法律和社会问题”，中欧合作的 BIONET 致力于生物学和生物医学研究的伦理管理，由中国科学院-马普学会计算生物学伙伴研究所和上海医学伦理学会联合承办。

背景

最近几年，许多科学观察家认为中国逐渐成为国际上正在兴起的干细胞研究中心之一。中国政府已经将干细胞研究定为重要战略领域，并通过中国科技部等有关部门直接提供经费支持。在中国，实验和临床两方面的干细胞研究都受到了重视。实验室研究侧重于优化干细胞株的获得和培养流程，临床研究侧重于干细胞在神经变性疾病，肌肉萎缩症和其他疾病的治疗方面的潜在应用。伴随这一系列的发展，面对这些研究引发的伦理挑战，中华人民共和国科技部和卫生部已联合出台了《人胚胎干细胞研究伦理指导原则》及其他的管理规范。

尽管对干细胞研究的管理关注越来越多，正如欧洲已经出现的情况那样，中国也出现了许多关于规范管理执行力度的担忧，特别是有关‘疗效未经证实’的干细胞治疗。同时中国学者对目前实施的同行评议审核体系是否能够确保干细胞的良好质量和制止科学不端行为持怀疑态度。

出于对这些干细胞研究和临床应用伦理挑战的关注，50 位中欧专家于 10 月 9-11 号相聚在上海，就干细胞研究和临床应用中相关伦理和监控等问题进行了热烈的讨论，并坦诚地交换了意见。

目的：

BIONET 简介

BIONET 是一个为中国和欧洲学者提供研究、培训、讨论以及会议的网络。同时各国专家将对生命科学和生物医学方面的伦理管理，为中

国和欧洲各国进行相关材料及文件的整理及研究。此项目于2006 年10 月启动，将于2009 年9 月结束。网址：www.bionet-china.org。

BIONET 研讨会有如下数个目标：

- 为具有不同文化和学术背景的学者提供一个交流平台，促进相互理解。
- 为中欧各领域的专业人员提供一个交流提高、促进能力建设的机会，这些人员包括生命科学领域的研究者、伦理研究者和决策者，还包括伦理审查委员会的成员。
- 探索中欧在伦理审查和管理方法及关注焦点，尤其在知情同意方面存在的差异。
- 加强对各种不同的生命医学研究和实践的管理方法的优缺点的理解。
- 收集因背景不同而出现的在伦理管理中的问题和案例等。
- 对医患关系以及其他可能出现的问题进行研究并制定未来研究路线
- 促进循证的社会科学研究的发展，提高对患者和受试者的尊重。
- 在辅助生殖技术的伦理管理方面相互学习。
- 对研究场所进行实地参观和考察，提高认识并促进相互理解。

参会者：

约有 50 名的中欧专家参与了 BIONET 关于干细胞研究的研讨会，包括：干细胞研究学者、生物伦理学家、律师、社会学家和政府官员等。

欢迎与伦敦政治经济学院 BIOS 中心的 BIONET 专家组的秘书的 Dr. Ayo Wahlberg 或与 CAS-MPG Partner Institute 的 Wolfgang Henning 教授联系采访工作或获得相关资料。

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