

SCIENCE AND LAW

Integrity in International Stem Cell Research Collaborations

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International collaborations in human embryonic stem cell research (hESCR) currently face ethical and policy challenges resulting from conflicting national regulations. To address these challenges, we convened more than 50 scientists, ethicists, journal editors, lawyers and policy-makers from 14 countries, in Hinxtton, Cambridge, UK (1). Through exploration of case studies (see Supporting Online Material) and deliberations, we came to consensus on guiding principles (see table, page 922) for international collaborations in hESCR (1).

Science, Society, and the Law

Society has the authority to regulate science, and scientists have moral and legal duties to obey the law. The Hinxtton Group engaged in discussion about the power of law to facilitate or to restrict hESCR and about the need, given the critical contribution science makes to the public good, for lawmakers to be circumspect in regulating science.

Even apparently well-crafted laws can have unintended consequences as science progresses. Since enacted legislation is difficult to change, a premium should be placed on flexible regulatory structures that can respond to the rapid evolution of scientific understanding. To strike the best possible balance between free scientific inquiry and social values, it is essential that lawmakers and scientists consult with each other and with the public.

We also call for clarity in the law. Scientists and clinicians have the right to know what is, and is not, permitted with respect to their research, the jurisdiction of any prohibitions, and related penalties so that they and their research institutions can regulate their behavior accordingly. The lack of

clarity in laws, for example, due to the ambiguous use of technical language [e.g. (2)], may have unintended chilling effects on science. It can lead to costly and time-consuming legal challenges, and in the face of ambiguity, scientists and research institutions may choose not to pursue a particular line of investigation or collaboration.

Governments have the authority to regulate science according to the values and histories of their nations. One of the most contested issues the Hinxtton Group discussed was whether or under what conditions governments should exert extraterritorial jurisdiction over hESCR. One case study that we debated involved an Italian scientist traveling to England to pursue collaborative work in which nuclear transfer will be used to develop patient-specific hESC lines. This is legal in England but illegal in Italy. Because Italian law does not address conduct of its scientists outside its borders, it appears that the Italian investigator would not be violating her country's laws. A second case study involved a German scientist planning travel to the United States to collaborate with a California colleague on research involving derivation of hESC lines from supernumerary in vitro fertilization (IVF) embryos. This is legal in California but illegal in Germany. In contrast to Italy, Germany appears to claim extraterritorial jurisdiction, regulating conduct of German scientists outside Germany.

The Hinxtton Group calls on lawmakers to be circumspect in restricting citizens' conduct extraterritorially with regard to hESCR. We agreed that if scientifically and ethically defensible hESCR is undertaken in a country in which it is legal, scientists should be free to participate without fear of being liable to prosecution, restriction, or discrimination in another jurisdiction. There was not, however, unanimity in the group on how far this point should be extended. For example, the apparent extraterritorial reach of German law is embedded in the German constitution and is not specific to hESC research or scientists, but rather

Although countries with different traditions, laws, and cultures may not agree on standards for stem cell research, a set of principles could clarify terms of collaboration.

applies to the conduct of federal employees, which includes most scientists. Insofar as this is a basic principle of German law, it may be inappropriate, and unrealistic, to expect that science should be treated as an exception.

In countries with laws that restrict elements of hESCR but that do not expressly prohibit citizens' participation in these practices abroad, research institutions should neither discriminate against nor restrict the

freedom of investigators who

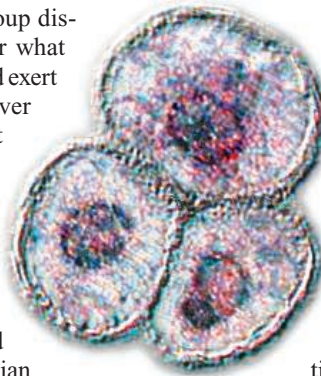
want to travel to do scientifically and ethically defensible research. For example, when the traveling Italian scientist is evaluated for promotion, his home institution should include in its assessment any publications that come from his collaboration in England. By contrast, the home institution of the German scientist, even if she is not prosecuted, may be legally constrained

from including in her review any publications that emerged from her work in California.

In some cases, scientists who are citizens of countries with restrictive laws may wish to collaborate with colleagues in more permissive countries without personally engaging in the activities that are illegal in their home countries. Particularly for such scientists, and also generally, journal editors should encourage authors to include in manuscripts explicit descriptions of their specific roles in the collaboration that led to the published research.

Promoting Integrity

Scientific and ethical integrity are crucial to scientific progress, which depends not only on the replication of results, but also on the public's trust. The Hinxtton Group proposed that scientists should submit stem cell lines they derive to national or international depositories (e.g., the U.K. Stem Cell Bank) that subscribe to internationally accepted standards of quality and that make cell lines and relevant information (e.g., DNA fingerprinting and microsatellite data) (3) publicly available. Journal editors should require authors



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HINXTON GROUP PRINCIPLES AND A SAMPLING OF NATIONAL POLICIES

| | Hinxton Group | Australia | China | United Kingdom | Germany | Israel |
|----------------------------------------------------|-------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|
| Flexible regulatory structures | Flexibility in hESC policy. | Relevant Acts were reviewed by the Lockhart Committee in 2005 and are awaiting government response. | Not addressed in the relevant policy. | Licensure guidelines are broadly written, allowing flexibility in case-by-case assessment of research proposals. | Not addressed in the relevant policy. | Current law is valid only until 1 March 2009. "Existing regulations... [to be] respected, and when necessary changed." |
| Consultation with scientists and the public | Consultation between lawmakers, scientists, and the public. | Extensive consultation was undertaken by the Lockhart Committee—over 1000 submissions. | Not addressed in the relevant policy. | An annual report from HFEA (focuses on its own activities). | Not addressed in the relevant policy. | Public discussion and an annual report from the advisory committee (issues include medicine, science, biotech, bioethics, and law) |
| Extraterritorial jurisdiction | Circumspection in exerting extraterritorial jurisdiction. | Jurisdiction is limited to Australia. | The Guiding Principle applies to "research activity related to [hESCs] conducted in the territory of the People's Republic of China." | Regulations extend to Northern Ireland and the Channel Islands. | The Embryo Protection Act and the German Penal Code imply that prohibited actions are illegal—and prosecutable—regardless of location of the transgression. | Not addressed in the relevant policy. |
| Human materials donors | Classification and protection as human research subjects. | Protections and procedures required for human subjects research. The Lockhart Committee recommended that the NHMRC develop guidelines for egg donation. | Protections and procedures required for human subjects research. | Implies that prohibited actions are illegal. Protections and procedures required for human subjects research. | Defers to national policies for the countries where stem cell lines were derived. | Informed consent for gamete donors in relation to IVF. (Oocyte donation is accepted only for cases of infertility.) |

Last updated 24 July 2006; for source documents, see (9). HFEA, Human Fertilisation and Embryology Authority; NHMRC, National Health and MRC.

(i) to provide specific information about the source of the cells used in research, (ii) to submit data verifying the authenticity of new hESC lines, and (iii) to explain how they have complied with accepted standards of good cell culture practice.

Journal editors and reviewers have a responsibility to promote ethical, as well as scientific, integrity. Journal editors should require a statement from scientists that their research conforms to local laws and policies and has been approved by all applicable oversight committees. Scientists should also be ready and willing to provide approved protocols, consent forms, and other related information that may bear on the ethics of their research.

The Hinxton Group is creating a public database for the deposition of relevant policies, information provided to potential human subjects and tissue donors, and other documents that bear on the ethics of hESCR. This site will also provide a forum for international conversation among scientists and the broader society. It should be available in the fall of 2006 (4).

Some ethical challenges facing hESCR can be addressed through national regulatory mechanisms and international norms of ethics for conduct of research involving human subjects. Although human materials donors in the context of hESCR may not normally be considered research subjects, for ethical oversight, we believe that they should be treated as

such. Currently, the status of human materials donors and the policies that pertain to their participation as donors in hESCR varies between countries (see table, above).

However, many ethical challenges in hESCR fall outside the traditional human subjects framework. As the science evolves, academies of science and relevant professional organizations, in consultation with the public, should continue to develop guidelines for the ethical conduct of hESC research and clinical trials. Several national and international bodies are currently attempting this (5–8). The process should include concerted efforts to engage people worldwide in honest and realistic conversations about the science and ethics of hESCR. Research institutions should create opportunities for scientists and trainees to learn about the social context and implications of research and to engage in ethical discussion and reflection among themselves and with the public. Funders of hESCR must satisfy themselves that the scientists they fund conduct their research ethically and in accordance with national regulations and international guidance.

Although we should not expect harmonization of international laws with respect to hESCR, we should strive to develop international consensus on ethical and scientific standards and practices. Stem cell scientists should be vigilant in anticipating coming ethical challenges to ensure that the science proceeds in an acceptable fashion.

References and Notes

1. See (www.hinxtongroup.org).
2. B. Hansen, *Med. Law* **23**, 19 (2004).
3. I. Wilmut *et al.*, *Science* **310**, 1903 (2005).
4. Public database (www.hinxtongroup.org) in design stage.
5. U.K.'s Human Fertilisation and Embryology Authority (www.hfea.gov.uk).
6. U.S. National Academy of Sciences (<http://dels.nas.edu/bls/stemcells/>).
7. International hESCR Guidelines Task Force of the International Society for Stem Cell Research (www.isscr.org/scientists/guidelines.cfm).
8. International Stem Cell Forum (www.stemcellforum.org/).
9. Country-specific sources that formed the basis for the table were as follows. **Australia:** Human Cloning Prohibition Act (2002); Research Involving Human Embryos Act (2002); National Health & Medical Research Council's Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research. **China:** Ethical Guiding Principles for Research on Human Embryonic Stem Cells (2003); The Guidelines on Human Assisted Reproductive Technology (July 2003), promulgated by the Ministry of Health. **United Kingdom:** Human Fertilisation and Embryology Act, Schedules 2 and 3 (1990); Human Fertilisation and Embryology (Disclosure of Information) Act (1992); Human Fertilisation and Embryology (Research Purposes) Regulations (2001). **Germany:** StGB (German Penal Code); Embryonenschutzgesetz—ESchG (1990); Stammzellgesetz—StZG (2002). **Israel:** Prohibition of Genetic Intervention (Human Cloning and Genetic Manipulation of Reproductive Cells) Law, 5759-1999 (this law was renewed, and slightly amended, in 2004, with the same sunset clause established for another 5 years); Report of the Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities: The Use of Embryonic Stem Cells for Therapeutic Research (2001); Public Health Regulations (1979).
10. Supported by the Greenwall Foundation; the Wellcome Trust; the British Embassy in Washington, DC; and the Juvenile Diabetes Research Foundation.

Supporting Online Material

www.sciencemag.org/cgi/content/full/313/5789/921/DC1

10.1126/science.1127990