Updating International Ethics Guidelines for Stem Cell Research

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Disclosures

- I serve on the Bioethics Advisory Panel and the Stem Cell Research Oversight Committee for Merck KGaA
- I receive consulting income for these activities

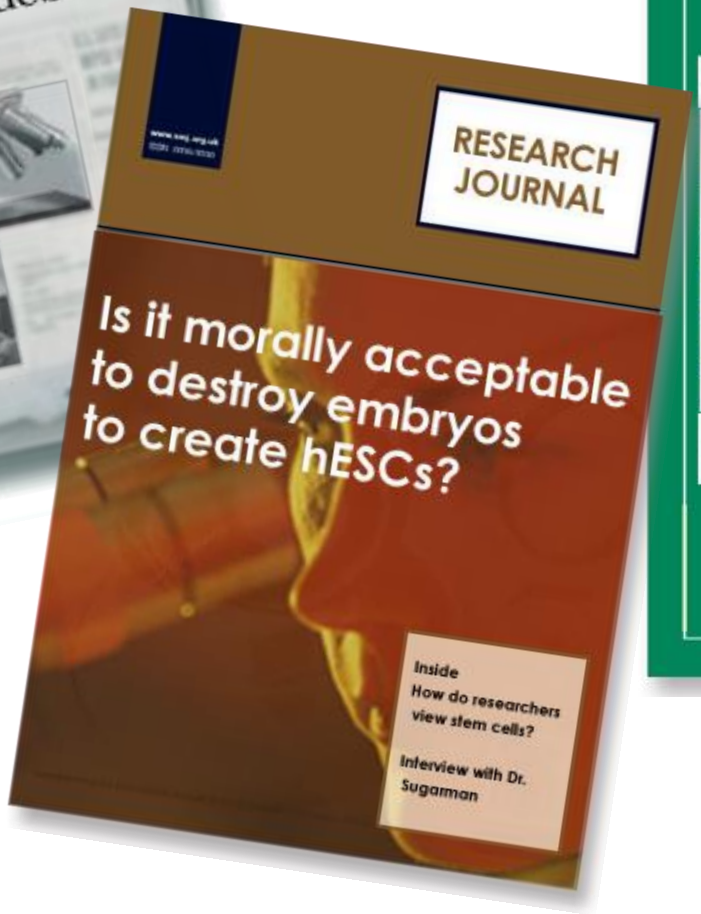
Background Conditions

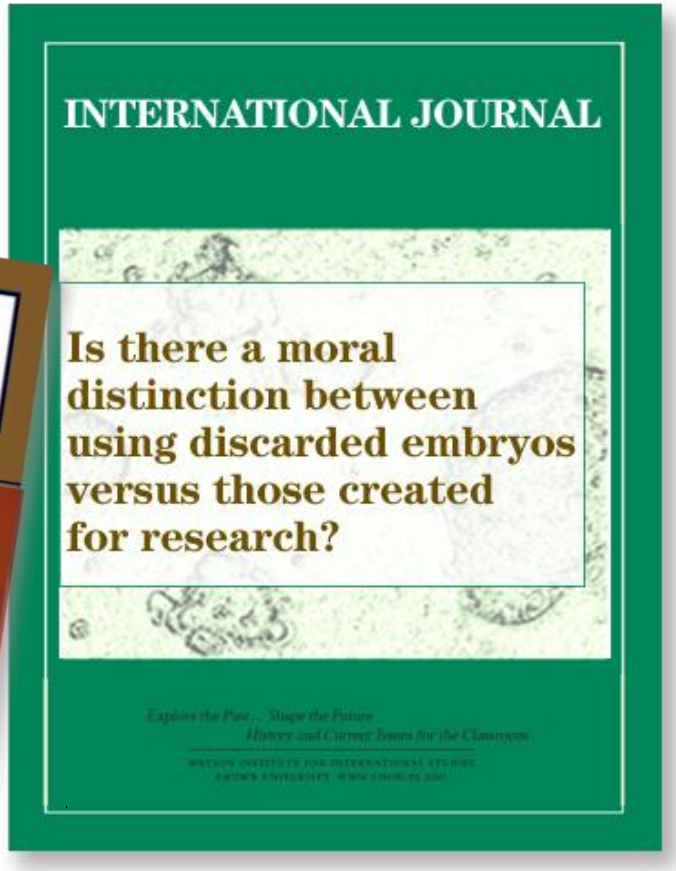
- Scientific excitement is high
- Desire for access to investigational treatments abounds, especially for devastating disorders
- The financial and moral stakes are high

Stem Cell Research: Excitement

Stem Cell Research: Scrutiny


FINAL EDITION
The Times
Moral status of embryo debated


RESEARCH JOURNAL
Is it morally acceptable to destroy embryos to create hESCs?
Inside
How do researchers view stem cells?
Interview with Dr. Sugarman


INTERNATIONAL JOURNAL
Is there a moral distinction between using discarded embryos versus those created for research?

Complexities in Collaboration

Difficulties at maintaining scientific integrity at a distance

Debates about appropriate practices, provenance, consent

Some countries facilitate hESC – others prohibit it

Which rules should be followed when collaborating?

Professional Guidelines

- National Research Council and Institute of Medicine (of the National Academies), 2005
- International Society for Stem Cell Research (ISSCR), 2006

Recommendations for Oversight of hESC Research

- **Local oversight:** Each institution should establish an oversight committee to review and monitor all proposals to conduct hESC research

- ESCRO/SCRO committees should include representatives of the public and persons with expertise in developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical and legal issues in hESC research

SCRO Review

- Ethically and scientifically sound
- Considers compliance with applicable government regulations and institutional policies related to stem cells and research

Guidelines for the Clinical Translation of Stem Cells

- Multidisciplinary task force representing 13 countries convened by the ISSCR
- Released 12/2008
- Available at www.isscr.org

Intent

…that basic stem cell research is responsibly translated into appropriate clinical applications for treating patients.

Scope of the Guidelines

- Cell processing and manufacturing
- Pre-clinical studies
- Clinical research
- Medical innovation
- Social justice

Introduction of hESCs into Humans

- Pre-clinical testing with animal models
- Quality control of hESC lines and their derivatives
- Selection of subjects (e.g., the appropriateness of using healthy volunteers in early human trials)
- Risk of diseases (e.g., from cells cultured in mouse feeder layers)
- Risk of transfer of genetic disorders
- Risks of misdifferentiation, mistargeting, tumor formation, and immune rejection
- Risk of uncontrolled cell growth

Scientific Advances

- Induced pluripotent stem cells
- Mitochondrial replacement therapy
- Gene editing technologies

Evolving Research Ethics Issues

- Immortalized cell lines
- Fetal tissue research
- Chimeras
- Clinical trial registration and reporting
- Expanded use of unproven stem cell-based interventions

Revising the Guidelines

- Multidisciplinary international task force
- Combine separate guidelines into a single document
- Account for scientific progress and emerging bioethics issues
- External review by over 100 individuals with diverse expertise
- Final guidelines scheduled for release in April 2016 (see www.isscr.org)

Highlights

- Review mechanisms
- Standards
- Clinical development

Highlights: Review Mechanisms

- iPSCs reviewed by human research ethics committees (not SCROs)
- SCROs review ethically sensitive research with pluripotent stem cells and embryos
- EMRO (Embryonic Research Oversight) process
  - Embryonic stem cell research
  - Embryo research and clinical translation

Highlights: Standards

- Disallows gene editing in assisted reproduction
- Provision of oocytes
  - Compensation possible
- Human-animal chimeras
  - Welfare of transgenic animals
  - Bans certain research (e.g., breeding nonhuman animals with human gametes)

Highlights: Clinical Development

- Design, reporting, and systematic review of preclinical evidence
- Safety and efficacy in relevant pre-clinical research
- Research design
  - Sham controls
  - Selection of subjects
- Transparency in clinical research
  - Registration
  - Reporting
- Patient funding of research only with independent oversight
- Condemns premature translation

Closing Comments

- Scientific and commercial interests along with the hopes of patients and other stakeholders need to be considered in light of scientific realities and not merely aspirations
- There are a clear set of ethical considerations involved with the derivation of stem cells, in moving to clinical trials, and in their therapeutic use

Thanks!