Ethics and the Clinical Translation of Stem Cell Research

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Disclosures

• I serve on Merck KGaA’s Bioethics Advisory Panel and Stem Cell Research Oversight Committee; Quintiles Ethics Advisory Panel; and have consulted with Novartis on bioethical issues.

• I am on the faculty at Johns Hopkins University and co-chair the Institutional Stem Cell Research Oversight Committee.
Objectives

1. Discuss the range of ethical issues associated with the clinical translation of stem cell research.

2. Explain why ethics oversight of the clinical translation of stem cell research is needed.

3. Describe emerging approaches to ethics oversight of the clinical translation of stem cell research.
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
Moral status of embryo debated

RESEARCH JOURNAL

Is it morally acceptable to destroy embryos to create hESCs?

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
- Some countries facilitate hESC – others prohibit it
- Debates about appropriate practices, provenance, consent
- 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
Selected Conditions Treated

• Cancers
  – ALL, AML, CML
• Bone marrow failure syndromes
  – Aplastic anemia, Fanconi’s
• Hemoglobinopathies
  – Sickle cell, thallassemia
• Inborn errors
  – SCID
HDCT/ABMT or Breast Cancer

• Rapid dissemination of an innovative therapy offering hope
• >30,000 women received it before it was shown to be ineffective
Groundbreaking Trachea Transplant Could Become Routine

Oct. 23, 2013

By KATIE MOISSE via GOOD MORNING AMERICA

Science 19 April 2013:
Vol. 340 no. 6130 pp. 266-268
DOI: 10.1126/science.340.6130.266

NEWS FOCUS

Trachea Transplants Test the Limits
stem cell treatments

Stem Cell Therapy - Stem Cell Treatment Specialists
www.stemgenex.com/Stem-Cell-Treatment
StemGenex® U.S. Stem Cell Leaders!
Over 8 Years Experience - Minimally Invasive & Safe - Free Candidate Evaluation
Novel Approaches to Therapies for Hard to Treat Diseases – PR Newswire
FAQ's - How Does it Work? - Patient Satisfaction Rate - Contact Us

Non-Surgical Alternatives - stemcellarts.com
www.stemcellarts.com
Same Day Stem Cell Procedures for Joint Injuries and Osteoarthritis

Stem Cell Therapy - Advanced Stem Cell Treatments
www.worldstemcellinstitute.org
Contact Us For Help Today!

Scholarly articles for stem cell treatments
... stem cell transplantation and cell therapy as an ... - Slavin - Cited by 2102
Treatment of severe acute graft-versus-host disease ... - Le Blanc - Cited by 2218
... mesenchymal stem cell infusion for treatment of ... - Koc - Cited by 660

Stem Cell Therapy
www.stemcelltherapyplus.com
(302) 483-7786
Stem Cell Therapy Switzerland
For Degenerative Diseases.

Stem Cell Therapy
www.dermamed.com.au
ISSCR Guidelines

- Cell processing and manufacturing
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ISSCR
Stem Cell-Based Medical Innovation
“Clinician-scientists may provide unproven stem cell-based interventions to at most a very small number of patients outside the context of a formal trial, provided….,”
Acceptable Stem Cell-Based Medical Innovation: Provisions

- There is a written plan
- Plan is approved through peer review
- Institution is accountable
- Personnel are qualified
- Voluntary informed consent
- Action plan for adverse events
- Resources for complications
- Commitment to contribute to generalizable knowledge
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 released 12 May 2016
GUIDELINES FOR
STEM CELL SCIENCE AND CLINICAL TRANSLATION

12 MAY, 2016
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!