Ethics and Stem Cell Research

Jeremy Sugarman, MD, MPH, MA
Harvey M. Meyerhoff Professor of Bioethics & Medicine
Department of Medicine
Berman Institute of Bioethics
Johns Hopkins University
Baltimore, Maryland  USA
Embryonic Stem Cell Lines Derived from Human Blastocysts

James A. Thomson,* Joseph Itskovitz-Eldor, Sander S. Shapiro, Michelle A. Waknitz, Jennifer J. Swiergiel, Vivienne S. Marshall, Jeffrey M. Jones
Moral status of embryo debated

Is it morally acceptable to destroy embryos to create hESCs?

Is there a moral distinction between using discarded embryos versus those created for research?
Stem Cell Research: Excitement
Stem Cell Research: Scrutiny
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
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
Clinical Pathways

Translational Research

Innovation

Clinical Care

Inappropriate Use
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
Clinical Pathways

Translational Research

Innovation

Clinical Care

Inappropriate Use

JOHNS HOPKINS
SCHOOL OF MEDICINE
MEDICAL INTELLIGENCE

HEMATOPOIETIC RECONSTITUTION IN A PATIENT WITH FANCONI'S ANEMIA BY MEANS OF UMBILICAL-CORD BLOOD FROM AN HLA-IDENTICAL SIBLING

Eliane Gluckman, M.D.,
Hal E. Broxmeyer, Ph.D.,
Arleen D. Auerbach, Ph.D.,
Henry S. Friedman, M.D.,
Gordon W. Douglas, M.D.,
Agnès Devergie, M.D., Hélène Esperou, M.D.,
Dominique Thierry, Ph.D., Gérard Socie, M.D.,
Pierre Lehn, M.D., Scott Cooper, B.S.,
Denis English, Ph.D., Joanne Kurtzberg, M.D.,
Judith Bard, and Edward A. Boyse, M.D., F.R.S.

THE NEW ENGLAND JOURNAL OF MEDICINE

Oct. 26, 1989
Selected Conditions Treated

- Cancers
  - ALL, AML, CML
- Bone marrow failure syndromes
  - Aplastic anemia, Fanconi’s
- Hemoglobinopathies
  - Sickle cell, thalassemia
- 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
Girl Dies After Groundbreaking Trachea Transplant
July 8, 2013

By KATIE MOISSE via WORLD NEWS
Clinical Translation of Stem Cells

1. Cell Processing and Manufacture
2. Preclinical Studies
3. Clinical Research
4. Stem Cell-based Medical Innovation
5. Clinical Application
Provision of Innovative Care

“Clinician-scientists may provide unproven stem cell-based interventions to at most a very small number of patients outside the context of a formal clinical trial and according to the highly restrictive provisions outlined in this section.”

(ISSCR, 2017, 3.4.1)
Provisions for Innovative Care

• There is a written plan
• Plan is approved through peer review
• Patient not eligible for a trial
• Institution is accountable
• Personnel are qualified
• Voluntary informed consent
• Action plan for adverse events
• Resources for complications
• Commitment to contribute to generalizable knowledge
Clinical Pathways

Translational Research

Innovation

Clinical Care

Inappropriate Use
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 2216
... mesenchymal stem cell infusion for treatment of ... - Koc - Cited by 660

Stem Cell 100 on Amazon
www.amazon.com/
4.4 ★★★★★ rating for amazon.com
Turn Back the Clock on Aging, Look and Feel Younger!

New Stem Cell Treatments
www.stemcellofamerica.com/stem-cell
Cutting Edge Stem Cell Procedures
Painless Procedure, Takes One Hour!

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

Stem Cell Therapy
Table 1. Nature of Therapies Offered across Surveyed Websites

<table>
<thead>
<tr>
<th>Stem Cell Type</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult, autologous</td>
<td>9</td>
<td>47</td>
</tr>
<tr>
<td>Fetal</td>
<td>6</td>
<td>32</td>
</tr>
<tr>
<td>Cord blood</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>Embryonic</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Adult, allogeneic</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Adjuncts</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unspecified</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stem Cell Source</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow</td>
<td>7</td>
<td>37</td>
</tr>
<tr>
<td>Blood or marrow donors</td>
<td>5</td>
<td>26</td>
</tr>
<tr>
<td>Peripheral blood</td>
<td>5</td>
<td>26</td>
</tr>
<tr>
<td>Fetuses</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>Fat</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Unspecified</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transplantation Procedure</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrathecal, into the CSF</td>
<td>6</td>
<td>32</td>
</tr>
<tr>
<td>Intravenous</td>
<td>6</td>
<td>32</td>
</tr>
<tr>
<td>Subcutaneous or intramuscular</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>Surgical transplantation</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>Catheterization of deep body vessels</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>By mouth</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Topical</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>
Table 1 Demographics of patient undergoing stem cell treatment as reported in news media articles from October 2006 to September 2009

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (adult versus minor)</th>
<th>Country of origin (in descending order)</th>
<th>Five most common conditions</th>
<th>Three most common treatment destinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Adult (126; 56.3%)</td>
<td>US (84; 37.5%)</td>
<td>Multiple sclerosis (22; 9.8%)</td>
<td>China (100; 44.6%)</td>
</tr>
<tr>
<td></td>
<td>(134; 59.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>Minors (98; 43.8%)</td>
<td>UK (80; 35.7%)</td>
<td>Cerebral palsy (18; 8.0%)</td>
<td>Germany (17; 7.6%)</td>
</tr>
<tr>
<td></td>
<td>(87; 38.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td>Australia (32; 14.3%)</td>
<td>Septo-optic dysplasia (15; 6.7%)</td>
<td>Mexico (17; 7.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3; 1.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Canada (12; 5.4%)</td>
<td>Optic nerve hypoplasia (13; 5.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>New Zealand (12; 5.4%)</td>
<td>Unspecified blindness (13; 5.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Israel (1; 0.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Brazil (1; 0.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Vision Loss after Intravitreal Injection of Autologous “Stem Cells” for AMD

Autologous Induced Stem-Cell–Derived Retinal Cells for Macular Degeneration

NEJM 2017; 376 (11)
Challenge of Unproven Therapies

- The delivery of unproven stem cell-based interventions has flourished as regulators have struggled to establish new rules for cellular therapies
  - Approximately 100 new clinics open in the US alone each year (Turner/Knoepfler)
  - Patchwork of regulations across the world, allows delivery to change jurisdictions to avoid regulations

- Clinics may mislead patients with exaggerated promises in direct to consumer advertising and using tokens of legitimacy

- Patients may not have all the information they need to make decisions about their care

Patient Handbook on Stem Cell Therapies

www.isscr.org
www.closerlookatstemcells.org
• Nine things to Know about Stem Cell Treatments
• Stem Cell Treatments: What to Ask

http://www.closerlookatstemcells.org/
One Hundred Fifteenth Congress of the United States of America

AT THE SECOND SESSION
Begun and held at the City of Washington on Wednesday, the third day of January, two thousand and eighteen

An Act
To authorize the use of unapproved medical products by patients diagnosed with a terminal illness in accordance with state law, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.
This Act may be cited as the “Trickiott Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017.”

Promoting Patient Interests in Implementing the Federal Right to Try Act

Needed Actions

• Regulators filling gaps in current policies and to enforce them
• Scientists engaging in responsible research
• Clinicians delivering SCBIs that are likely to be helpful
• Professional societies articulating appropriate standards and guidelines

*Stem Cell Reports* 2018; 11: 1021-1025
Additional Approaches

• ISSCR Consent Template
• Properly curated registries
• Sophisticated social media engagement
Closing Comments

• Stem cell research raises ethical issues across the clinical translation cascade

• Innovation and early access to cell-based interventions has resulted in enormous benefits and enormous harms
Thanks!