Ethics and Stem Cell Research

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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

SCIENCE VOL 282 6 NOVEMBER 1998

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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

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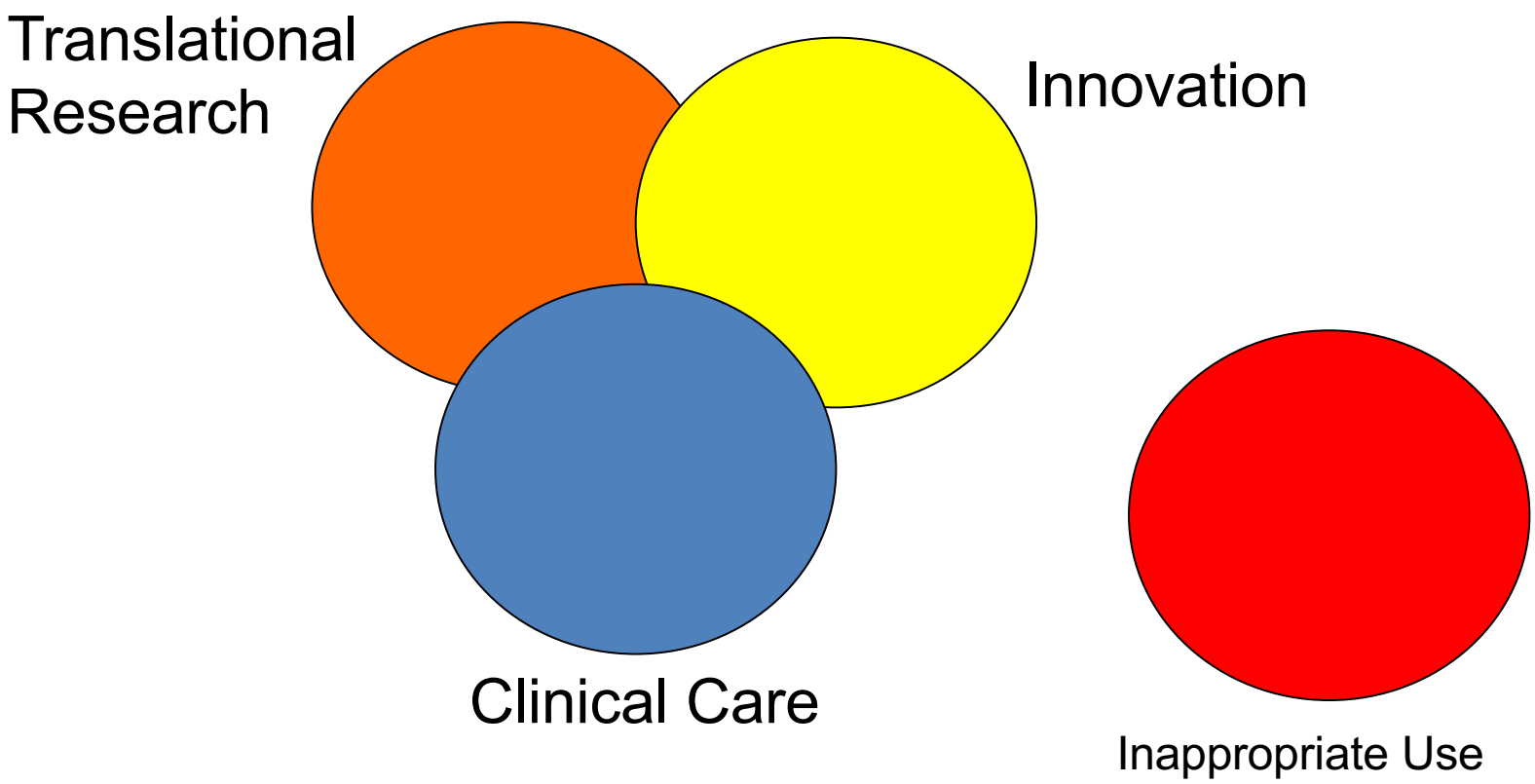
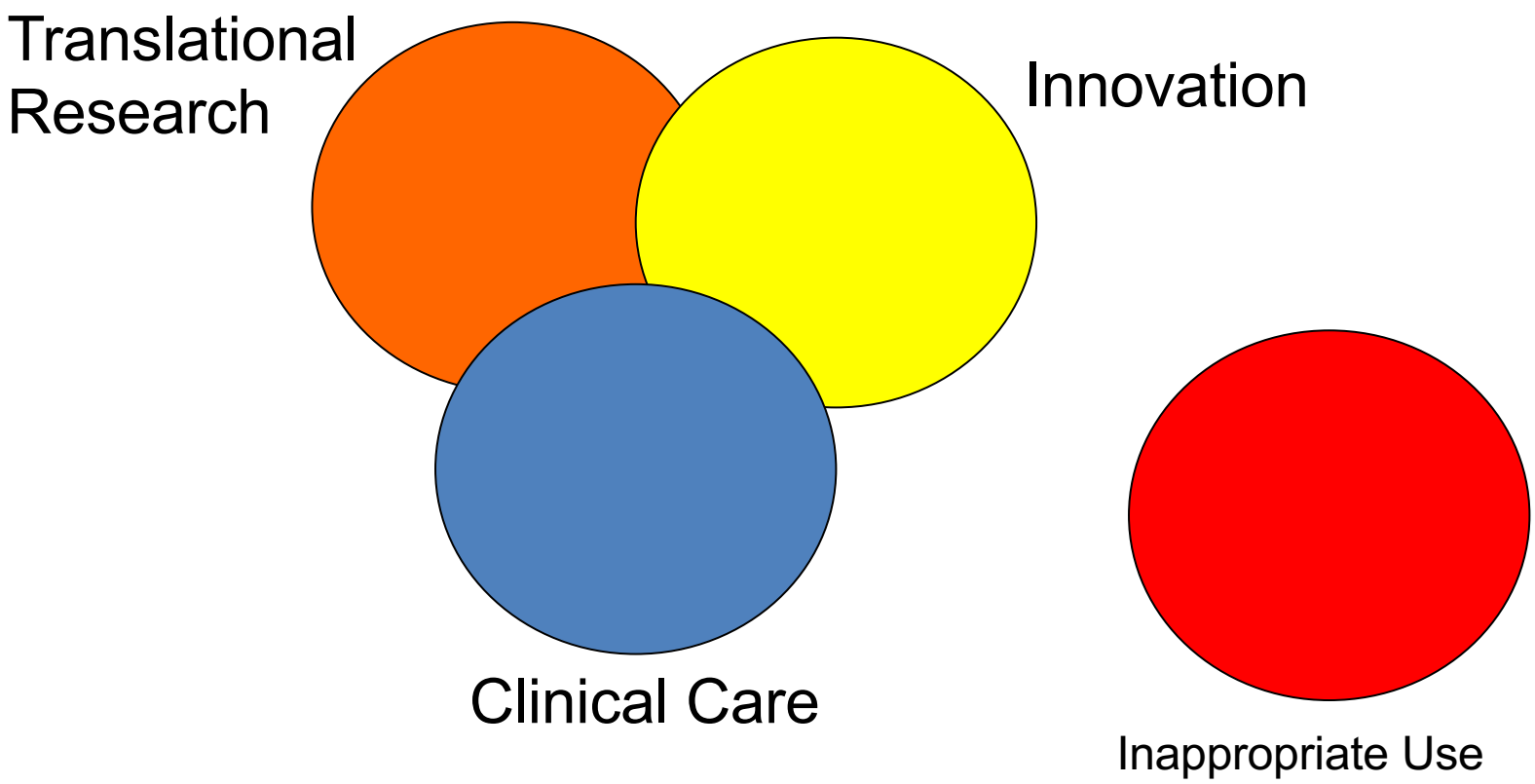
Clinical Pathways



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



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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.

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30 year anniversary

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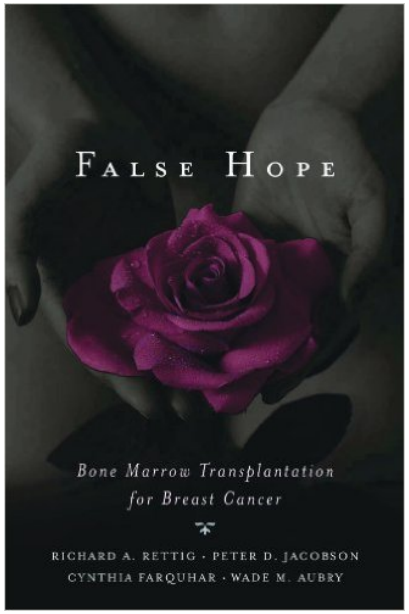
Selected Conditions Treated

- 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



THE LANCET

The Lancet, Early Online Publication, 23 October 2013
doi:10.1016/S0140-6736(13)62033-4

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

Help Hannah Breathe

$50,000 of $50,000

100%

609 donations

0 days left

Fundraiser ended on
August 22nd, 2013

Share on Facebook

Like Sign Up to see what your friends like.

Girl Dies After Groundbreaking Trachea Transplant

July 8, 2013

By KATIE MOISSE via **WORLD NEWS**

share Tweet +1 4 30 Comments

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https://www.vanityfair.com/news/2016/01/celebrity-surgeon-nbc-news-producer-scam

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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

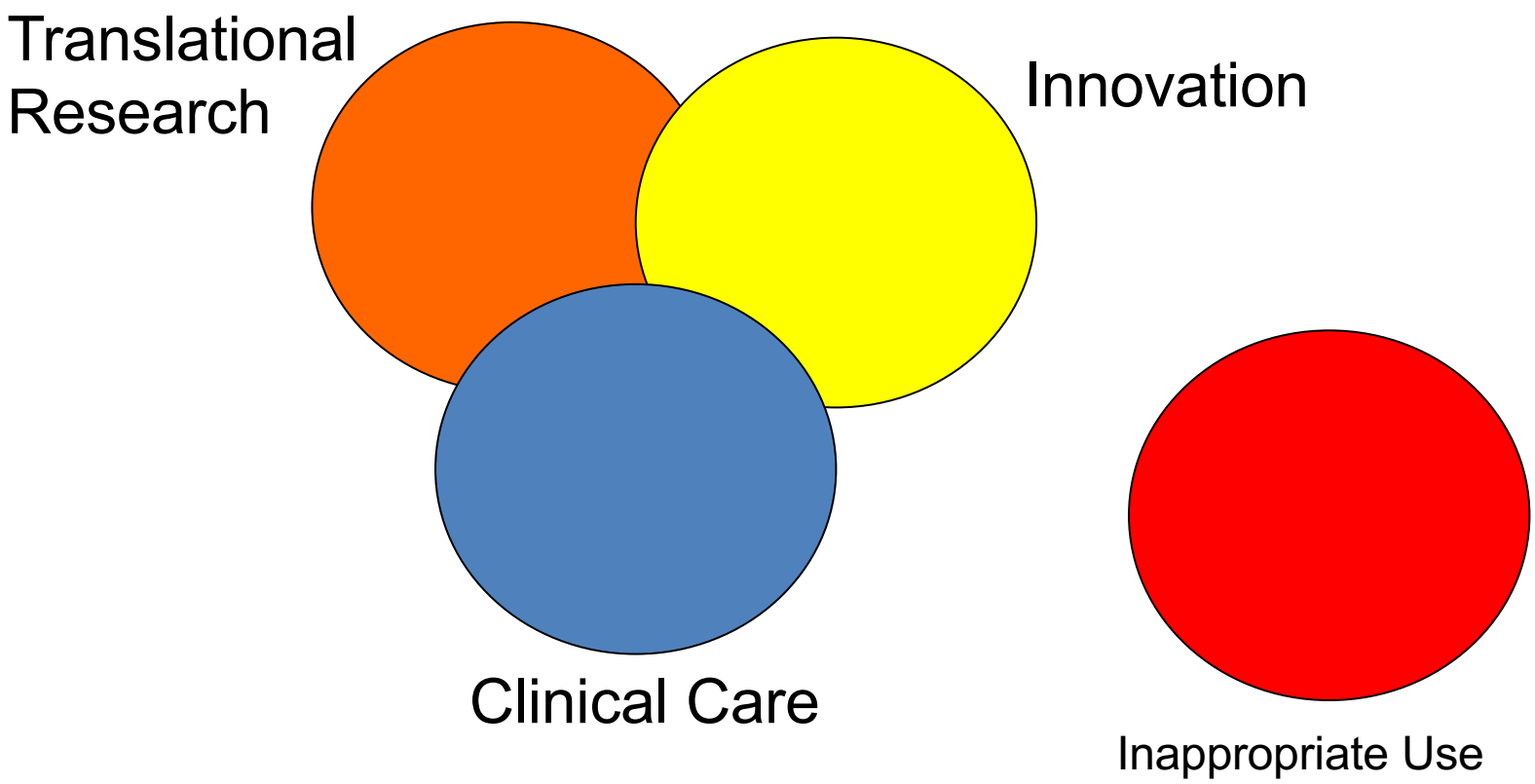
"Clinician-scientists may provide unproven stem cell-based interventions to at most a very small number of patients outside the context of a formal clinical trial and according to the highly restrictive provisions outlined in this section."

(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




STEM CELL THERAPY
CALL NOW
Appointments available
AR

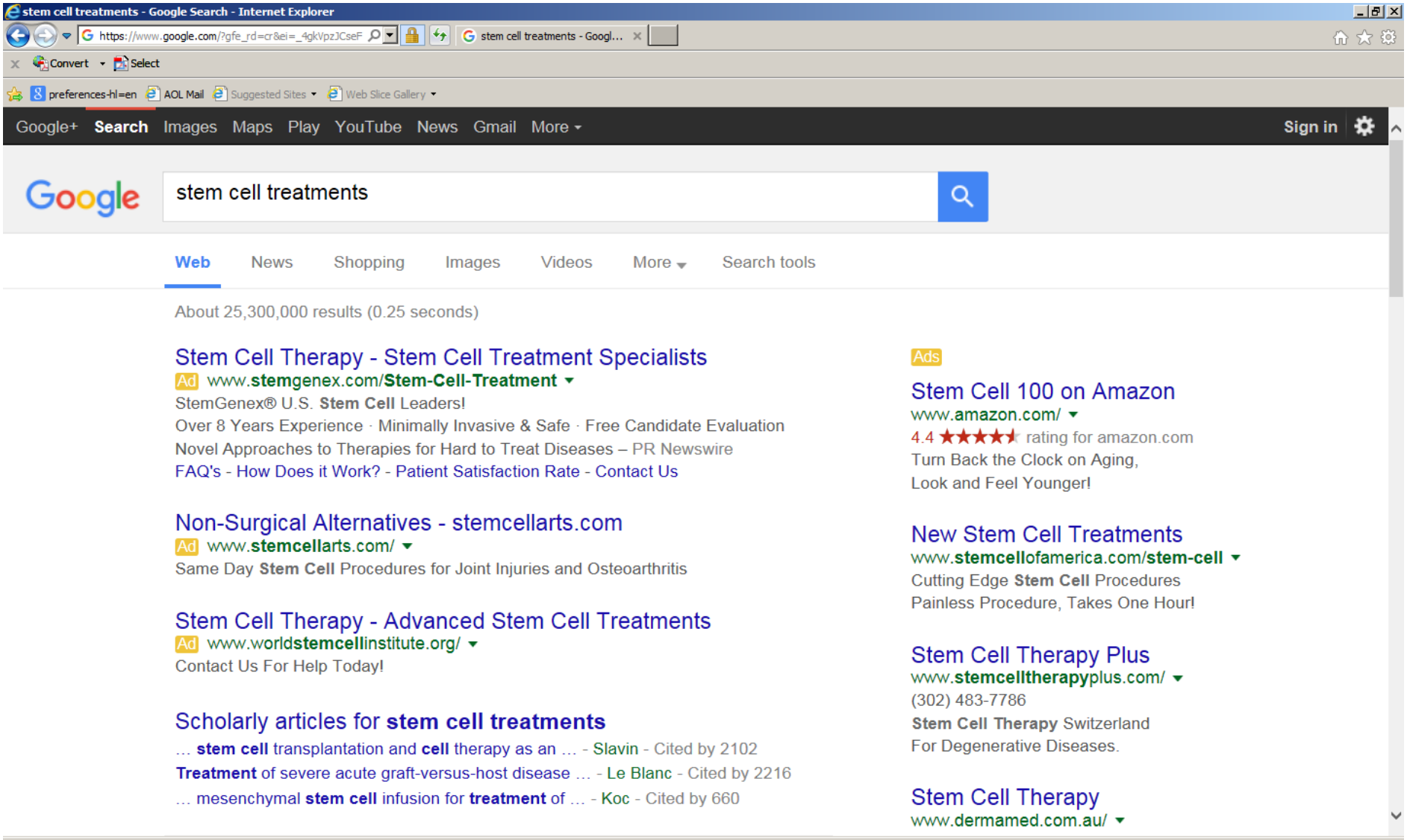


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Table 1. Nature of Therapies Offered across Surveyed Websites

Stem Cell Type	Frequency	%
Adult, autologous	9	47
Fetal	6	32
Cord blood	4	21
Embryonic	2	11
Adult, allogeneic	2	11
Adjuncts	0	0
Unspecified	0	0
Stem Cell Source	**Frequency**	**%**
Bone marrow	7	37
Blood or marrow donors	5	26
Peripheral blood	5	26
Fetuses	4	21
Fat	2	11
Unspecified	2	11
Other	3	16
Transplantation Procedure	**Frequency**	**%**
Intrathecal, into the CSF	6	32
Intravenous	6	32
Subcutaneous or intramuscular	4	21
Surgical transplantation	4	21
Catheterization of deep body vessels	3	16
By mouth	1	5
Topical	1	5

Lau, et al. *Cell Stem Cell*, 2008

Table 1 Demographics of patient undergoing stem cell treatment as reported in news media articles from October 2006 to September 2009

Gender	Age (adult versus minor)	Country of origin (in descending order)	Five most common conditions	Three most common treatment destinations
Male (134; 59.8%)	Adult (126; 56.3%)	US (84; 37.5%)	Multiple sclerosis (22; 9.8%)	China (100; 44.6%)
Female (87; 38.8%)	Minors (98; 43.8%)	UK (80; 35.7%)	Cerebral palsy (18; 8.0%)	Germany (17; 7.6%)
Unspecified (3; 1.3%)		Australia (32; 14.3%)	Septo-optic dysplasia (15; 6.7%)	Mexico (17; 7.6%)
		Canada (12; 5.4%)	Optic nerve hypoplasia (13, 5.8%)	
		New Zealand (12; 5.4%)	Unspecified blindness (13; 5.8%)	
		Israel (1; 0.5%)		
		Brazil (1; 0.5%)		

Zarzeczny, et al. *Nature Biotechnology*, 2010

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The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Vision Loss after Intravitreal Injection of Autologous "Stem Cells" for AMD

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

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

NEJM 2017; 376 (11)

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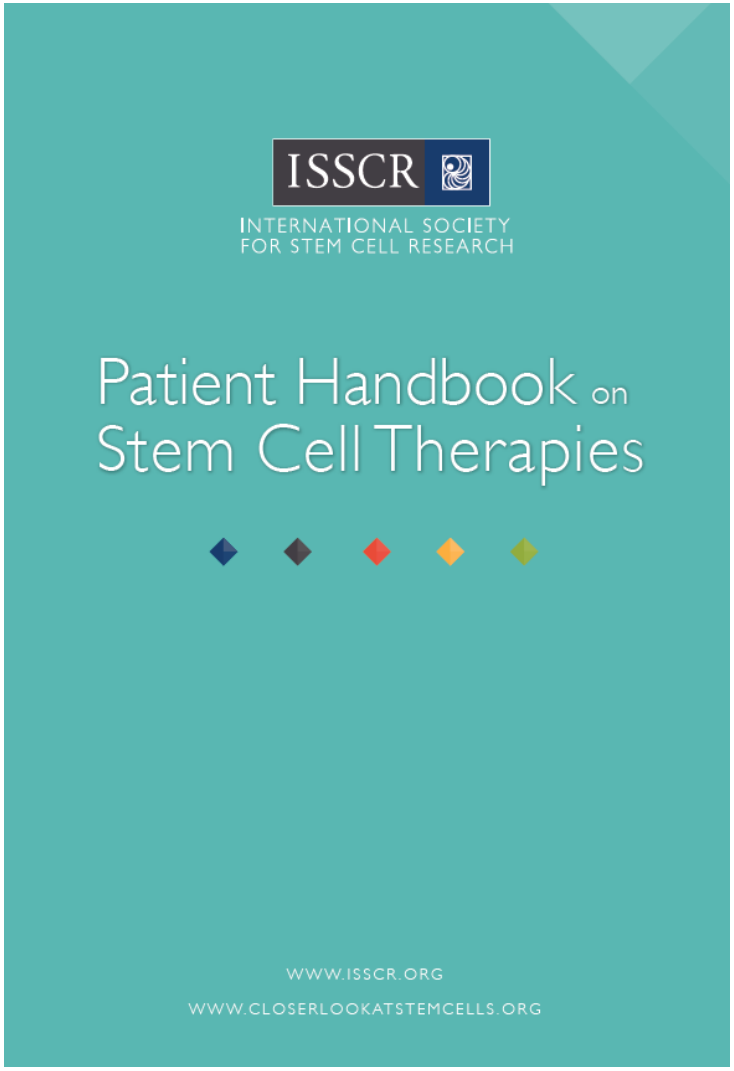
Challenge of Unproven Therapies

- 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

Perspect Biol Med 2018; 61: 1-6.



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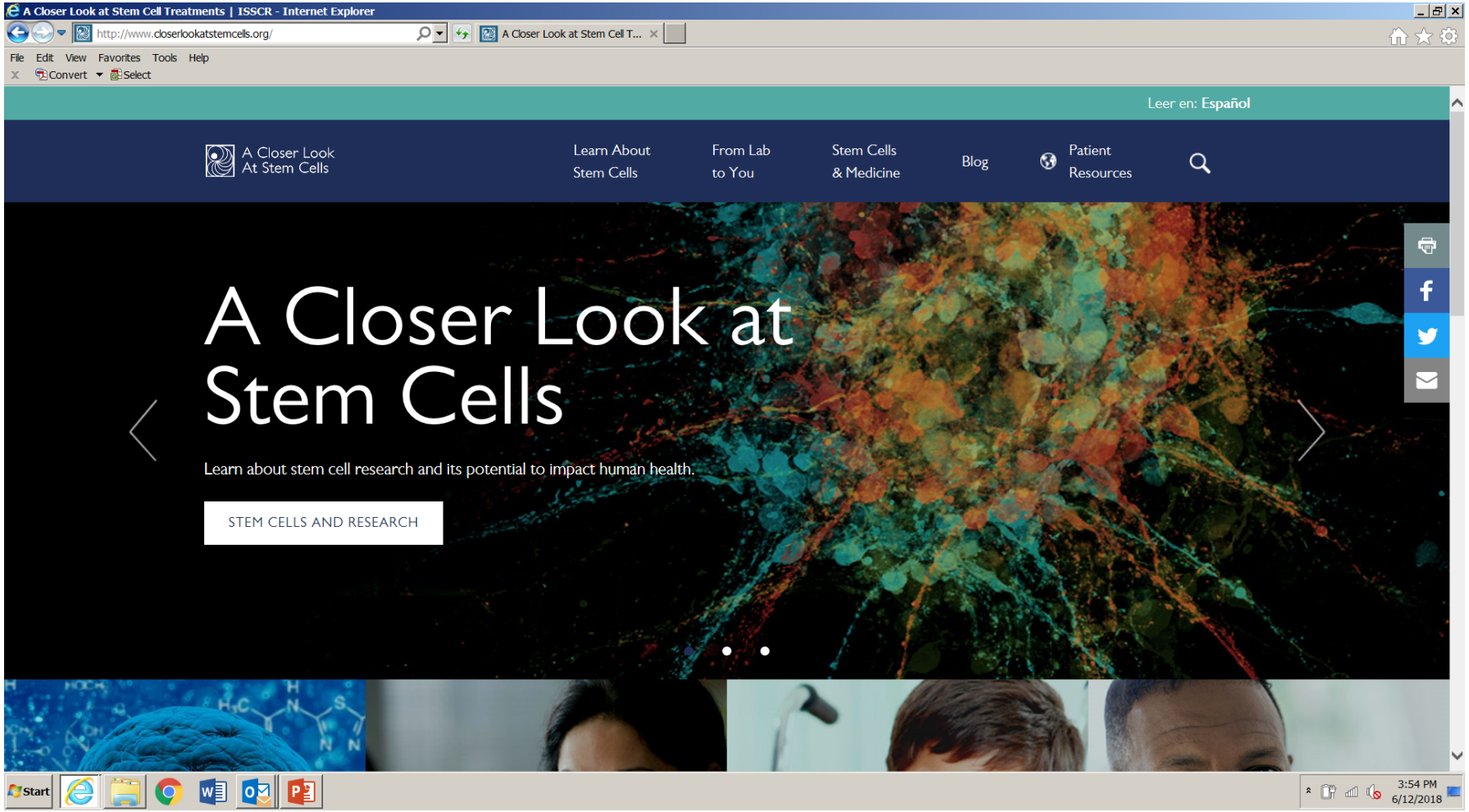

- *Nine things to Know about Stem Cell Treatments*
- *Stem Cell Treatments: What to Ask*

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http://www.closerlookatstemcells.org/

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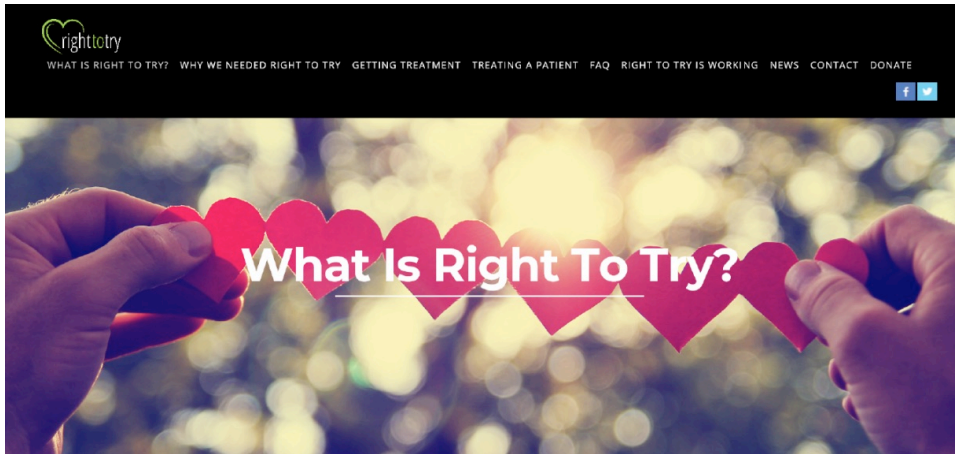

S. 204

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 "Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017".

VIEWPOINT

Promoting Patient Interests in Implementing the Federal Right to Try Act

Lynch HF, Zettler PJ, Sarpatwari A. *JAMA* 2018;320:869-870.

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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!