Stem Cells in Context: 
What’s our global positioning system for policy & research?

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www.sts.wisc.edu
Main elements of GPS
Rhetoric of anti-aging, replaceable parts, natural remedies, endless supply

Tissue Eng early 1990s
SC 1997 ->

Racing Toward Immortality
(Or at Least Your 150th Birthday)

The spectacular — and scary — promise of embryonic-cell research.
By Stephen S. Hall

McEnroe’s Midlife Tantrum · Bad-Girl Art · Mary Tyler Moore’s Imaginary Friend
Mapping the territory:

• Health care environment
• Scientific research environment
• Legal/ regulatory environment
• Business environment
• User environments: patients but also other users
But proposed budget will cut $36 billion in next 5 years  (-2.3% next yr) while military will increase $28.5 billion  (+ 6.9% next yr)
Health Care Spending Continues to Grow

Source: CMS
How the Nation’s Spending its Health Care Dollar

Source: CMS, Office of the Actuary
Personalized medicine or population health?
Clinical judgement or evidence-based?
### U.S. Federal funding for stem cells

<table>
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<tr>
<th>Cell type</th>
<th>2002</th>
<th>2003</th>
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<tr>
<td>Human embryonic cells</td>
<td>$10.7</td>
<td>$24.8</td>
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<tr>
<td>Human nonembryonic cells</td>
<td>170.9</td>
<td>190.7</td>
<td>203.3</td>
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<td>Nonhuman nonembryonic</td>
<td>134.0</td>
<td>192.1</td>
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Sources: Wall Street Journal (August 11, 2004)  
Red Herring June 2005  
NIH

### Venture capital past 5 years

<table>
<thead>
<tr>
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<th>US</th>
<th>Israel</th>
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<tbody>
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<td></td>
<td>$441 mm</td>
<td>10mm</td>
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Additional funding from foundations, donors
U.S. Stem Cell Line Providers
(examples)

- Reproductive Medicine & Genetics (Chicago) (n=50)
- Harvard (n=17)
- UCSF/Geron (n=12 + new non-mouse)
- U Wisconsin (n=5+2 new non-mouse)

Harvard will provide free; others charge fee
• Fed gov’t attempts to ‘plug holes’ with NIH bank and “roadmap” initiative (2004), but that ship has sailed – too little, too late
• In a reversal, private orgs and fdn are supporting corporations: (JDRP & Athersys)

• New organizational forms: physically separate from academic research facilities, often affiliated with transplant centers (NOT a biotech model)
Academic Institutions

- Harvard Institute for Stem Cell Biology
- Stanford Institute for Cancer and Stem Cell Biology ($120 MM)
- *UCSF ($11 MM - ½ UC, ½ donor)
- UCLA ($20MM)
- MIT /BPEC (Boston)
- *McGowan Institute for Regenerative Medicine (U Pittsburgh/Carnegie Mellon)
- *U Minnesota ($50 MM)
- Cambridge (€30 MM)
- *New Jersey Stem Cell Institute/ Rutgers-NJ College of Medicine & Dentistry ($10 MM)
- UW – $750mm, 10 yr (but includes many other initiatives)

*Indicates public-private partnership
Ambivalence at federal and state levels?

- 20 states have pending legislation re therapeutic sc research and/or cloning, however, half also have initiatives in play to allow state funding.
  
  Note: 41 states have declared that biotech will be an investment priority, and each of these intends to be in the “top 5” of the field.

- Increased “culture of life” efforts at all levels of regulatory and science oversight. However, new federal bill to loosen restrictions to funding & access.
Patchwork of institutions & guidelines

- Universities-IRB (teeth)
- Federal government (potential teeth)
- FDA & regulatory bodies (incisors, but no bite yet)
- NIH & other funding sources (incisors)
- National Academies of Science (??)
- President’s Commission on Bioethics (gums, baby teeth)
- Corporate advisory boards (dentures)
- Industry & professional associations
National Academies of Science
Guidelines for Stem Cell Research

- private, nonprofit society of science scholars
- May 2005--23 recommendations (local oversight - procedures for review, responsibilities)
  - do not deal with NT for reproduction
  - not allowed: embryo > 14d; chimeras
  - focus on research protocols, not derivation
- Apply to U.S. researchers only
- ESCRO committees (for universities conducting hES research)
  - each univ will accept, modify, reject guidelines
    --each univ will review protocols (with IRB & FDA)
• Little oversight of IVF clinics
• Varying practices in creating embryos, disposition, consent practices, handling practices, payment to donors
Regulatory context: FDA

• FDA claims right to regulate tissue (1990s)
• Divisions embattled, clashing
  – Gene therapy failures, postmarket drug problems
  – Competition for resources; budget & staff cuts
  – Political appointees
• FDAMA (1997) – downsize government
• Nat’l Tech Transfer and Advancement Act (1995) requires gov’t agencies to use privately developed stds
Regulatory context: Existing culture

- Pro-industry environment, but growing mistrust from public
- Political appointees; sensitivity to “culture of life” issues (ex: NIST)
- Changes in expertise, forms of evidence
• Tiered approach, risk-based (proposed 1997, before hES)

• Some items highly regulated (gene) others not at all (organs, blood)

• Limited authority to address tissue quality and function

• Relies on old, existing structures, forms of expertise, authority
Office of Cellular, Tissue and Gene Therapies (CBER)

• Efforts in counterterrorism
• Repair, Replace, Restore, Regenerate
  – Human Tissues
    • Finalize rules for framework
  – Hematopoetic Stem cell transplantation
    • Reviewing data for possible ‘deemed’ licensing for stem cell facilities
  – Other Stem Cells (Neural, pancreatic, mesenchymal)
    • Guidance for stem cells
    • Outreach to stem cell providers
  – Tumor vaccines
    • International Workshop, April 2003
    • Development of guidance
Regulation: Quality Control

- Cellular, Tissue & Gene Therapies Advisory Committee (formerly Biological Response Modifiers Advisory Committee)
- Focus on donor issues and processing/handling

- Infectious agents
  - Follow existing safety regs for tissue transfer, but must deal with both embryo & gamete donor if hES

- Genetic transfer
  - How much/what kind of genetic screening of donors?
  - Does it matter if a mutation occurs that is unrelated to the condition being treated?

- Good tissue manufacturing practices (GTP)
Quality control issues:

*key questions but no funding to answer*

Cell passage & expansion

- *unlike autologous transplants or hematopoetic, sc lines can be passaged for many generations*
- Genetic drift
- Need to be karyotyped often
- Definition of “passage” not consistent
Preparing for clinical trials

• What kinds of preclinical data?
  – Animal models? (‘chimera’ issues)
  – New models?

• Against what will trials be compared? i.e. how to test “efficacy” esp in disorders where no comparable therapy exists

• Long term follow up
  – Who will do? Pay for?
Business models

Regenerative medicine can’t be thought of as pharmaceutical or biotech industry!

--novel arrangements with service providers
--different forms of expertise
--different organizational cultures

Funding highly variable

Therapeutic and non-therapeutic markets
• Social considerations of clinicians
  – Is this a “disruptive” technology?
  – Will product design or delivery create new problems to address? (half-way technologies)
  – Can my patients pay for this? Can I recommend in light of cheaper, std-of-care therapies?
  – How will I get paid for this? (less-invasive procedures, followup time & tests)
Intracoronary injection of stem cells

“Pharmacologic potential of embryonic stem cells” Gorba, T and Allsopp, T
Pharmacological Research 47(4) 2003
Preparing for the Future

• Technology assessment, outcomes research analyses that include evaluation of social & ethical implications

New ways of analyzing risk:
Combine scenario analyses, risk models
Include relevant political & social elements
(nano, xeno)
• Cross-training ethicists, policymakers, scientists (Cluster initiative at UW)

• Multidisciplinary perspectives for specific problem-solving (‘Words & Images’ Workshop)

• International: Solutions may not be one-size-fits all—different cultures, clinical needs, politics