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

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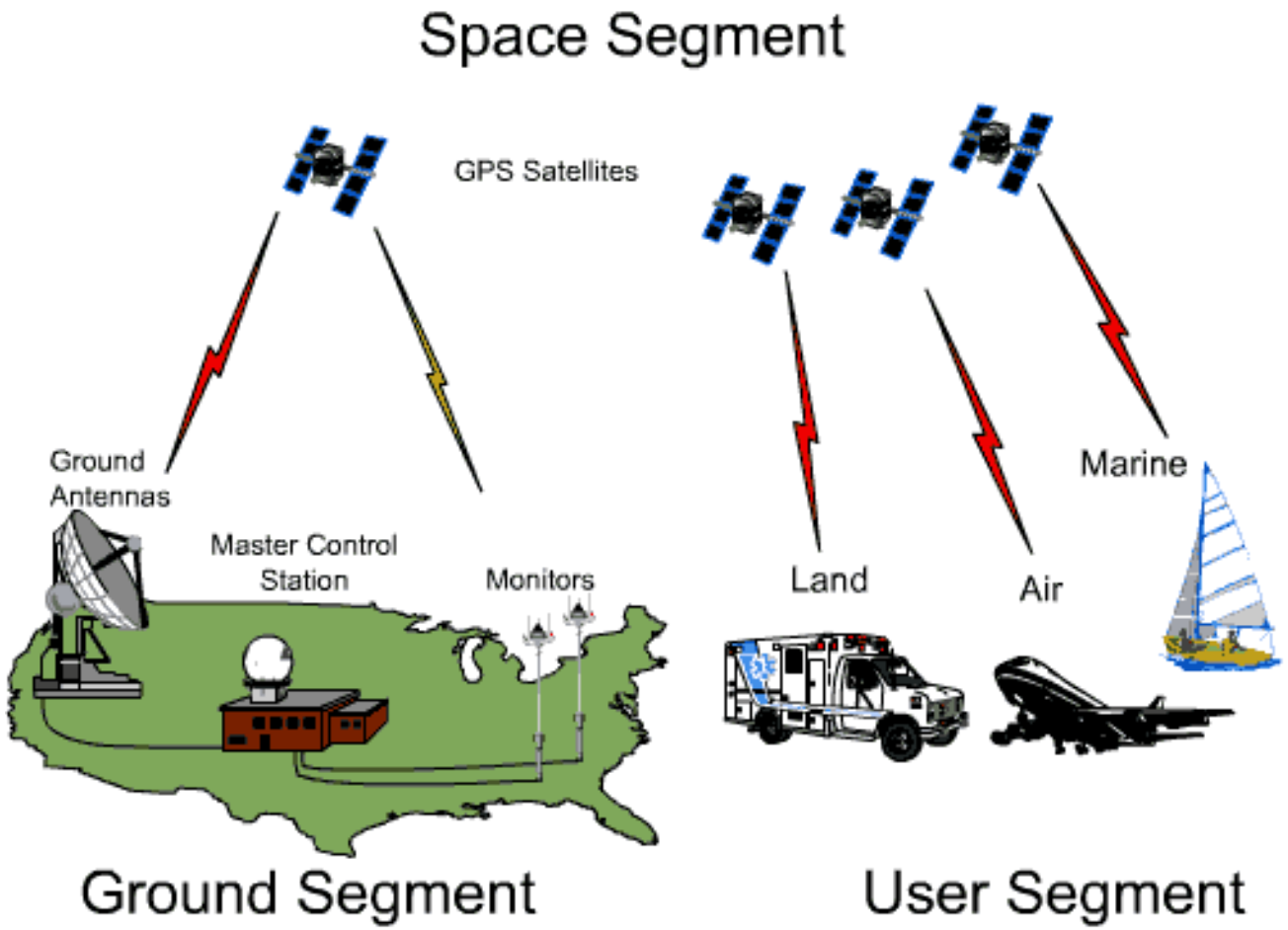
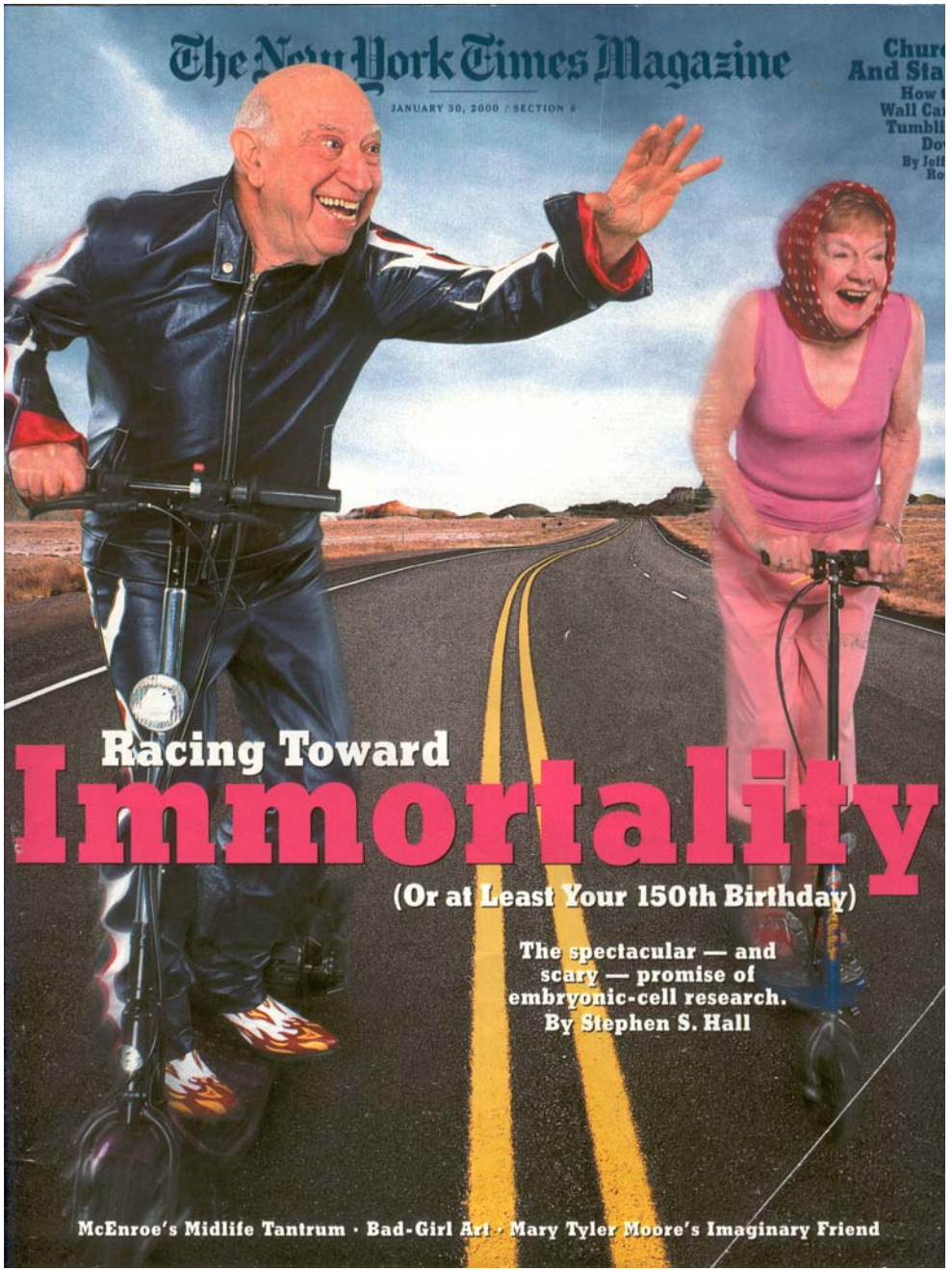
Main elements of GPS



Tissue Eng early 1990s
SC 1997 ->

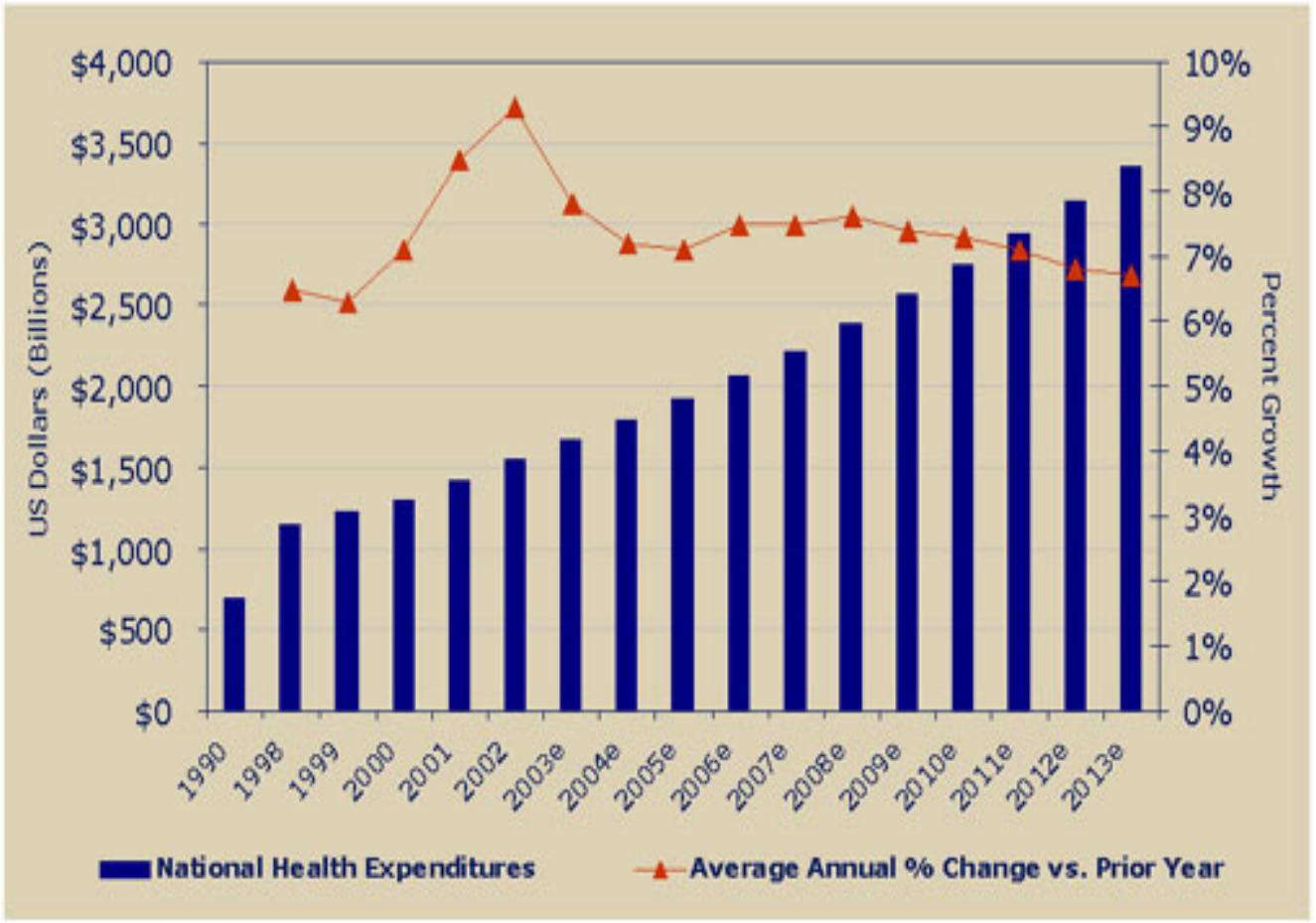
Rhetoric of anti-aging,
replaceable parts,
natural remedies,
endless supply



Mapping the territory:

- Health care environment
- Scientific research environment
- Legal/ regulatory environment
- Business environment
- User environments: patients but also other users

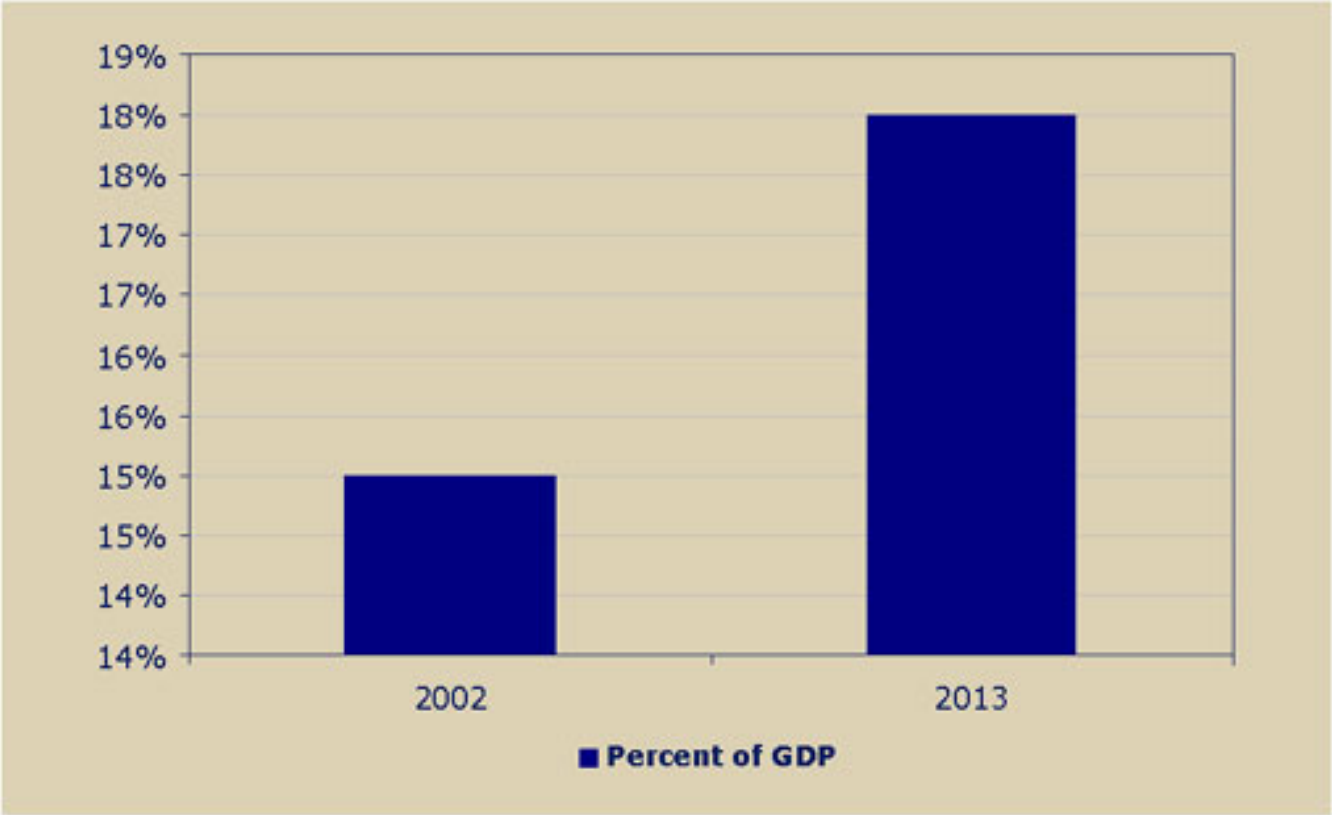
Growth in National Health Care Expenditures



Source: CMS, Office of the Actuary

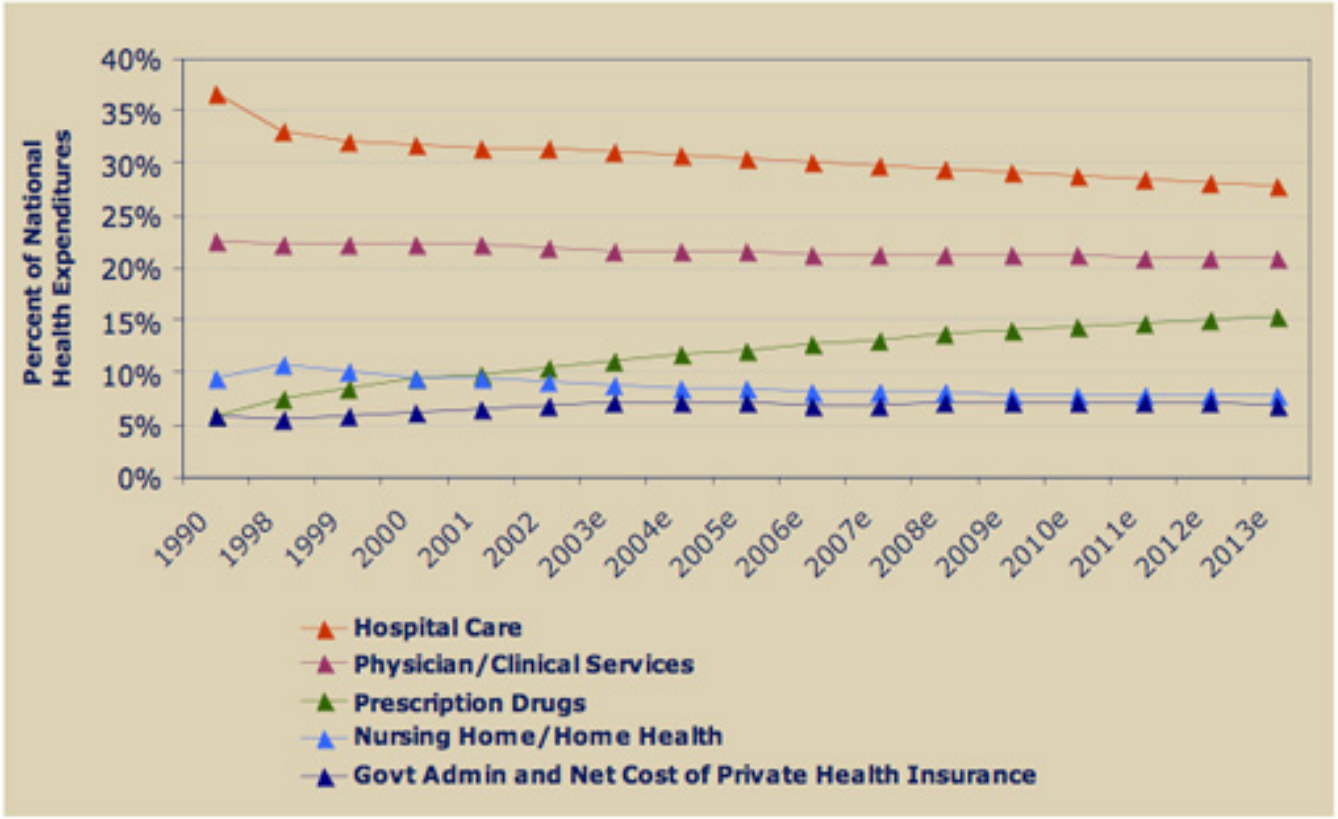
But proposed budget will cut $36 billion in next 5 years (-2.3% next yr)
while military will increase $28.5 billion (+ 6.9% next yr)

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

Cell type	2002	2003	2004
Human embryonic cells	$10.7	$24.8	$24.3
Human nonembryonic cells	170.9	190.7	203.3
Nonhuman nonembryonic	134.0	192.1	n/a

Sources: Wall Street Journal (August 11, 2004)
Red Herring June 2005
NIH

Venture capital past 5 years

US	Israel
$441 mm	10mm

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

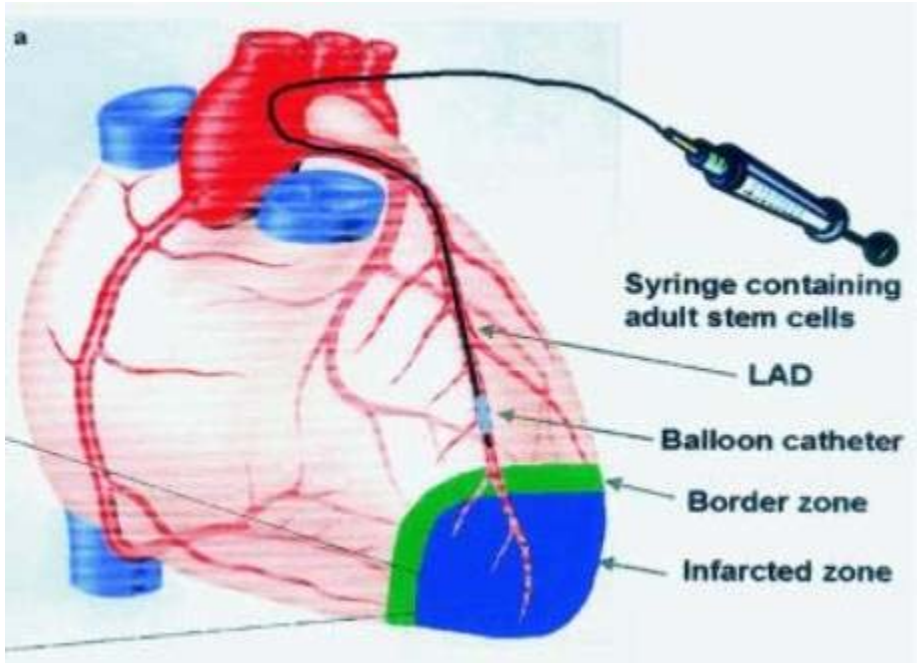
--different organizational cultures

Funding highly variable

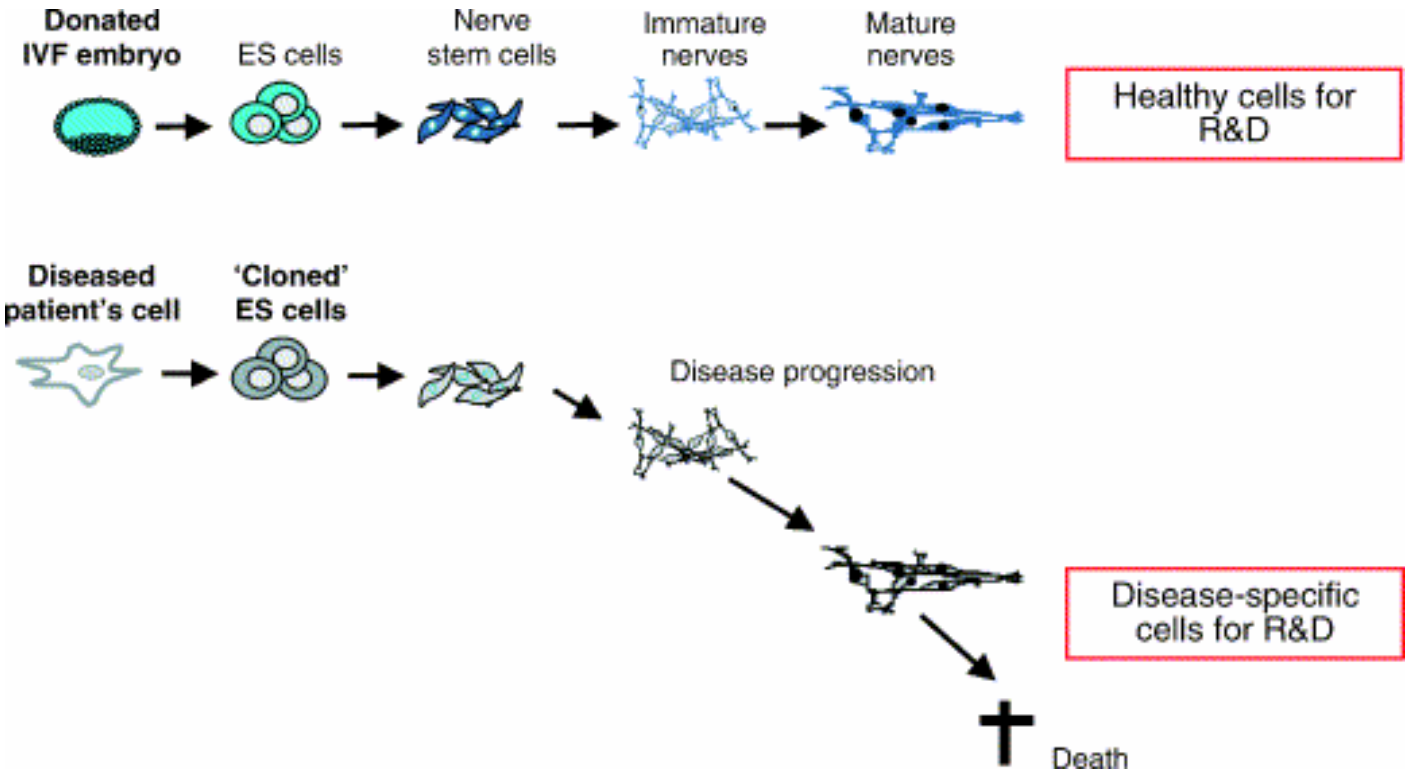
Therapeutic and non-therapeutic markets

- **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



Strauer BE, et al. Repair of Infarcted Myocardium by Autologous Intracoronoary Bone Marrow Cell Transplantation in Humans.C*irculation* 2002;106:1913-1918. American Heart Association.



"Pharmacologic potential of embryonic stem cells" Gorba, T and Allsopp, T *Pharmacological Research* 47(4) 2003

Preparing for the Future:

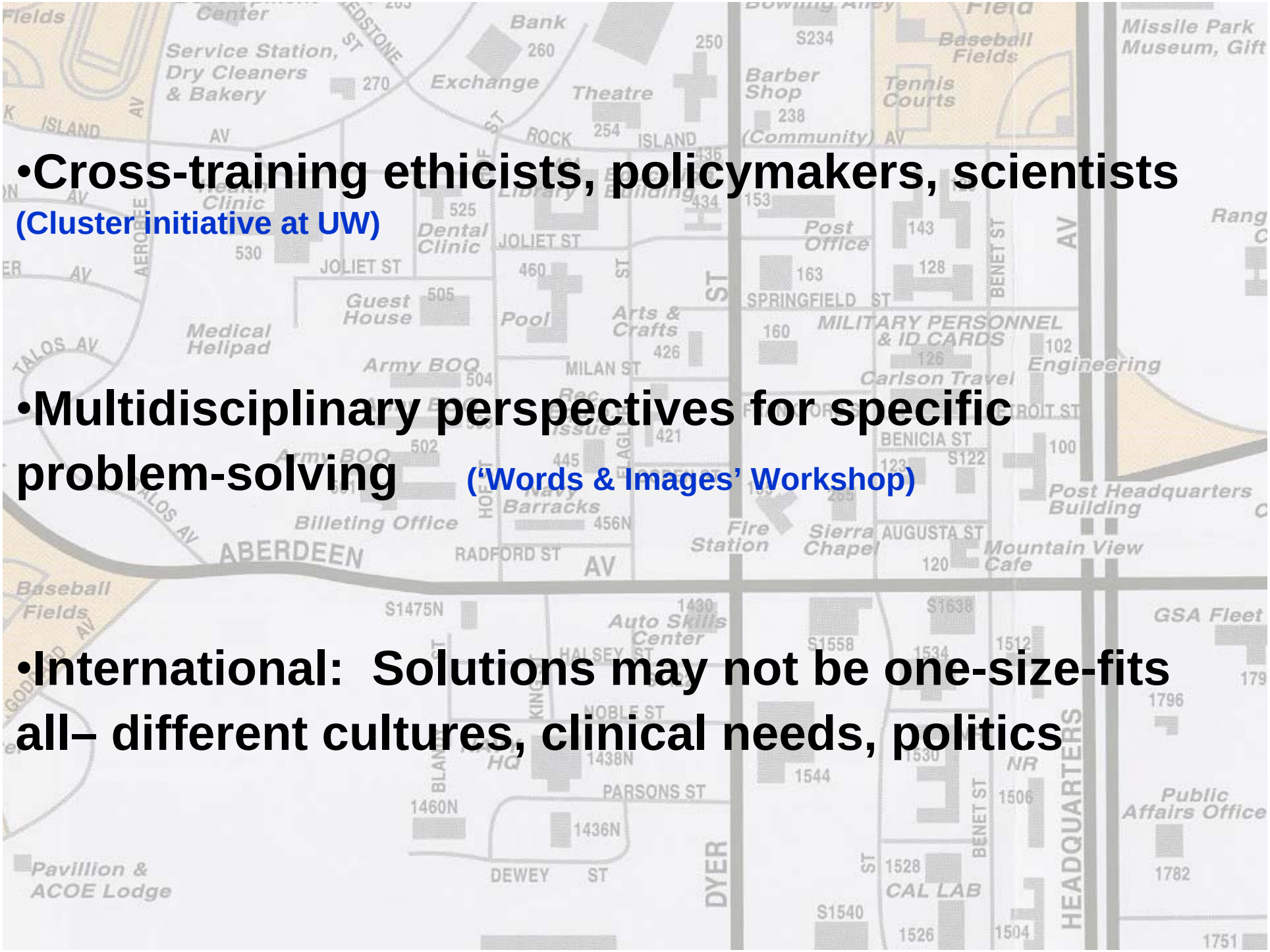
- **Technology assessment, outcomes research analyses that include evaluation of social & ethical implications**

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**