Stem Cells and Regenerative Medicine: Myth vs Reality

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Harvard Stem Cell Institute
Saints Damian and Cosmas replace a leg.

~275 A.D. 

Image courtesy of the Wellcome Trust
A stem cell is either . . .

**Pluripotent** (makes all tissues)

**Adult** (makes specific tissues)

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Embryonic

Induced pluripotent (iPS cells)

reprogramming

Blood

White cells

Red cells

Platelets

Connective

Bone

Muscle

Fat

....Not all tissues regenerate from stem cells
Stem Cells in Research and Therapy

Disease Models

CULTURED iPS CELLS

Drugs

Cell Therapy
Clinical translation of stem cells…

- Stem cell therapy established for blood, skin, cornea

- Stem cells hold promise as new treatments…
  - but ALL such interventions are EXPERIMENTAL

- Successful stem cell therapy will require
  - scientific and clinical advances
  - attention to regulatory, ethical, and societal issues
Popular stem cell types:
Hematopoietic > Neural > Mesenchymal > Embryonic

~1750 open clinical trials

Stem cell types employed in interventional clinical trials
(www.clinicaltrials.gov)
Numbers of Trials Rising Fast

Trends in trials on clinicaltrials.gov:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune</td>
<td>43</td>
</tr>
<tr>
<td>Heart disease</td>
<td>35</td>
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<tr>
<td>Fanconi anemia</td>
<td>21</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>19</td>
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<tr>
<td>MI</td>
<td>16</td>
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<tr>
<td>Thalassemia</td>
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<td>MS</td>
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<td>Sickle cell anemia</td>
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<td>Systemic Lupus Erythematosus</td>
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<tr>
<td>CGD</td>
<td>7</td>
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<tr>
<td>Stroke</td>
<td>4</td>
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<tr>
<td>Amyotrophic lateral sclerosis</td>
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<tr>
<td>Alzheimer's</td>
<td>1</td>
</tr>
<tr>
<td>Parkinson's</td>
<td>1</td>
</tr>
<tr>
<td>Spinal chord injury</td>
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</tr>
</tbody>
</table>

Year

Number of Trials Started

- All SCT
- NOT Leukemia, NOT Lymphoma
Practice of stem cell trials is global
New ISSCR Guidelines Underscore Major Principles for Responsible Translational Stem Cell Research

- Principles to guide clinical trials of stem cell products
- Promote standards, protect patients, advance science
- Prohibitions against marketing of unproven therapies

Guidelines for the Clinical Translation of Stem Cells

December 3, 2008
Why are stem cells different from drugs?

• Stem cells and derivatives represent novel products

• Stem cell self-renewal, differentiation are variable, posing major challenges to manufacture

• Stem cells persist indefinitely, raising bar for safety
Core principles in clinical translation

• Scientific and clinical conduct subject to peer-review

• High standards of voluntary informed consent
  – Note unique risks, and unknown long-term risk

• Conducted with institutional oversight
Standards for preclinical studies

- Proof-of-principle for efficacy should be obtained first in animal models (most often rodents)

- Plausible biological mechanisms

- Rigorous testing for adverse effects and toxicity
Guidelines for clinical studies

• Manufacturing should ensure quality, safety, purity, stability, and potency of cells to be delivered

• Novel interventions should be delivered via clinical trial

• Imperative for follow-up
  – Meticulous patient monitoring
  – Adverse events reporting
  – Publication of results (positive and negative)
Medical innovation (outside clinical trial)
Medical innovation (outside clinical trial)

• Few, seriously ill patients

• Written treatment plan articulating compelling rationale
  – Reviewed by experts

• Rigorous voluntary informed consent
  – Institutional accountability

• Expansion to larger numbers through clinical trials
If you were a patient, how would you go about looking for information on stem cell treatments?
Conditions and diseases

ALS
Alzheimer's Disease
Anemia
Anti-Aging Treatment
Arterial Hypertension
Autism
Cancer
Diabetes Treatment
Eye Diseases
HIV/AIDS
Idiopathic Encephalopathy
Ischemic Heart Disease
Liver Diseases
MD Treatment
Multiple Sclerosis Treatment
Parkinson Treatment
Rheumatoid Arthritis
SMA
Ulcerative Colitis, Crohn's Disease

Stem cell treatments, cell therapy, stem cells

Welcome to Cell Therapy Center EmCell!

Testimonial for stem cell treatment at EmCell c...

Testimonials for Fetal Stem Cell Treatment

Kiev, Ukraine
Websites magnify benefits
Trivialize risks
(Lau et al, 2008)

Multiple sclerosis treatment with stem cells

Cell Therapy Center EmCell offers stem cell therapy for multiple sclerosis. Multiple sclerosis treatment with fetal stem cells results in the pronounced positive effect in all cases. The most successful results of the therapy are reported in patients with relapsing-remitting multiple sclerosis (successful rate up to 90%) but in other types of multiple sclerosis patients also report improvement of their condition (successful rate up to 59%).
Conclusions

This is the first report of a human brain tumor complicating neural stem cell therapy. The findings here suggest that neural stem/progenitor cells may be involved in gliomagenesis and provide the first example of a donor-derived brain tumor. Further work is urgently needed to assess the safety of these therapies.
Summary

• Stem cells hold promise
• Stem cells are largely unproven
• Interventions may be risky
• Best approach is clinical trial

• For more info…www.closerlookatstemcells.org
Summary

[Website Screenshot]

**A Closer Look at Stem Cell Treatments**

Find out what's possible. Know what to ask.

We have all heard about the extraordinary promise that stem cell research holds for the treatment of human diseases. Clinics all over the world claim to offer stem cell treatments for a wide variety of conditions. But are all of these treatments likely to be safe and effective?

The ISSCR provides information to help you evaluate these claims.

Learn more about what this site can provide.