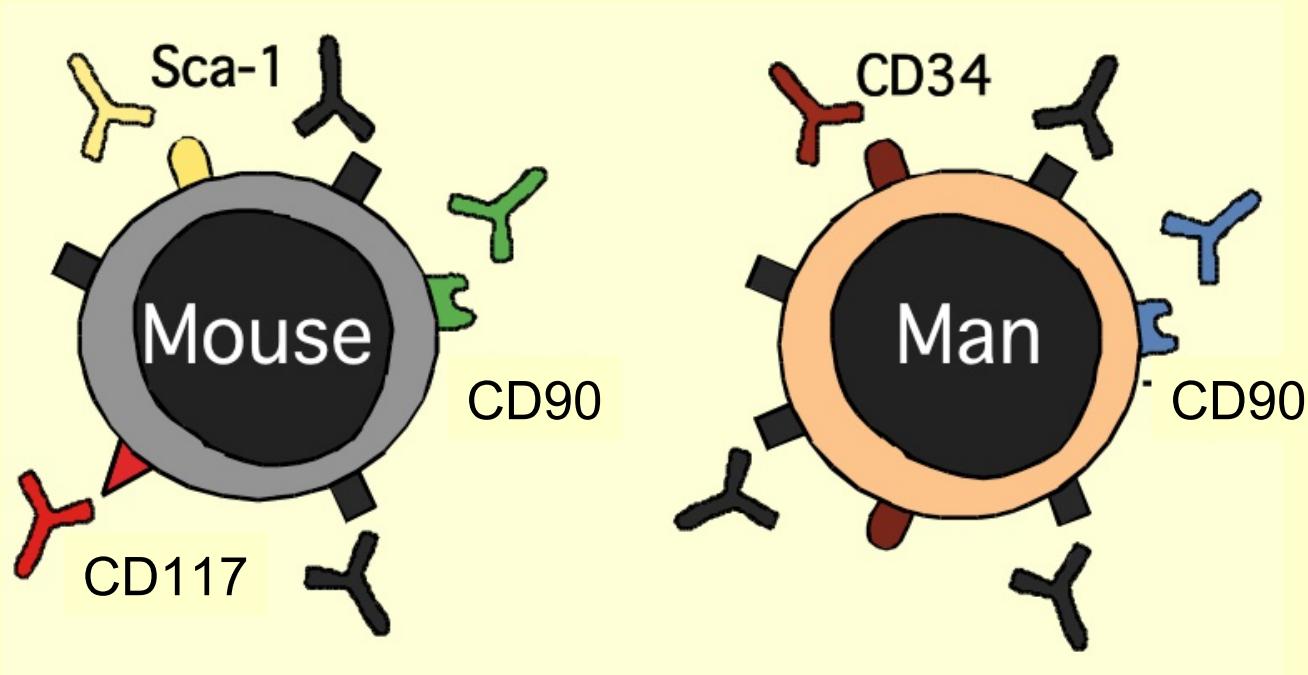
Genomics & Medicine

http://biochem118.stanford.edu/

Stem Cell Therapies

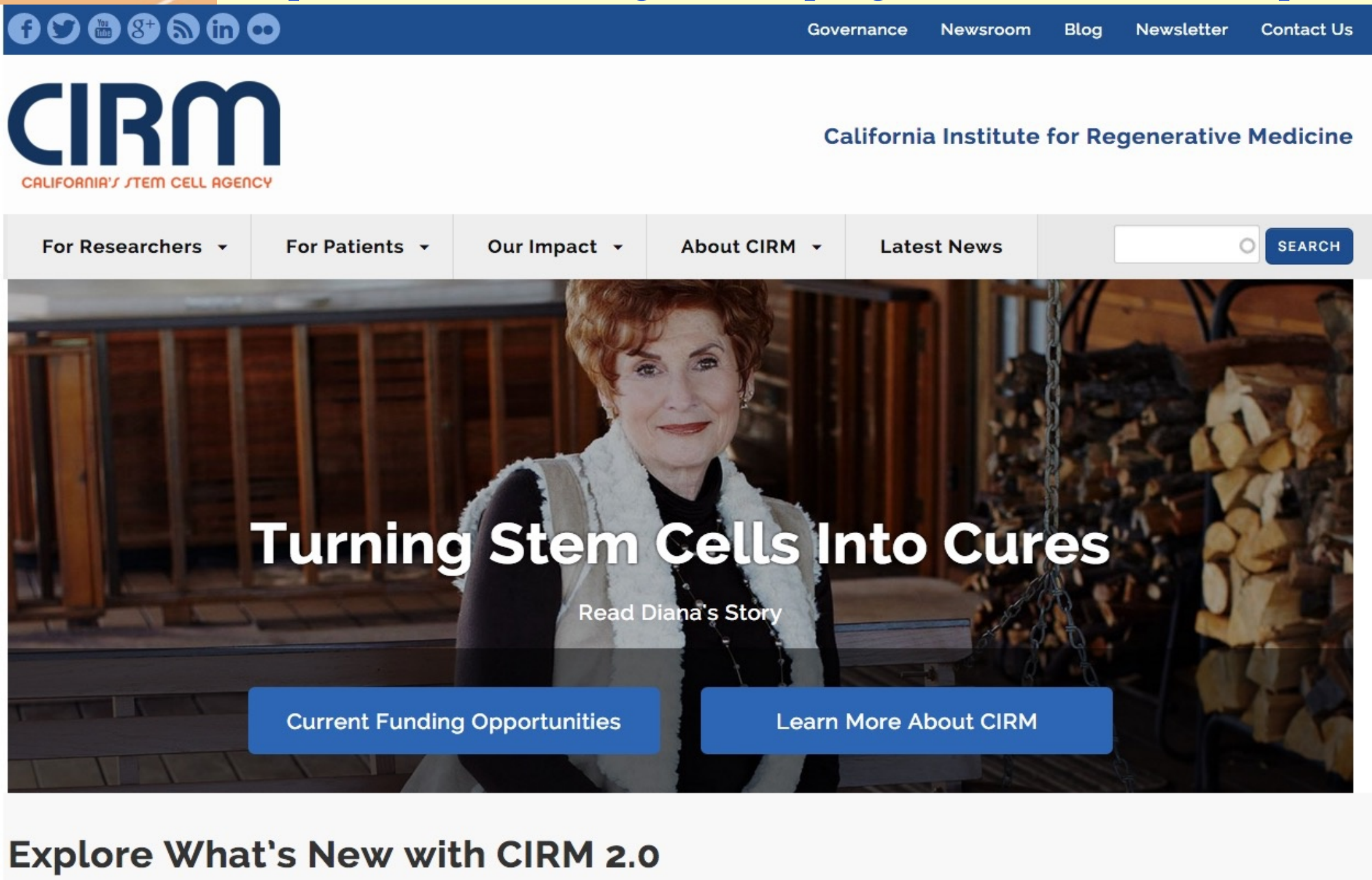
http://biochem118.stanford.edu/13%20Stem%20Cell%20Therapies.html



Doug Brutlag
Professor Emeritus of Biochemistry & Medicine (by courtesy)
Stanford University School of Medicine

California Institute for Regenerative Medicine

http://www.cirm.ca.gov/our-progress/stem-cells-therapies



California Institute for Regenerative Medicine

http://www.cirm.ca.gov/our-progress/stem-cells-therapies

Turning stem cells into therapies

Stem cells have the potential to treat a wide range of diseases, including diabetes, neurodegenerative diseases, spinal cord injury, and heart disease. Learn why these cells are such a powerful tool for treating disease as well as what the current hurdles are before new therapies can become available.

- How can stem cells treat disease?
- What diseases could be treated by stem cell research?
- How can I learn more about CIRM-funded research in a particular disease?
- Are there any stem cell-based therapies currently available?
- When will therapies based on embryonic stem cells become available?
- What about the therapies that are available oversears?
- Why does it take so long to create new therapies?
    - Differentiation
    - Testing the therapy
    - Propensity for the cells to cause tumors
    - Immune rejection of the cells
    - Growing the cells in consistent conditions

How can stem cells treat disease?

The most common way of thinking about stem cells treating disease is through a stem cell transplant. Embryonic stem cells are differentiated into the necessary cell type, then those mature cells replace tissue that is damaged by disease or injury. This type of treatment could be used to replace neurons damaged by spinal cord injury, stroke, Alzheimer's disease, Parkinson's disease, or other neurological problems. Cells grown to produce insulin could treat people with diabetes and heart muscle cells could repair damage after a heart attack. This list could conceivably include any tissue that is injured or diseased.

These are all exciting areas of research, but embryonic stem cell-based therapies go well beyond cell transplants. What researchers learn from studying how embryonic stem cells develop into heart muscle cells, for example, could provide clues about what factors may be able to directly induce the heart muscle to repair itself. The cells could be used to study disease, identify new drugs, or screen drugs for toxic side effects. Any of these would have a significant impact on human health without transplanting a single cell.

What diseases could be treated by stem cell research?

In theory, there's no disease that is exempt from a possible treatment that comes out of stem cell research. Given that researchers may be able to study all cell types via embryonic stem cells, they have the potential to make breakthroughs in any disease.

How can I learn more about CIRM-funded stem cell research in a particular disease?

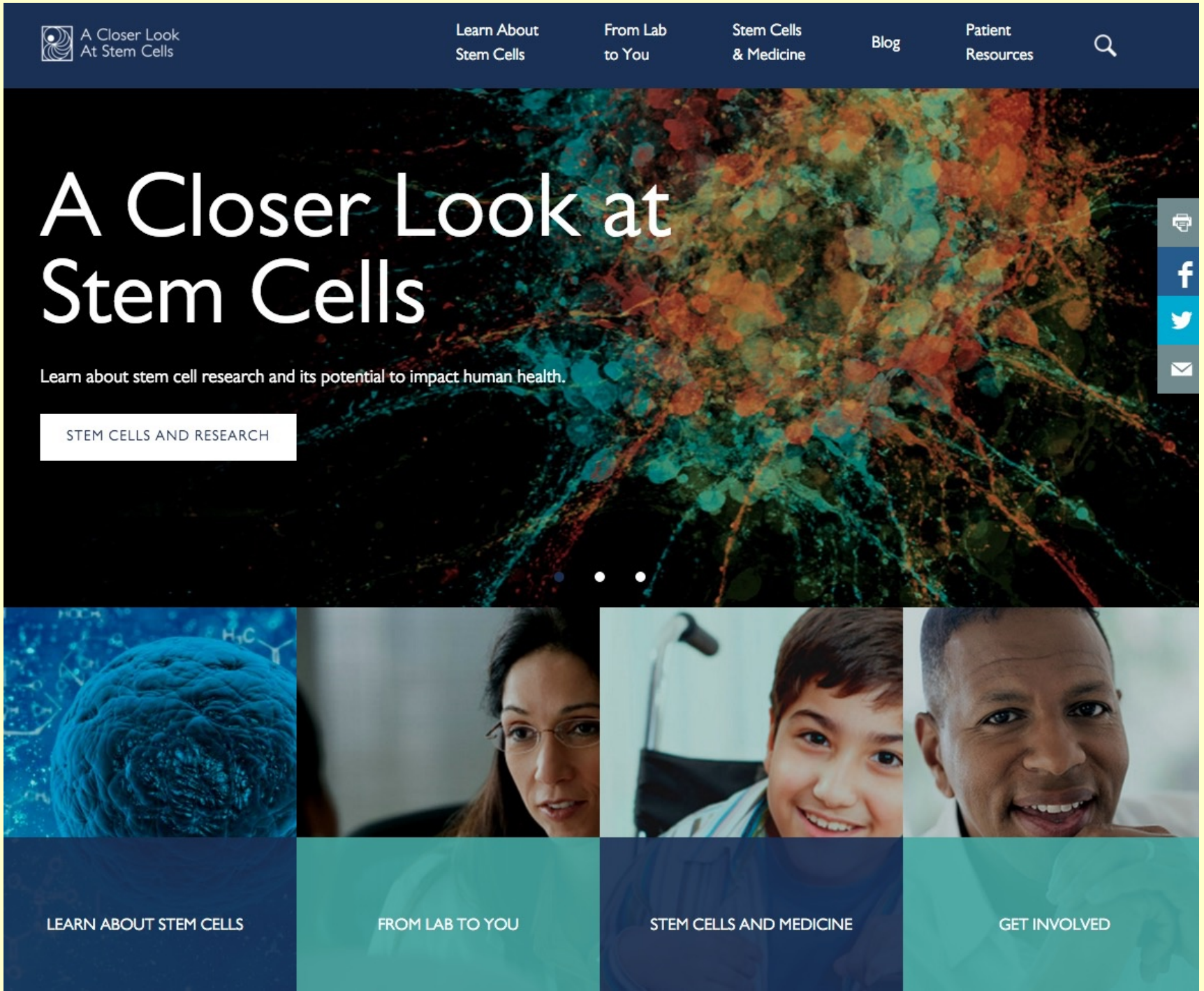
CIRM has created disease pages for many of the major diseases being targeted by stem cell scientists. You can find those disease pages here.

International Society for Stem Cell Research

http://www.isscr.org/

International Society for Stem Cell Research

http://www.closerlookatstemcells.org/



Stem Cell Promise & Stem Cell Therapeutics ClinicalTrials.gov

- Deborah Zarin, Director of Clinical Trials.gov
  - Selective publication, Suspect Analyses and Other Maladies: has ClinicalTrials.gov Helped?
  - http://med.stanford.edu/irt/edtech/video/re/?v=projects/mgr-public/grmed-04-
- Parkinson's Disease (9 clinical trials)
- Spinal Cord Injury (34 clinical trials)
- Bone Marrow and Hematopoietic Stem Cell Transplants (BMT & HSCs) (1435clinical trials)
- Sickle Cell (57 trials) , Thalassemias (44 trials) and other blood diseases with iPSCs and HSCs
- Autoimmune Diseases with Stem Cells (HSCs)
  - Rheumatoid arthritis (15 clinical trials)
  - Systemic Lupus Erythematosus (17 clinical trials)
  - Type 1 diabetes mellitus (28 clinical trials)
  - Multiple sclerosis (47 clinical trials)

Fetal Cell Transplants Can Cure Parkinson's

David Iverson's Frontline film: My Father, My Brother & Me

Removing Viral DNA from iPSCs

Parkinson's Disease Patient-Derived Induced Pluripotent Stem Cells Free of Viral Reprogramming Factors

Frank Soldner,[1,4] Dirk Hockemeyer,[1,4] Caroline Beard,[1] Qing Gao,[1] George W. Bell,[1] Elizabeth G. Cook,[1] Gunnar Hargus,[3] Alexandra Blak,[3] Oliver Cooper,[3] Maisam Mitalipova,[1] Ole Isacson,[3] and Rudolf Jaenisch[1,2,*]
[1]The Whitehead Institute, 9 Cambridge Center, Cambridge, MA 02142, USA
[2]Department of Biology, Massachusetts Institute of Technology, 31 Ames Street, Cambridge, MA 02139, USA
[3]Udall Parkinson Disease Research Center of Excellence, Center for Neuroredegeneration Research, McLean Hospital/Harvard Medical School, Belmont, MA 02478, USA
[4]These authors contributed equally to this work
*Correspondence: jaenisch@wi.mit.edu
DOI 10.1016/j.cell.2009.02.013

Soldner et al. Cell. 2009 Mar 6;136(5):964-77.

iPSC formed Neurons Cures Parkinson's in Rats

PNAS

Neurons derived from reprogrammed fibroblasts functionally integrate into the fetal brain and improve symptoms of rats with Parkinson's disease

Marius Wernig*, Jian-Ping Zhao†, Jan Pruszak‡, Eva Hedlund‡, Dongdong Fu*, Frank Soldner*, Vania Broccoli§, Martha Constantine-Paton†, Ole Isacson‡, and Rudolf Jaenisch*¶‖

*The Whitehead Institute for Biomedical Research, Cambridge, MA 02142; †The McGovern Institute for Brain Research and ¶Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139; ‡Udall Parkinson's Disease Research Center of Excellence and Neuroregeneration Laboratories, McLean Hospital/Harvard University, Belmont, MA 02478; and §San Raffaele Scientific Institute, 20132 Milan, Italy

Soldner et al. Cell. 2009 Mar 6;136(5):964-77.

Direct Conversion of Fibroblasts to Neural Precursor Cells Directly

Direct conversion of mouse fibroblasts to self-renewing, tripotent neural precursor cells

Ernesto Lujan[a,b], Soham Chanda[a,c], Henrik Ahlenius[a,d], Thomas C. Südhof[c,e,1], and Marius Wernig[a,d,1]

[a]Institute for Stem Cell Biology and Regenerative Medicine, Departments of [d]Pathology, [b]Genetics, and [c]Molecular and Cellular Physiology, and [e]Howard Hughes Medical Institute, Stanford University School of Medicine, Stanford, CA 94305

Contributed by Thomas C. Südhof, December 21, 2011 (sent for review August 4, 2011)

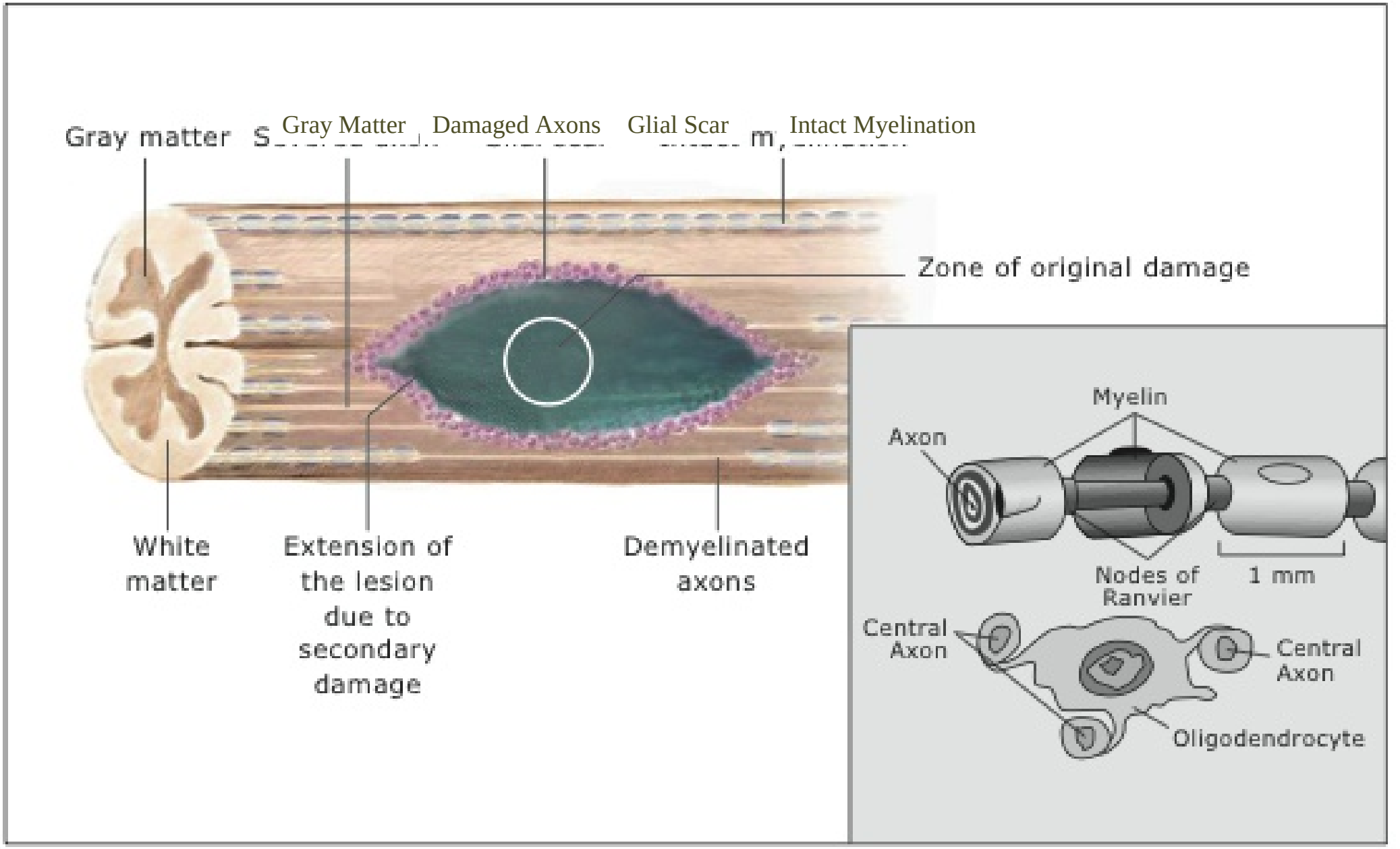
Using three transcription factors, FoxG1, Sox2 and Brn2 they could generate tripotent neural precursor cells directly from f broblasts that would differentiate into neural cells, astrocytes and oligodendrocytes.

Human Embryonic Stem Cell Therapy: Pathway to the Clinic

Stanford University
Stem Cell Policy Symposium:
Understanding the Scientific and Legal Challenges Ahead

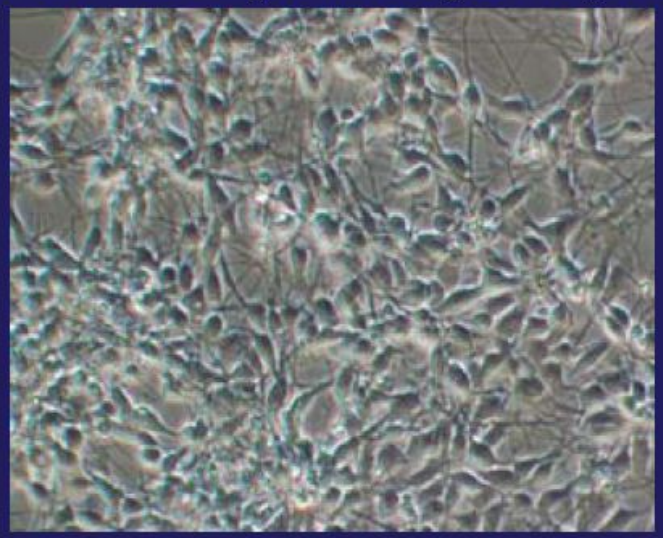
October 2, 2009

Spinal Cord Injury
Pathology at the Lesion



GRNOPC1 Improves Locomotor Behavior after Spinal Cord Injury

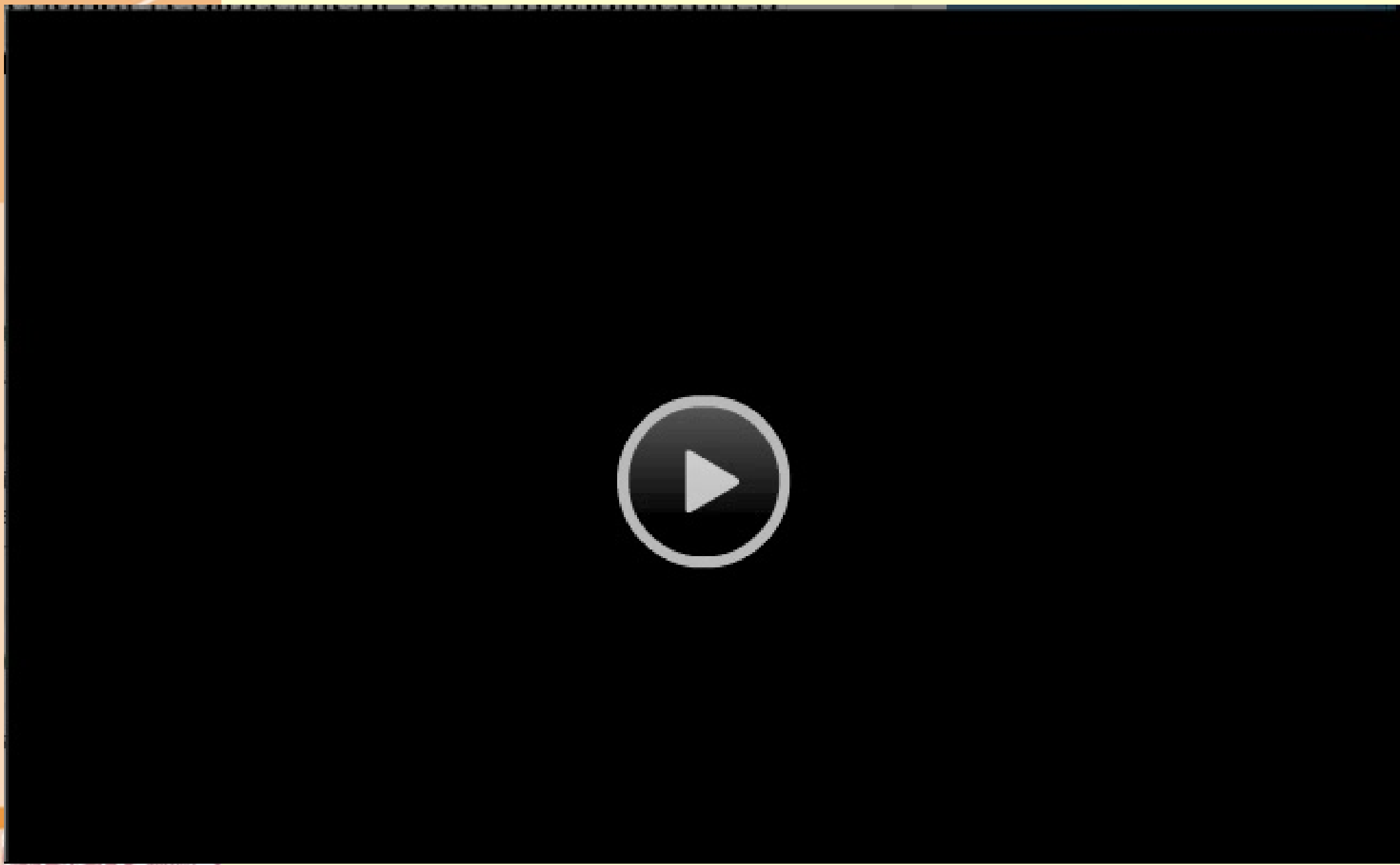
hESC-Derived Oligodendrocyte Progenitors



Control

GRNOPC1

Spinal Cord Injury



Spinal Cord Injury

http://www.geron.com/GRNOPC1Trial/

geron

Phase I Trial of GRNOPC1

A new chapter in medical therapeutics — one that reaches beyond pills to a new level of healing: the restoration of organ function achieved by the injection of healthy, functional replacement cells manufactured from human embryonic stem cells.

Video Illustration of GRNOPC1 in an Animal Model of Spinal Cord Injury

About GRNOPC1

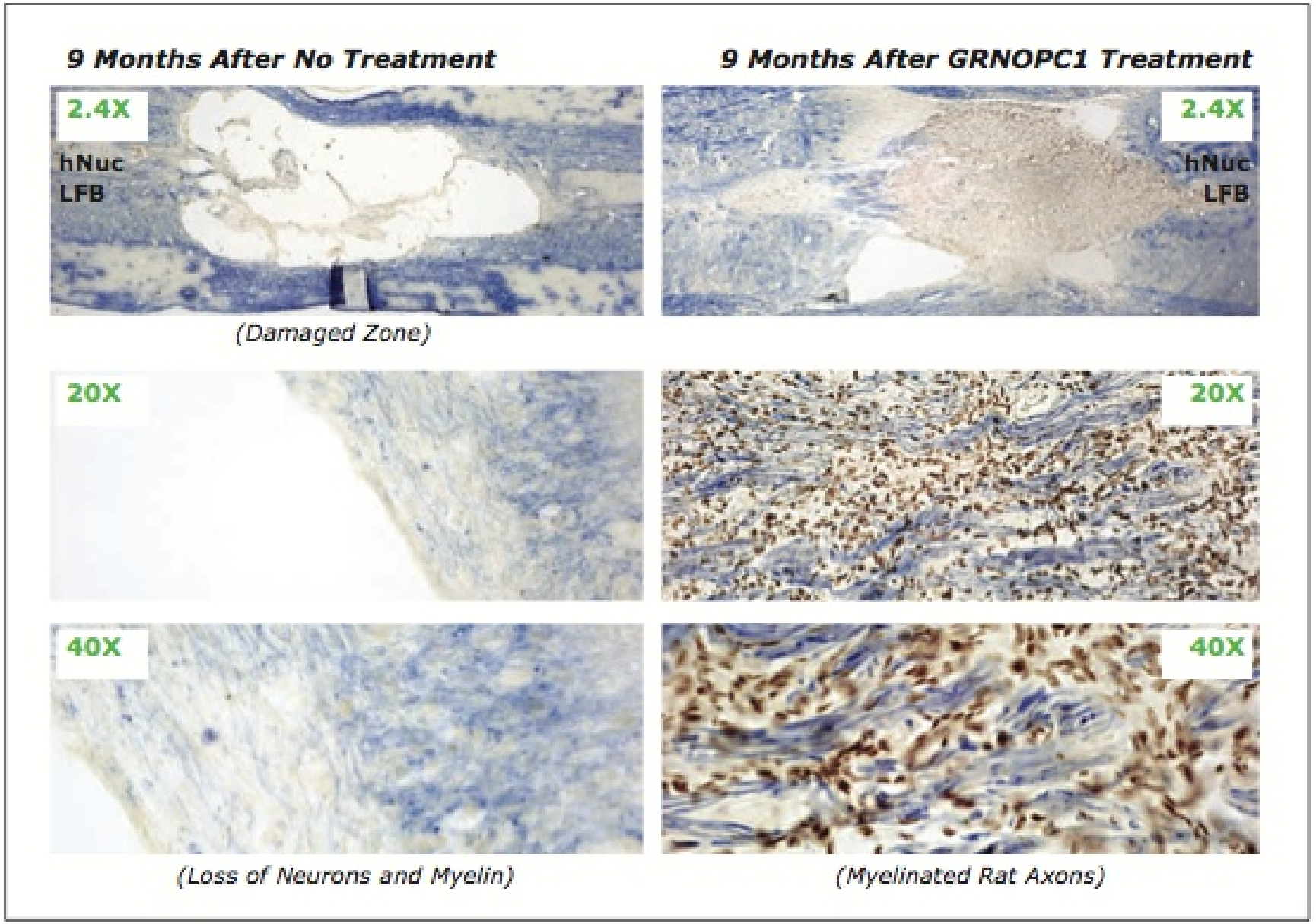
1. Human Embryonic Stem Cells (hESCs)
2. Oligodendrocyte Progenitor Cells (GRNOPC1)
3. Preclinical Safety Studies
4. Clinical Program
5. Manufacturing
6. Intellectual Property

Video of GRNOPC1 Manufacturing

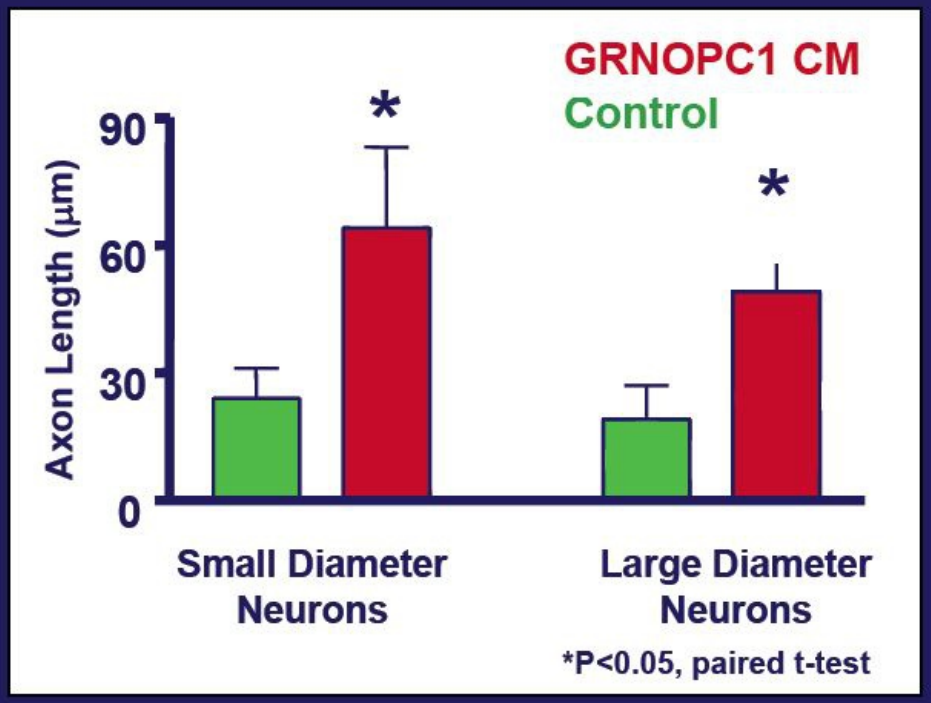
News Release

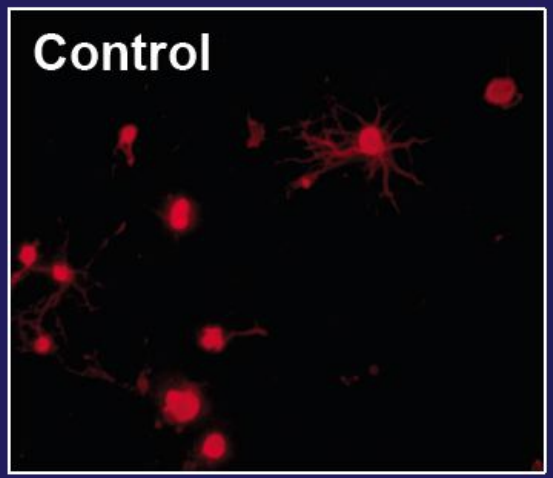
Geron Initiates Clinical Trial of Human Embryonic Stem Cell-Based Therapy

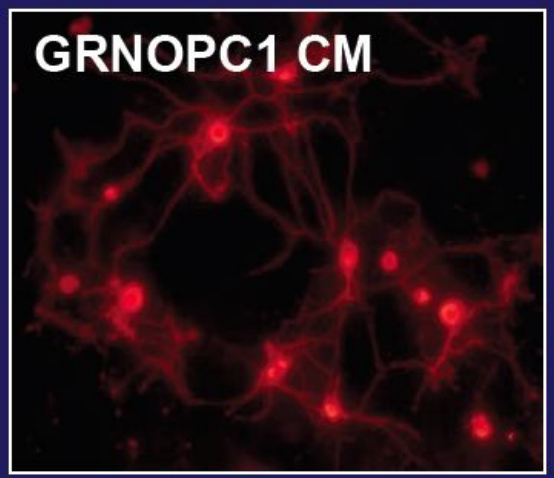
GRNOPC1 Induces Remyelination after Spinal Cord Lesions in Rodents



GRNOPC1 Promotes Neural Outgrowth



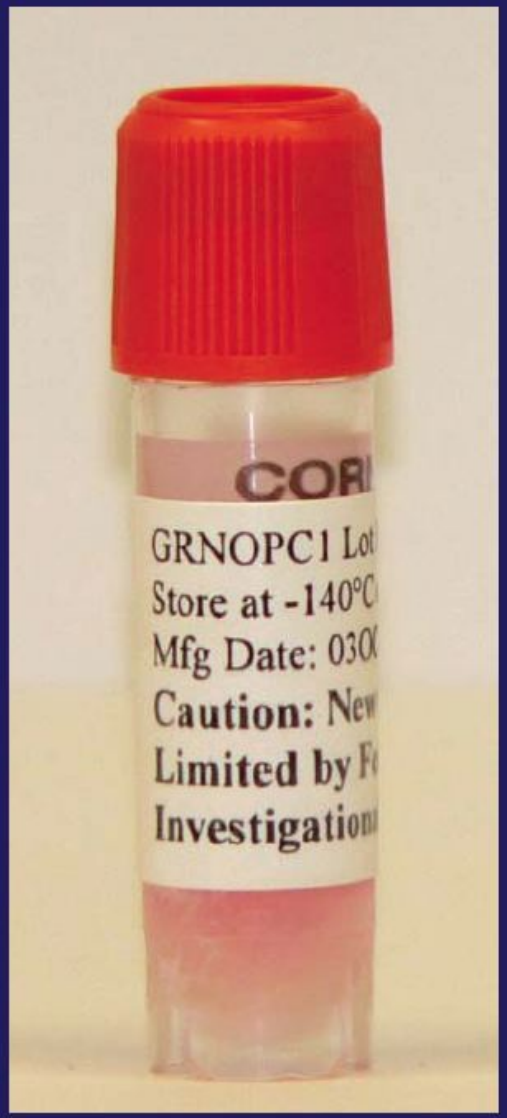




Concentrations of Neurotrophic Proteins in GRNOPC1 Conditioned Medium

Midkine	7.7 ± 2.3 ng/ml	(n = 6)
Activin A	13.2 ± 1.6 ng/ml	(n = 6)
BDNF	48 ± 13 pg/ml	(n = 9)
TGF-β2	95 ± 18 pg/ml	(n = 9)
HGF	1.2 ± 0.5 ng/ml	(n = 5)

Geron Oligodendrocyte Progenitor Cells GRNOPC1



GRNOPC1

- Cryopreserved Allogeneic Cell Population
- Derived from Human Embryonic Stem Cells
- Characterized Composition of Cells
- Contain Oligodendrocyte Progenitor Cells
- Produces Neurotrophic Factors
- Induces Myelination of Denuded Axons

Intended Application

- "Off-the-Shelf" Product
- Spinal Cord Injury
- Other CNS Disorders

Properties of GRNOP1

24 Studies

1977 Rodents

858 Injected with GRNOPC1

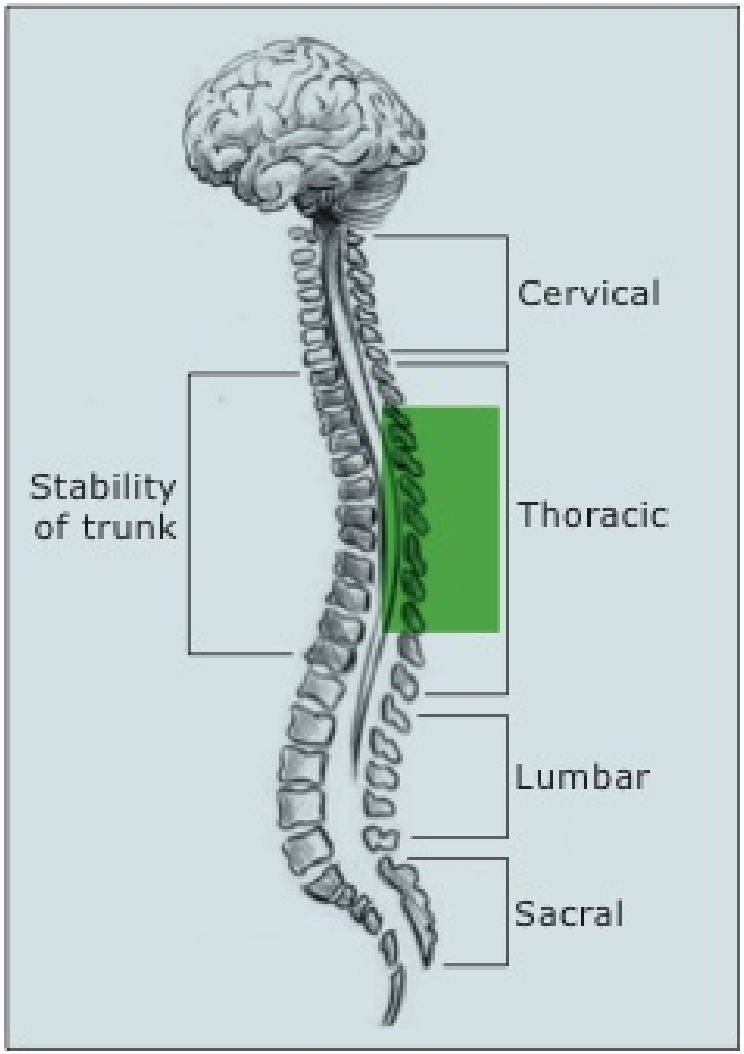
5 x 10^9 OPC1 Tested in Studies

GRNOPC1

- Survives in the Spinal Cord
- Produces Neurotrophic Factors
- Can Induce Myelination
- Improves Locomotor Activity
- Reduces Parenchymal Cavitation
- Migrates Through the Spinal Cord
- Does Not Increase Mortality
- Does Not Induce Allodynia
- Does Not Induce Systemic Toxicity
- Predominantly Neural Cells Types
- Some Non-Neural Cell Types Observed
- Does Not Produce Teratomas
- Not Highly Susceptible to Direct Immune Responses

GRNOP1 Phase 1 Multi-Center Spinal Cord Injury Trial

- **Open Label Trial**
- **Subacute, Functionally Complete Spinal Cord Injury with a Neurological Level of T3 to T10**
- **$2x10^6$ Cells**
- **Transplant 7-14 Days Post Injury**
- **Temporary Immunosuppression with Low Dose Tacrolimus**
- **Primary Endpoint: Safety**
  - *Neurological*
  - *Overall*
- **Secondary Endpoint: Efficacy**
  - *ASIA Sensory Score*
  - *Lower Extremity Motor Score*



Clinical Trials Database

http://clinicaltrials.gov/

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. Learn more about clinical studies and about this site, including relevant history, policies, and laws.

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ClinicalTrials.gov currently lists 178,531 studies with locations in all 50 states and in 187 countries.

Text Size

Search for Studies

Example: "Heart attack" AND "Los Angeles"

Search

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See Studies on a Map

Search Help

- How to search
- How to find results of studies
- How to read a study record

Locations of Recruiting Studies

- Non-U.S. Only (52%)
- U.S. Only (43%)
- Both U.S. and Non-U.S. (6%)

Total N = 34,089 studies
Data as of November 12, 2014

- See more trends, charts, and maps

For Patients & Families

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- ClinicalTrials.gov Online Training
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For the Press

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Clinical Trials Stem Cell Interventions

http://clinicaltrials.gov/

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"

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4252 studies found for: stem cell

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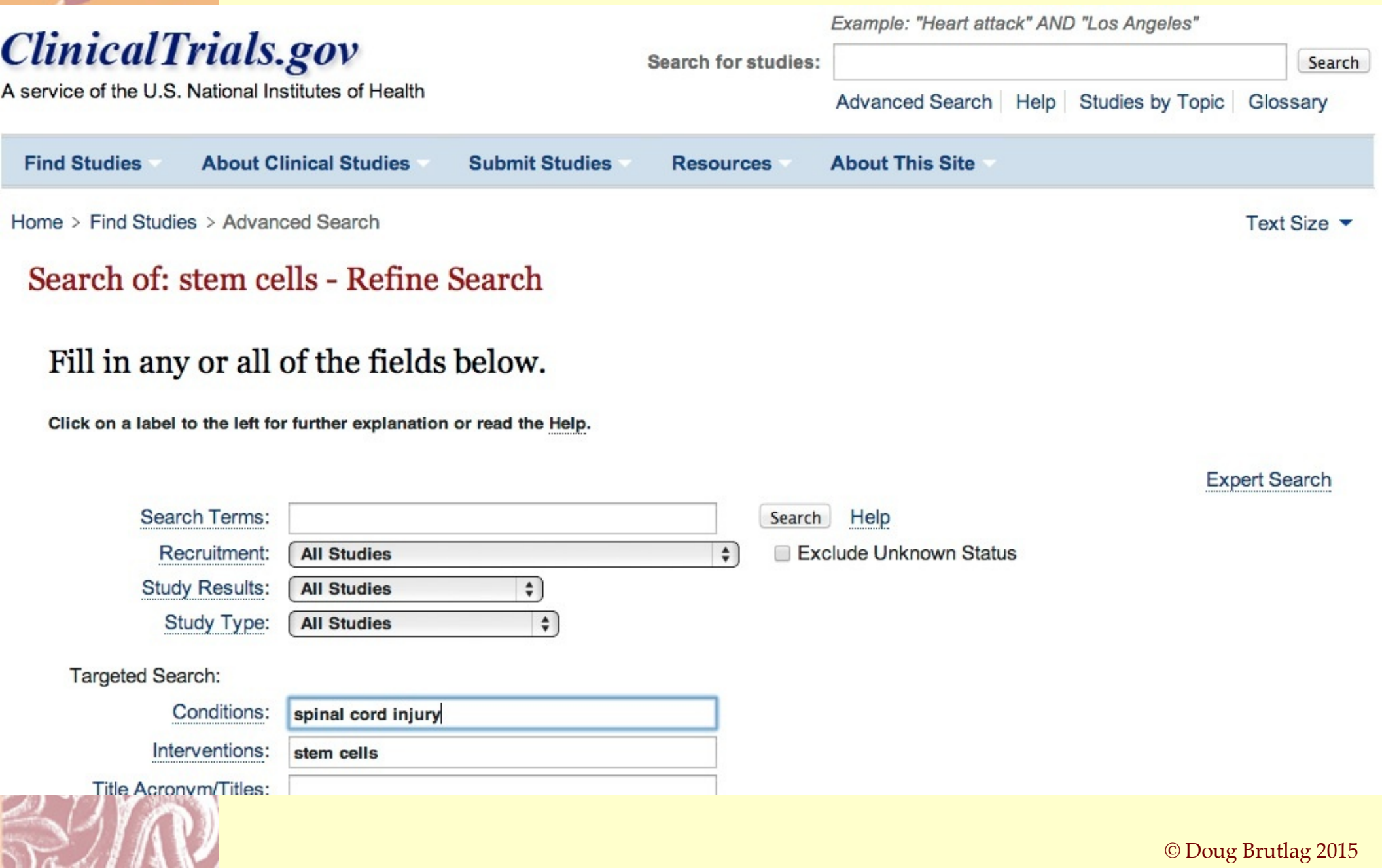
[ ] Include only open studies [ ] Exclude studies with Unknown status

Rank	Status	Study
1	Unknown †	**Tissue Distribution of F18-FDG Labelled Autologous Bone Marrow Derived Stem Cells in Patients With Type 2 DM** **Condition:** Type 2 Diabetes Mellitus **Interventions:** Other: Stem cell therapy- SPD artery; Other: Stem cell therapy- splenic artery; Other: Stem cell therapy-intravenous; Other: Normal saline placebo -sham procedure
2	Recruiting	**Hematopoietic Stem Cell Support in Vasculitis** **Condition:** Vasculitis **Interventions:** Biological: Autologous Stem Cell Transplant; Biological: Allogeneic Stem Cell Transplant
3	Recruiting	**Bortezomib, Melphalan, and Total-Body Irradiation Before Stem Cell Transplant in Treating Patients With Multiple Myeloma** **Conditions:** DS Stage I Plasma Cell Myeloma; DS Stage II Plasma Cell Myeloma; DS Stage III Plasma Cell Myeloma; Refractory Plasma Cell Myeloma **Interventions:** Drug: Bortezomib; Radiation: Total-Body Irradiation; Drug: Melphalan; Procedure: Autologous Bone Marrow Transplantation; Procedure: Autologous Hematopoietic Stem Cell Transplantation; Procedure: Peripheral Blood Stem Cell Transplantation; Other: Laboratory Biomarker Analysis

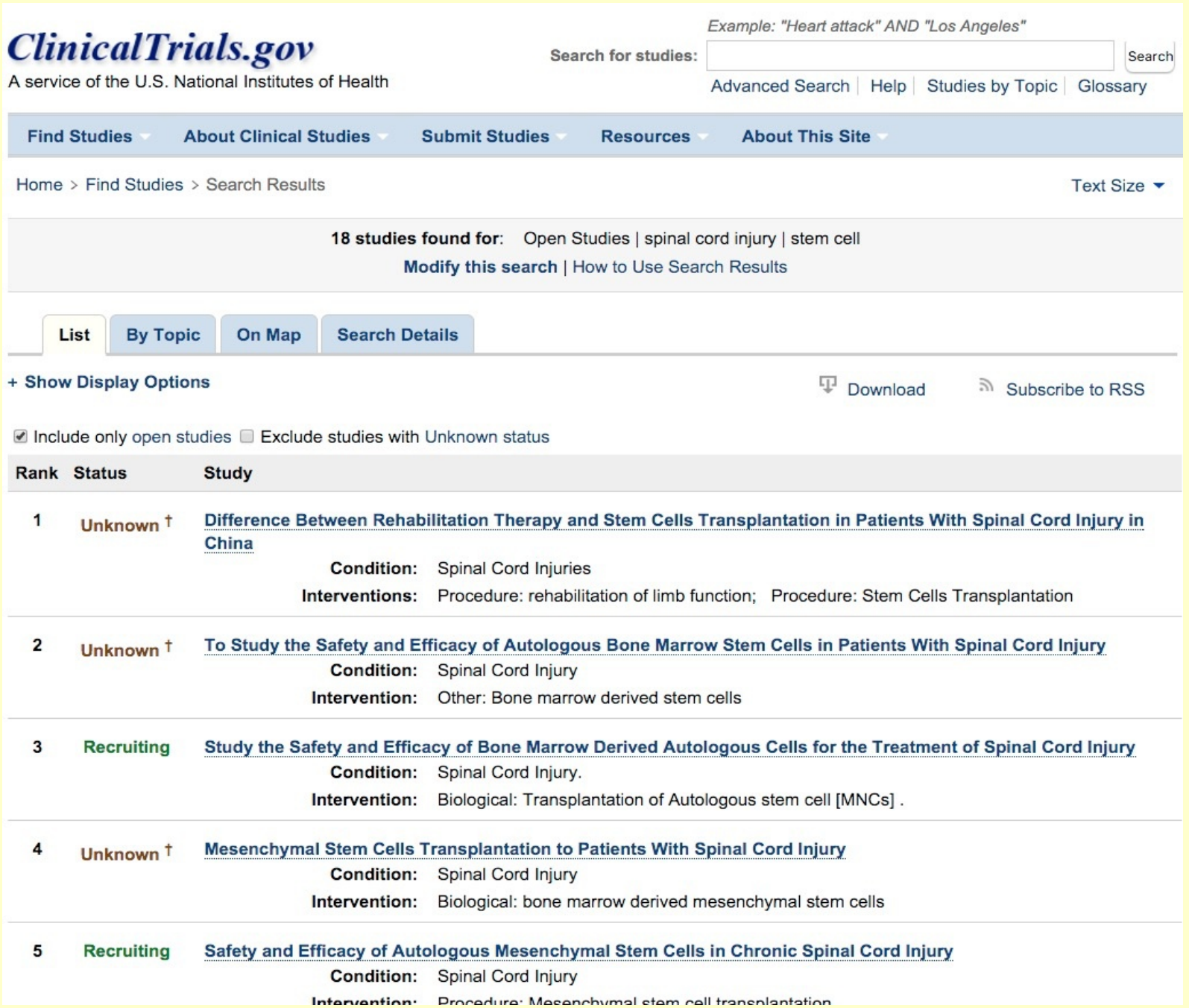
Clinical Trials Search for Spinal Cord Injury (SCI)

http://clinicaltrials.gov/



Clinical Trials for SCI and Stem Cells

http://clinicaltrials.gov/



ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"

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18 studies found for: Open Studies | spinal cord injury | stem cell

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☑ Include only open studies ☐ Exclude studies with Unknown status

Rank	Status	Study
1	Unknown †	Difference Between Rehabilitation Therapy and Stem Cells Transplantation in Patients With Spinal Cord Injury in China **Condition:** Spinal Cord Injuries **Interventions:** Procedure: rehabilitation of limb function; Procedure: Stem Cells Transplantation
2	Unknown †	To Study the Safety and Efficacy of Autologous Bone Marrow Stem Cells in Patients With Spinal Cord Injury **Condition:** Spinal Cord Injury **Intervention:** Other: Bone marrow derived stem cells
3	Recruiting	Study the Safety and Efficacy of Bone Marrow Derived Autologous Cells for the Treatment of Spinal Cord Injury **Condition:** Spinal Cord Injury. **Intervention:** Biological: Transplantation of Autologous stem cell [MNCs] .
4	Unknown †	Mesenchymal Stem Cells Transplantation to Patients With Spinal Cord Injury **Condition:** Spinal Cord Injury **Intervention:** Biological: bone marrow derived mesenchymal stem cells
5	Recruiting	Safety and Efficacy of Autologous Mesenchymal Stem Cells in Chronic Spinal Cord Injury **Condition:** Spinal Cord Injury **Intervention:** Procedure: Mesenchymal stem cell transplantation

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Clinical Trials Recruiting for SCI and Stem CELLS

http://clinicaltrials.gov/

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☑ Include only open studies ☑ Exclude studies with unknown status

Rank	Status	Study
1	Recruiting	**Study the Safety and Efficacy of Bone Marrow Derived Autologous Cells for the Treatment of Spinal Cord Injury** **Condition:** Spinal Cord Injury. **Intervention:** Biological: Transplantation of Autologous stem cell [MNCs] .
2	Recruiting	**Safety and Efficacy of Autologous Mesenchymal Stem Cells in Chronic Spinal Cord Injury** **Condition:** Spinal Cord Injury **Intervention:** Procedure: Mesenchymal stem cell transplantation
3	Not yet recruiting	**Evaluation of Autologous Mesenchymal Stem Cell Transplantation in Chronic Spinal Cord Injury: a Pilot Study** **Condition:** Spinal Cord Injury **Intervention:** Other: Mesenchymal stem cell transplantation
4	Recruiting	**Safety Study of Human Spinal Cord-derived Neural Stem Cell Transplantation for the Treatment of Chronic SCI** **Condition:** Spinal Cord Injury (SCI) **Intervention:** Device: Human spinal cord stem cells.

Clinical Trials of Hematopoietic Cell Transplantation

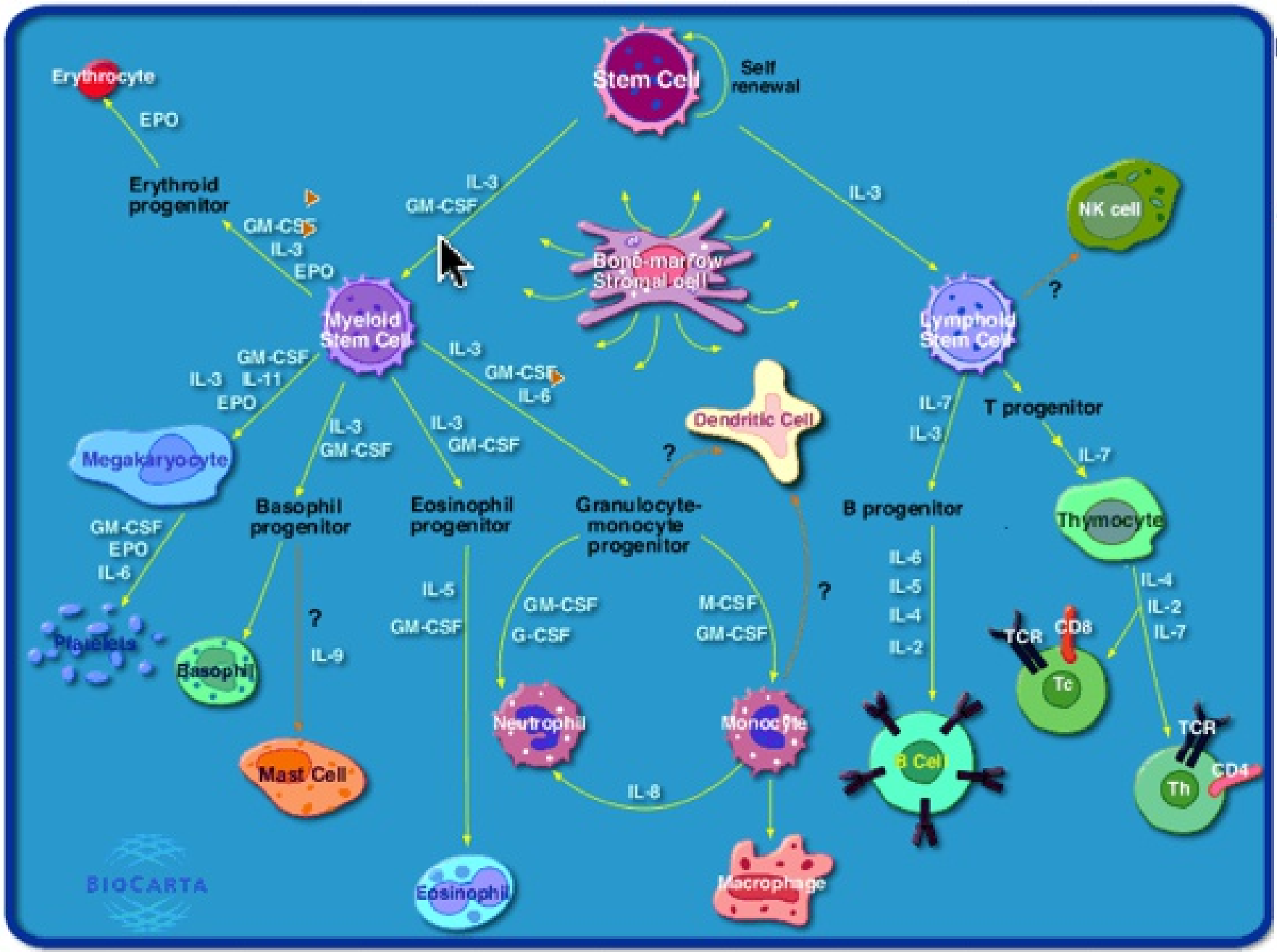
Judith A. Shizuru, M.D., Ph.D.

Division of Blood and Marrow Transplantation

Stanford University Medical Center

Hematopoiesis

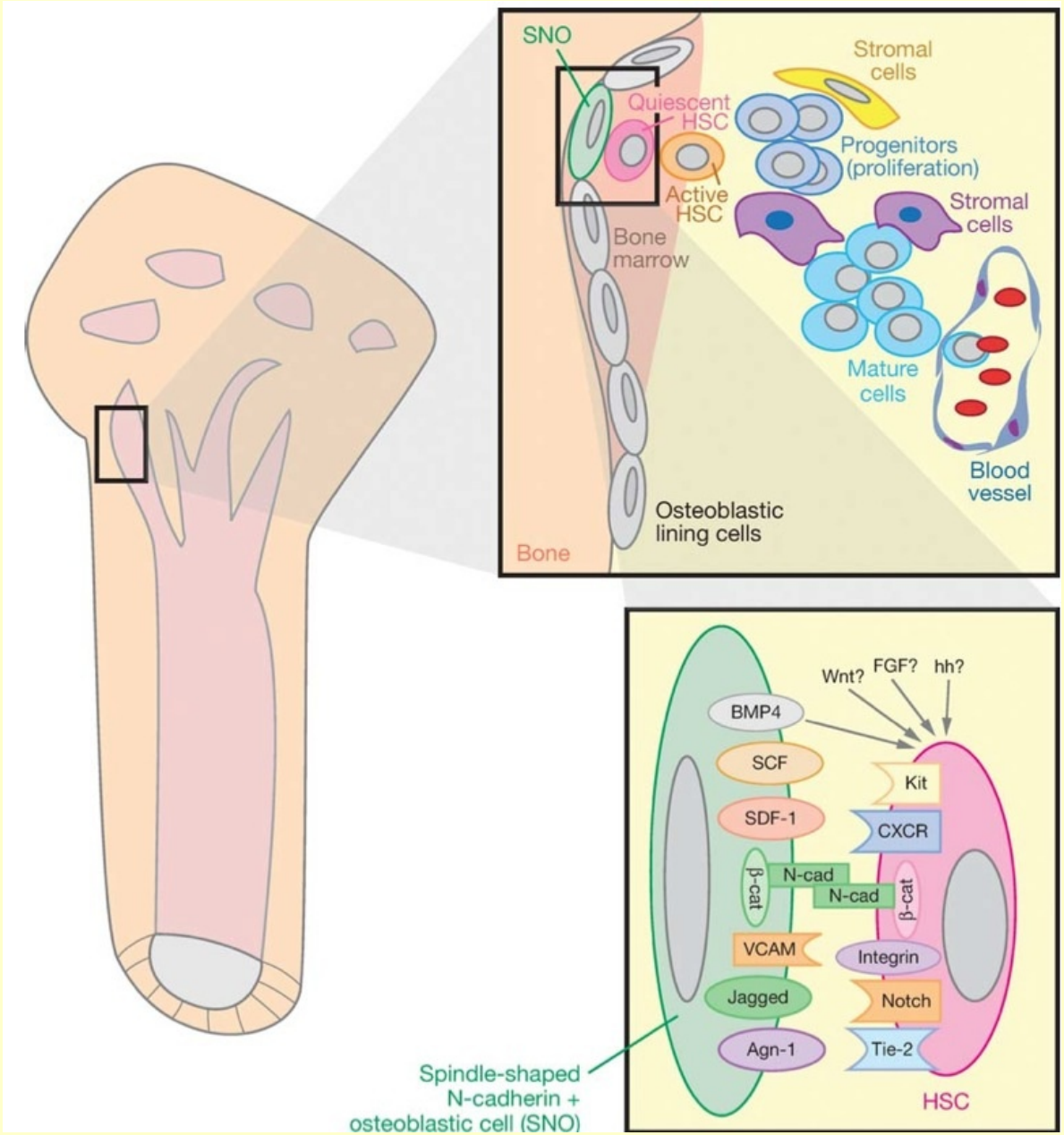
http://www.biocarta.com/pathfiles/h_stemPathway.asp



Hematopoietic Stem Cell Niche

Joy Wu: Bone & Blood: Role of Osteoblasts in Hematopoeisis

http://med.stanford.edu/irt/edtech/video/rea/?v=fall2014auth/video/grmed-09-03-2014-08r.mp4



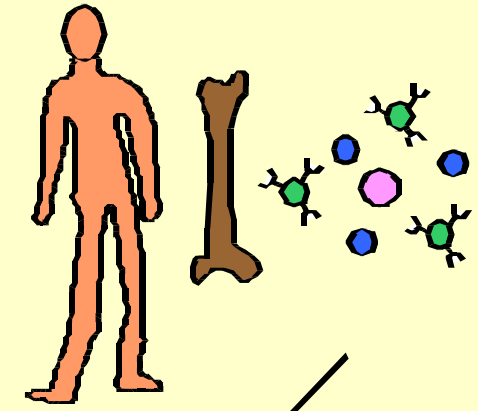
Li and Xie, Ann. Rev. Dev. Biol. 2005, 605-663

Bone Marrow Transplants to Cure Lymphomas/Thymomas

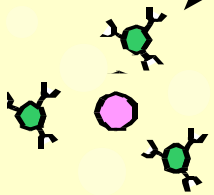
- Whole body irradiation to remove endogenous immune system and tumor
  - Also total lymphoid irradiation with antithymocyte serum
- Injection of bone marrow from a well matched donor to re-establish immune system
- Regulation of immune response to prevent graft versus host reaction.
- Autologous donation possible if one can purify and remove tumor cells, enriching for stem cells..
- Allogeneic donors have advantage of graft versus tumor reaction to kill any remaining tumor cells.
- Allogeneic donors have the disadvantage of graft versus host reaction if they are not well matched.

Autologous vs. Allogeneic Transplants

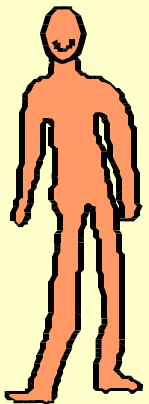
Autologous



Purify from Tumor cells

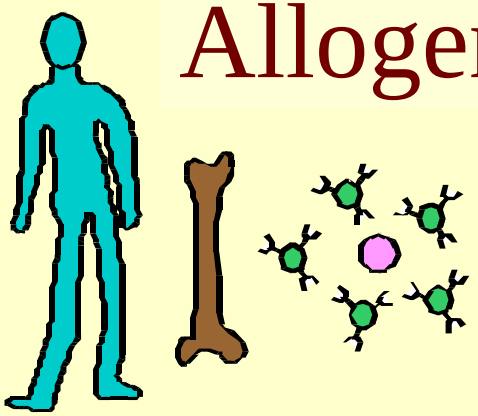


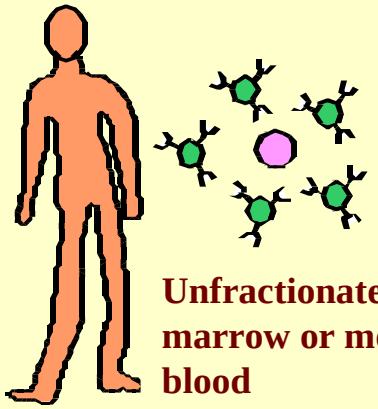
Transplant



Allogenic

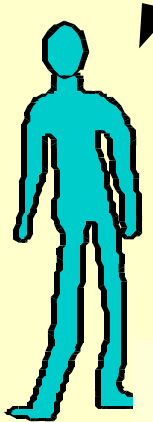
Healthy Donor





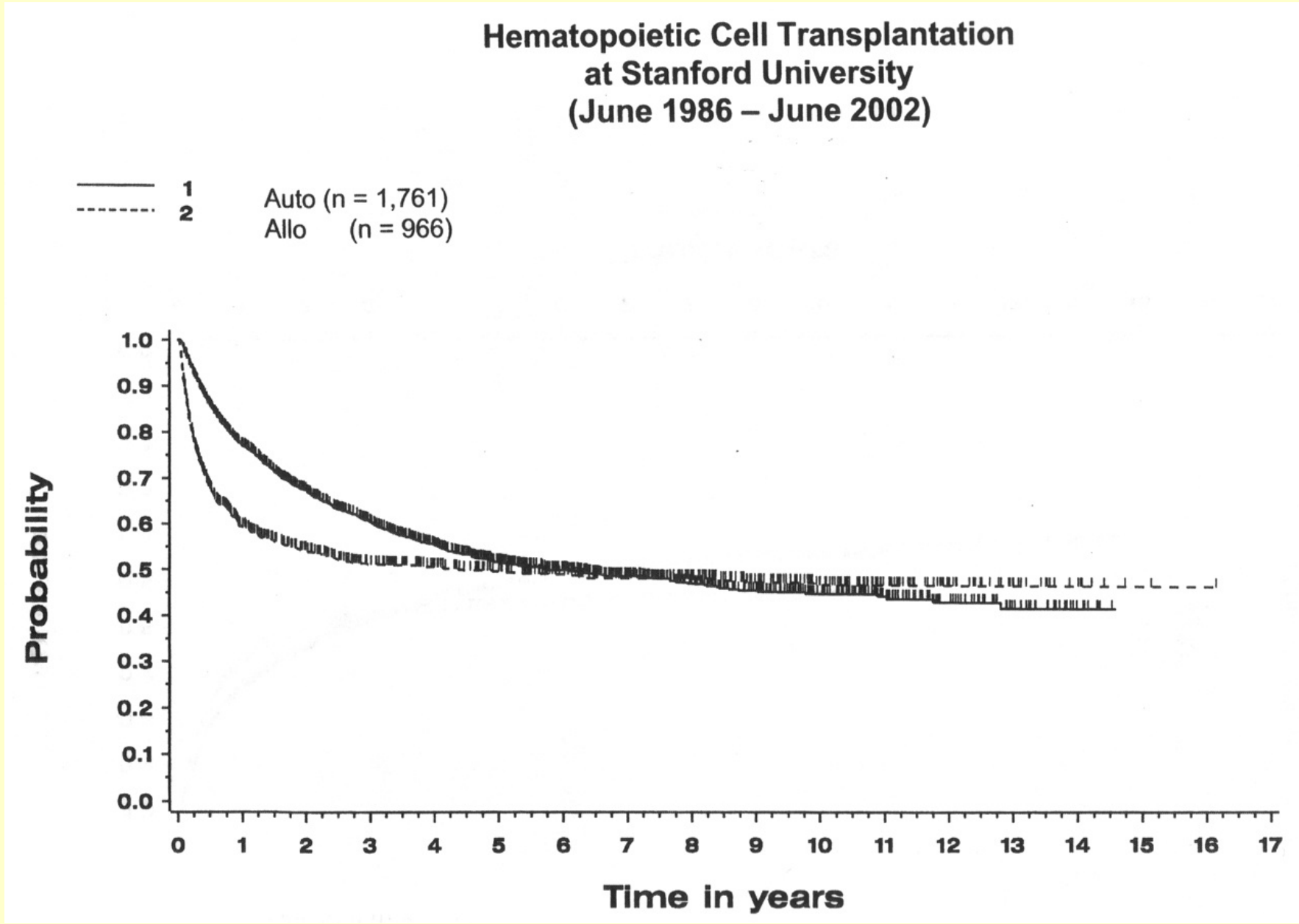
Unfractionated bone marrow or mobilized blood

Transplant



Donor blood formation, graft-vs-tumor effect

Judith Shizuru



Judith Shizuru

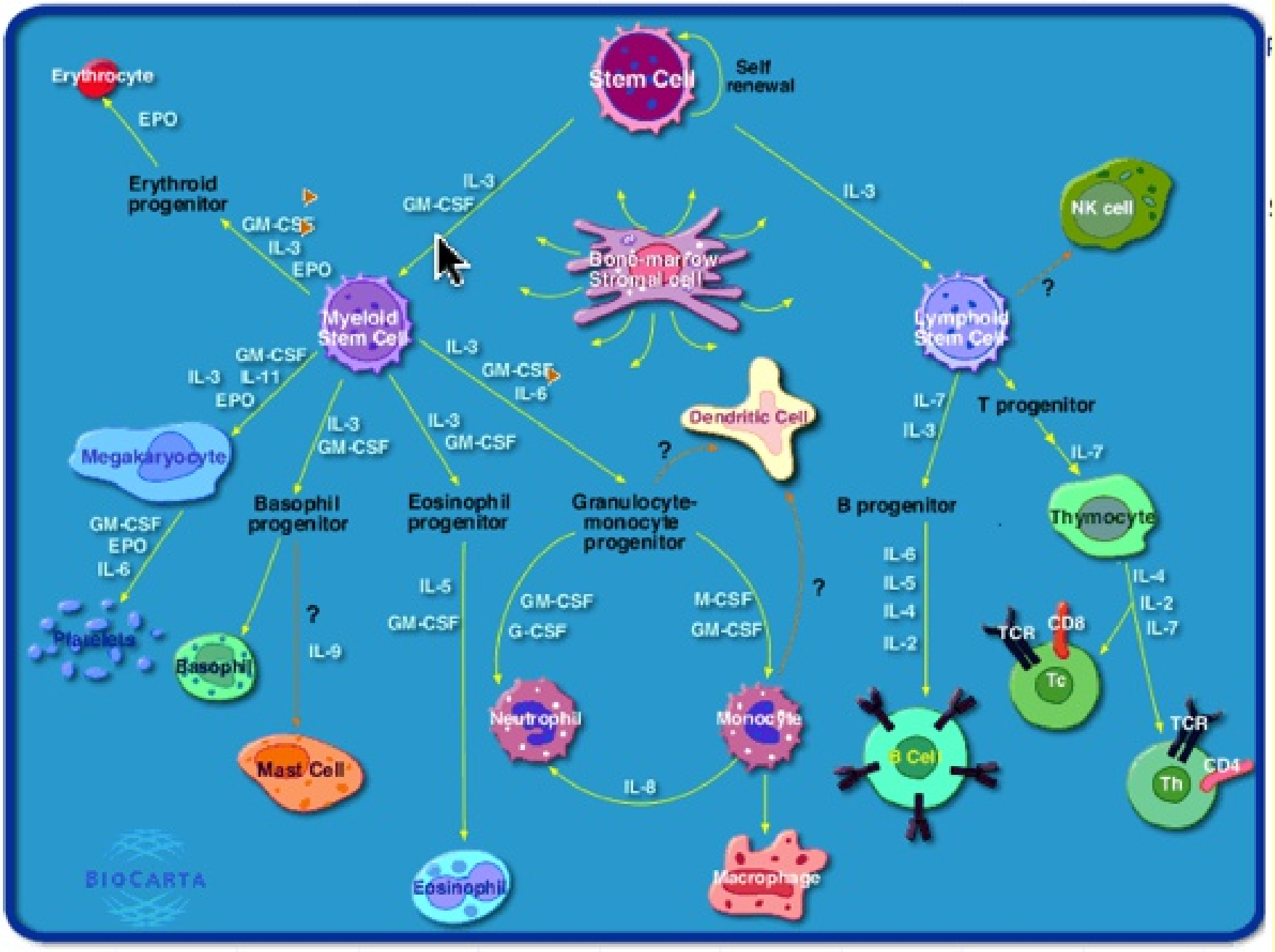
Complications of Allogeneic Transplants

Transplant related mortality = 10 - 15%

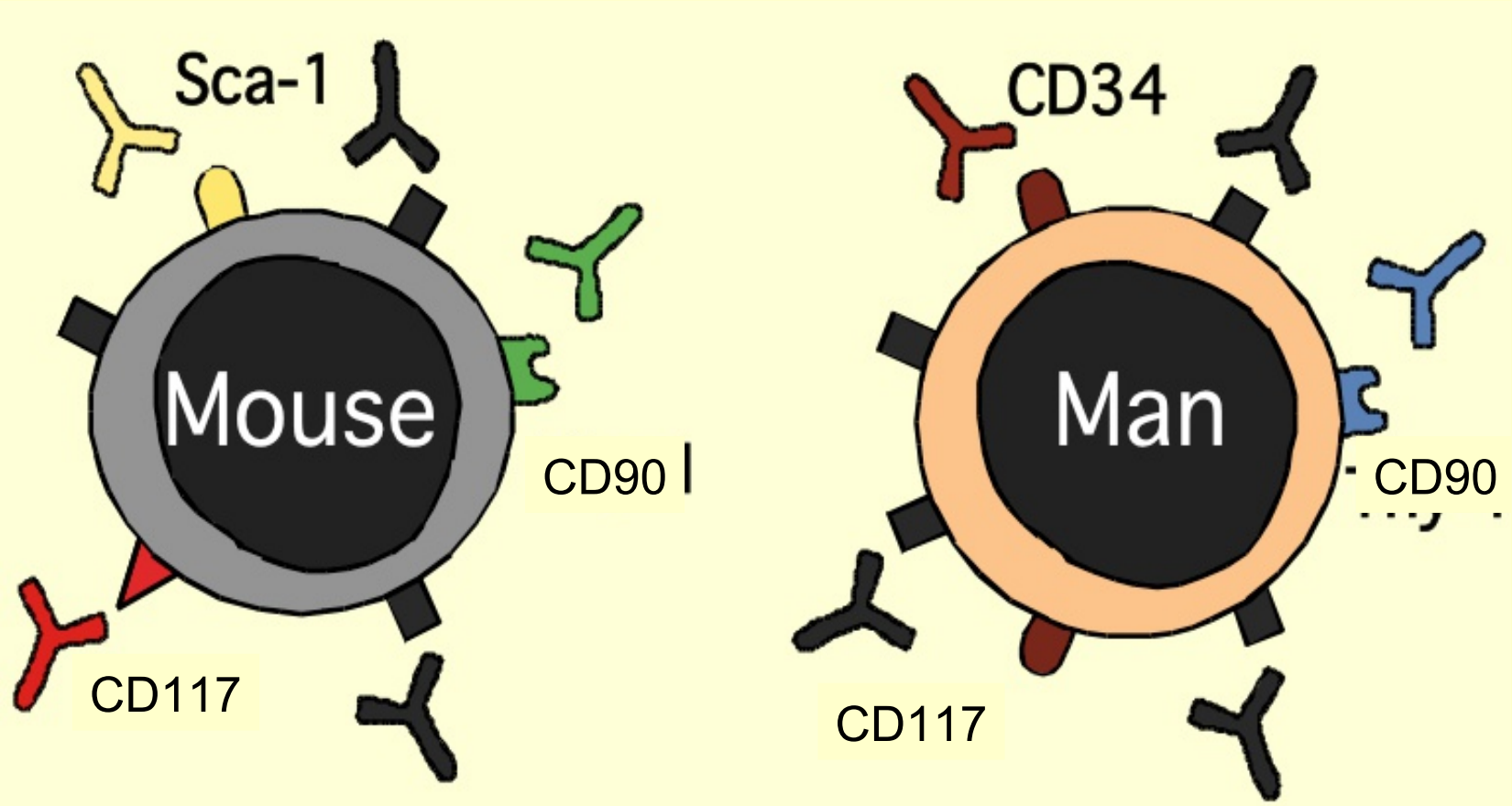
- Regimen related toxicity
- Infectious complications
- Engraftment failure (resistance)
- Graft-versus-host disease

Regulation of hematopoiesis by cytokines

http://www.biocarta.com/pathfiles/h_stemPathway.asp



Isolation of Hematopoietic Stem Cells



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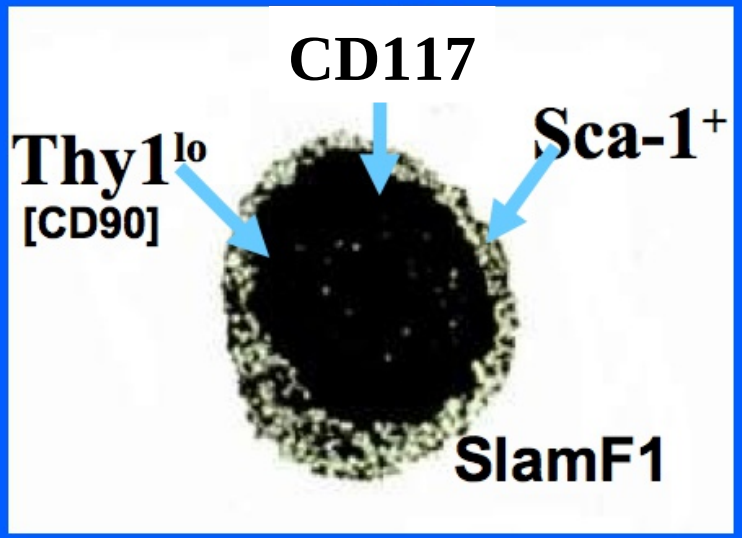
Isolation of Hematopoietic Stem Cells

MOUSE



Negative for:

B220

Mac-1

Gr-1

CD3, 4, 8

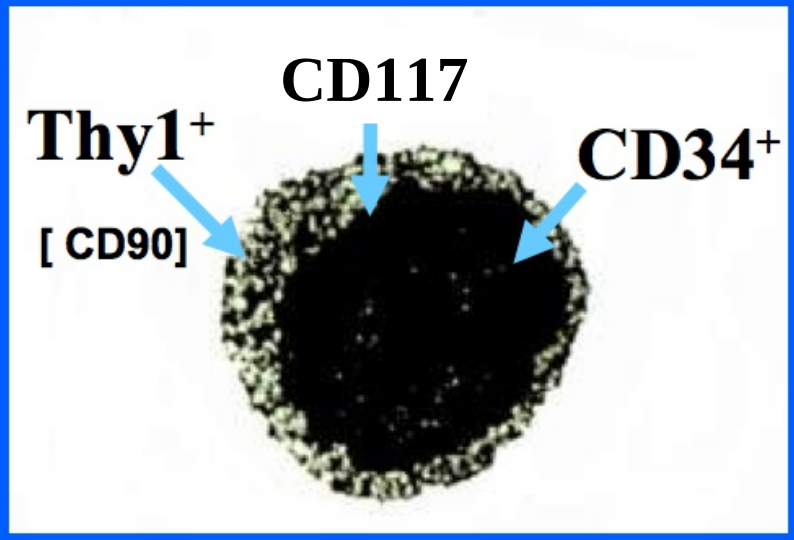
Ter119

Flk2

CD34

Spangrude, Muller, Heimfeld

MAN



Negative for:

CD10
CD14
CD15
CD16
CD19
CD20
CD 38

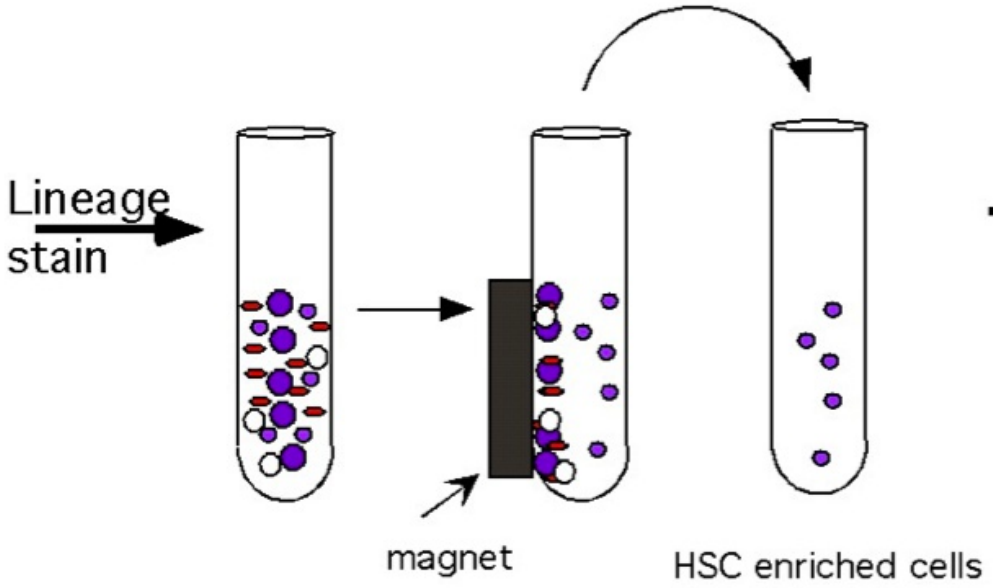
CD 3,4,8
Glycophorin A

Baum, Buckle, Peault, Tsukamoto

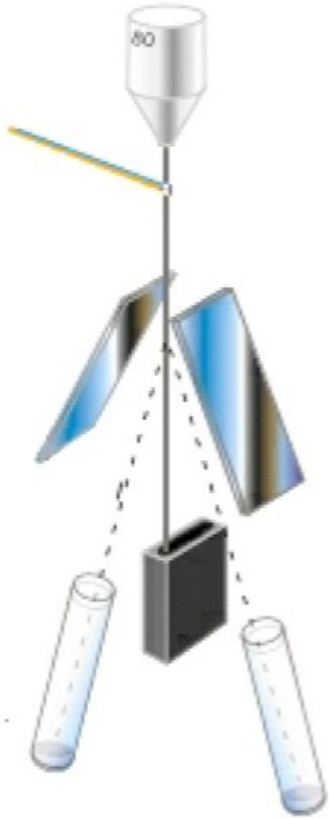
Courtesy Irv Weissman

Isolation of Pure Hematopoietic Stem Cells

Collect bone marrow cells



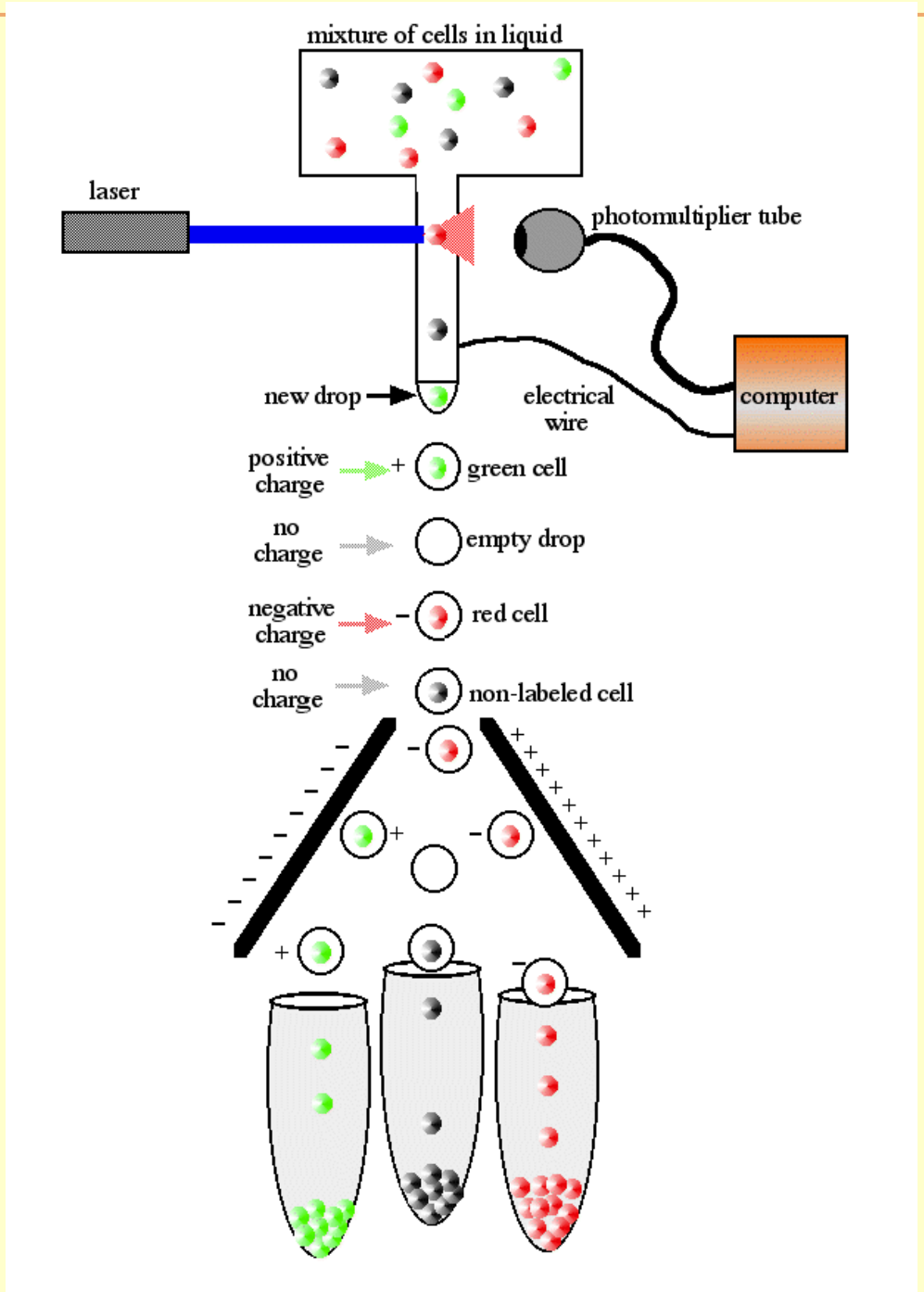
Deplete mature blood cells by labeling with magnetic antibodies



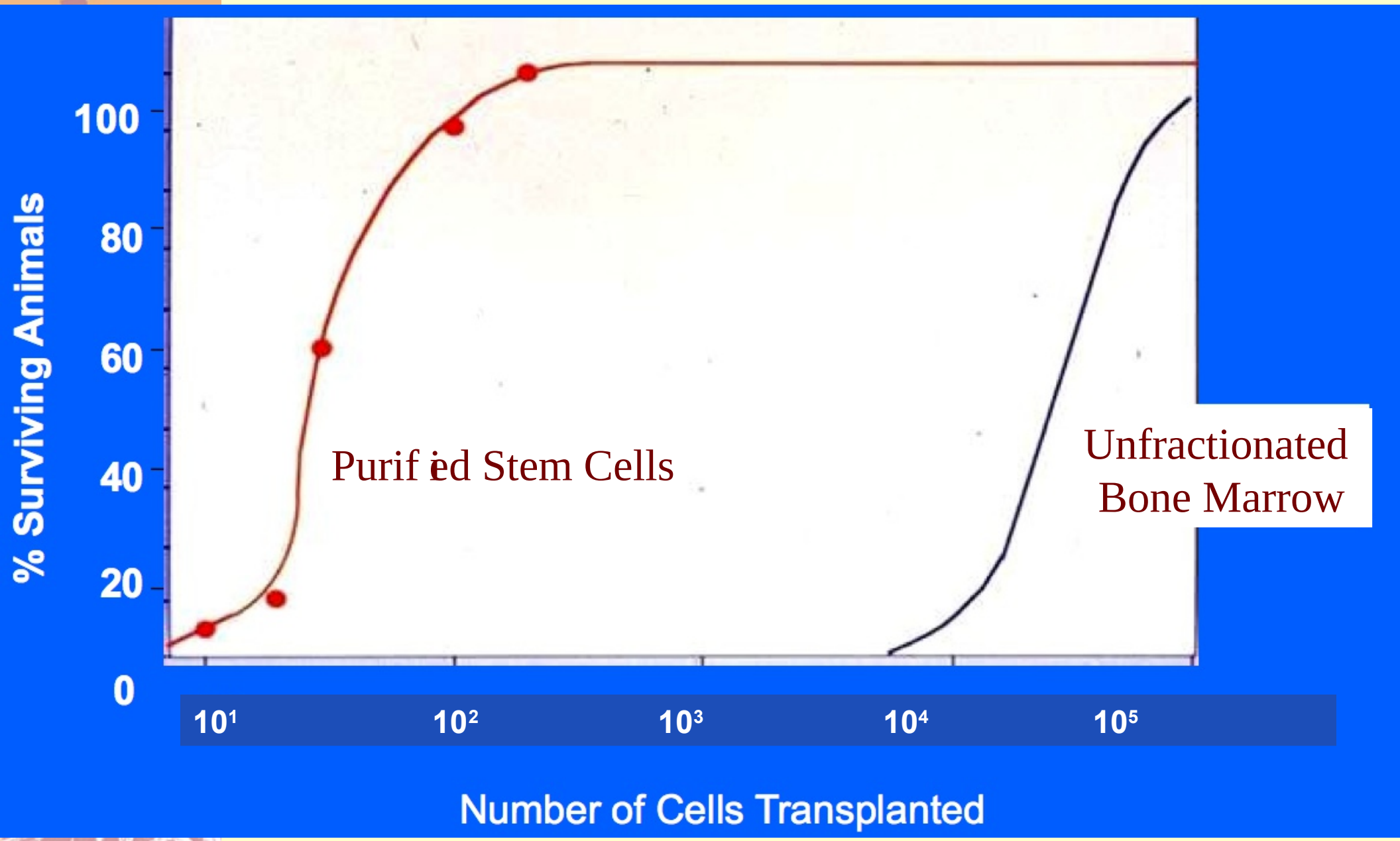
Sort stem cells

Courtesy Irv Weissman

Fluorescent Activated Cell Sorter (FACS)
Len Herzenberg & Lee Herzenberg

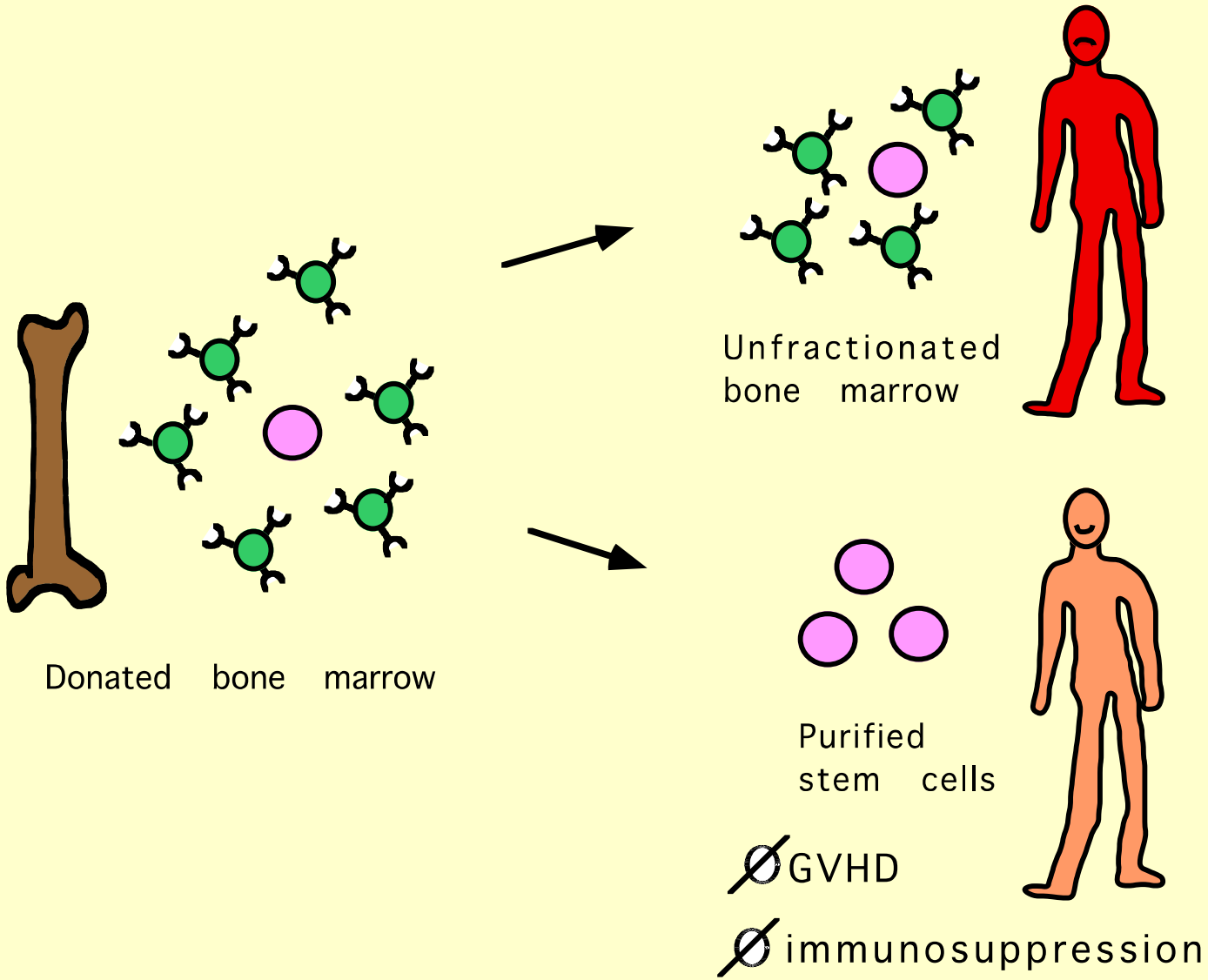


Purified Hematopoetic Stem Cells are 2000 Times More Effective in Transplants



Courtesy Irv Weissman

Why Transplant Purified Allogeneic HSCs?



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Applications of Hematopoietic Stem Cell Transplantation

- Treatment of patients with blood tumors.
- Treatment of autoimmune disease
  - Patients treated with bone marrow transplants are often cured of autoimmune disease
  - Bone marrow transplant donors with autoimmune disease can pass the disease on to recipients
- Organ tolerance induction
  - Mice receiving organ transplant and HSC transplant together are tolerant and no rejection occurs. No immune suppressants are needed.
- Very high dose chemotherapy
  - Breast caner patients receive very high dose chemotherapy that kills tumor and immune system.
  - Autogenic hematopoietic stem cell transplants recover patient's immune system.

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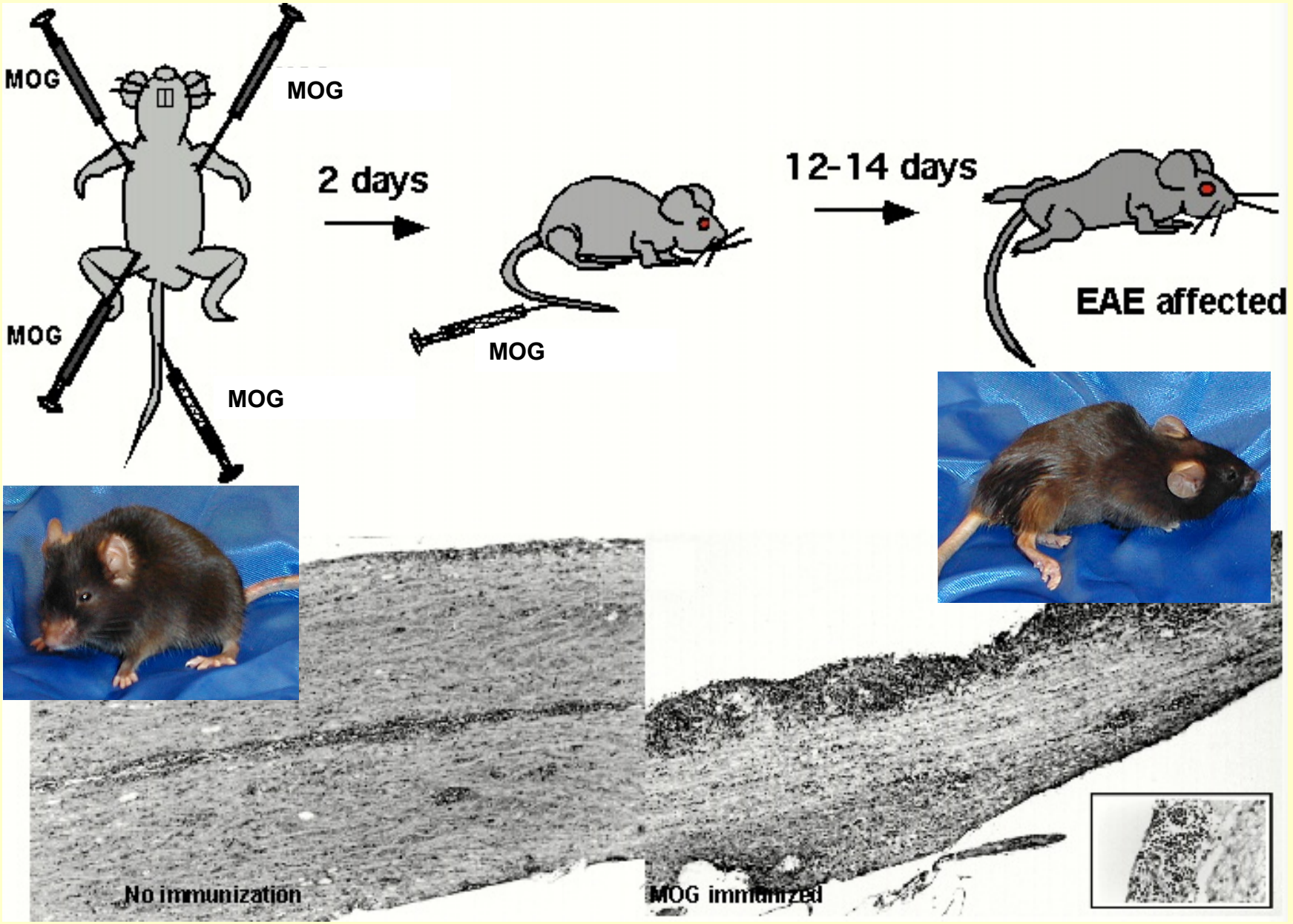
Experimental Autoimmune Encephalomyelitis (EAE) Model for Multiple Sclerosis in Mice



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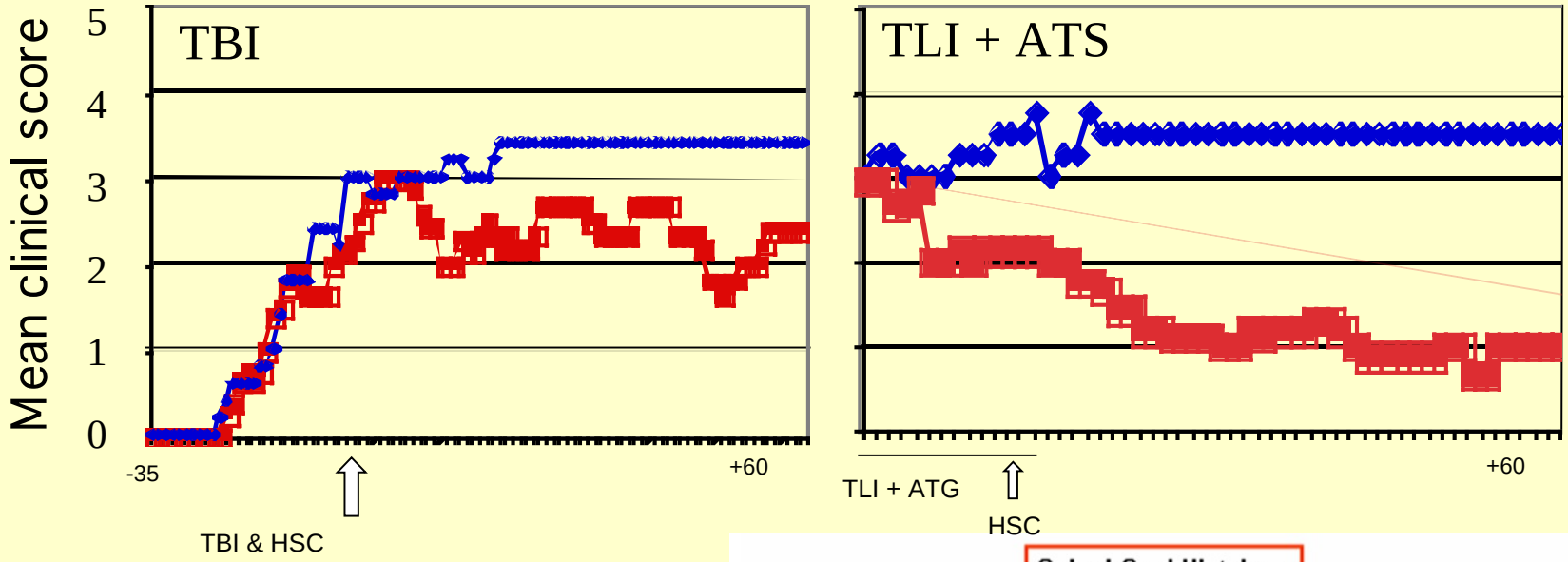
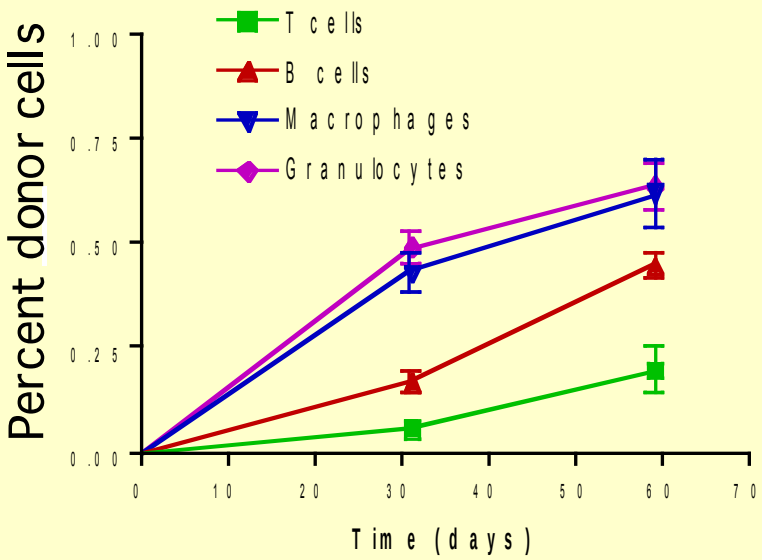
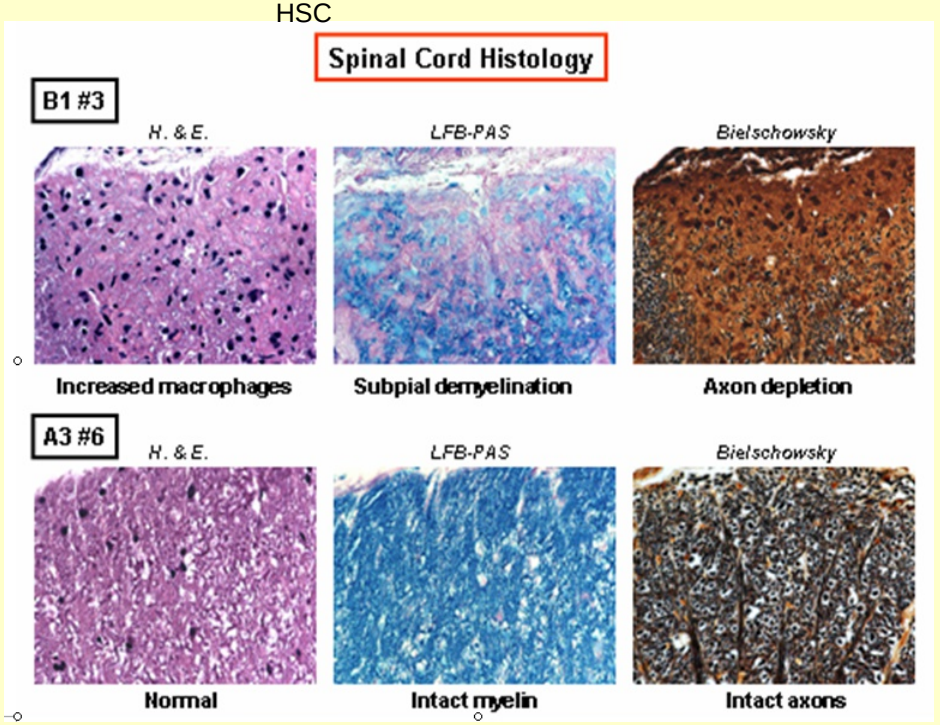
Partial Chimerism Results in Disease Amelioration







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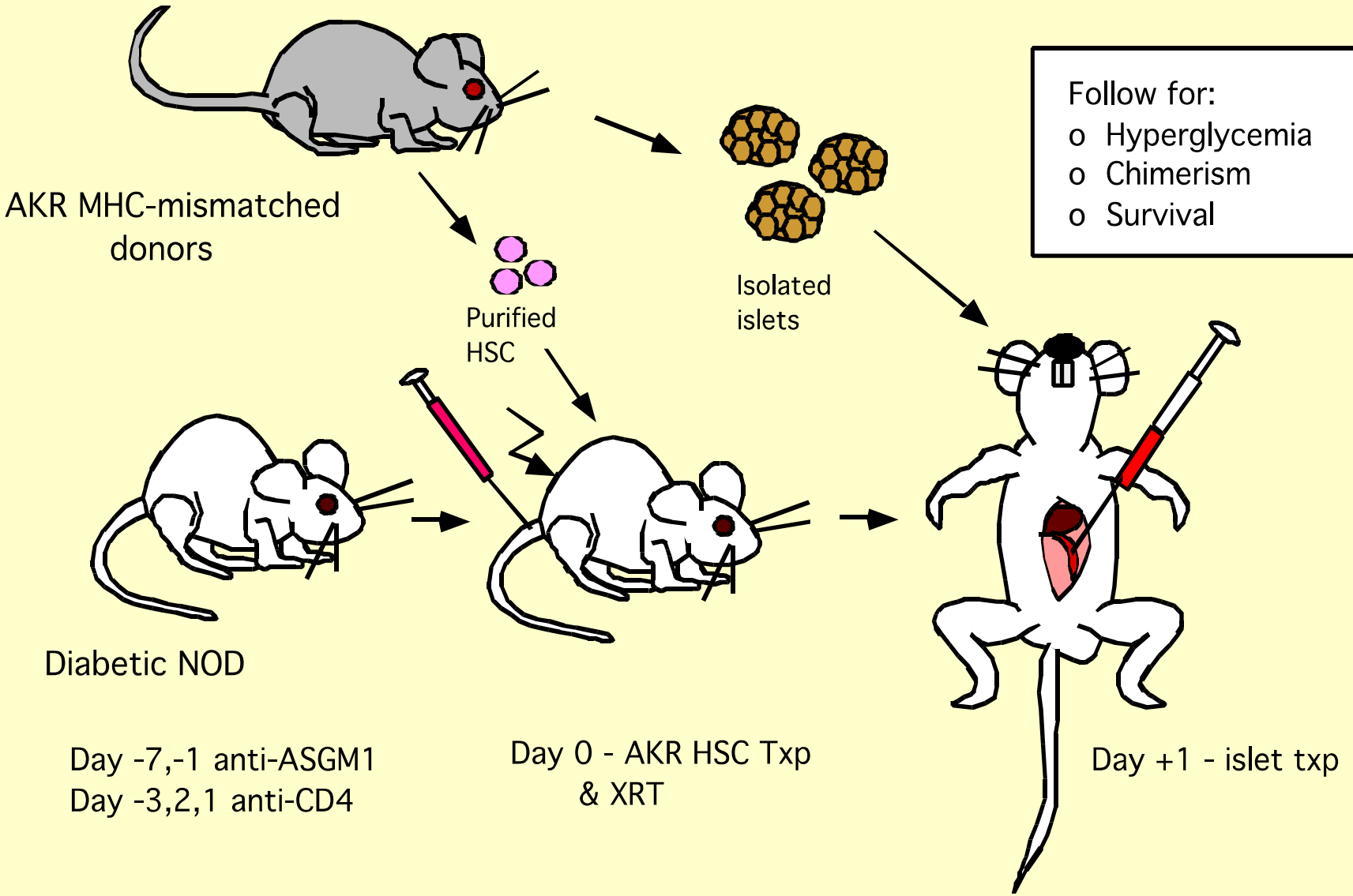
Combined HSC & islet transplantation



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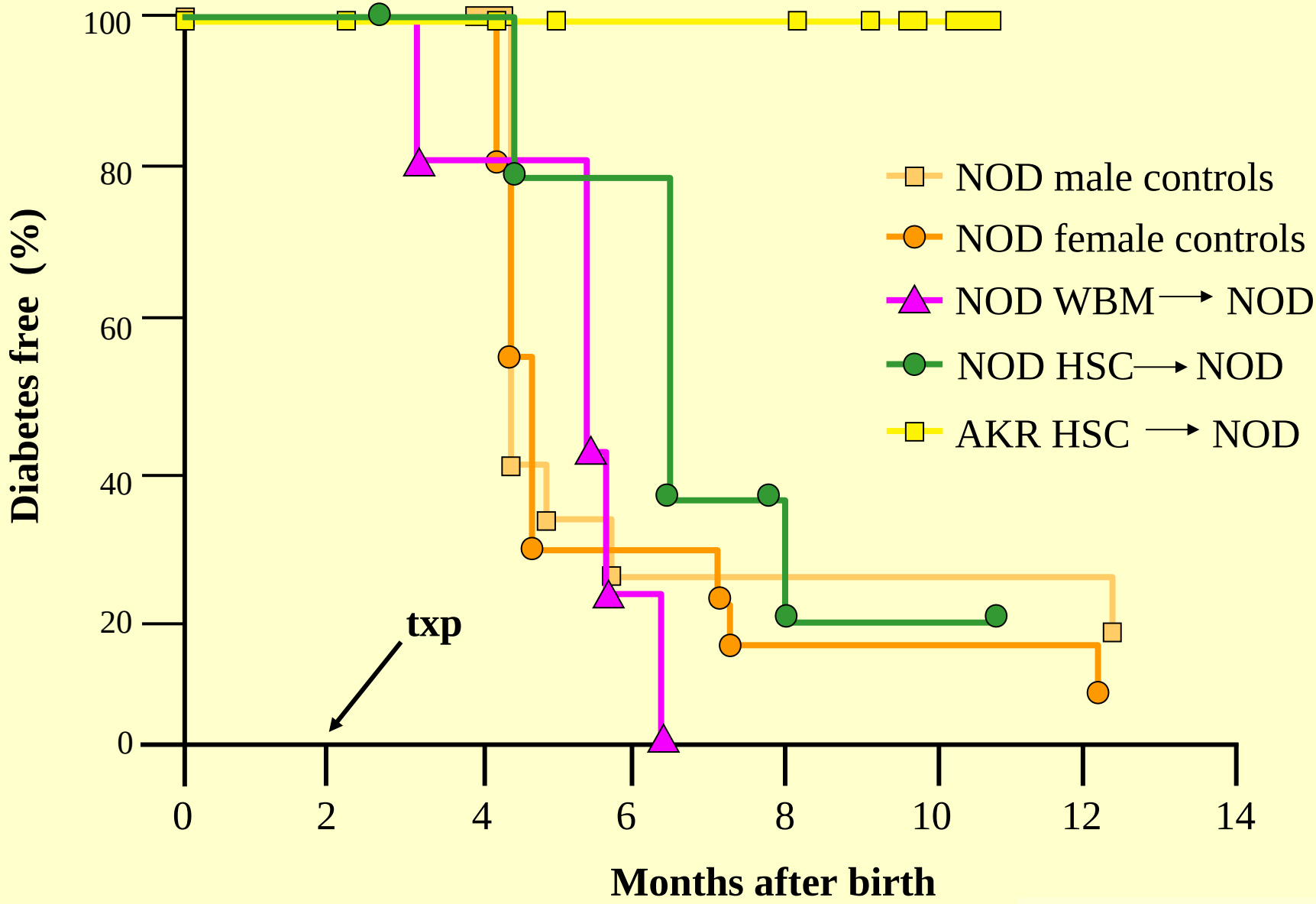
Treatment of Diabetic Mice (NOD) with Hematopoietic Stem Cell Transplants



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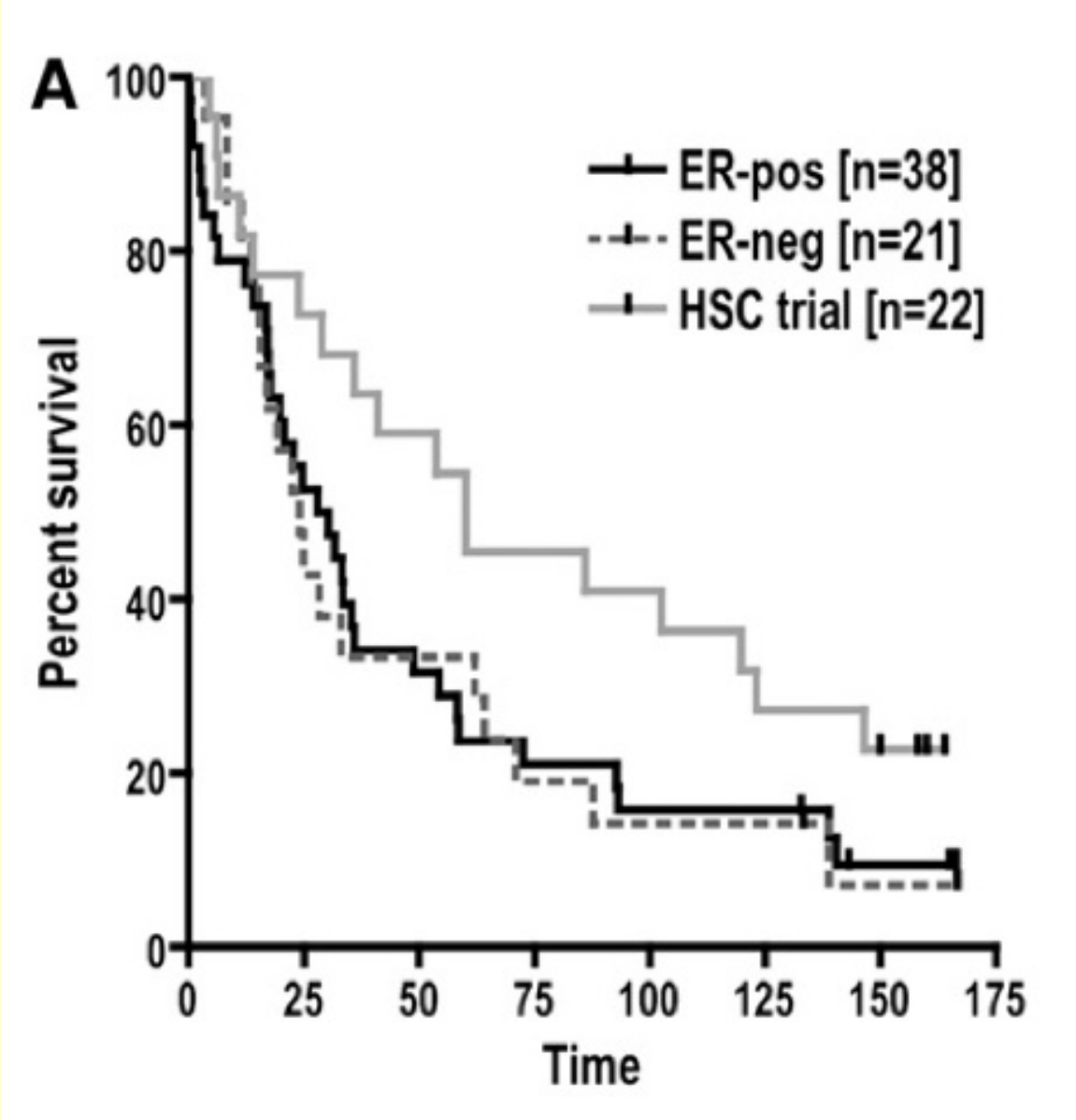
Hematopoietic Cell Treatment Coupled with High Dose Breast Cancer Chemotherapy



Stage Four Metastatic Breast Cancer

Müller et al. (2011) Biol. Blood Marrow Transplant

Stem Cell Therapy Research Project

http://biochem118.stanford.edu/Homeworks/06%20stem-cell-project.html

Many inherited diseases can be treated with drugs, hormones or other biological products that are missing or abnormally regulated in the disease. Some diseases can also be treated by nutritional methods, especially those diseases that alter metabolism. However, many diseases that are missing membrane proteins or protein complexes in the patient's cells cannot be treated so easily. These diseases of missing membrane proteins, missing protein complexes or even missing or defective cell types or tissues are candidates for treatment with stem cell therapies.

For this homework, I would like you to choose a disease not mentioned in class, that is a candidate for stem cell therapy and describe:

1) why the disease might be best treated by stem cell

2) which stem cells might be used

3) can the patients own stem cells (iPSCs or others) be used

4) is genetic therapy on the stem cells required to replace a defective gene

5) has a protocol for a clinical trial been submitted and

6) what is the preclinical evidence that the method will work.

The best way to discover a potential candidate disease is to go to the web site clinicaltrials.gov and search either for a disease of interest or for the term stem cell. If you use the Advanced Search button on clinicaltrials.gov you can specify the condition (disease) and the intervention (stem cells) at the same time. This will give you an extensive list of clinical trials involving stem cells (over 3,600 at the moment). Please write a short report (4 pages max) that answers the 6 questions above. Please send the paper to brutlag@stanford.edu.

In vitro fertilization and Preimplantation Genetic Diagnosis

- *In vitro* fertilization (IVF) to aid fertility
  - Heterologous using sperm donors
  - Homologous to improve fertility
- Preimplantation genetic diagnosis (PGD)
  - IVF to generate multiple 3 day embryos
  - Single cell removal and diagnosis
    - PCR
    - FISH
    - *In situ* hybridization
  - Selection
    - Absence of genetic abnormality
    - For a sibling donor compatibility
    - Sex selection
    - Other desirable traits?

Dignitas Personae

- Holiness of the conjugal act
  - Technical means to avoid it are illicit
  - Technical means to improve it are licit
- Sanctity of human life
  - All stages of human life should be treated with dignity and respect
    - Zygotes
    - Embryos
    - Fetus
    - Infants
    - Elderly and infirm

Am I for the creation-and-destruction of human embryos solely for research or am I against it?

Should parents be permitted to select their child's traits by preimplantation genetic selection?

Sandel and Genetic Eugenics

- Science moves faster than moral understanding.
- Example if cloning were perfect and easy should we do it?
- What is wrong with recreating a child who died?
- An admired scientist?
- The deeper danger is that they aspire to remake nature to serve our purposes and satisfy our desires.
- The problem is the drive to mastery.
- Defenders of enhancement reply that genetic choices freely made are not really eugenic—at least not in the pejorative sense.
- Sorting out the lesson of eugenics is another way

Genetic Eugenics

- Autonomy
- Fairness
- Equality
- Individual rights
- Nothing wrong with genetic engineering and enhancement, provided they are freely chosen rather than state-imposed.
- Puts a value on life buying and selling eggs and gametes.

Prenatal Diagnosis
Power and Perils

- Early medical diagnosis for known carriers
- Amniocentesis and chorionic villus sampling (CVS)
  - Early fetal genetic diagnosis
  - Termination of pregnancy
- *In vitro* fertilization (IVF) has lead to preimplantation genetic diagnosis (PGD)
  - Disease
  - Gender
  - Familial Traits

Eugenics

- Natural selection according to Darwin
- Human selection against a disease gene
- Human selection for specific traits.
- Human selection against races: genocide

Ethical Considerations

- Value and human rights of the individual
- Autonomy and political rights of individuals
- Health and welfare of offspring
- Health and overall welfare of society
- Cost of treatment to the individual or to society
- What are the rights of an egg, fertilized egg, embryo, implanted embryo, fetus, child?
- Who owns eggs, embryos, stem cells?
- When do human rights transfer from mother & father to the offspring?

Gender Selection

- Societal pressures
  - China one child law
  - India boys preferred
- Medical motivations
  - Sex linked diseases (hemophilia, Duchenes muscular dystrophy)
  - Autism
- Family balancing or imbalancing
- Religious, cultural or economic reasons

Reasons for IVF

- Fertility
- Preimplantation genetic diagnosis
- Sperm donors
- Egg donors
  - Older mothers
  - Infertility
  - After chemotherapy

Anonymity of Sperm Donors

- Right of donor to remain anonymous
- Right of child to know father
- Right of child to know biological siblings

Should society permit?

- IVF for treatment of fertility?
- IVF for sperm donor?
- IVF for egg donor?
- PGD for gender selection?
- PGD for disease avoidance?
- PGD for trait selection?
- PGD for compatible sibling tissue donor?

Should society pay for?

- IVF for treatment of fertility?
- IVF for sperm donor?
- IVF for egg donor?
- PGD for gender selection?
- PGD for disease avoidance?
- PGD for trait selection?
- PGD for compatible sibling tissue donor?

Should society screen for

- Cystic fibrosis
- Down's syndrome
- Thalassemia
- Sickle Cell disease
- Breast Cancer genes
- Familial colorectal cancer genes
- Huntington's disease
- Will screening result in genetic discrimination?

Anecdotes on selection for the abnormal

- Two deaf lesbians wanted a deaf child using PGD with a deaf sperm donor.
- Two deaf heterosexual parents in Australia wanted to use IVF and PGD to ensure a deaf offspring.
- Parents permitting a Down's child to be borne are often made to feel guilty.

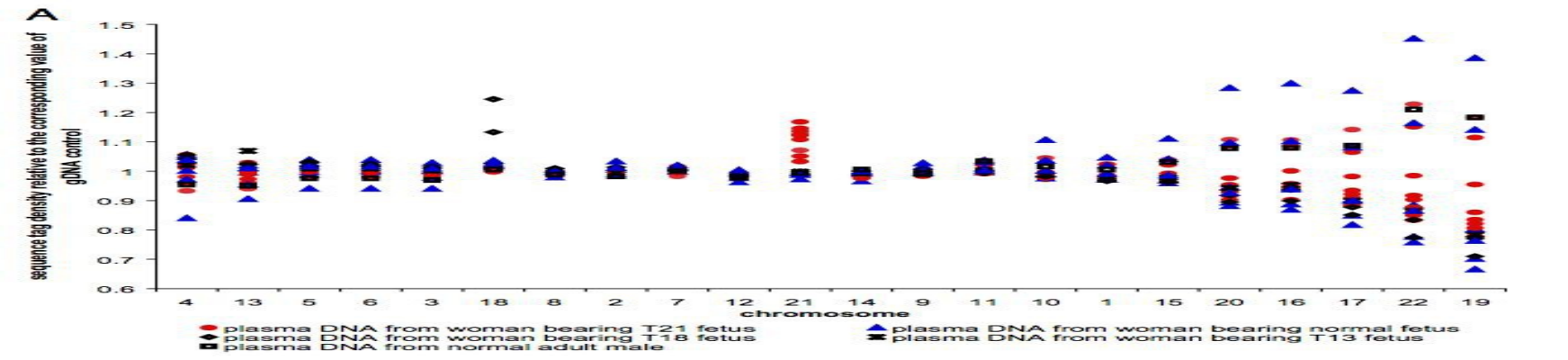
Noninvasive diagnosis of fetal aneuploidy by shotgun sequencing DNA from maternal blood

H. Christina Fan*, Yair J. Blumenfeld†, Usha Chitkara†, Louanne Hudgins‡, and Stephen R. Quake*§

We directly sequenced cell-free DNA with high-throughput shotgun sequencing technology from plasma of pregnant women, obtaining, on average, 5 million sequence tags per patient sample. This enabled us to measure the over- and underrepresentation of chromosomes from an aneuploid fetus. The sequencing approach is polymorphism- independent and therefore universally applicable for the noninvasive detection of fetal aneuploidy. Using this method, we successfully identi ed all nine cases of trisomy 21 (Down syndrome), two cases of trisomy 18 (Edward syndrome), and one case of trisomy 13 (Patau syndrome) in a cohort of 18 normal and aneuploid pregnancies; trisomy was detected at gestational ages as early as the 14th week. Direct sequencing also allowed us to study the characteristics of cell-free plasma DNA, and we found evidence that this DNA is enriched for sequences from nucleosomes.

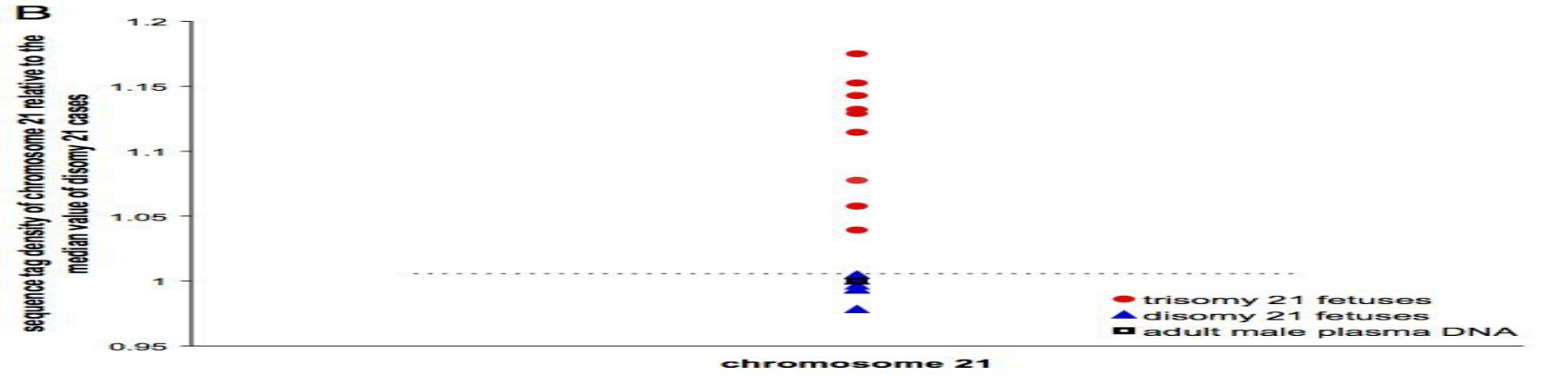
Fan et al. (2008) PNAS 105; 16266-16271.

Fetal Aneuploidy Detected by Sequencing Maternal Blood



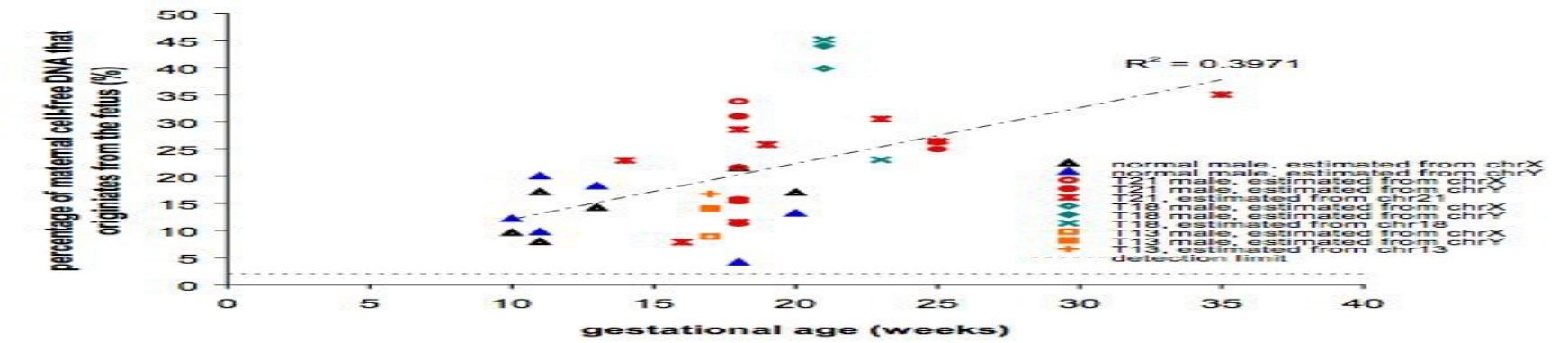
Fan et al. (2008) PNAS 105; 16266-16271.

Chromosome 21 Aneuploidy



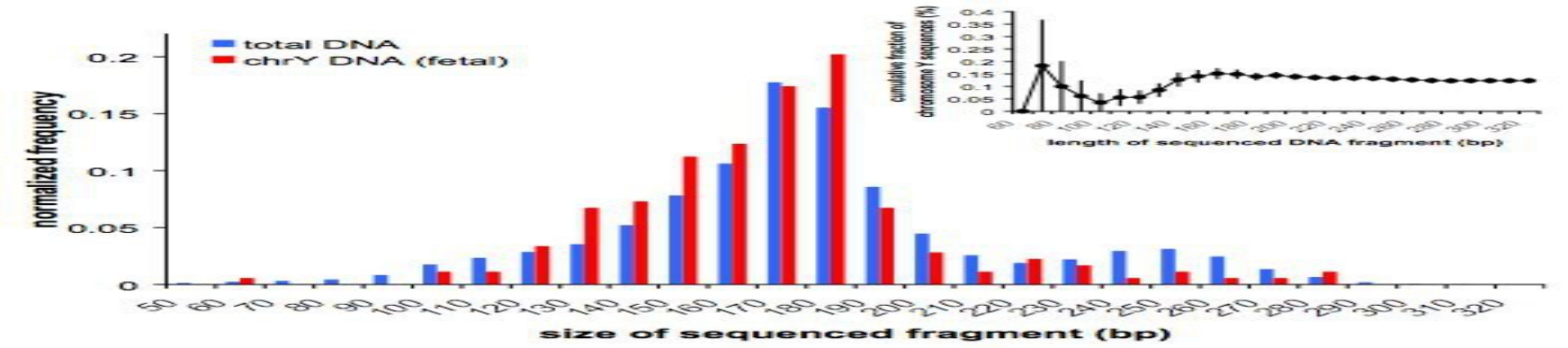
Fan et al. (2008) PNAS 105; 16266-16271.

Fraction of Fetal DNA in Maternal Blood with Gestational Age



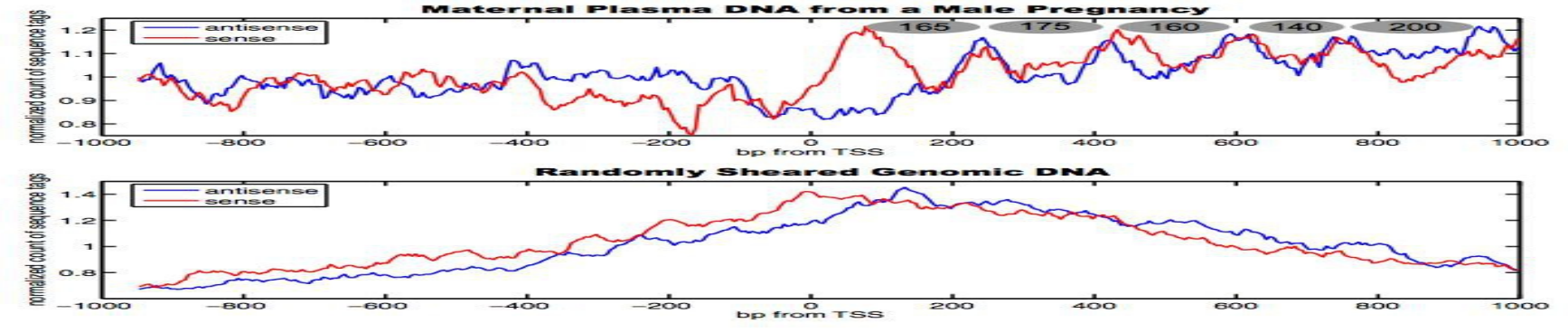
Fan et al. (2008) PNAS 105; 16266-16271.

Size of Fetal and Maternal DNA Fragments



Fan et al. (2008) PNAS 105; 16266-16271.

Presence of Fetal DNA as a distance from Transcription Start Site



Fan et al. (2008) PNAS 105; 16266-16271.

THE WHITE HOUSE

Office of the Press Secretary

For Immediate Release March 9, 2009

EXECUTIVE ORDER

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REMOVING BARRIERS TO RESPONSIBLE SCIENTIFIC RESEARCH INVOLVING HUMAN STEM CELLS

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

Section 1. Policy. Research involving human embryonic stem cells and human non-embryonic stem cells has the potential to lead to better understanding and treatment of many disabling diseases and conditions. Advances over the past decade in this promising scientific field have been encouraging, leading to broad agreement in the scientific community that the research should be supported by Federal funds.

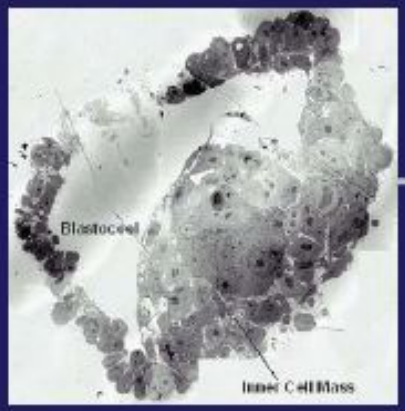
For the past 8 years, the authority of the Department of Health and Human Services, including the National Institutes of Health (NIH), to fund and conduct human embryonic stem cell research has been limited by Presidential actions. The purpose of this order is to remove these limitations on scientific inquiry, to expand NIH support for the exploration of human stem cell research, and in so doing to enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind.

Sec. 2. Research. The Secretary of Health and Human Services (Secretary), through the Director of NIH, may support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law.

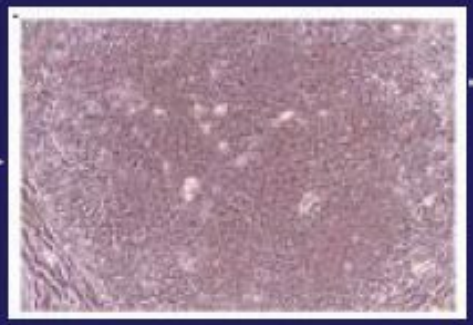
Sec. 3. Guidance. Within 120 days from the date of this order, the Secretary, through the Director of NIH, shall review existing NIH guidance and other widely recognized guidelines on human stem cell research, including provisions establishing appropriate safeguards, and issue new NIH guidance on such research that is consistent with this order. The Secretary, through NIH, shall review and update such guidance periodically, as appropriate.

Human Embryonic Stem Cells

Self-Renewing Source for the Scalable Manufacturing of Replacement Cells for Every Tissue in the Body

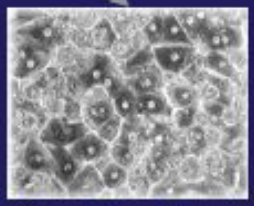


Blastocyst

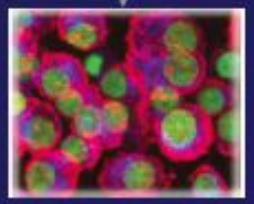


Human Embryonic Stem Cells

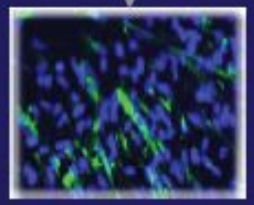
Large Characterized cGMP Banks



Hepatocytes



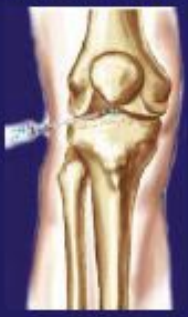
Chondrocytes



Osteoblasts

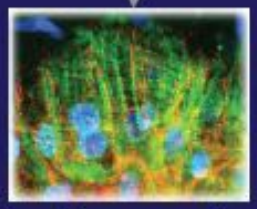
Dendritic Cells

Drug Discovery
Liver Failure



Arthritis

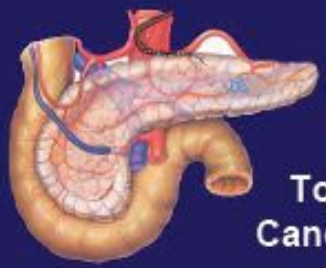
Islets



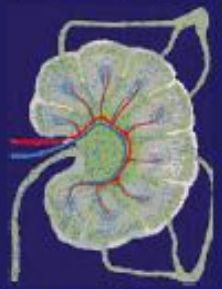
Cardiomyocytes

Neural Cells

Osteoporosis
And Bone
Fractures



Diabetes



Tolerance Induction
Cancer Immunotherapy

Heart Failure

Spinal Cord
Injury

geron