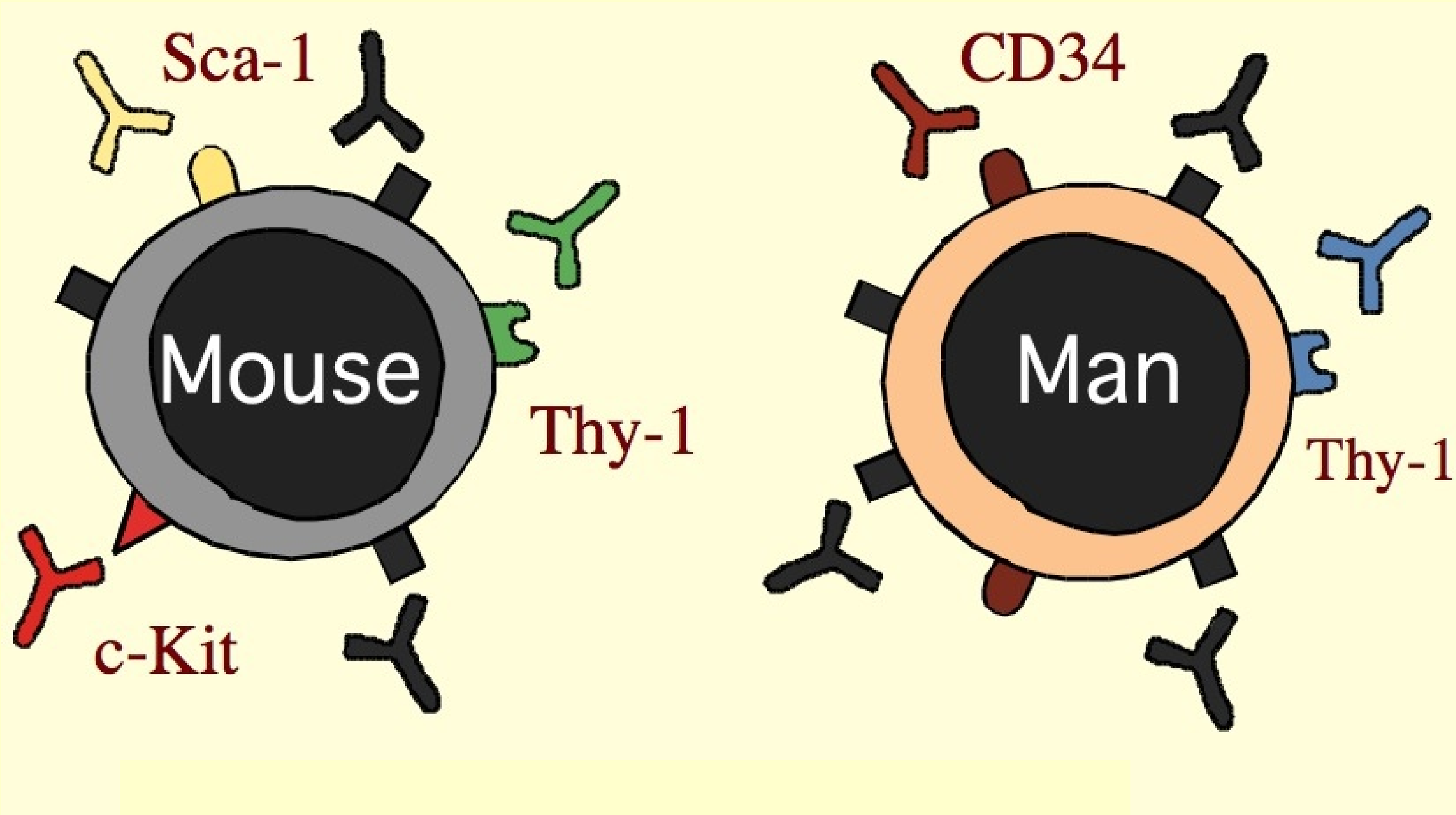
Genomics, Bioinformatics & Medicine

http://biochem158.stanford.edu/

Stem Cell Therapies

http://biochem158.stanford.edu/Stem%20Cell%20Therapies.html



Doug Brutlag
Professor Emeritus of Biochemistry & Medicine
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

California Institute for Regenerative Medicine

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

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/

ISSCR — International Society for Stem Cell Research

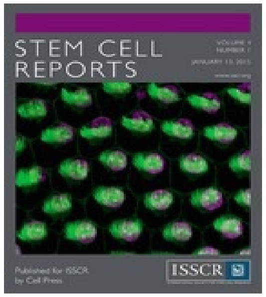
MEMBERS | PUBLIC | MEDIA

About Us | Annual Meeting | International Symposia | ISSCR Connect | Awards | Events | Publications | Resources | Donate

ISSCR CONNECT

Click here to LOGIN

Your online link to the latest stem cell research



Events

ISSCR 2015
ANNUAL MEETING
STOCKHOLM | SWEDEN
24-27 JUNE
Stockholmsmässan

For the Public

considering STEM CELL treatment?
www.closerlookatstemcells.org

What's New?

The Vancouver Sun, Op Ed: Gordie Howe's Pursuit of Stem Cell Treatment Abroad is an Awakening for Continued Education and Informed Choice
05 February, 2015
An opinion piece by Drs. Judy Illes and Fabio Rossi, available here. Dr. Illes is Canada research chair in neuroethics, professor of neurology and director of the National Core for Neuroethics, Faculty of Medicine, University of British Columbia. Dr. Rossi is Canada research chair in regenerative medicine and professor of Medical Genetics Biomedical Research Centre, UBNC. Both are investigators with the Stem Cell Network.
Read more

ISSCR 2015 Annual Meeting Abstract Submission Extended
05 February, 2015
Read more

Member Spotlight on Beck Tsai, PhD
26 January, 2015
CIRM Postdoctoral Scholar at the City of Hope National Medical Center and podcast enthusiast Dr. Becky Tsai aims to develop tools that contribute to improving patient diagnosis and treatment. She also aids in the personal development of Southern California's youth. Find out how and why in this month's Member Spotlight.
Read more

The International Society for Stem Cell Research Announces the 2015 Recipients of the McEwen Award for Innovation, the ISSCR-BD Biosciences Outstanding Young Investigator and the ISSCR Public Service Awards
20 January, 2015

International Society for Stem Cell Research

http://www.closerlookatstemcells.org/

Stem Cell Promise & Stem Cell Therapies

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

- Parkinson's Disease with iPSCs (Michael J. Fox Foundation)
- Spinal Cord Injury with human embryonic stem cells (hESCs)
- Sickle Cell, Thalassemias, hemophilia and other blood diseases with iPSCs (Matthew Porteus, Stanford)
- Bone Marrow Transplants (BMT) & hematopoietic stem cell therapy (HCT) (Judith Shizuru)
  - Lymphomas and thymomas
  - Hematopoietic cells
  - Metastatic cancers of other origins
- Autoimmune Diseases with hematopoietic stem cells (HSCs)
  - Rheumatoid arthritis
  - Systemic Lupus Erythematosus
  - Type 1 diabetes mellitus
  - Multiple sclerosis
  - Pernicious anemia

Fetal Cell Transplants Can Cure Parkinson’s

David Iverson’s Frontline Film: My Father, My Brother and Me

Geron Stem Cell Therapy

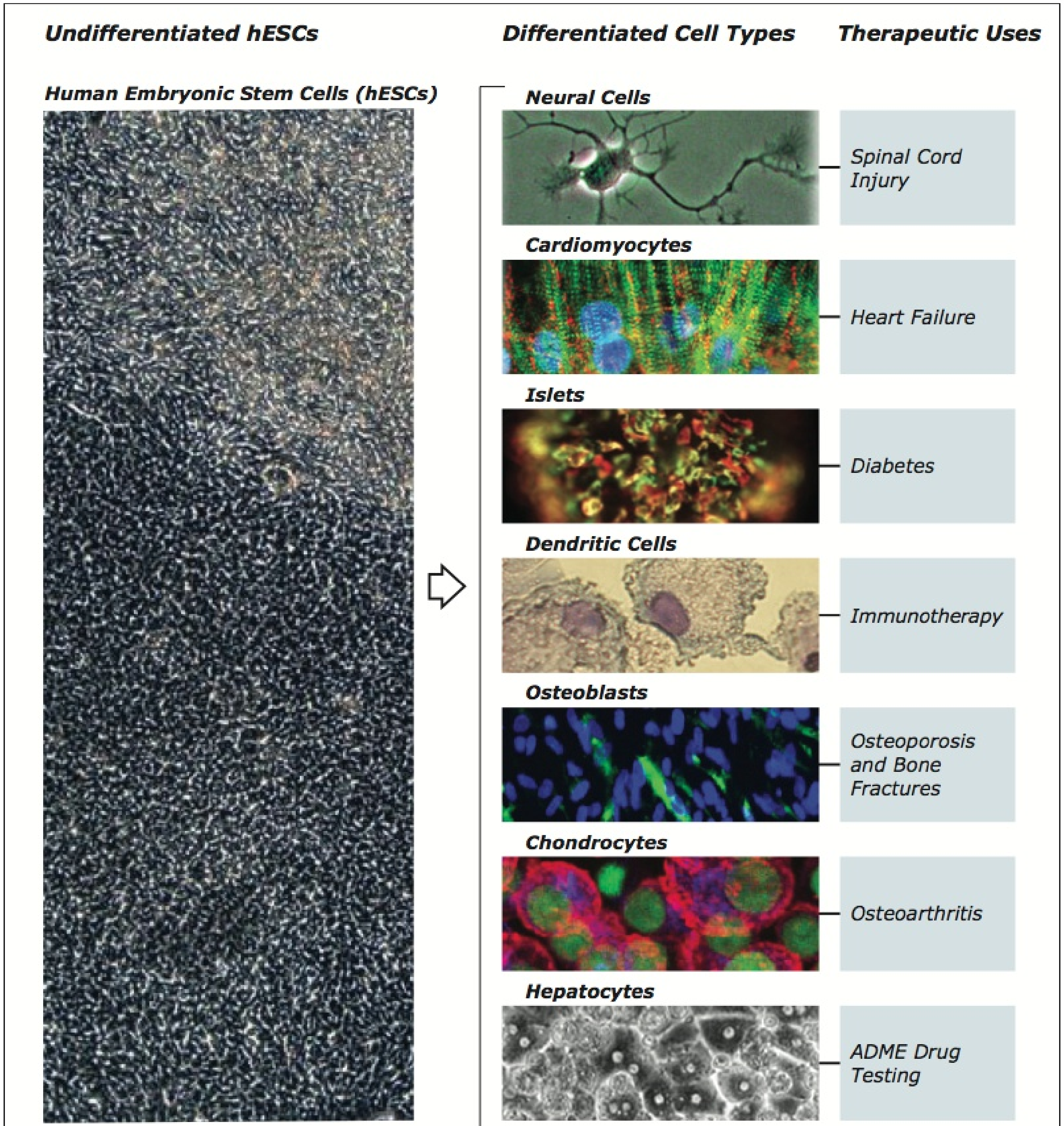
geron

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

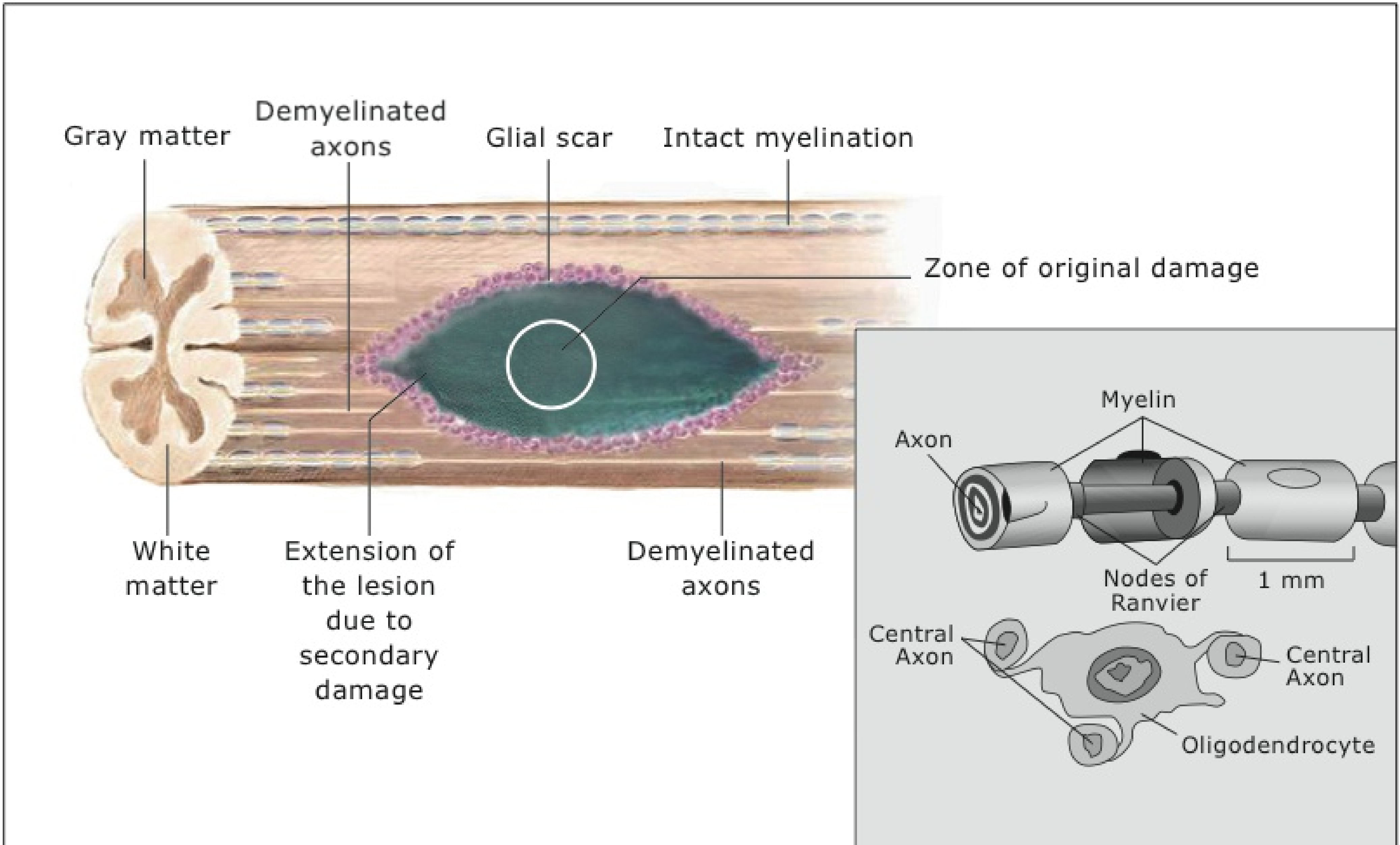
Human Embryonic Stem Cells



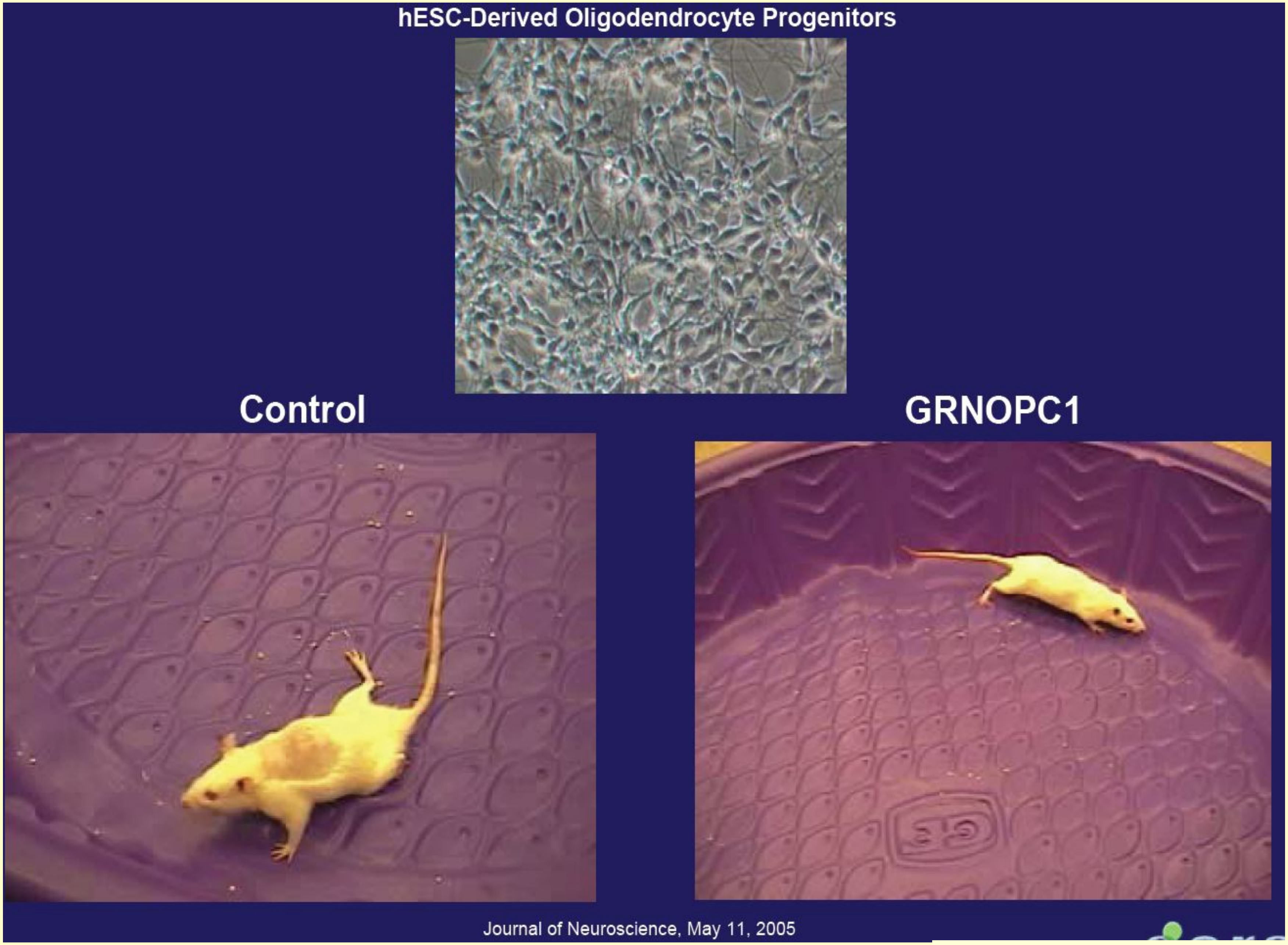
Geron has developed proprietary processes to convert hESCs into therapeutic cells.

Tom Okarma - Geron

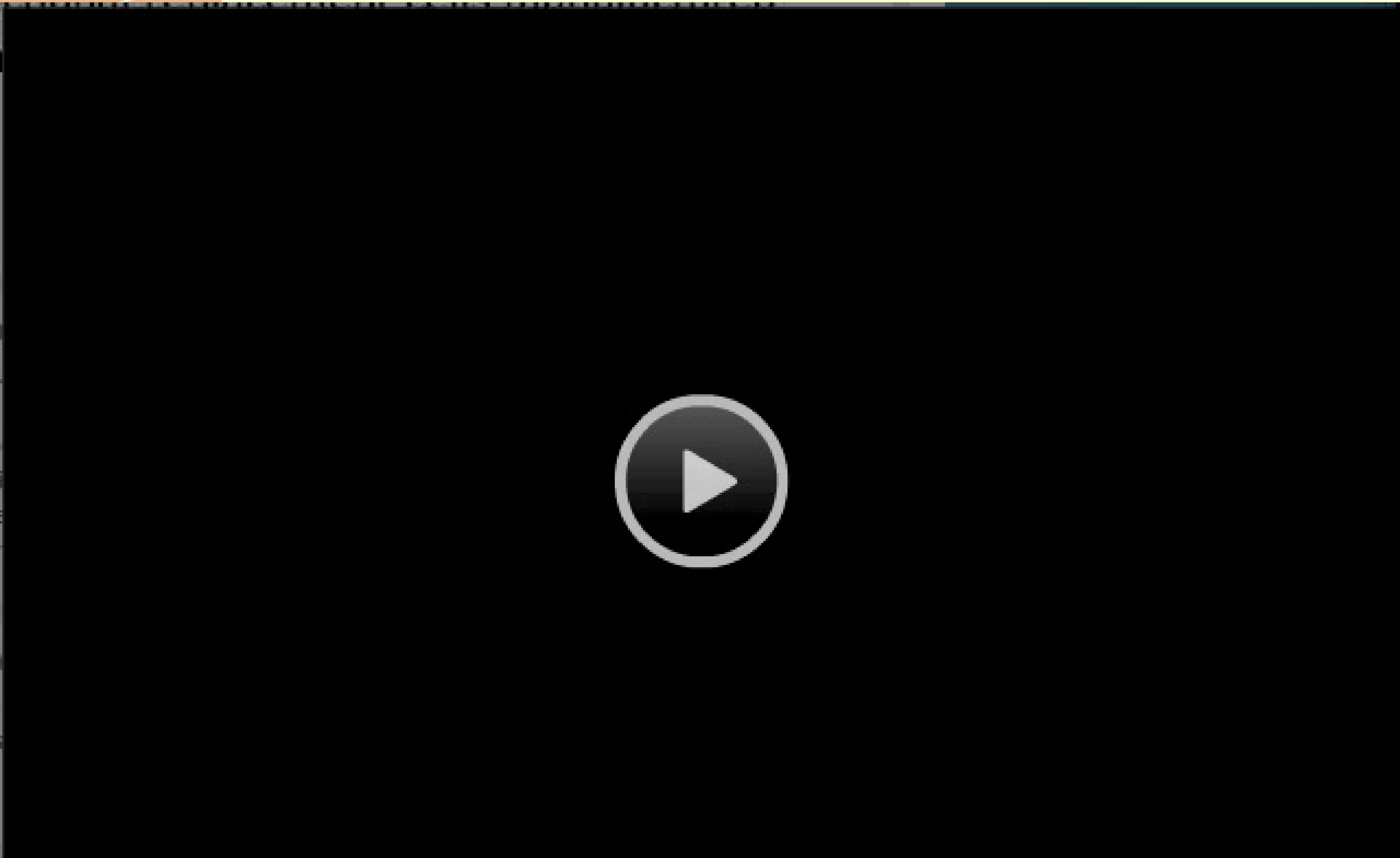
Spinal Cord Injury
Pathology at the Lesion



GRNOPC1 Improves Locomotor Behavior after Spinal Cord Injury



GRNOPC1 Improves Locomotor Behavior after 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

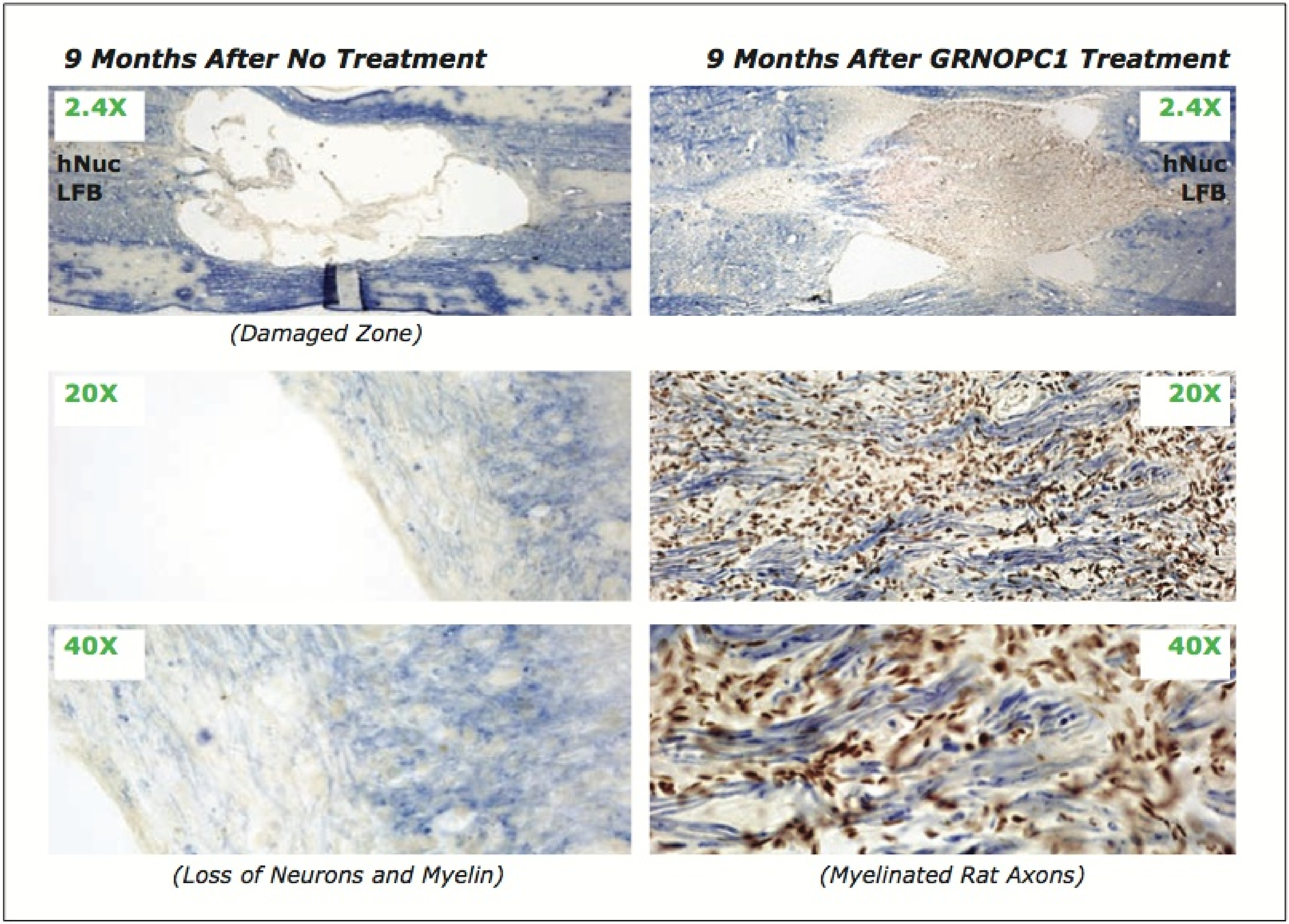
1. Human Embryonic Stem Cells (hESCs)
2. Oligodendrocyte Progenitor Cells (GRNOPC1)
3. Preclinical Safety Studies
4. Clinical Program
5. Manufacturing
6. Intellectual Property

Video of GRNOPC1 Manufacturing

News Release

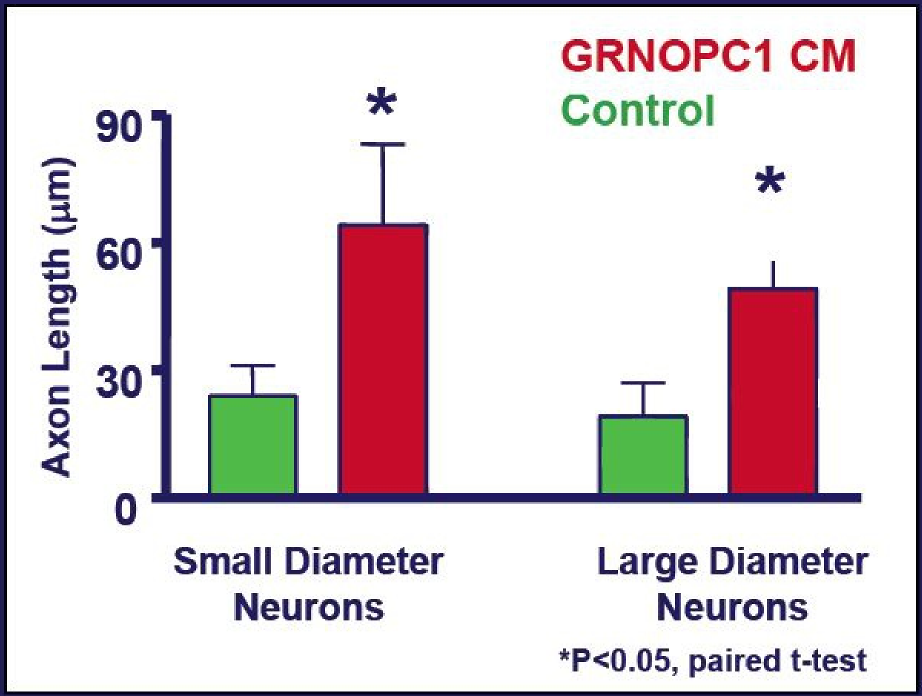
Geron Initiates Clinical Trial of Human Embryonic Stem Cell-Based Therapy

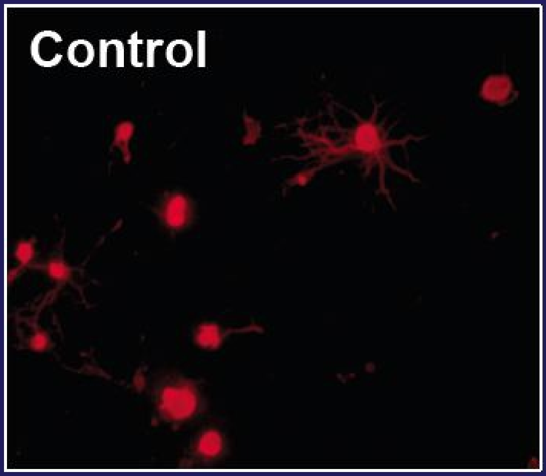
GRNOPC1 Induces Remyelination after Spinal Cord Lesions in Rodents

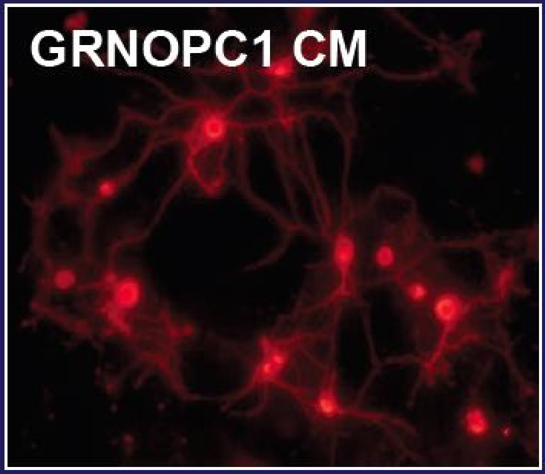


Tom Okarma - Geron

GRNOPC1 Promotes Neural Outgrowth







Concentrations of Neurotrophic Proteins in GRNOPC1 Conditioned Medium

Midkine 7.7 ± 2.3 ng/ml (n = 6)
neurite growth-promoting factor 2

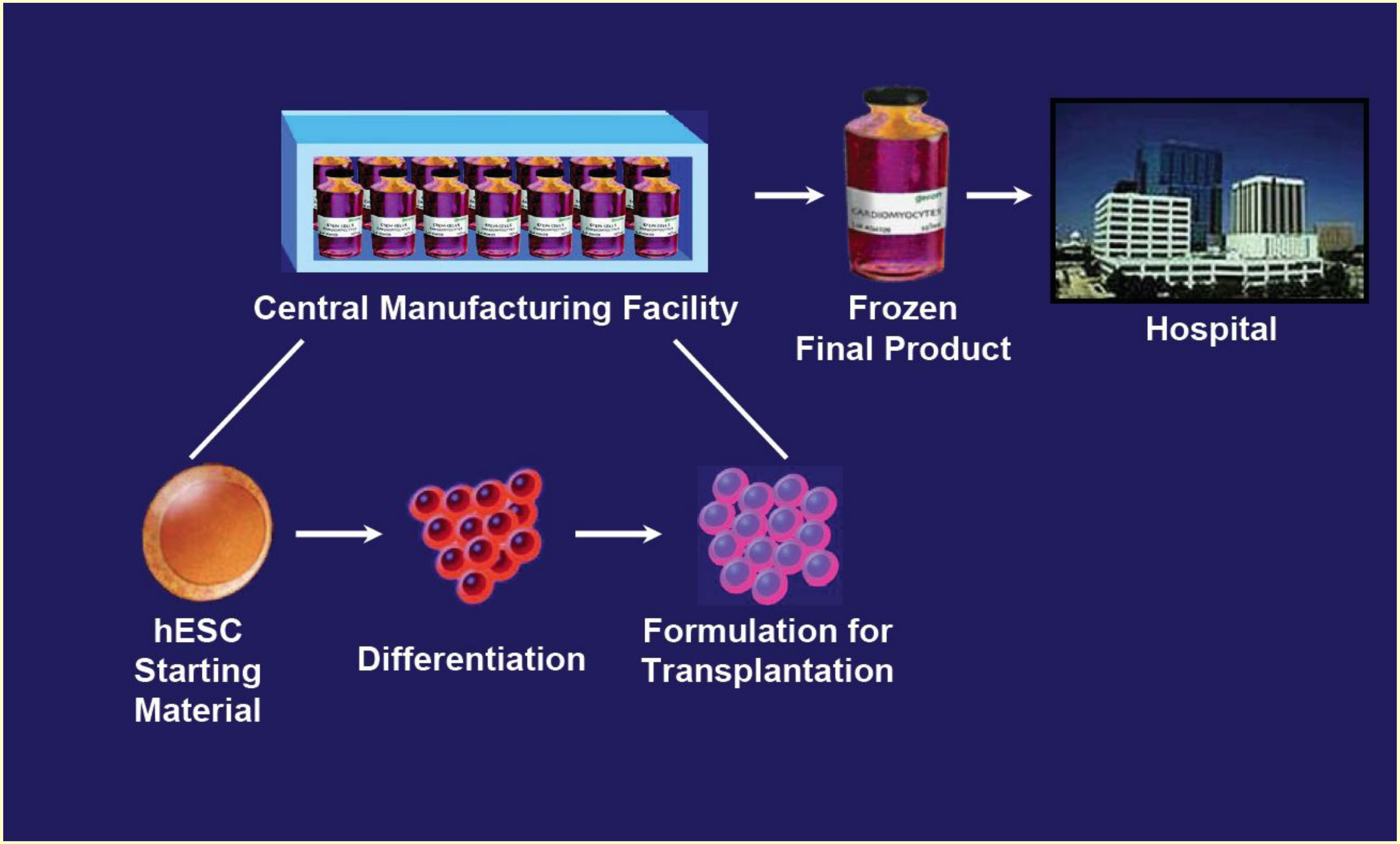
Activin A 13.2 ± 1.6 ng/ml (n = 6)
growth & differentiation factor in TGF family

BDNF 48 ± 13 pg/ml (n = 9)
brain-derived neurotrophic factor

TGF-β2 95 ± 18 pg/ml (n = 9)
transforming growth factor-beta 2

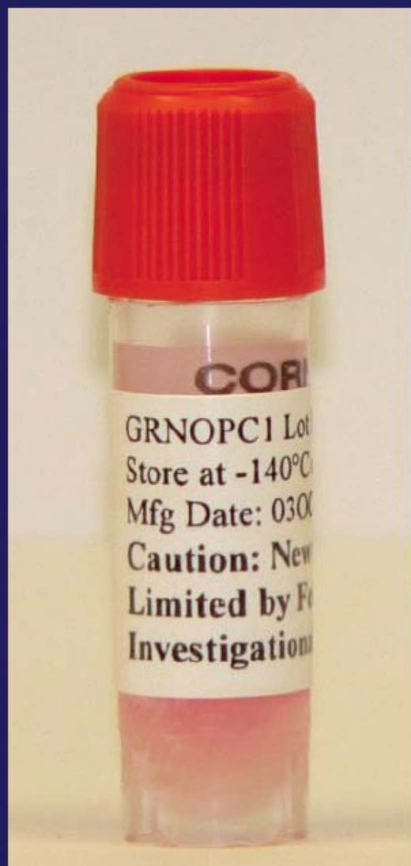
HGF 1.2 ± 0.5 ng/ml (n = 5)
hepatocyte growth factor

Human Embryonic Stem Cell (hESC) Based Therapy



Tom Okarma - Geron

Geron Oligodendrocyte Progenitor Cells GRNOPC1



GRNOPC1

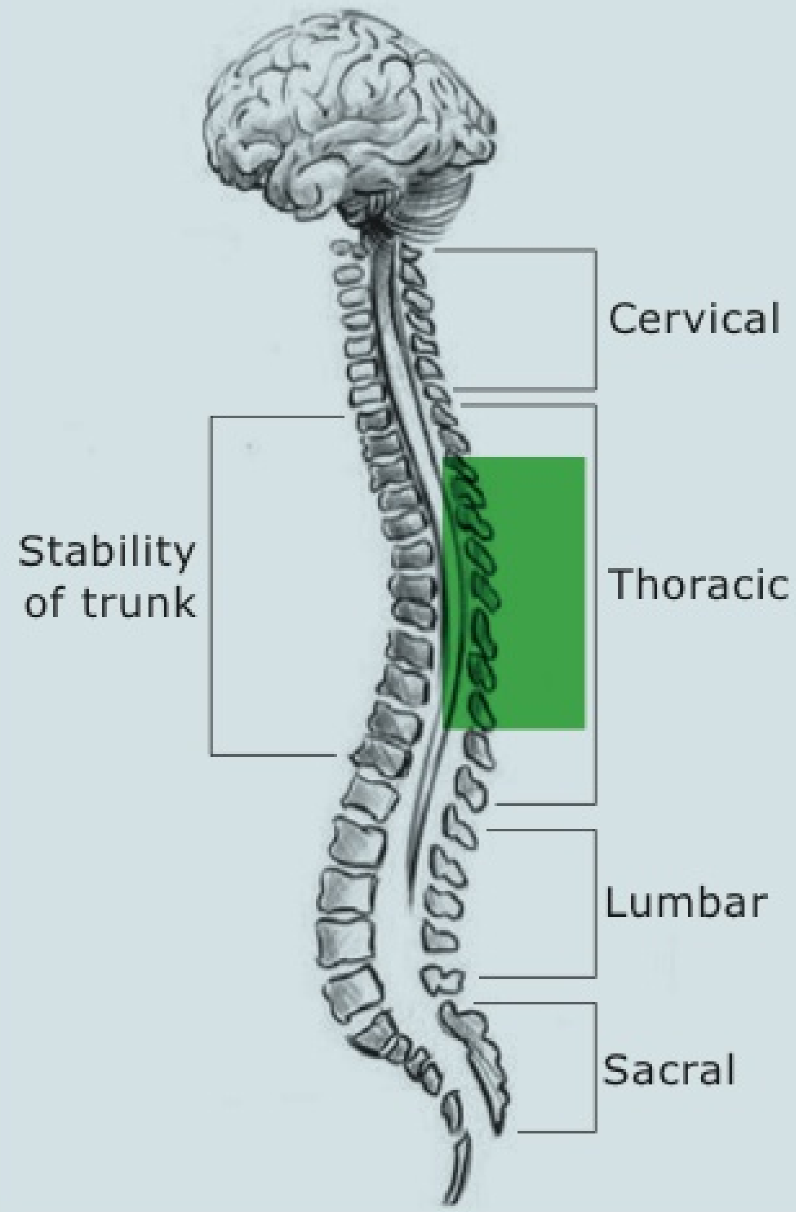
- Cryopreserved Allogeneic Cell Population
- Derived from Human Embryonic Stem Cells
- Characterized Composition of Cells
- Contain Oligodendrocyte Progenitor Cells
- Produces Neurotrophic Factors
- Induces Myelination of Denuded Axons

Intended Application

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

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.

Comment Period Extended to 3/23/2015 for Notice of Proposed Rulemaking (NPRM) for FDAAA 801 and NIH Draft Reporting Policy for NIH-Funded Trials

Find Studies | **About Clinical Studies** | **Submit Studies** | **Resources** | **About This Site**

ClinicalTrials.gov currently lists 184,118 studies with locations in all 50 states and in 187 countries.

Text Size

Search for Studies

Example: "Heart attack" AND "Los Angeles"

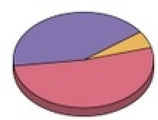
stem cells | Search

Advanced Search | See Studies by Topic
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 (42%)
- Both U.S. and Non-U.S. (6%)

Total N = 34,400 studies
Data as of February 12, 2015

- See more trends, charts, and maps

For Patients & Families

- How to find studies
- See studies by topic
- Learn about clinical studies
- Learn more…

For Researchers

- How to submit studies
- Download content for analysis
- About the results database
- Learn more…

For Study Record Managers

- Why register?
- How to register study records
- FDAAA 801 Requirements
- Learn more…

Learn More

- ClinicalTrials.gov Online Training
- Glossary of common site terms

For the Press

Using our RSS Feeds

Deborah Zarin, Director, Hum Bio Grad.

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

Clinical Trials Database

https://clinicaltrials.gov/

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

Example: "Heart attack" AND "Los Angeles"

Search for studies: Search

Advanced Search | Help | Studies by Topic | Glossary

Comment Period Extended to 3/23/2015 for Notice of Proposed Rulemaking (NPRM) for FDAAA 801 and NIH Draft Reporting Policy for NIH-Funded Trials

Find Studies **About Clinical Studies** **Submit Studies** **Resources** **About This Site**

Home > Find Studies > Search Results Text Size

4831 studies found for: stem cells

Modify this search | How to Use Search Results

List | **By Topic** | **On a Map** | **Search Details**

+ Show Display Options Download Subscribe to RSS

Include only open studies Exclude studies with unknown status

Rank	Status	Study
1	Unknown †	**Stem Cell Educator Therapy in Alopecia Areata** **Condition:** Alopecia Areata **Intervention:** Device: Stem Cell Educator
2	Unknown †	**Tissue Distribution of F18-FDG Labelled Autologous Bone Marrow Derived Stem Cells in Patients With Type 2 DM** **Condition:** Type 2 Diabetes Mellitus

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

Clinical Trials Database

https://clinicaltrials.gov/

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

Example: "Heart attack" AND "Los Angeles"

Search for studies: Search

Advanced Search | Help | Studies by Topic | Glossary

Comment Period Extended to 3/23/2015 for Notice of Proposed Rulemaking (NPRM) for FDAAA 801 and NIH Draft Reporting Policy for NIH-Funded Trials

Find Studies **About Clinical Studies** **Submit Studies** **Resources** **About This Site**

Home > Find Studies > Search Results Text Size

1900 studies found for: stem cells | Open Studies

Modify this search | How to Use Search Results

List **By Topic** **On a Map** **Search Details**

+ Show Display Options Download Subscribe to RSS

Include only open studies Exclude studies with unknown status

Rank	Status	Study
1	Unknown †	**Stem Cell Educator Therapy in Alopecia Areata** **Condition:** Alopecia Areata **Intervention:** Device: Stem Cell Educator
2	Unknown †	**Tissue Distribution of F18-FDG Labelled Autologous Bone Marrow Derived Stem Cells in Patients With Type 2 DM** **Condition:** Type 2 Diabetes Mellitus

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

Clinical Trials Database

https://clinicaltrials.gov/

14 studies found for: Open Studies | Exclude Unknown | spinal cord injury | stem cells

Modify this search | How to Use Search Results

List | By Topic | On a Map | Search Details

+ Show Display Options

Download   Subscribe to RSS

☑ 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	**Neural Stem Cell Transplantation in Traumatic Spinal Cord Injury** **Condition:** Spinal Cord Injury **Intervention:** Biological: Autologous Stem Cell Transplantation
3	Recruiting	**Safety and Efficacy of Autologous Mesenchymal Stem Cells in Chronic Spinal Cord Injury** **Condition:** Spinal Cord Injury **Intervention:** Procedure: Mesenchymal stem cell transplantation
4	Recruiting	**Nerve Regeneration-guided Collagen Scaffold and Mesenchymal Stem Cells Transplantation in Spinal Cord Injury Patients** **Condition:** Spinal Cord Injury

Clinical Trials of Hematopoietic Cell Transplantation

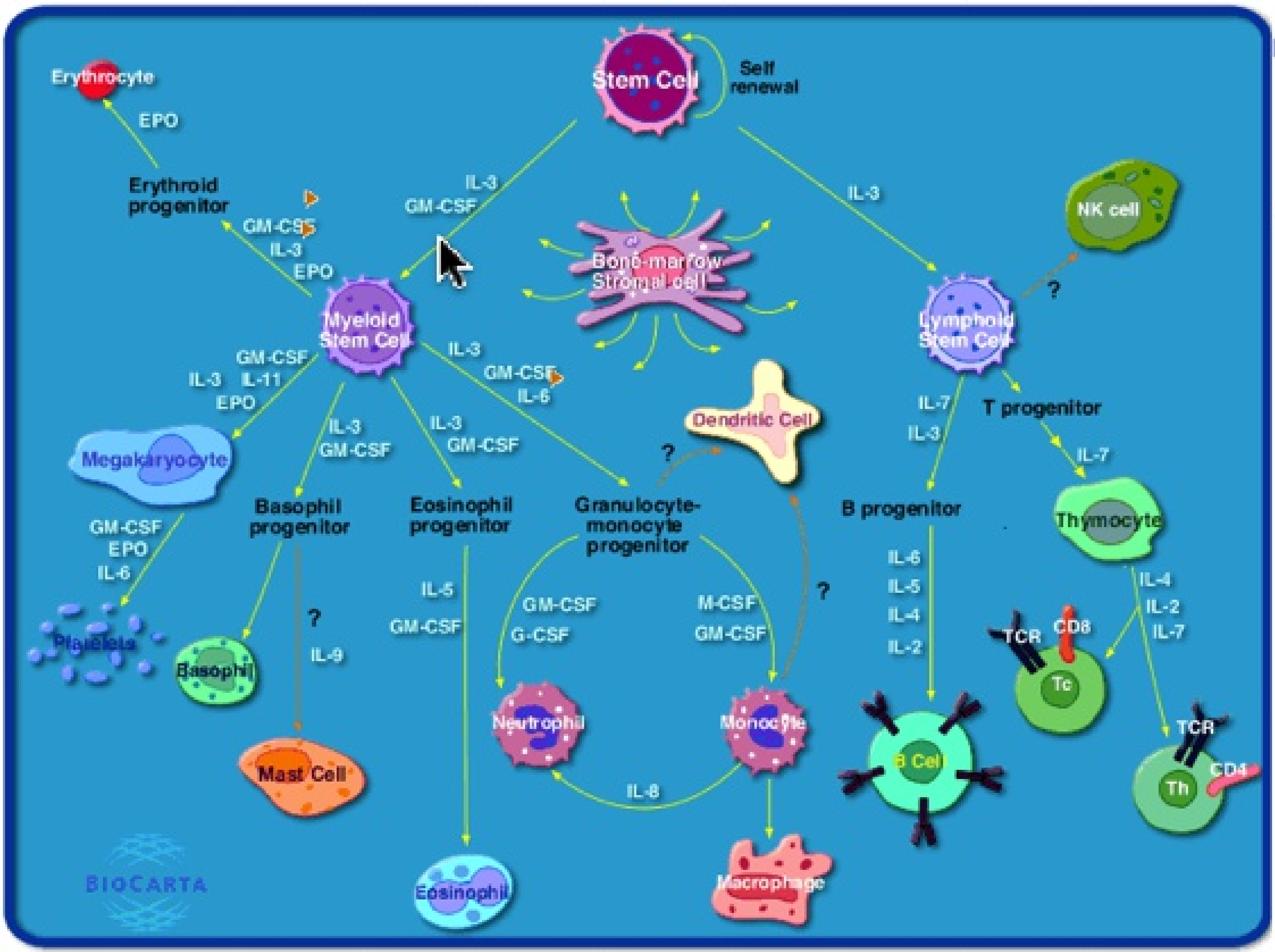
Judith A. Shizuru, M.D., Ph.D.

Division of Blood and Marrow Transplantation

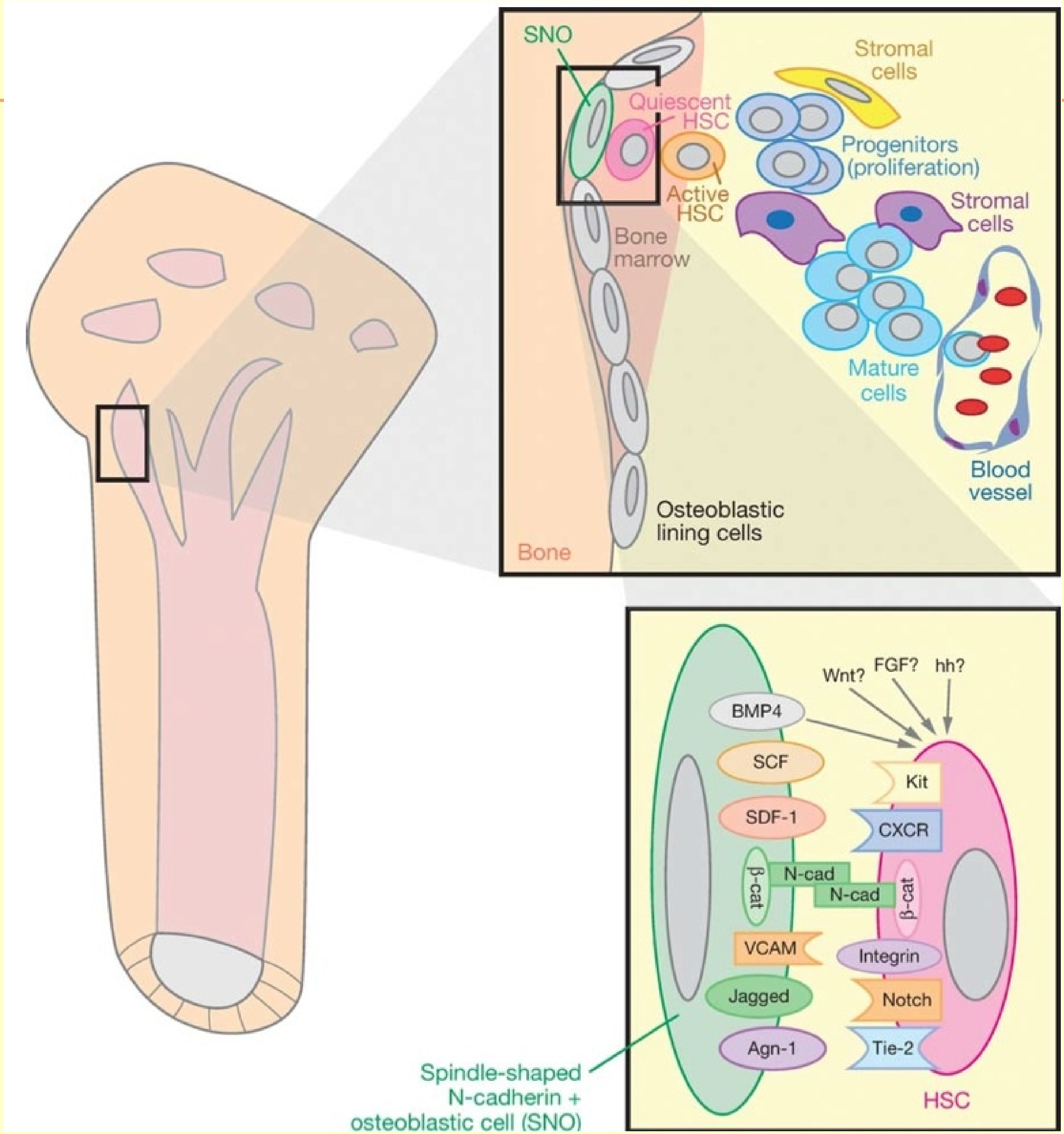
Stanford University Medical Center

Hematopoiesis

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



Hematopoietic Stem Cell Niche



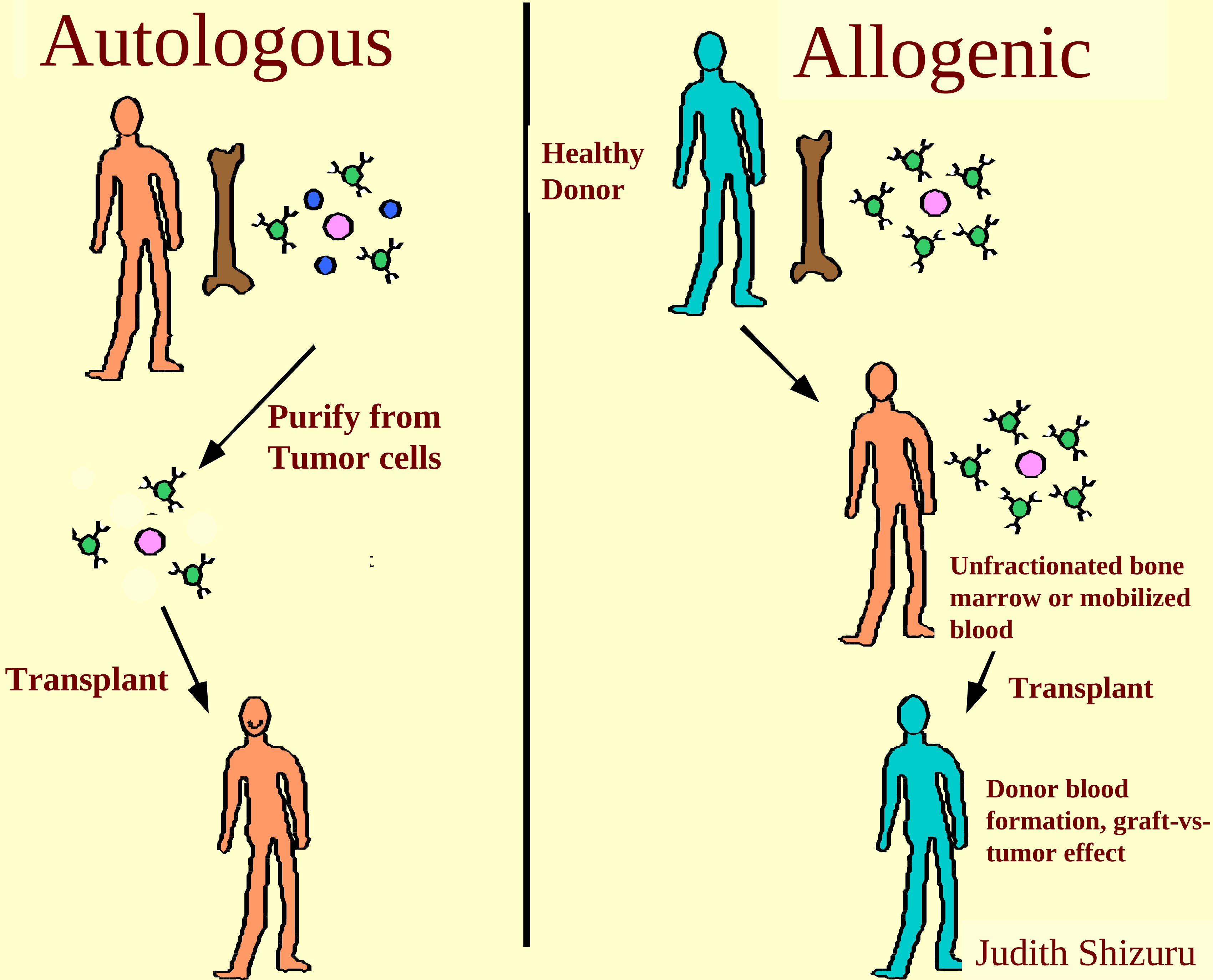
Li and Xie, Ann. Rev. Dev. Biol. 2005, 605-663

Bone Marrow Transplants to Cure Lymphomas/Thymomas

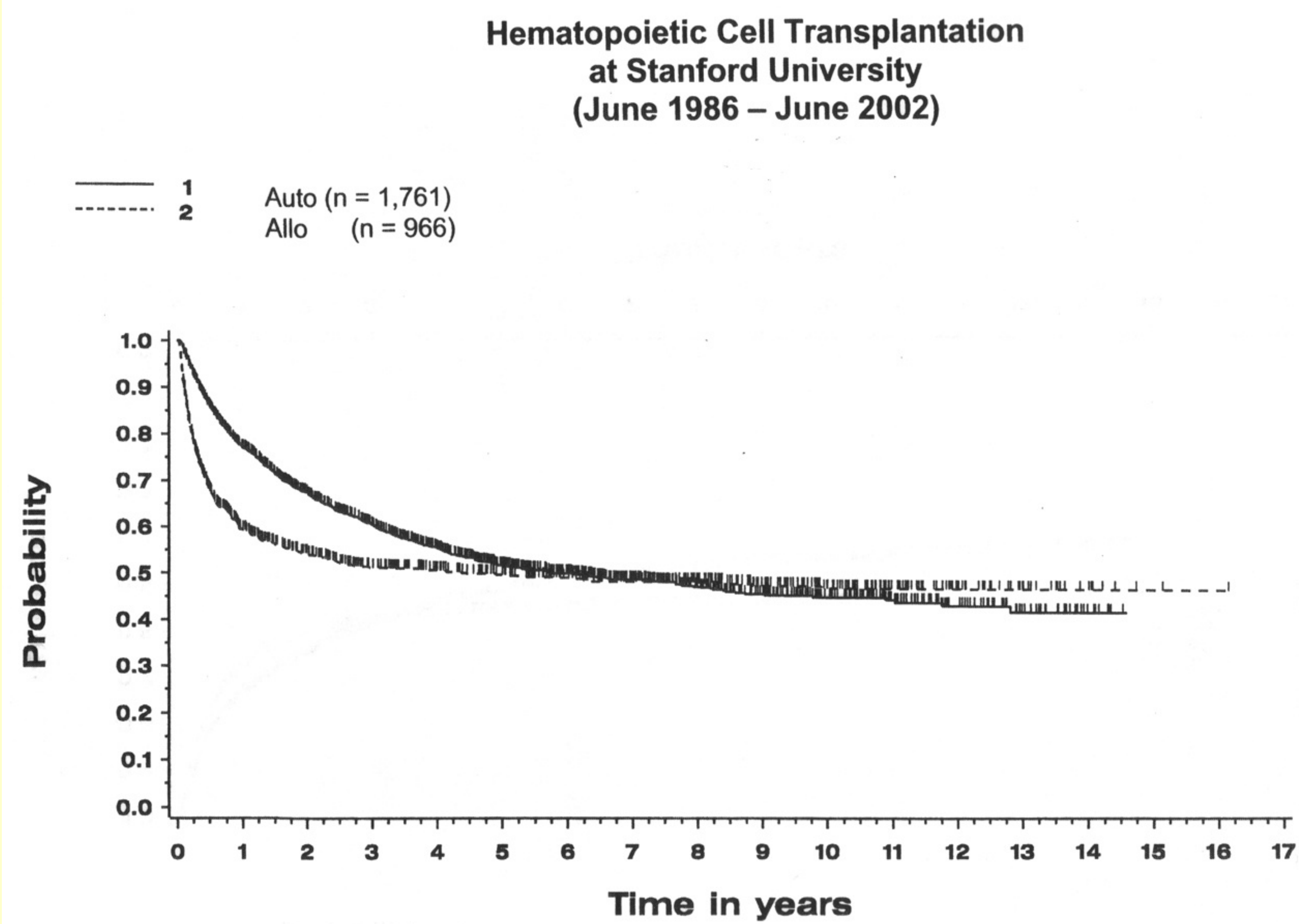
- Whole body irradiation (WBI) to remove endogenous immune system and tumor
  - Also total lymphoid irradiation (TLI) with antithymocyte serum (ATS)
- Injection of bone marrow from a well matched donor to re-establish immune system
- Regulation of immune response to prevent graft versus host reaction.
- Autologous donation possible if one can purify and remove tumor cells, enriching for stem cells > 10^6 fold
- 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.

Judith Shizuru

Autologous vs. Allogeneic Transplants



Judith Shizuru



Judith Shizuru

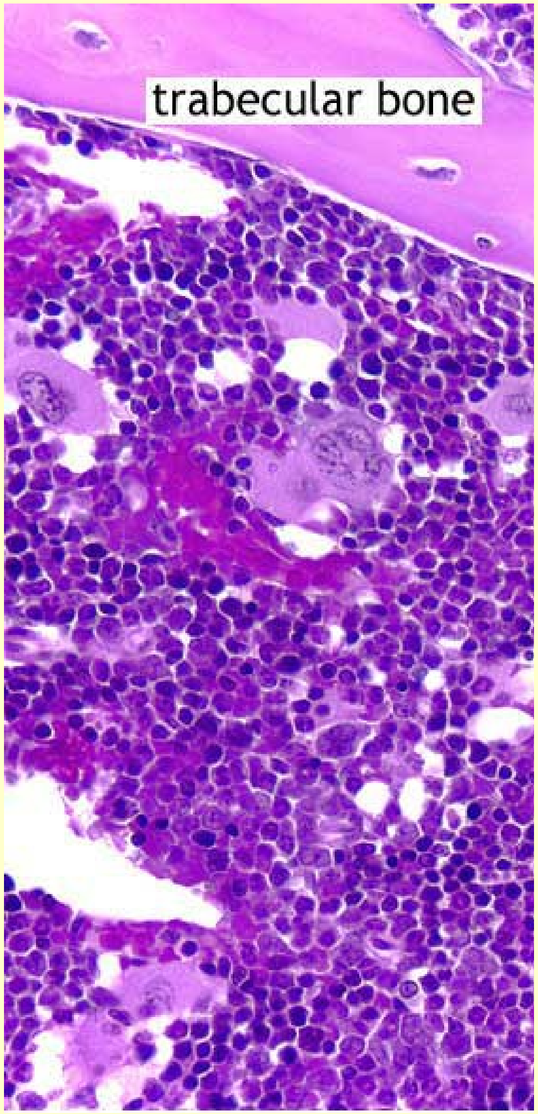
Complications of Allogeneic Transplants

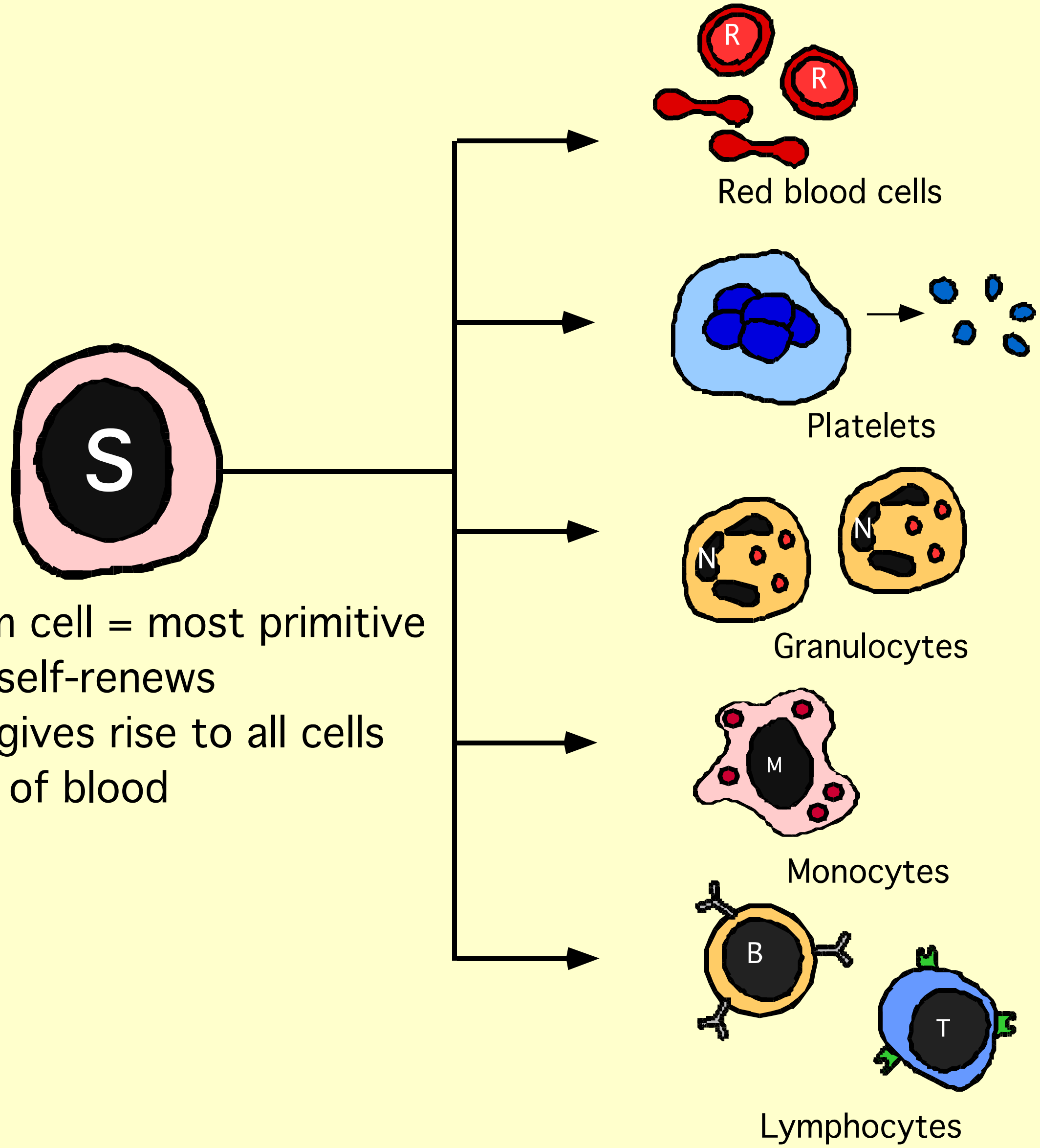
Transplant related mortality = 10 - 15%

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

Judith Shizuru

Cells of the Bone Marrow





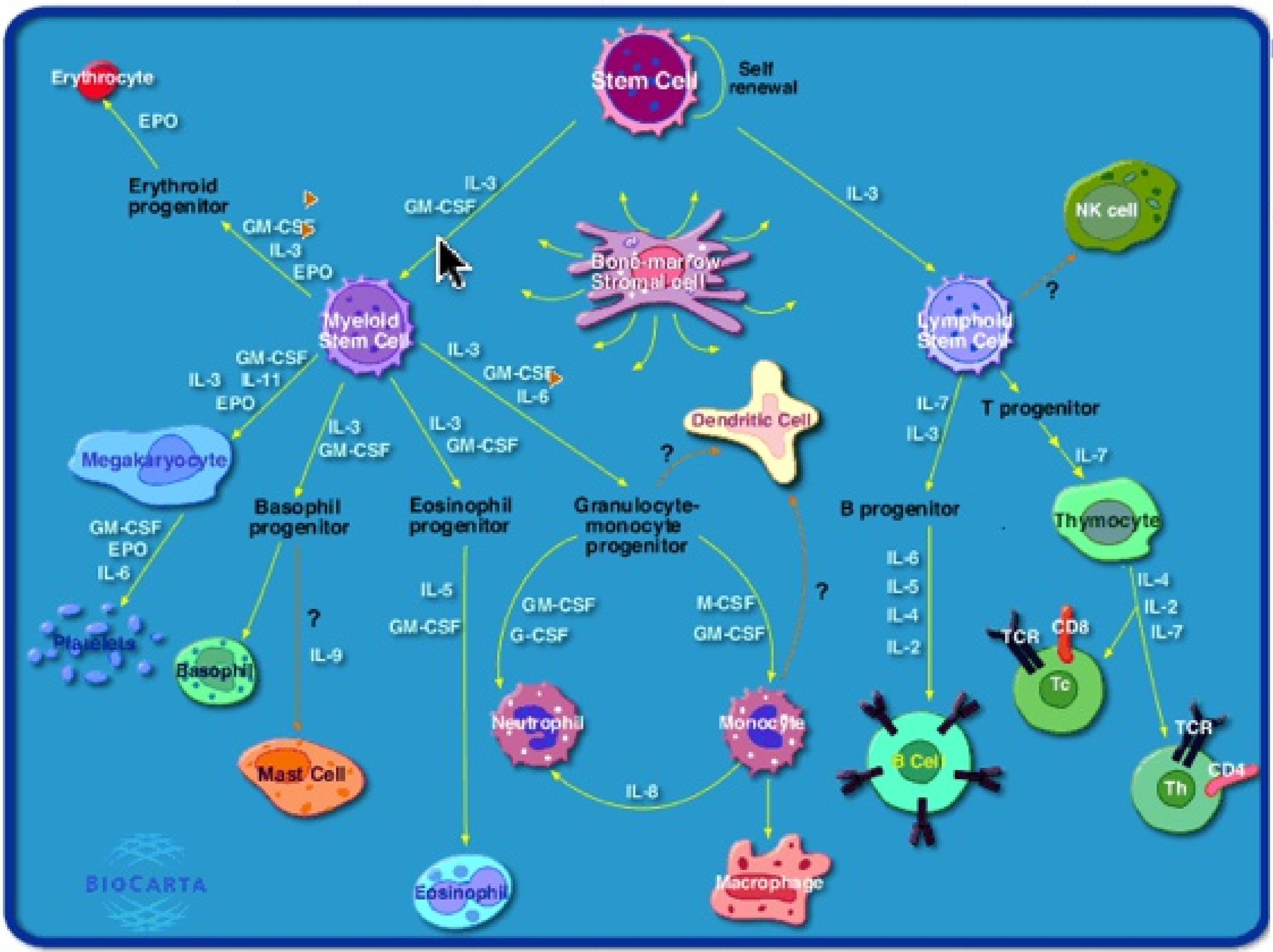
Stem cell = most primitive

- self-renews
- gives rise to all cells of blood

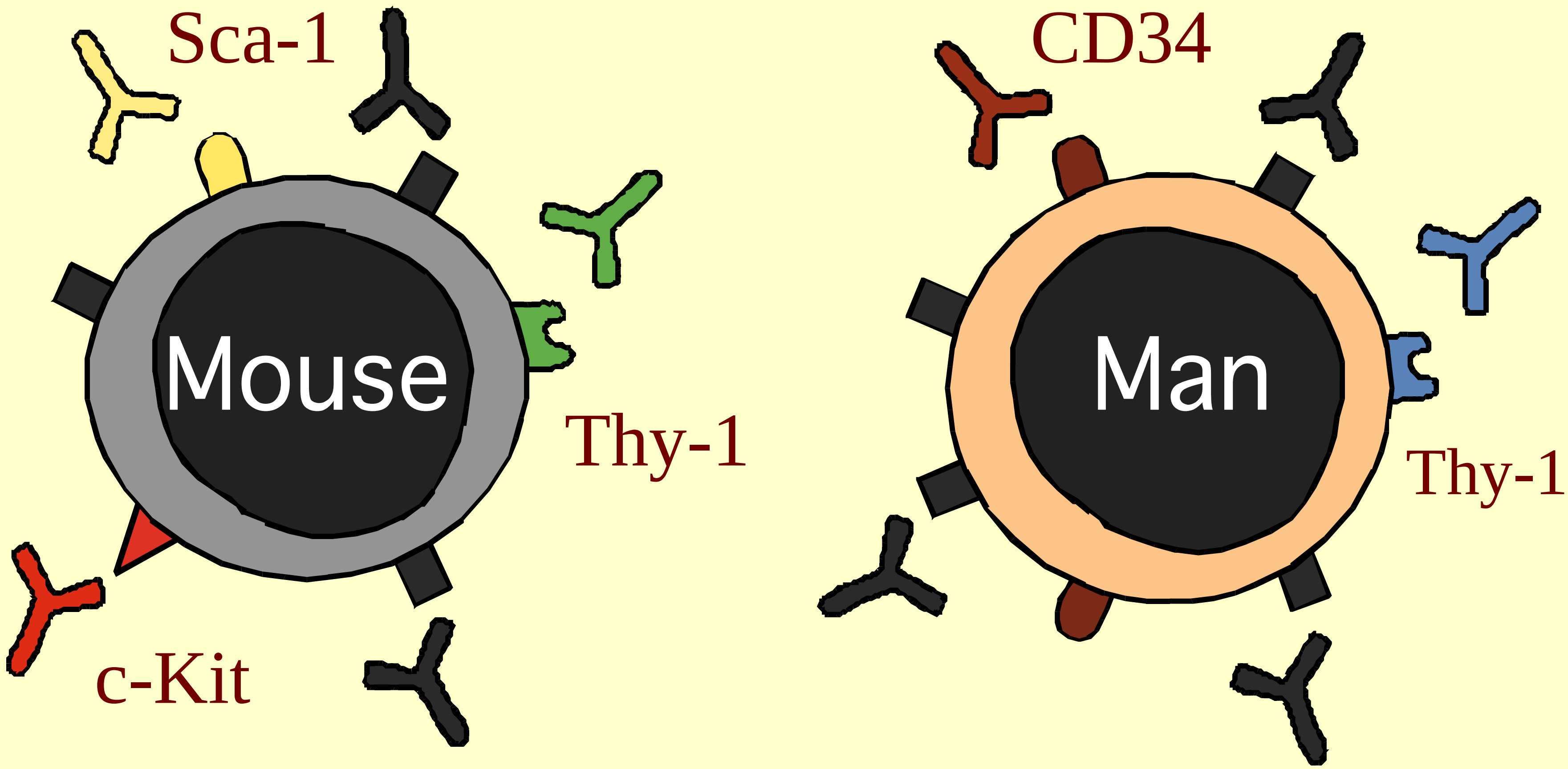
Judith Shizuru

Regulation of hematopoiesis by cytokines

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



Isolation of Hematopoietic Stem Cells

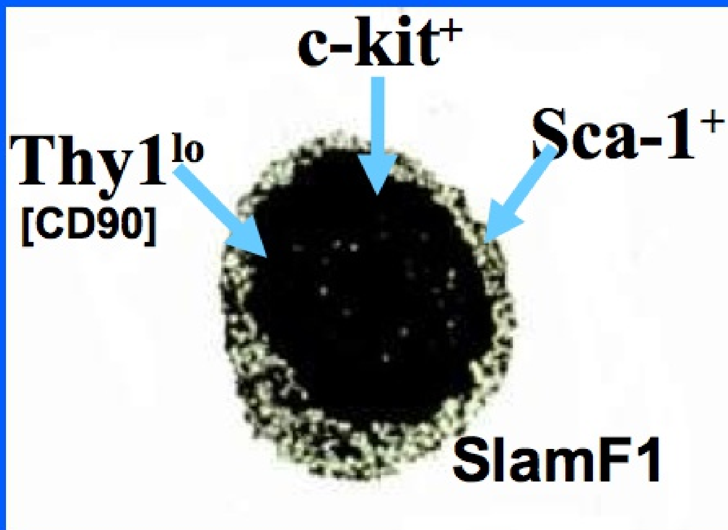


Lineage: T, B, Macrophage/Monocyte
Granulocyte, Red Blood Cells

Judith Shizuru

Isolation of Hematopoietic Stem Cells

MOUSE



Negative for:

B220

Mac-1

Gr-1

CD3, 4, 8

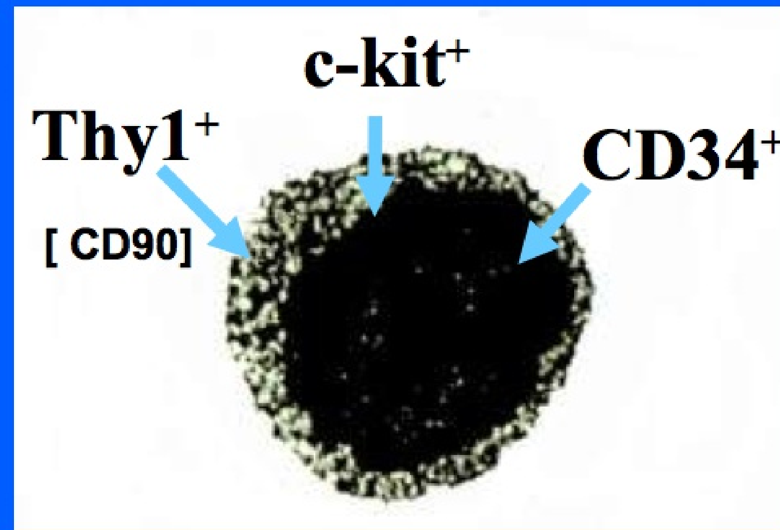
Ter119

Flk2

CD34

Spangrude, Muller, Heimfeld

MAN



Negative for:

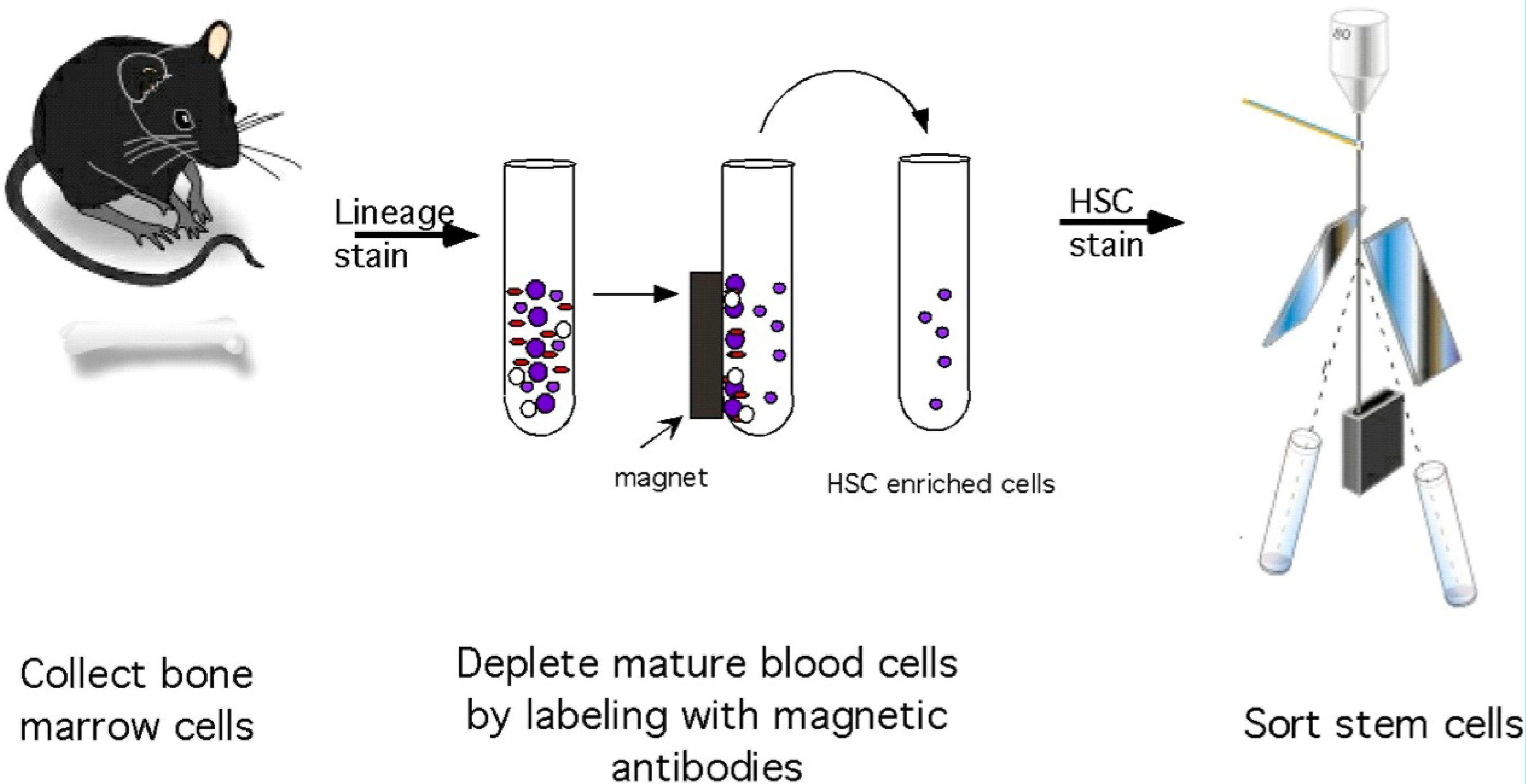
CD10
CD14
CD15
CD16
CD19
CD20
CD 38

CD 3,4,8
Glycophorin A

Baum, Buckle, Peault, Tsukamoto

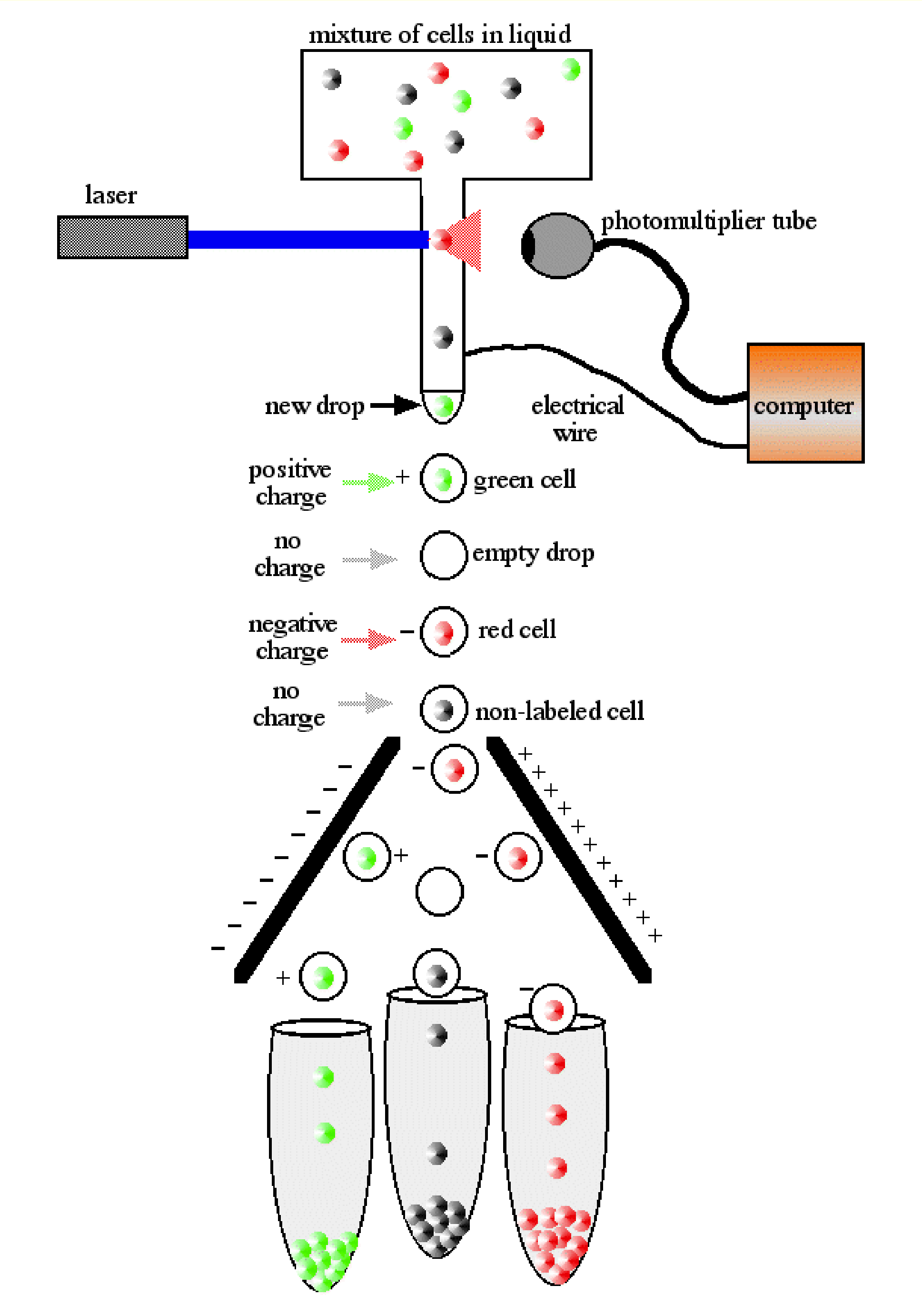
Courtesy Irv Weissman

Isolation of Pure Hematopoietic Stem Cells

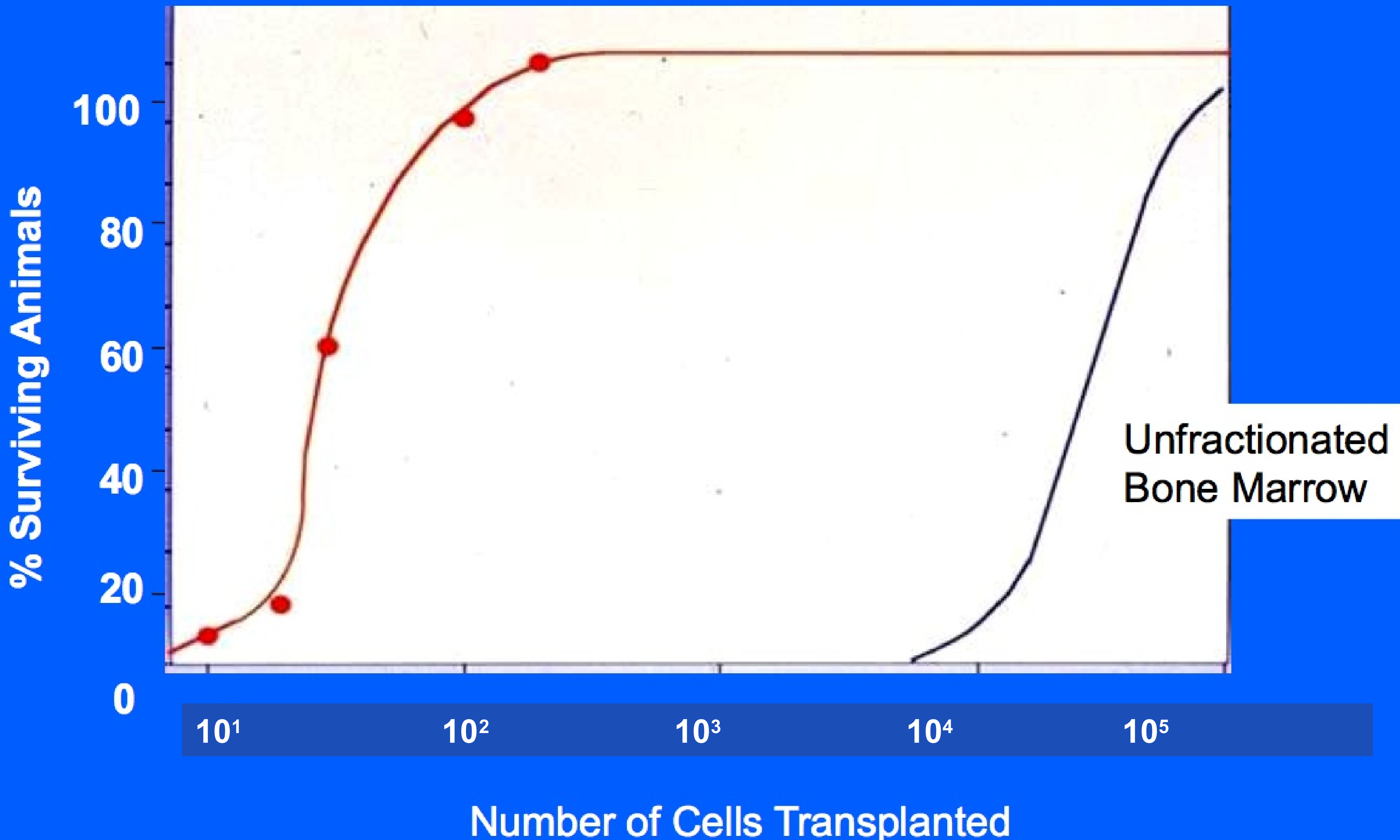


Courtesy Irv Weissman

Fluorescent Activated Cell Sorter (FACS) Herzenberg & Herzenberg

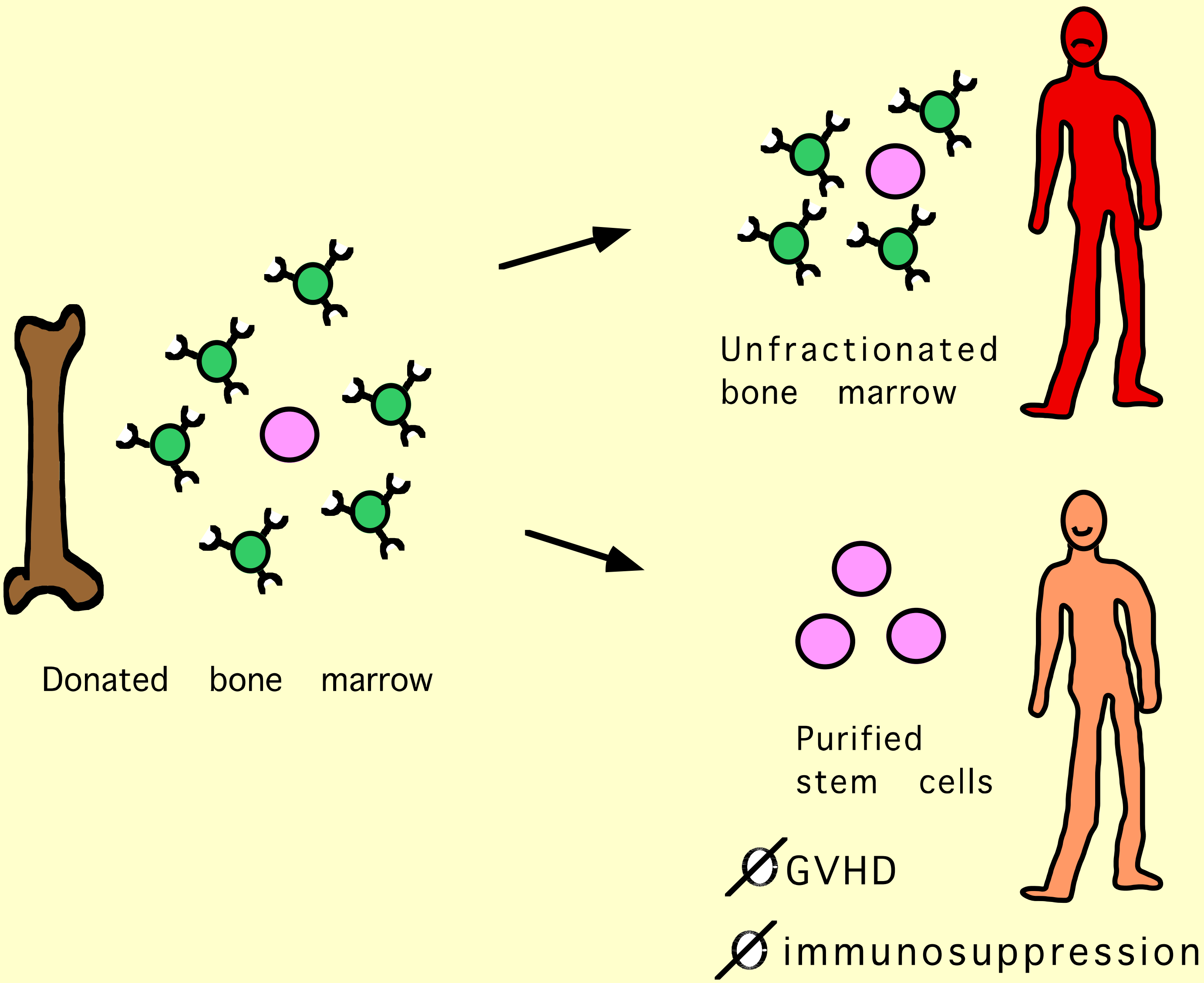


Purified Hematopoetic Stem Cells are 2,000 Times More Effective in Transplants



Courtesy Irv Weissman

Why Transplant Purified Allogeneic HSCs?



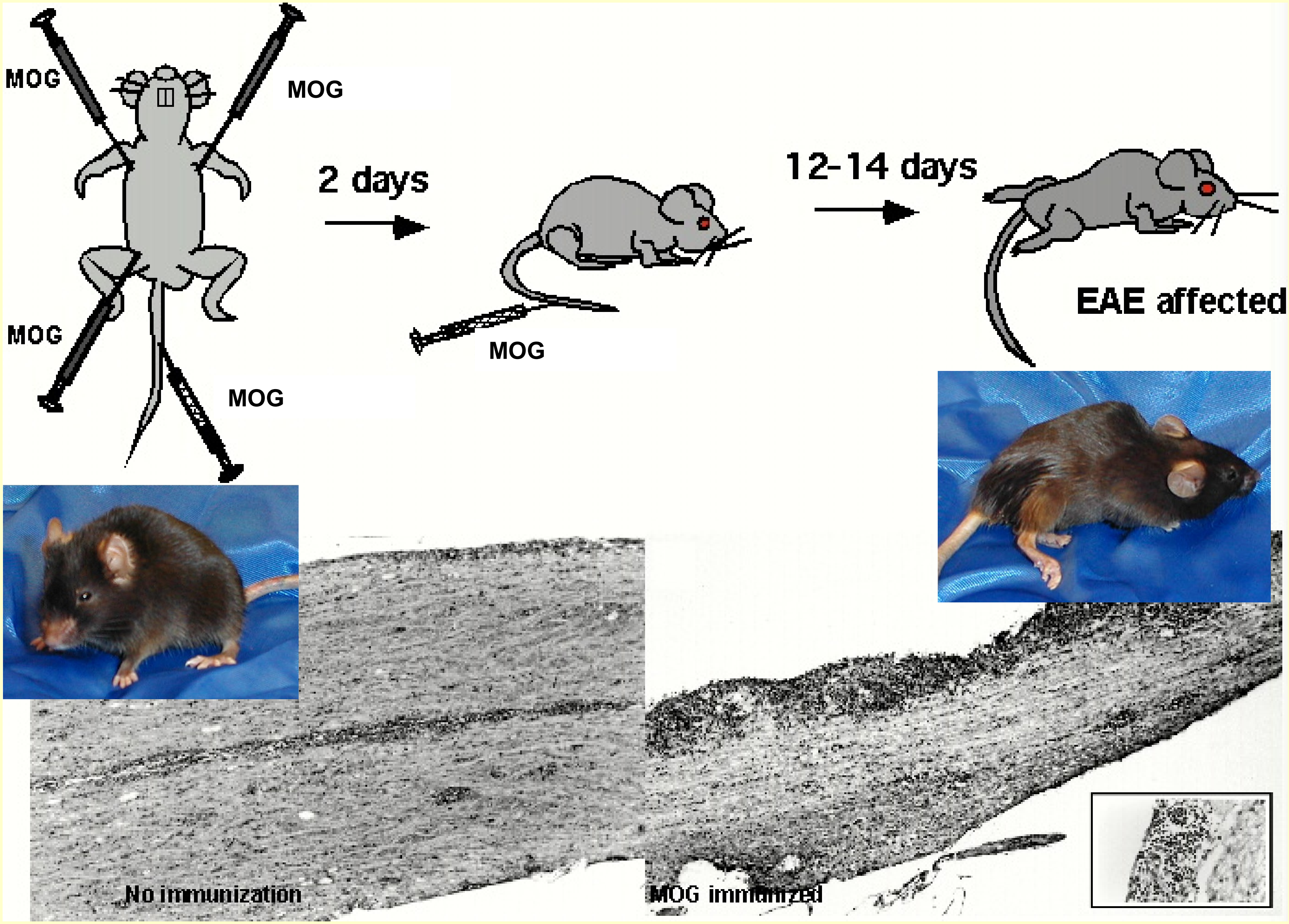
Judith Shizuru

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 does chemotherapy that kills tumor and immune system.
  - Autogenic hematopoietic stem cell transplants recover patient's immune system.

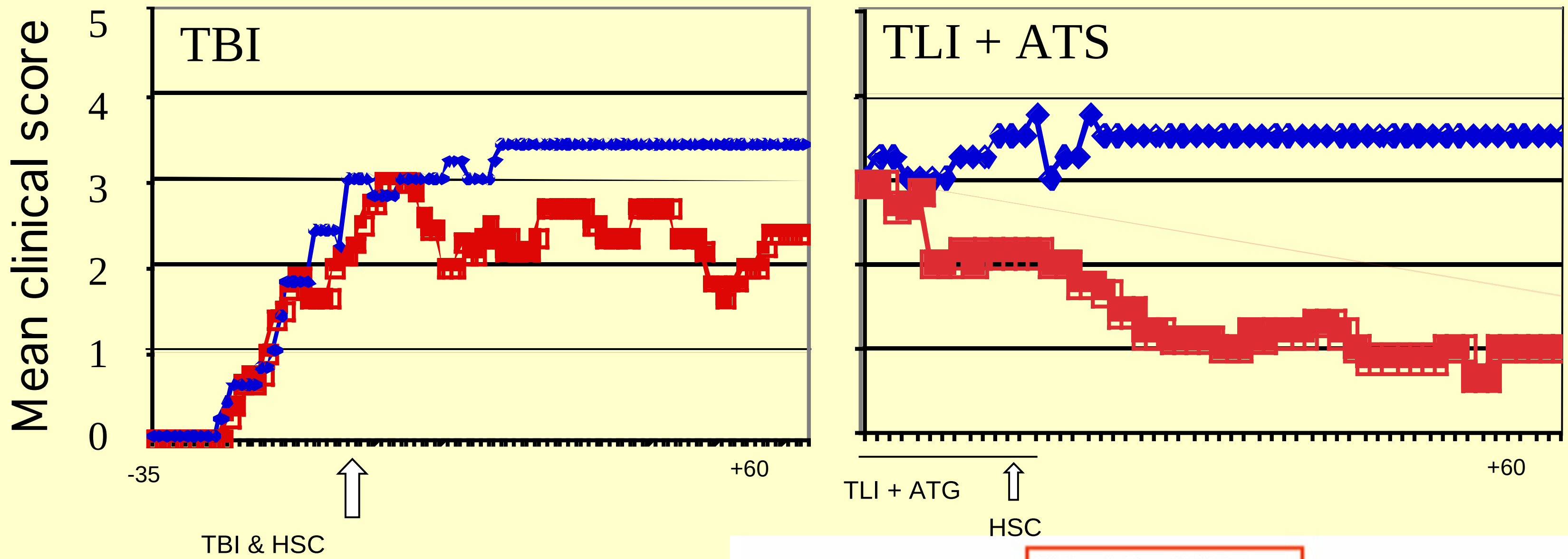
Judith Shizuru

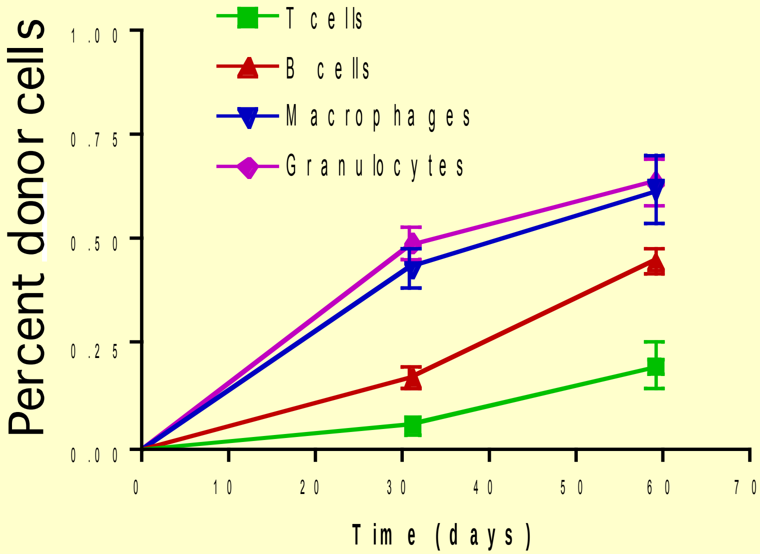
Experimental Autoimmune Encephalomyelitis (EAE) Model for Multiple Sclerosis in Mice

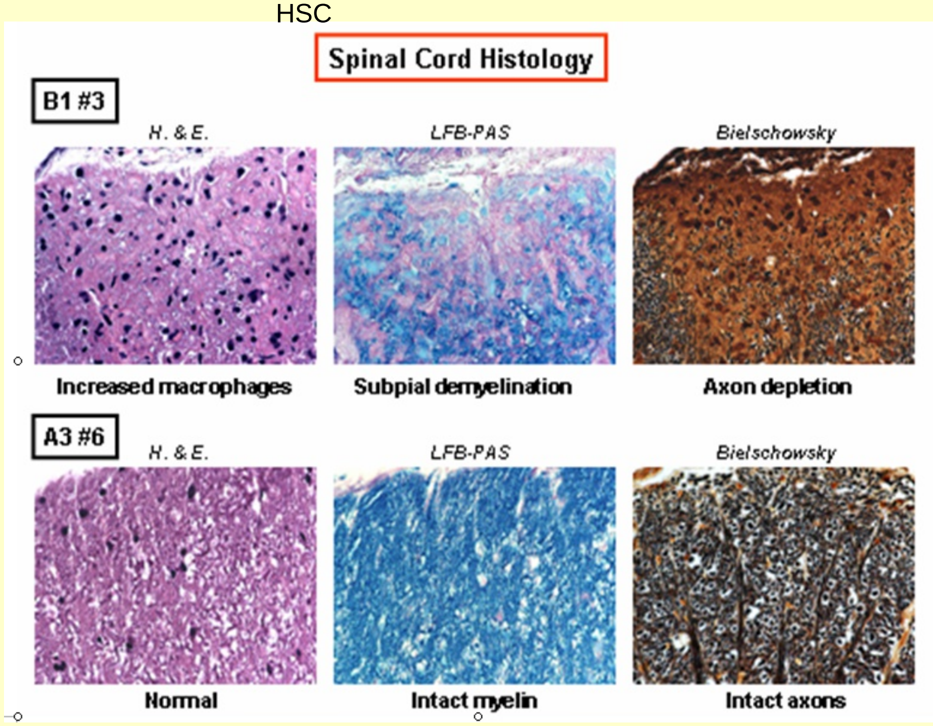


Judith Shizuru

Partial Chimerism Results in Disease Amelioration

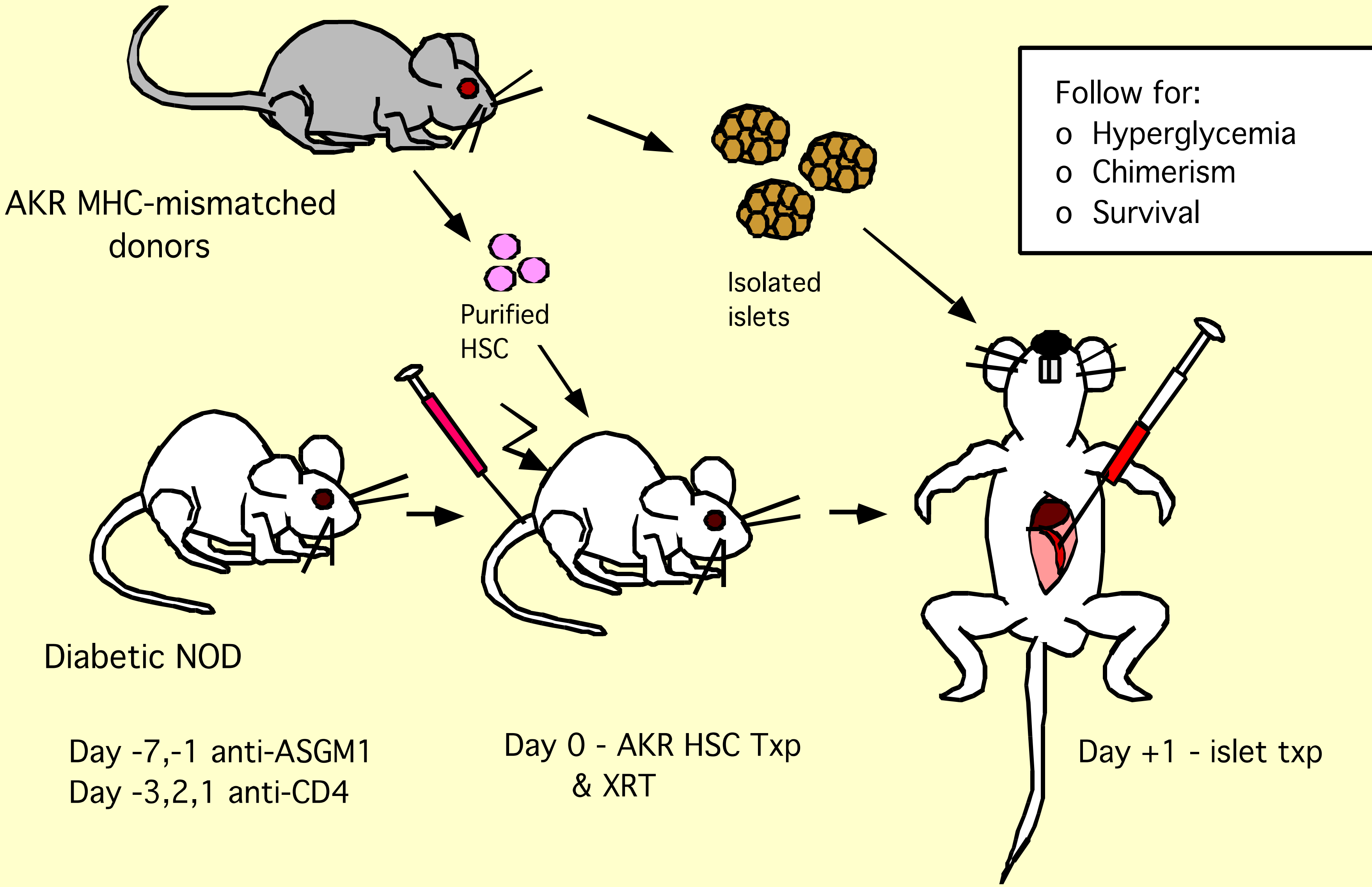






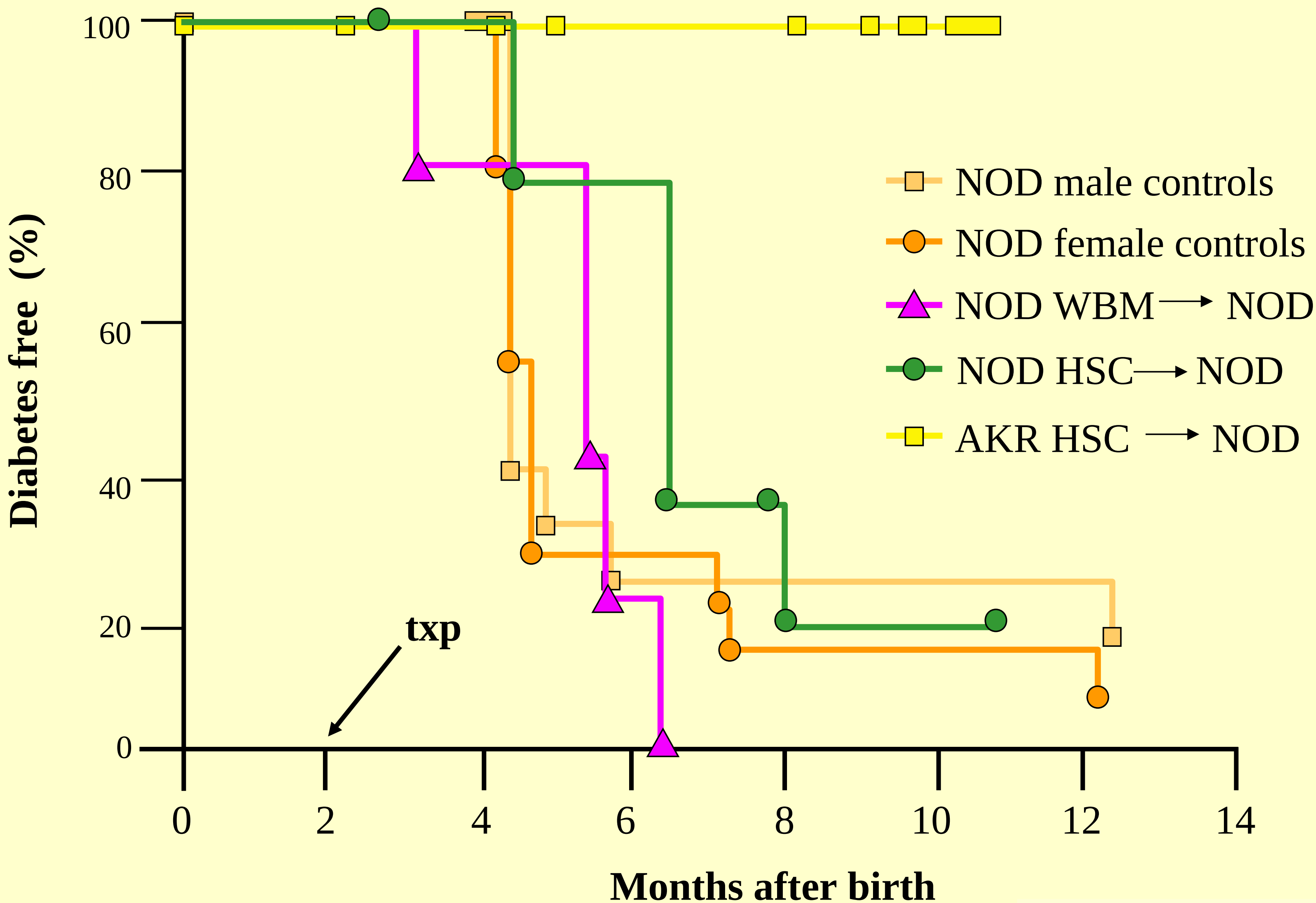
Judith Shizuru

Combined HSC & islet transplantation



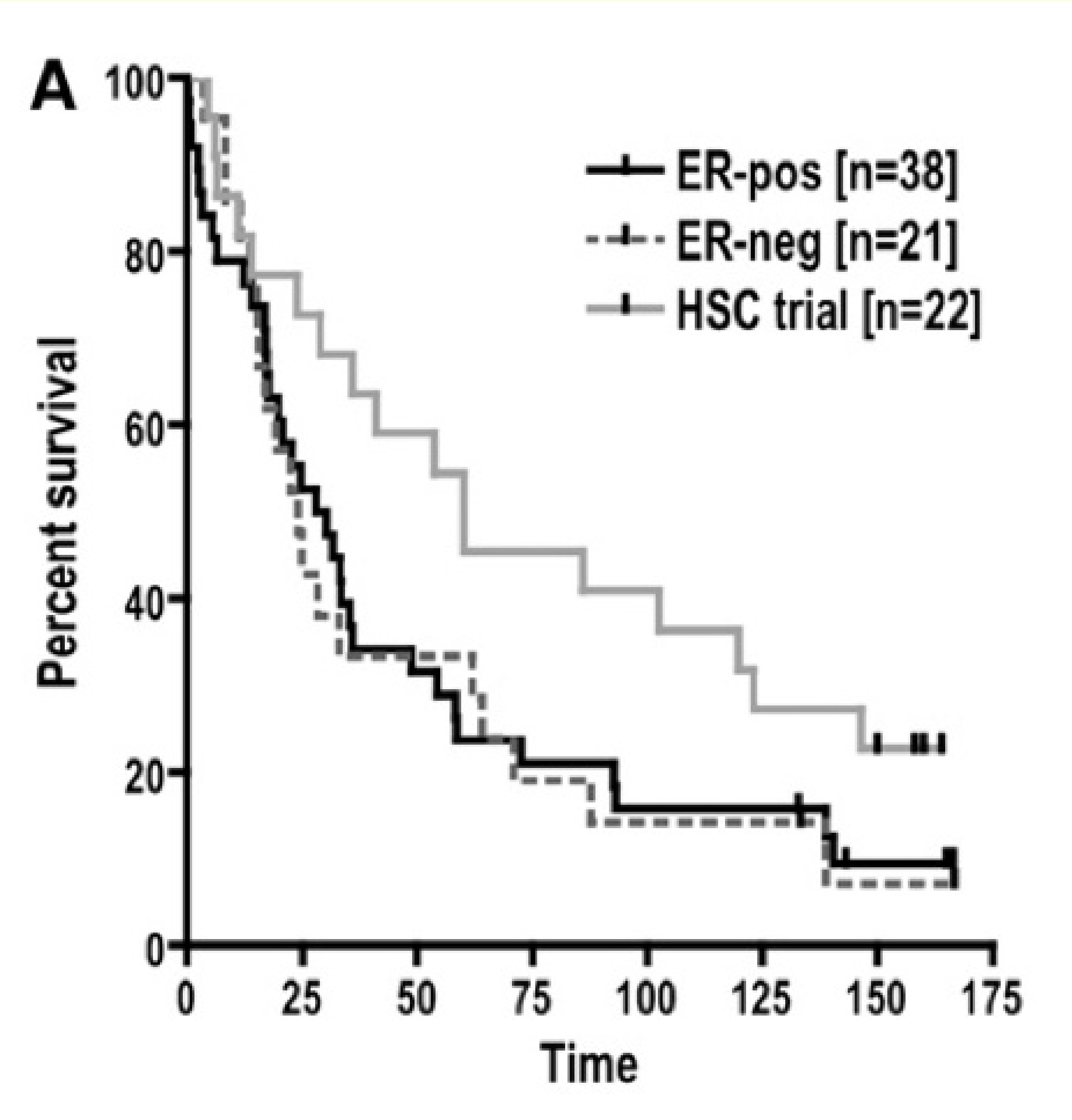
Judith Shizuru

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



Judith Shizuru

Hematopoietic Cell Treatment Coupled with High Dose Breast Cancer Chemotherapy



Stage Four Metastatic Breast Cancer

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