Stem Cells as a Source of Regenerative Tissues

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What are stem cells?

The human body is comprised of over 200 different cell types that are organized into tissues and organs that provide viability and reproduction.

Stem Cells are characterized by the ability to

- renew themselves through asymmetric cell division
- differentiate into a diverse range of cell types.

Two categories of Stem Cells: **Embryonic and Adult.**

Potential therapeutic use of stem cells

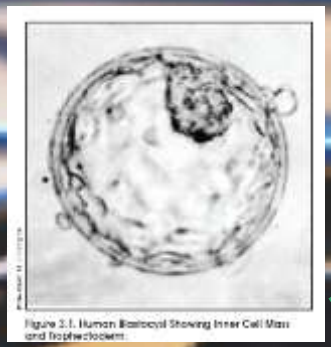
DEGENERATIVE DISEASES

TRANSPLANTATION

DRUG DEVELOPMENT

TISSUE ENGINEERING

TOXICICOLOGY



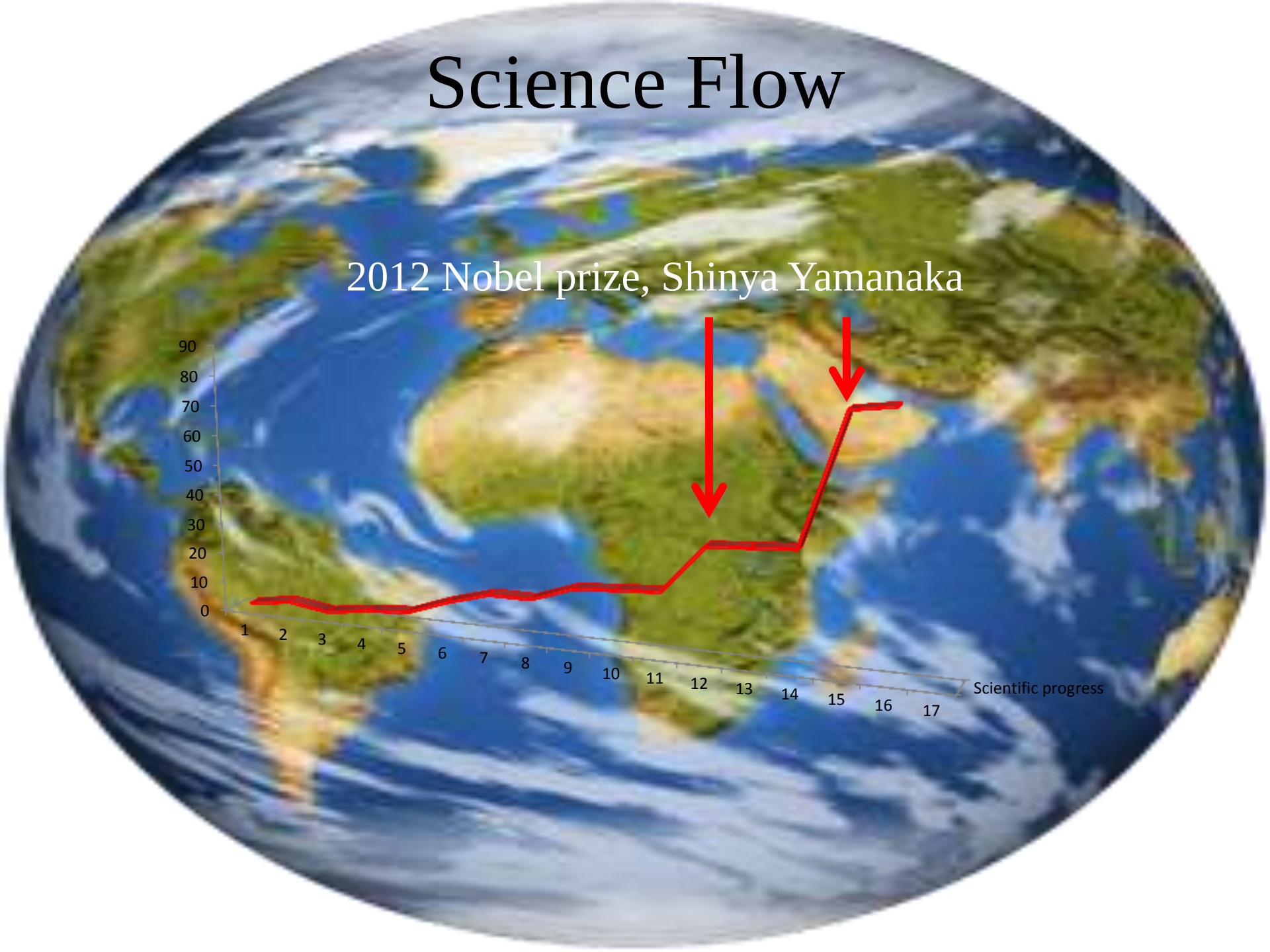
AGING

TRAUMA:
Spinal cord
Burns
Head injury

CANCER SURVIVAL

Early Development

Science Flow



Timeline: induced pluripotency in human cells: iPS cells

- 1962 John Gurdon cloned a tadpole from a frog
- 2007 Takahashi and Yamanaka used same concept
  retroviral vector with 4 TF: Oct4, Sox2, Klf4 and c-Myc
- 2007 Yu and Thomson
  lentiviral vector 4 TF: Oct4, Nanog, Sox2 and Lin28
- 2007 Thompson et al, non-integrating viral vector
  Epstein-Barr virus, 4 TF: Oct4, Nanog, Sox2 and Lin28
- 2012 Drug assisted reprogramming require only 2-3 TF

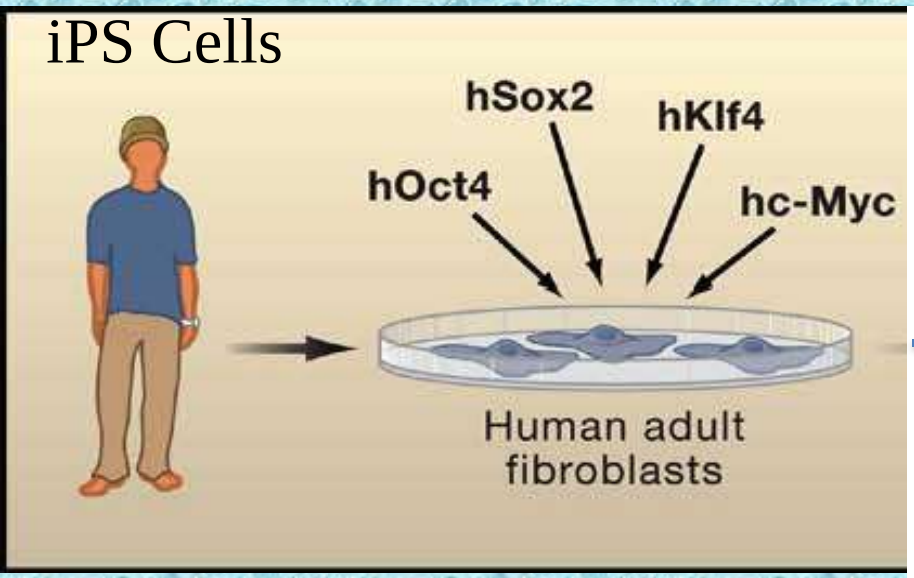
2012

Sir John Gurdon (79) and Shinya Yamanaka (50) were awarded the Nobel Prize

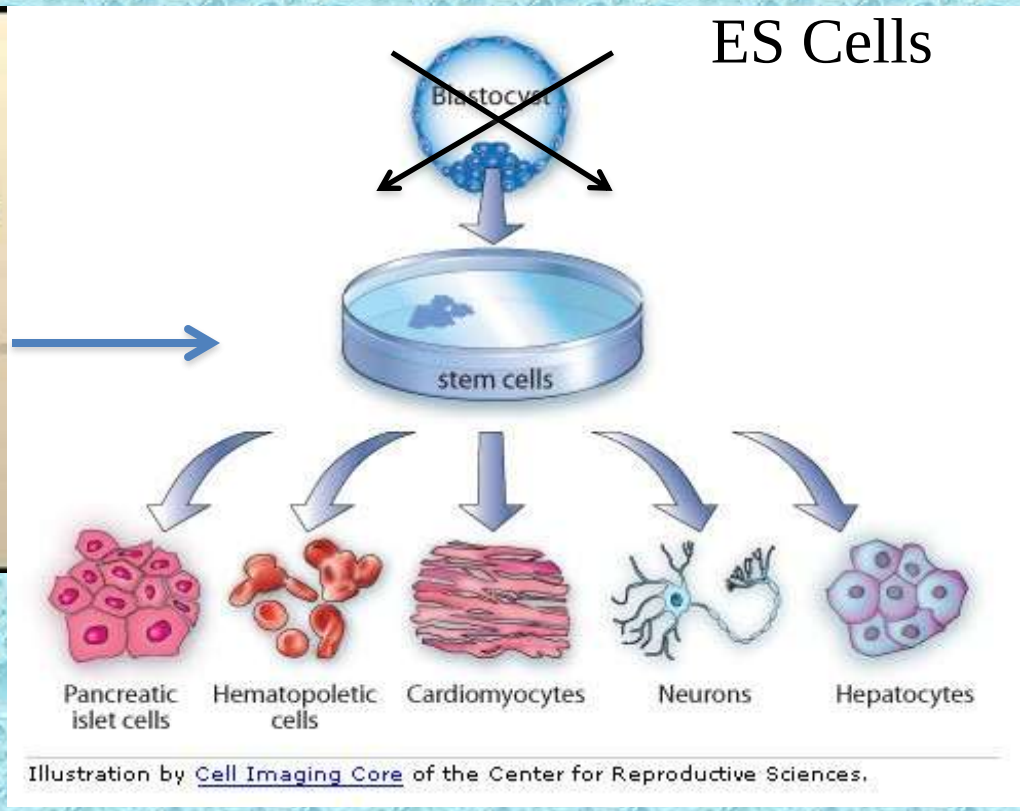
Sources of Stem Cells

A long-debated mater-will be put to rest?

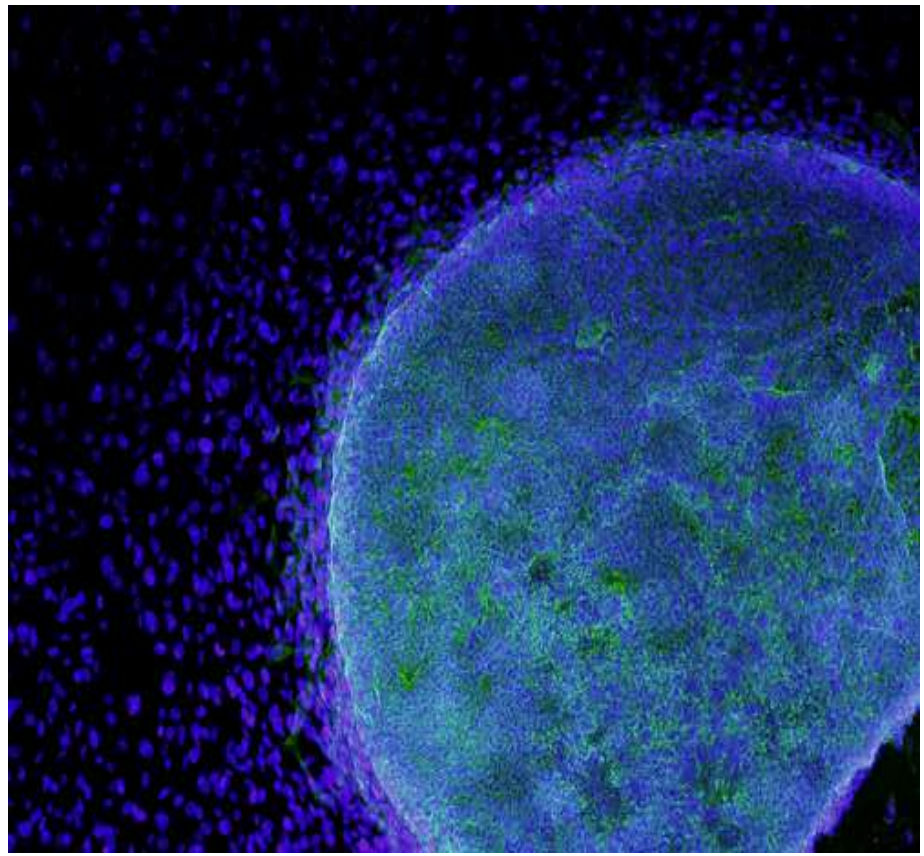
iPS Cells

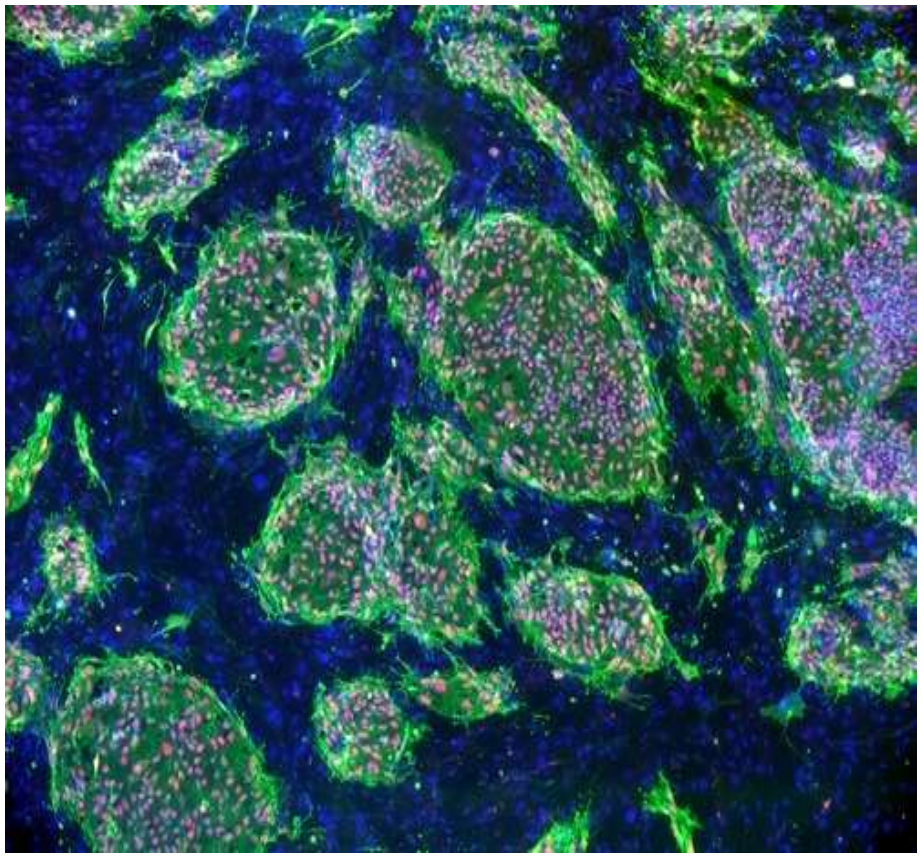


ES Cells



Fluorescent imaging of ES or iPS colonies.





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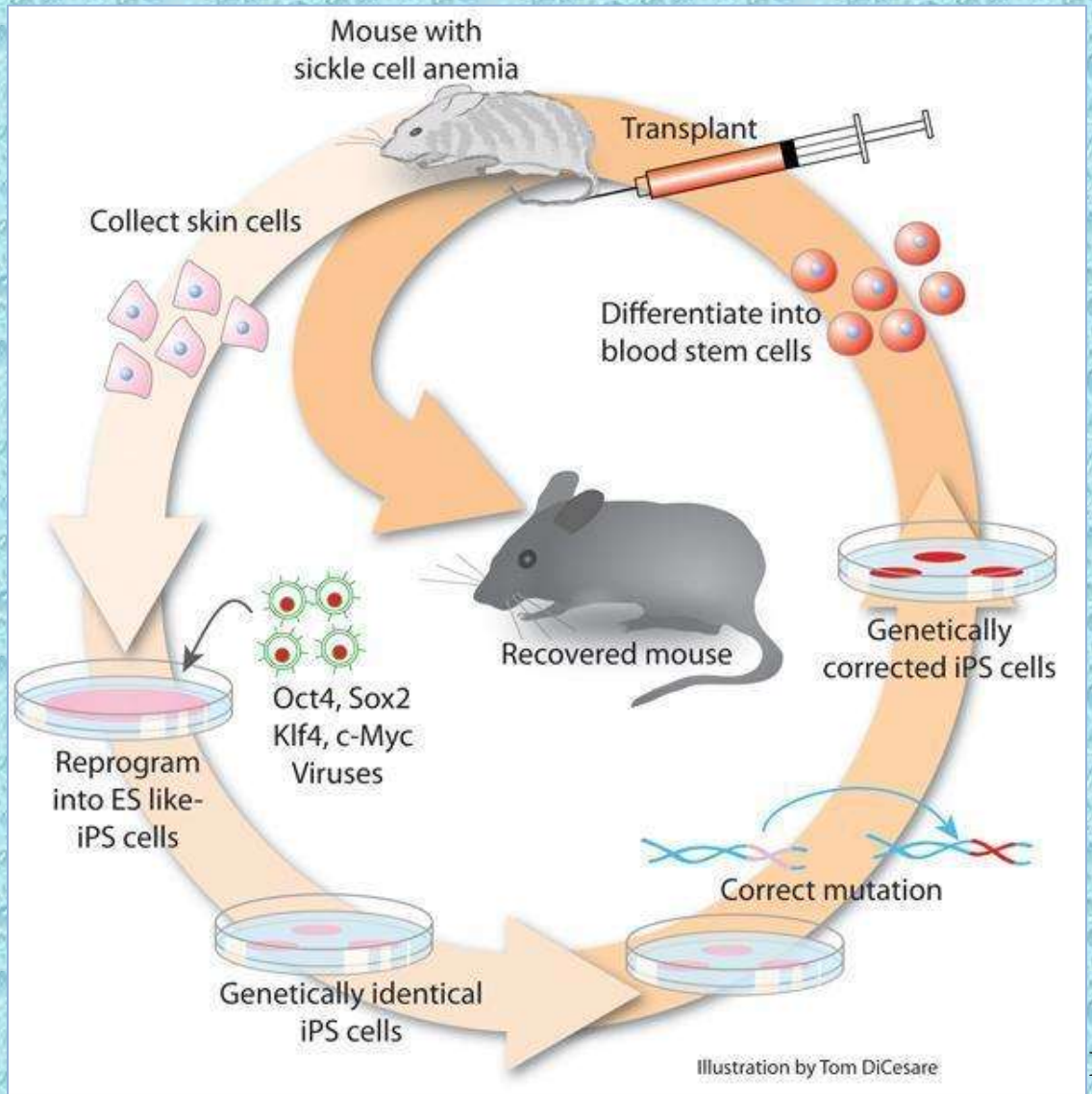
Treatment of Sickle Cell Anemia Mouse Model with iPS Cells from Autologous Skin



Hanna et al, Science 2007

Inducible pluripotent stem cells as a source of regenerative tissues

Pluripotent stem cells can self-renew and **differentiate** into various types of mature cells *in vitro*, and are **considered an ideal source for donor tissues**

Pluripotent stem cells can be manipulated to correct genetic defects before transplantation into a patient

Stemcells.nih.gov

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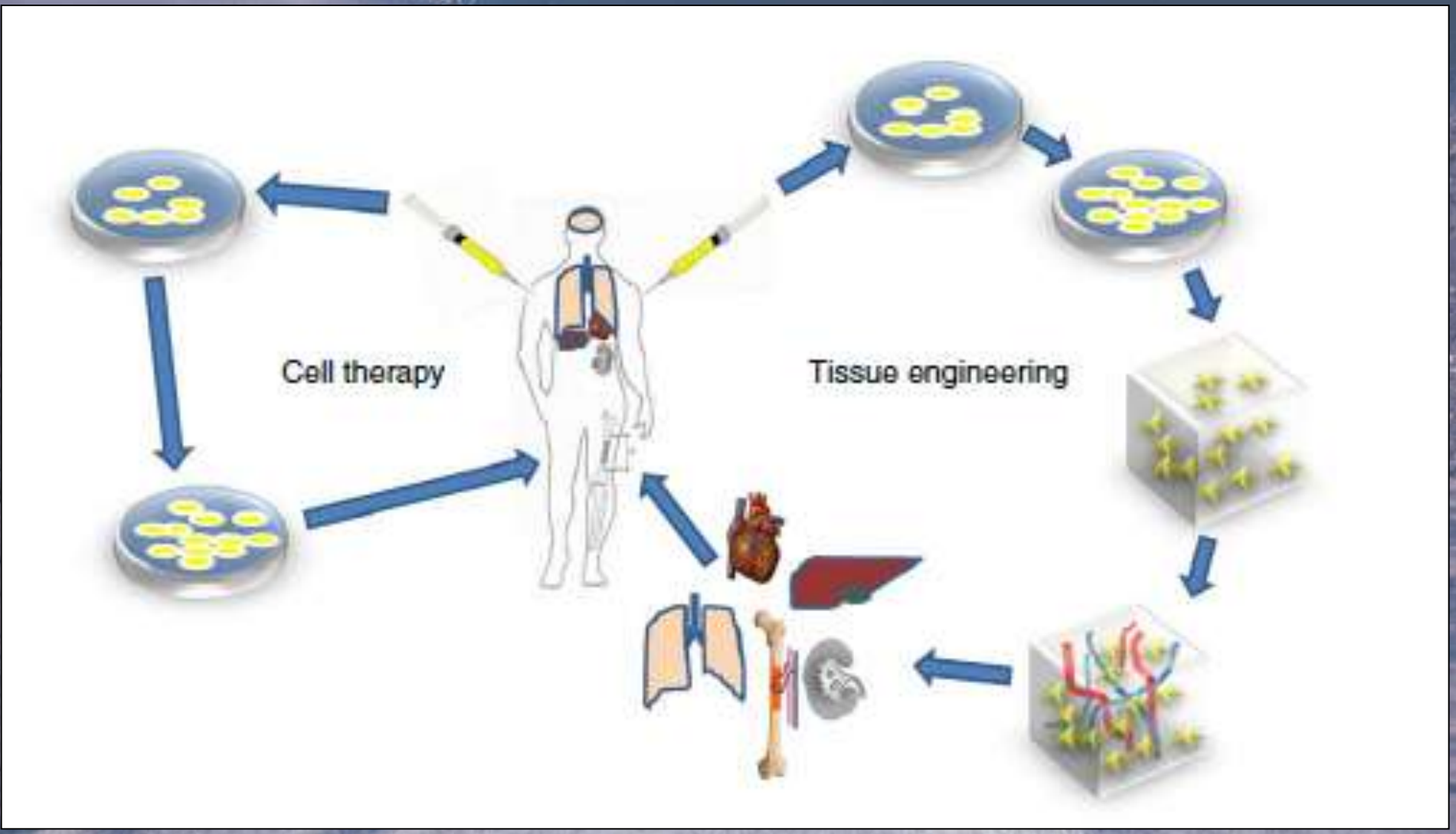
Cell Therapy and Tissue Engineering



CURRENT STATUS

iPS cells generation from skin fibroblasts

- Parkinson's disease (Wernig and Jaenisch, 2008, Maehr and Melton PNAS 2009).
- Amyopathic Lateral Sclerosis, (Dimos and Eggan Science 2008)
- Type I diabetes (Maehr and Melton PNAS 2009)
- ADA-SCID, SBDS, Gaucher disease, Duchenne and Becker Muscular dystrophin, Parkinson's disease, Huntington disease, JDM, Down syndrome, Lesch-Nyhan syndrome. (Park and Daley Cell 2008).

iPS cells generation from other cell types

- Blood cells (Loh and Daley 2009). B-cells (Hanna and Jaenisch Cell 2008)
- Blood stem cells (Emiinli and Hochedlinger Nat Genet 2009)
- Pancreatic b-cells (Stadtfeld and Hochedlinger Cell Stem Cell2008)
- Hepatic and gastric endoderm (Aoi and Yamanaka Science 2008)
- Neural stem cells (Kim and Scholar, Nature 2008)

Potential clinical use of iPS cells

- Pros:
  - Cells would be genetically identical to patient or donor cells (no immune rejection!)
  - Do not need to use an embryo
  - Can be manipulated in vitro for gene therapy
- Cons:
  - Cells would still have genetic defects
  - One of the pluripotency genes is a cancer gene (myc)
  - In vitro manipulation may introduce other mutations and viral sequences.

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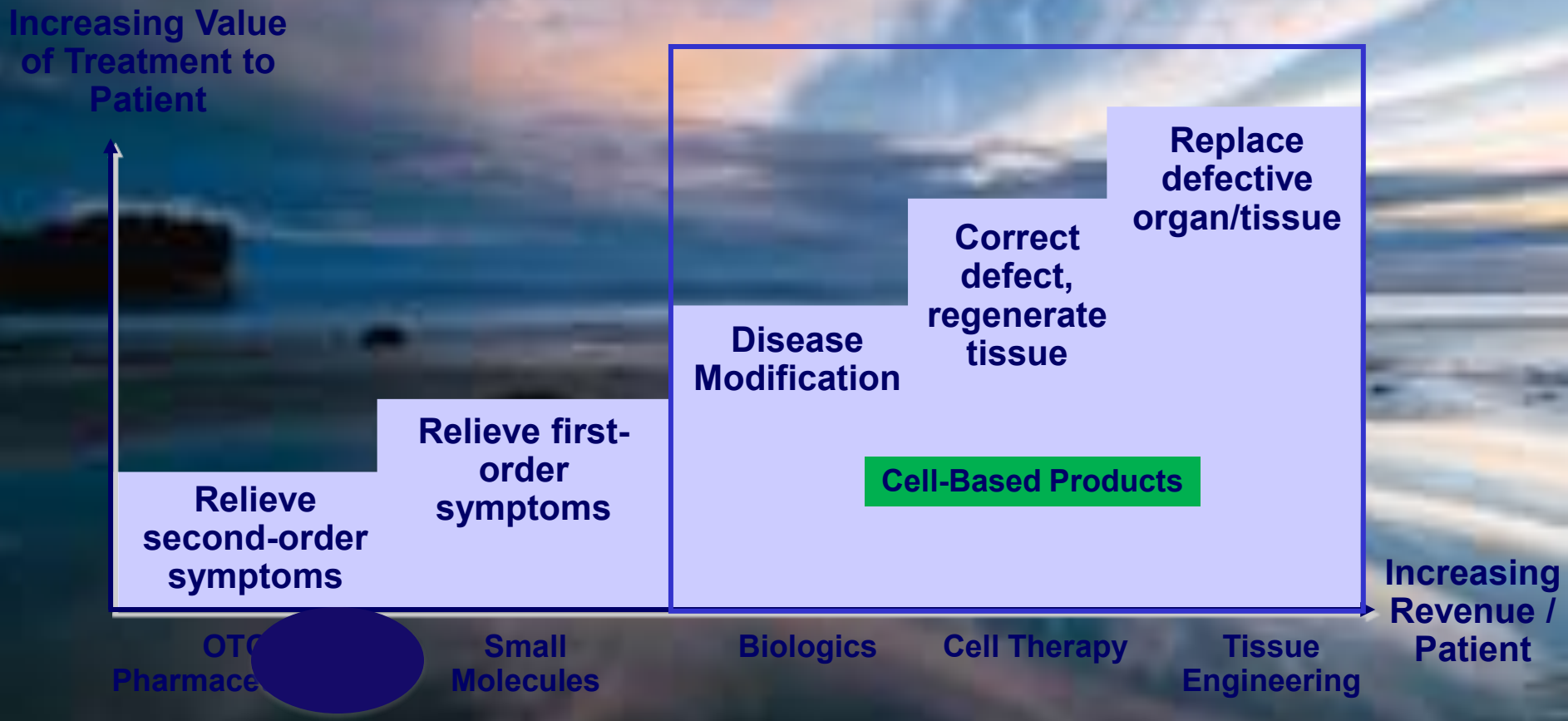
Potential use of iPS cells



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Summary: New era in Personalized Medicine

- Direct reprogramming generates induced pluripotent stem (iPS) cells that are functionally and phenotypically similar to embryonic (ES) stem cells.
- “Safer” protocols in generating clinically approved iPS cells are rapidly evolving.
- More work is needed for tissue replacement and therapeutics.

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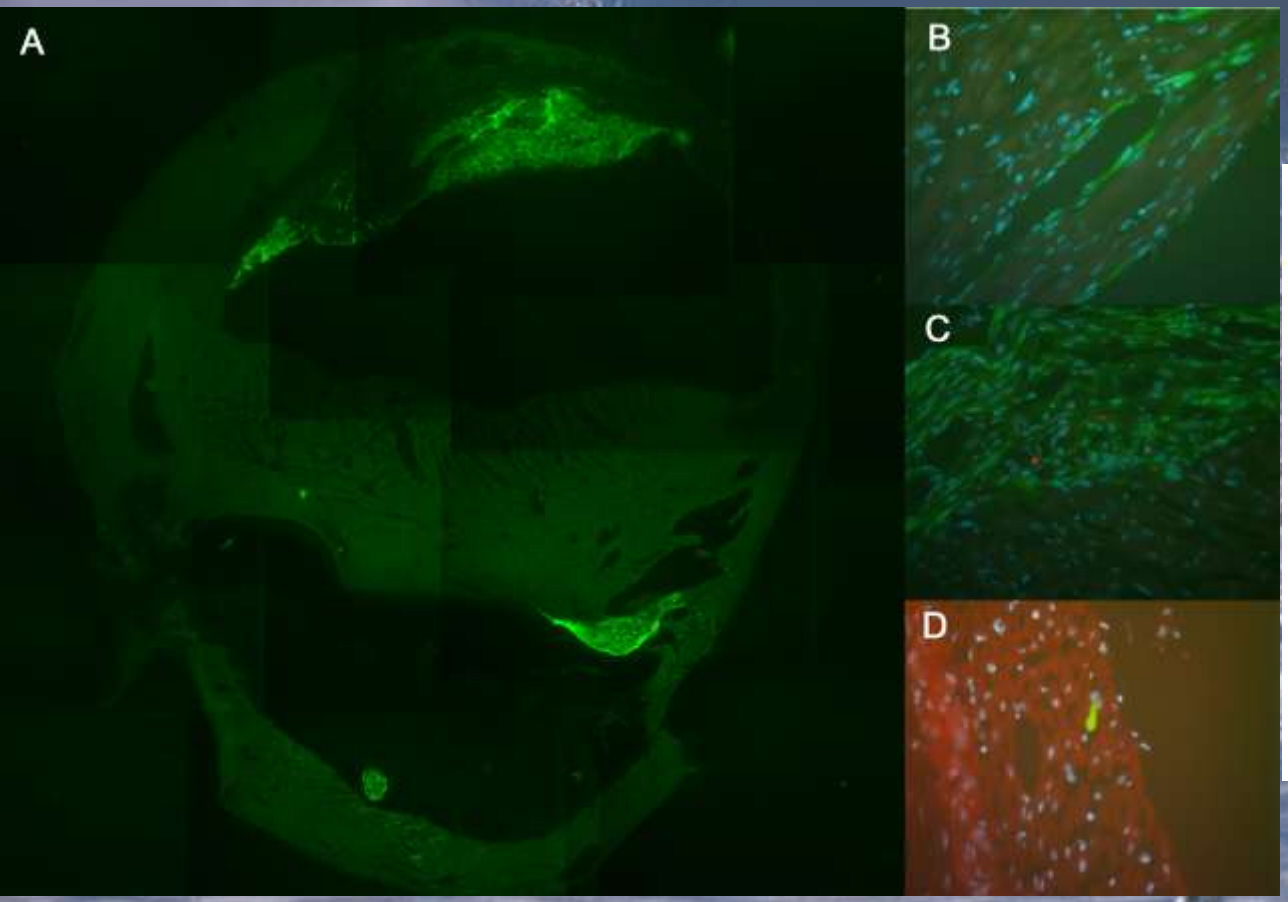
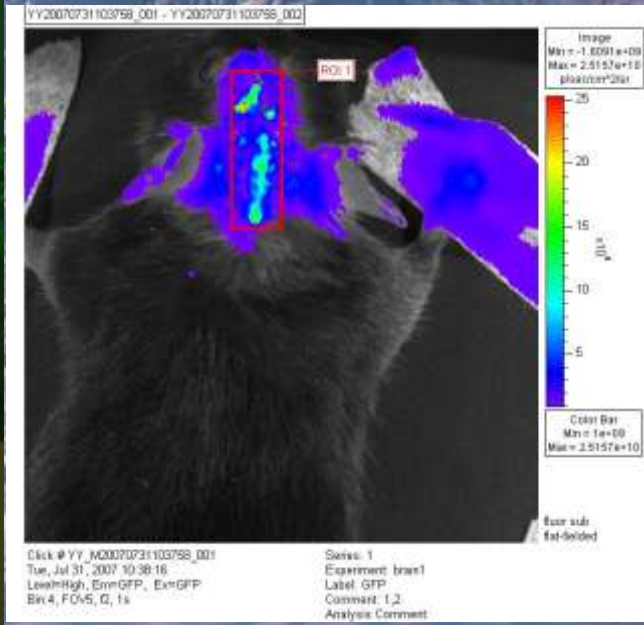
Any Questions?

MSCs home to areas of ischemia and tissue injury



Xenogen Bioluminescence



Surgical incision
Skin Wound healing
24 hrs

Heart MI (DLC) 14 days post-MI

- GFP-labeled MSCs from bone marrow

-Sca1 expressing progenitors along with differentiated fibroblasts