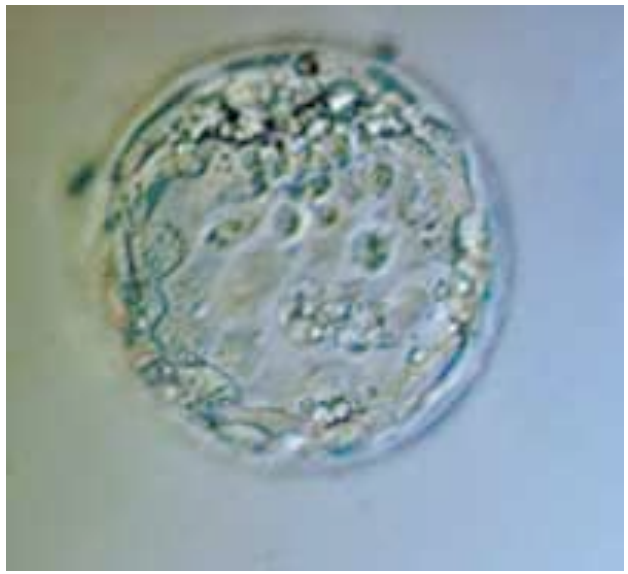

STEM CELLS – A CLOSER LOOK

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Bio 118Q

DIFFERENT KINDS OF STEM CELLS

- Embryonic Stem Cells
- Adult Stem Cells
  - From Bone Marrow:
    - Mesenchymal stem cells
    - Haematopoietic stem cells
    - Endothelial stem cells
  - Induced Pluripotent Cells
  - Mammary, Testicular, Neural, Dental, Umbilical cord, etc.

EMBRYONIC VERSUS ADULT

Embryonic:

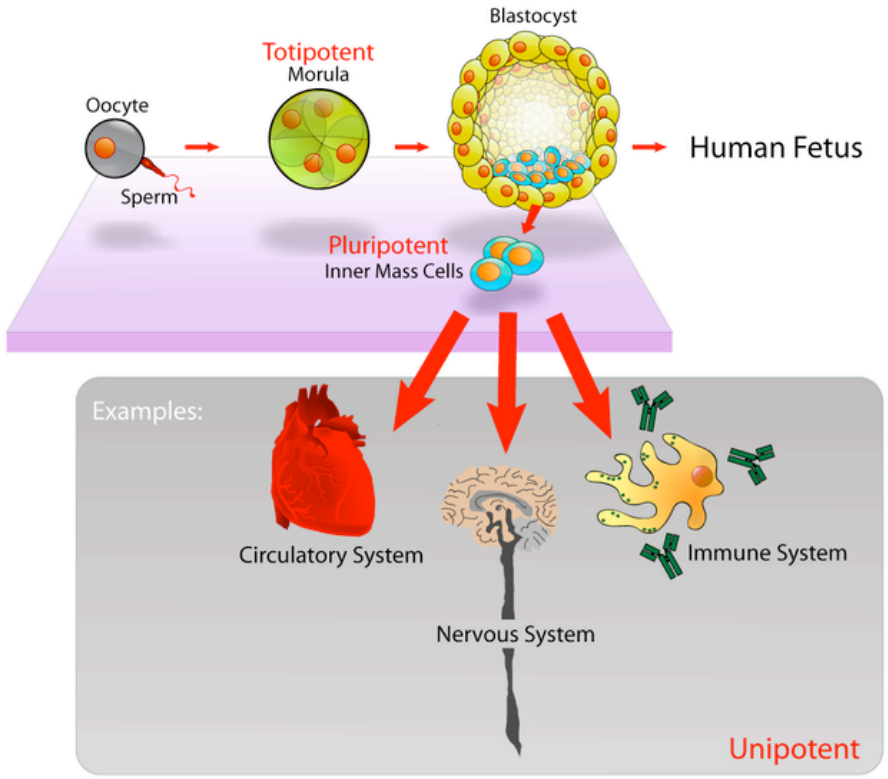
- Can differentiate into any cell type
- Easier to harvest(no invasive surgery)

Adult:

- Limited Differentiation (excluding induced)
- Invasive surgery sometimes required (bone marrow)
- Fewer Ethical Concerns
- Autografts

POTENCY OF CEI

- Totipotent(Omnipotent): Can differentiate into entire organism
- Pluripotent: can turn into nearly all cell types(all three germ layers)



- Multipotent: Can differentiate into several types, usually closely related
  - Ex: hematopoietic stem cells differentiate into red blood cells, white blood cells, platelets.
- Unipotent: Can only differentiate into one kind of cell.
  - Ex: Muscle stem cells can both regenerate and turn into muscle cells. Skin cells.

4 WAYS TO HARVEST STEM CELLS

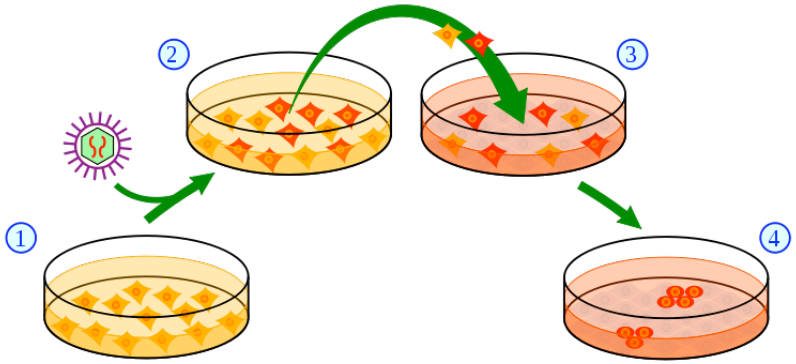
1. Alter Embryonic Cells
   - Remove developmental genes and create an embryo
2. Rescue Embryonic Cells
   - Use only dead embryos
3. Biopsy Embryonic Cells
   - Take only several cells, before implantation
4. Reprogram Adult Cells
   - Take adult cells, revert them back

OPEN QUESTIONS ABOUT ADULT STEM CELLS

- **How do adult stem cells arise?**
- **Which adult tissues have stem cells?**
- **Are stem cells found in different locations unique?**
- **What molecular factors enable stem cell plasticity?**

INDUCED PLURIPOTENT STEM CELLS

- iPSCs first produced in mice in 2006, in humans 2007.
- Derived by forced expression of certain genes.
  - Oct-3/4, SOX2, c-Myc, and Klf4
- Believed to be identical to embryonic stem cells (pluripotent).
- Uses fibroblasts(but theoretically could use any cell)



- Used retrovirus to write genes into adult cells.
  - Possibly caused tumors
- Konrad Hochedlinger and his Harvard University research team successfully used adenovirus in a mouse.

ADVANTAGES OF IPSC'S

- Combines the best of both worlds.
- Can be harvested very easily.
- Little ethical debate.
- Can use patient's own cells.

However,

- Using retroviruses can cause tumors.
- More research is needed.

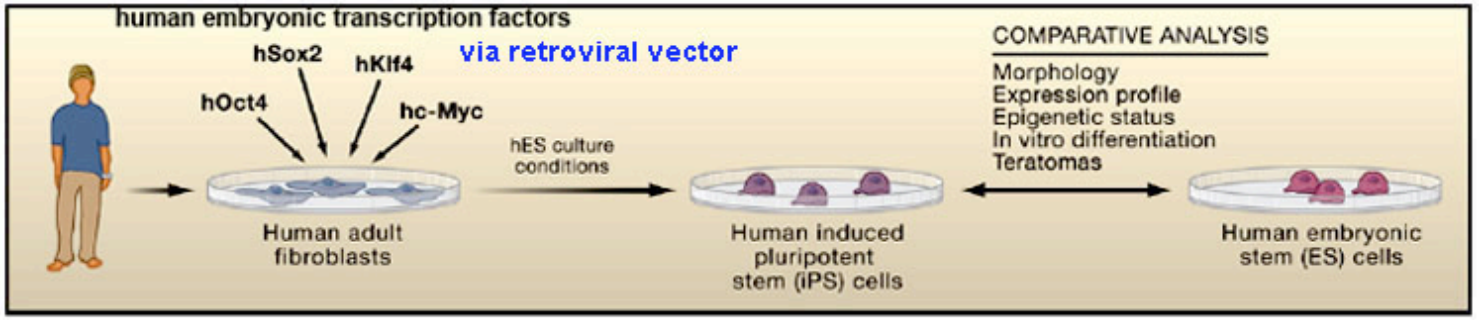
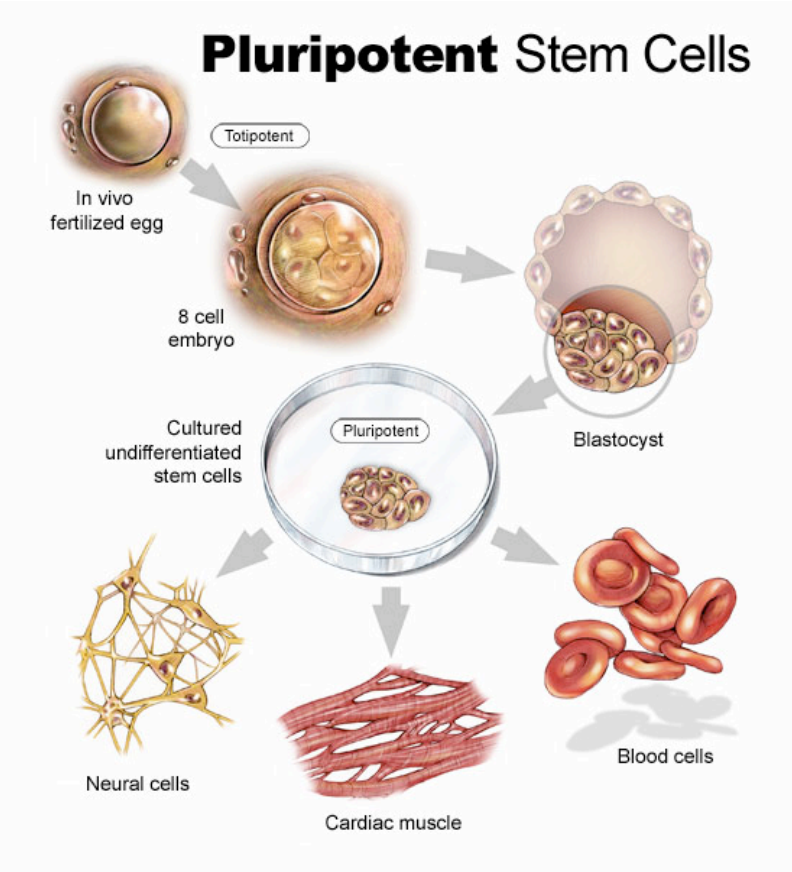


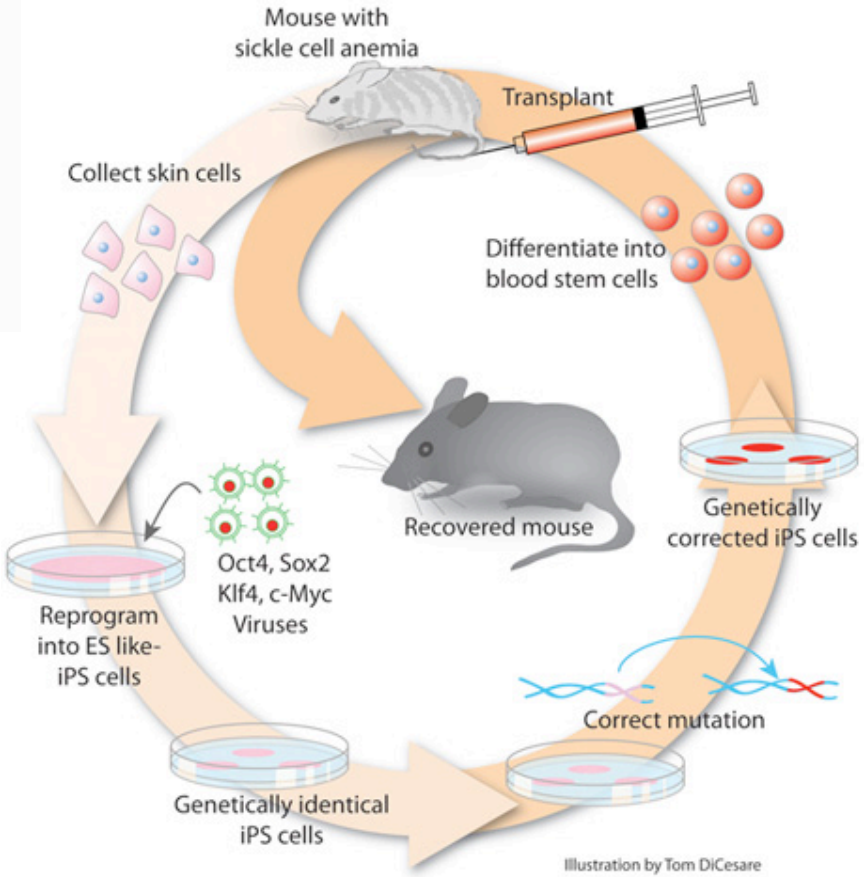
Figure 1. Transcription Factor-Induced Pluripotency

Adult fibroblasts from human donors were exposed to retroviral vectors expressing a cocktail of four transgenes encoding the human factors hOct4, hSox2, hKlf4, and hc-Myc (Takahashi et al., 2007). Thirty days after transduction and further cultivation under human ES cell growth conditions, human induced pluripotent stem (iPS) cell colonies (among others) that could be propagated and expanded further were isolated. Comparative analysis of human iPS cells and human ES cells using assays for morphology, surface-marker expression, gene expression profiling, epigenetic status, and in vitro and in vivo differentiation potential revealed a remarkable degree of similarity between these two pluripotent stem cell types.

RESEARCH IS IN PROGRESS

- June 2008, By using adult neural stem cells, they managed to induce pluripotency with only 2 of the 4 genes required.
- Oct 2008 “Nature”, An article showed a lab managed to create pluripotent stem cells from adult human sperm.
- 30 Oct 2008 A lab managed to create pluripotent stem cells from a single human hair.
- Still much progress to be done.

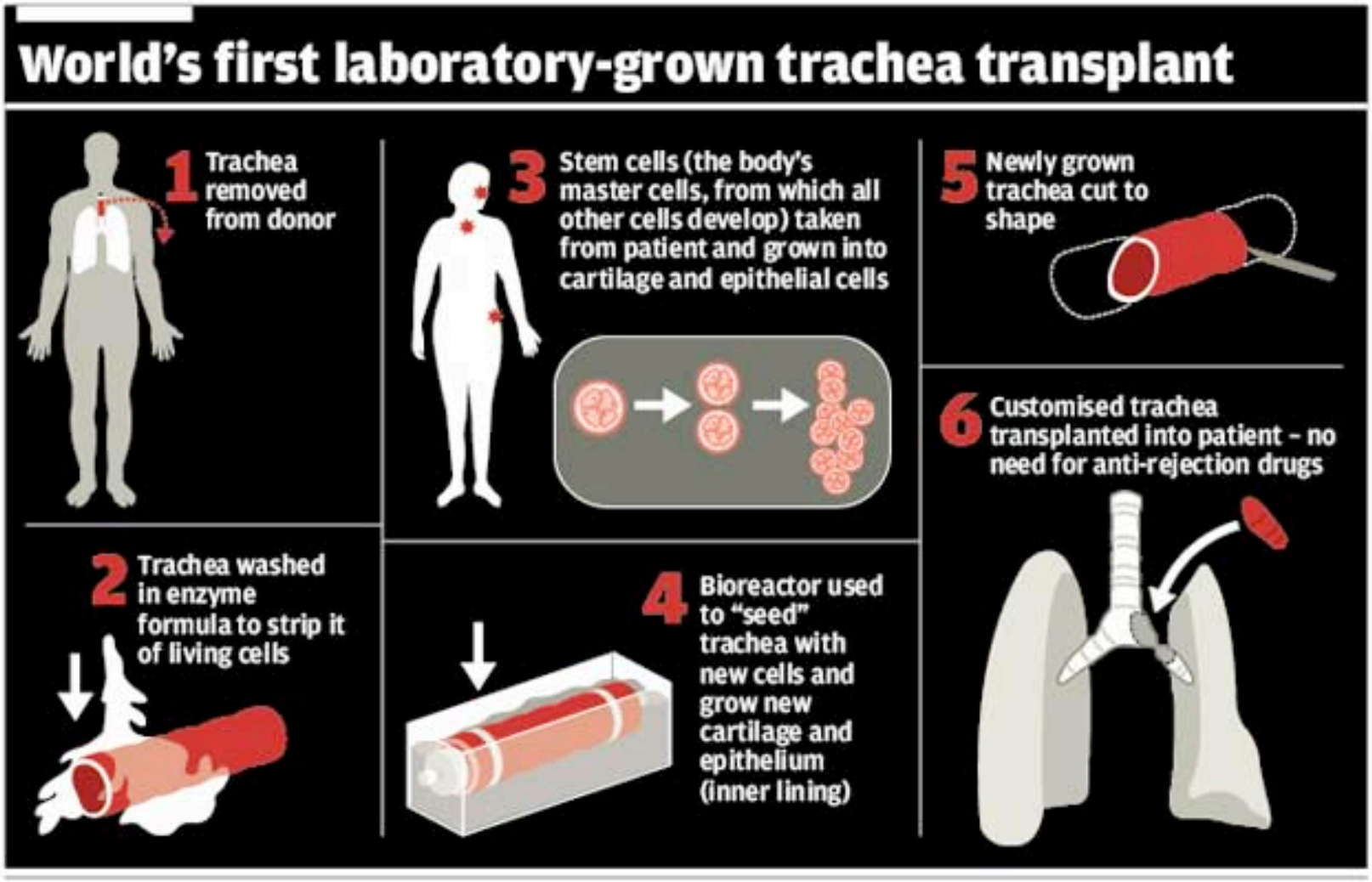

Pluripotent Stem Cells
Totipotent
In vivo
fertilized egg
8 cell
embryo
Blastocyst
Cultured
undifferentiated
stem cells
Pluripotent
Neural cells
Cardiac muscle
Blood cells


Mouse with
sickle cell anemia
Transplant
Collect skin cells
Differentiate into
blood stem cells
Recovered mouse
Genetically
corrected iPS cells
Oct4, Sox2
Klf4, c-Myc
Viruses
Reprogram
into ES like-
iPS cells
Correct mutation
Genetically identical
iPS cells
Illustration by Tom DiCesare

A SMALL CASE STUDY OF STEM CELLS

- 2008 – Prof. Macchiarini in Barcelona.
- Full transplant of trachea.
- Decellularized windpipe acted as a scaffold/ECM, while the cells also secreted their own cartilage matrix proteins.
- They used chondrocytes made from mesenchymal stem cells.
- Avoided rejection because was autografted.

CONTINUED


World's first laboratory-grown trachea transplant
1 Trachea removed from donor
2 Trachea washed in enzyme formula to strip it of living cells
3 Stem cells (the body's master cells, from which all other cells develop) taken from patient and grown into cartilage and epithelial cells
4 Bioreactor used to "seed" trachea with new cells and grow new cartilage and epithelium (inner lining)
5 Newly grown trachea cut to shape
6 Customised trachea transplanted into patient – no need for anti-rejection drugs

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