Human Embryonic Stem (ES) Cells
and
Induced Pluripotent Stem (iPS) Cells

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Cells are the fundamental, structural, and functional units of living organisms.
Step-wise restriction of differentiation potential during human development
Neurological Diseases
Parkinson’s Disease

- Caused by the death of dopaminergic neurons
- 1.5 million people affected in the U.S.
- $5.6 billion total cost in the U.S.
- Fetal tissue transplants have been performed, but the source of tissue is inadequate.

ALS (Lou Gehrig’s Disease)

- Caused by death of motor neurons
Heart Disease

- Afflicts 1 in 3 people ... over 70 million Americans
- The #1 killer in U.S. and every Wisconsin county ... over 920,000 people a year (2002)
- Prevalence increasing as population ages
- Costs our nation $393 billion estimated in 2005
- There is a severe shortage of heart donors to treat end stage heart failure
- The adult heart does not have a stem cell
Juvenile Onset Diabetes

- Juvenile onset diabetes is caused by the death of specific pancreatic cells (islet cells).
- 1 million people affected in the U.S.
- More than 15% of U.S. healthcare dollars.
- The transplantation of pancreatic islet cells has been successful, but the source of cells is inadequate.
- It is not yet possible to sustainably culture adult pancreatic stem cells, and they may not exist.
Embryonic Stem Cells Can Become Any Tissue in the Body

Scientific manipulations entice stem cells to become specialized tissues (blood, muscle, neuron, etc.).

- Blood cells
- Muscle cells
- Neuron (brain) cells

Blastocyst
Cultured laboratory stem cells
Placenta cell
Stem cell
Challenges For ES Cell-Based Transplantation Therapy

- Immune Rejection
- Making the Cell Type of Interest
- Safety Concerns, Including Cancer
- Preventing the Process That Killed the Cells Originally
- Integration in a Physiologically Useful Form
Nuclear Cloning

A donor cell is taken from a sheep's udder.

Donor Nucleus

These two cells are fused using an electric shock.

Egg Cell

The nucleus of the egg cell is removed.

An egg cell is taken from an adult female sheep.

The fused cell begins dividing normally.

Embryo

The embryo is placed in the uterus of a foster mother.

Cloned Lamb

The embryo develops normally into a lamb—Dolly.
Producing primate embryonic stem cells by somatic cell nuclear transfer.

Byrne JA, Pedersen DA, Clepper LL, Nelson M, Sanger WG, Gokhale S, Wolf DP, Mitalipov SM.

Oregon National Primate Research Center, Oregon Health & Science University, 505 N.W. 185th Avenue, Beaverton, Oregon 97006, USA.
Human Embryonic Stem Cells are able to reprogram human blood cells

Stem Cells. 2006 Jan

Human embryonic stem cells reprogram myeloid precursors following cell-cell fusion.

Yu J, Vodyanik MA, He P, Slukvin II, Thomson JA.

Wisconsin National Primate Research Center, University of Wisconsin, Madison, WI 53706, USA.
Human Embryonic Stem Cells are able to reprogram human blood cells

Embryonic stem cells  Blood cell

Cell-cell Fusion
What are the factors in human embryonic stem cells involved in reprogramming?

- genes whose expression are enriched in human embryonic stem cells.
Identification of genes with enriched expression in human embryonic stem cells

- Gene expression analysis

~ 150 genes of interest
Screening

Skin cells ➔ iPS cells
Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells.


Genome Center of Wisconsin, Madison, WI 53706-1580, USA.; Wisconsin National Primate Research Center, University of Wisconsin-Madison, Madison, WI 53715-1299, USA.
New and Existing Methods

Researchers take skin cell samples from patients.

Scientists reprogram cells by injecting retroviruses carrying four genes.

Researchers can induce both cells to become any human tissue.

Scientists take fertilized human egg.

Egg develops into blastocyst, a 70 -100 cell mass.

Researchers harvest stem cells, destroying the embryo.
Why Are Human iPS Cells Important?

- They allow the development of accurate in vitro disease models

- iPS cells with diversity of genetic background can be used for drug screening.

- iPS cell technology solves the problem of immune rejection for transplantation therapies.
Human regeneration?
Urodele Regeneration

QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture.
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