

1 **Stem Cell Notes**

From National Academies of Science

2 **Stem cells**

- Can replicate itself
- Can differentiate into many cell types
- Not all stem cells are pluripotent (nor are they all totipotent)

- Pluripotent:

3 **The difference between totipotent and pluripotent**

- Totipotent: capable of developing into a complete embryo or organ
- Pluripotent: capable of developing into any of the three germ layers (epiderm, mesoderm, or endoderm)
- It is not possible to develop an entire human being because they cannot develop extraembryonic tissues
- Multipotent cells can develop into limited cell types, not any layer

4 **Cytokines of the immune system**

- These are pluripotent; that is they can evoke different responses from a variety of cells
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5 **Interferon gamma is an example of a pluripotent cell of immune system**

- In somatic cells it inhibits growth
- It upregulates major histocompatibility complex antigens in a general anti-viral response
- In B cells, it stimulates antibody class switching
- It stimulates maturation of natural killer cells
- It induces macrophages to intracellular attacks

6 **2 main types of stem cells**

- Embryonic stem cells: blastocyst (5 days after fertilization, hollow sphere about 64 cell stage)
 - There are about 30-34 cells forming the inner cell mass that are pluripotent
- Adult stem cells from bone marrow

7 **Embryonic stem cell lines**

- Can be induced to replicate as undifferentiated cells
 - These cannot be used for treatment; they develop into teratomas
- Later the cells could become specialized

8 **Sources of embryonic stem cells**

- In vitro fertilization is the largest source
- All donated eggs are fertilized, but not all are implanted
- Remainder are frozen

- Many of these are prestem cell research and donors were not asked to give permission for use in research of the excess blastocysts
- Nuclear transfer

9 **Nuclear transfer**

- Insert nucleus of an already differentiated cell from adult into an enucleated egg
- The resulting egg is then induced to become a blastocyst, providing an inner cell mass of stem cells
- As of summer of 2006, this has not been accomplished (great idea, not working yet)

10 **Research cloning vs reproductive cloning**

- If nuclear transfer works in the future, it would be considered research cloning
- It is a clone of the adult cell, but is not used to clone an individual
- therapeutic cloning is used to generate tissues for treatment
- Reproductive cloning would be used a cloned embryo to generate an entire organism (like Dolly the sheep)
- Incidentally, reproductive clones have been short lived and fraught with many cellular problems like tumors

11 **Embryonic stem cells from nuclear transfer treatments**

- Generate tissues from individual needing transplant-avoiding rejection issues and need for continuous medications to fight immune rejection of organ

12 **Sources of adult stem cells**

- Found in bone marrow, gut, skin, and even brain (although regeneration is not known at this point in time)
- Limited capabilities once harvested
- Difficult to isolate
- Stem cell therapies still limited and success uneven

13 **Identifying stem cells**

- Hard to find, found in low numbers
- Look for molecular identification by markers on surface
- Markers can then be added to help differentiate stem cells from other cells
- May be separated by observing their behavior (should self generate and remain unspecialized)

14 **Cell culture**

- In VITRO, outside of body
- Cell line: propagation of of genetically identical cells
- Give long-term supply of cells that can be shared
- Spontaneous mutations and accumulation of booboos –genetic mutations

15 **Getting the cells to differentiate**

- Cells that form tissues communicate with one another to maintain the tissue by telling when and how to differentiate
- These are often protein messengers
- They must be identified and proliferated to help differentiate cells in vitro

16 **In vitro vs in vivo**

- Not all applications can be tested in a petri dish
- Animals (mammals) are used to test stem cells that have been differentiated
- There are many drawbacks to testing in animals but the greatest advantage is it is as close to humans as we can get and not use humans for testing purposes
- Scientific chimeras contain more than one source of cells

17 **Alternatives to embryos**

- Collect a cell from a morula (16-30 cell stage) currently practiced to test for genetic defects
- Long term effects not known
- Mouse morula cells have given rise to mouse stem cells

18 **Alternatives to embryos**

- Altered nuclear transfer (ANT)
- Variation of nuclear transfer technique
- Create blastocyst with altered genetic material (no implantation and subsequent development in uterus possible)
- Remember nuclear transfer isn't working yet
- Some argue that "creating" blastocyst for destruction is immoral

19 **Alternatives to embryos**

- Cause adult cell to act as stem cell
- Most adult cells no longer use all code-some is permanently turned off to allow specialization and continuing to behave as tissues
- Hoping to reprogram cell to use all code

20 **Possibilities of stem cell research**

- Only few therapies currently available using stem cells, but those are promising
- Blood and skin transplants were among the first to be relatively successful

21 **Loss of single type of cell or tissue**

- This holds great promise
- Type I diabetes loss of insulin producing cells of the pancreas
- Treat symptoms, but can't alter the course of the disease

22 **Hematopoietic stem cells**

- Found in blood and bone marrow
- Used to treat patients with leukemia, sickle cell anemia, bone marrow damage, and some metabolic disorders and immunodeficiencies (bone marrow transplants)
- These cells can become blood cells of different types
- So far, only make blood cells-not undifferentiated cells that are pluripotent

23 **Stem cells of the skin**

- Are found in the dermis
- They are producing cells to replace those that have been shed
- If burn victim loses these cells, if there are cells from skin of the victim that are intact, they can be used to create sheets of skin that can be grafted for better

survival and appearance

24 **Parkinson's disease**

- Nerve cells that prevent muscle enervation of unneeded muscles for an action degenerate
- They are not able at this time to be replaced
- No cure-drugs tamp down all firing of muscle neurons
- One cell type needs replacing and have successfully transplanted these cells in rat brains
- Another possibility would be to induce patient's own stem cells to repair the damaged nerves

25 **Stem cell therapies**

- Still a pipe dream-not in the "pipeline" as yet
- Time line! Decades from therapies and practical use
- Moral and ethical issues
- Money issues (getting it for research and then who gets profits)
- Who owns the genes?

26 **Diseases that are close to resolution or hold particular promise**

- Type I diabetes
- Parkinson's
- Some blood diseases
- Understanding cancer stem cells

27 **General knowledge gained from stem cell research**

- Clarify roles of genes in development
- How genetic mutation affect normal processes
- How infectious agents invade and attach cells
- Investigate genetic and environmental factors involved in cancer and other diseases
- Understand aging processes
- Could be a new way to test drugs-use human cells that aren't in a human-safer and more cost effective

28 **Ethics, morals, and law in US**

- Nebulous definition of embryo and legal moral debate over at what point cells are human being
- No consensus on use or creation of human blastocysts for research purposes
- Some say it is same as in vitro fertilization and abortion-immoral

29 **Ethical considerations**

- Documentation
- Informed consent
- Dealing with chimeras
- Morality of chimeras (no human consciousness)
- No introduction of human cells into different animal blastocyst is current guideline and no reproduction of chimeras

30 **Legal but not funded federally**

- Legal or research embryonic stem cells lines and make or work with new cell lines
- Federal funding only for stem cells lines available before 9 Aug 2001
- Old stem cell lines accumulate mutations