**Stem Cells**

- **Characteristics**
  - Unspecialized cells
  - Have the potential to form other cell types
  - Self-renewal
    - Can make unlimited copies of themselves

**Types of stem cells**

- "Adult" or tissue-specific stem cells
  - More restricted; give rise to cells within a tissue family
- Embryonic stem cells
  - Pluripotent = can become any cell type
  - Created in a laboratory by reprogramming a previously specialized cell

**Tissue specific or “adult” stem cells**

- Replenish cells that turnover rapidly
  - Blood cells and skin
- Rare
- Tissue-specific
  - Able to develop into most of the cells in their specific tissue
- Not pluripotent
  - They are part way along the road to differentiation

**Embryonic stem cells**

- Originate as inner mass cells in an embryo
- Pluripotent – ES cells can develop into any of the 220 cell types
- Need chemical signals to differentiate
- Ethical concerns

**ES cells come from in vitro fertilization**

- Most ES cells come from IVF
- They are donated for research with consent
- Easily grown in culture in the lab
Using ES cells to combat paralysis

- In Oct 2010 Geron treated a paralyzed patient with spinal cord injury with embryonic stem cells
- 1st ever FDA-approved clinical trial of stem cell therapy
- 5 patients enrolled
- Trial has been discontinued

Using embryonic stem cells to combat paralysis

- Embryonic stem cells → neural support cells that form the myelin sheath
- Cells re-insulate the affected neurons
- Damage to the myelin sheath is a common cause of paralysis

iPS cells (reprogrammed cells)

- iPS cells = induced pluripotent stem cells
- Mature body cells that are reprogrammed
- Important step toward treating diseases with a patient’s own ‘repaired’ cells

Creating iPS cells

- A retrovirus is used to introduce four regulatory genes → stem cells.

Advantages

- Start with adult cells, not embryonic cells
- Able to use skin cells
- Use patients own cells—no problems with tissue rejection
- A work in progress
Stem cell breakthrough

- Specialized cells can be induced to assume new ID without passing thru a stem cell state

Why is stem cell research important?

- A question you need to be able to answer

Custom-tailored cells to cure disease

Applications

- Disease modeling
  - Convert IPS cells to the diseased cell type
  - Study disease progression
  - Treat cells in culture, response to drugs

- Cell therapy
  - Convert IPS cells derived from a sick patient into healthy cells, then transplant them back into that patient

Importance of Stem Cells

- A source of replacement cells to treat diseases
  - Parkinson’s and Alzheimer’s diseases
  - Spinal cord injury
  - Stroke and heart disease
  - Diabetes
  - Osteoarthritis and rheumatoid arthritis

Transforming stem cell science into stem cell medicine

Unanswered questions:

- Need safer and more effective techniques for creating IPS cells
- Will IPS cells work in humans?
- Will IPS cells created in the lab find their way to a diseased organ?
- Will they hook up with the healthy cells in that organ to work in harmony with them?

The AIDS pandemic
HIV/AIDS

- The problem is massive
  - 4th leading cause of death worldwide
  - ~30 million people are infected
  - 95% live in developing countries
  - And over 50% are women

AIDS at 30

- 7000 new infections a day
  - 1 in 3 in Africa
- US: 1 in 5 don’t know they’re HIV+
  - Most new infections are ‘men with men’, half are African American
  - In Africa as many as 90% don’t know they’re infected

What makes HIV so lethal?

- The virus highjacks immune cells
- HIV infects and destroys helper T cells
  - the very cells that normally suppress viral infections
- Long incubation period
  - The victim feels healthy but is highly infectious

HIV highjacks immune cells

- HIV binds to the plasma membrane of helper T cells
- Penetrates the cell
- Viral RNA is converted to DNA and integrated into the cell genome
- Human cells ‘manufacture’ the virus

It’s not always DNA → RNA

http://www.youtube.com/watch?v=FDugpEny0Zo&feature=related
HIV budding from an immune cell in culture

- The viruses bud so rapidly that the cell eventually lysed.
- The number of helper T cells drops, and the body cannot fight off other infections.
- These secondary infections cause AIDS.
  - Acquired immune deficiency syndrome.

HIV Infects Helper T Cells

- HIV infects and kills helper T Cells.
- How does this impact the body’s immune responses?

Why is HIV so lethal?

Q1: What is the difference between HIV and AIDS?

- HIV is the virus that causes AIDS.
- AIDS is the end stage disease.

Q2: Name the 3 main ways HIV is transmitted

- Sexual intercourse.
- Blood or blood products.
- Mother-to-child transmission.

Q3: How can we avoid HIV infection? (AIDS prevention)

- Use condoms.
- Don’t share needles.
- Get tested.
  - Many people infected with HIV have no symptoms.
Q4. Where is the virus?
- HIV is found in all body fluids
- Only semen, blood, breast milk and vaginal discharge have enough virus to transmit HIV
- Saliva, tears and sweat do not

How is HIV transmitted?
- Unprotected sexual intercourse
  - Heterosexual or homosexual
- Direct contact with infected blood
  - Sharing needles
  - Blood transfusions
    - blood is tested for HIV (not always in poor countries)
- Mother-to-child
  - HIV can infect the fetus in utero, or during birth
    - Without treatment, rate of transmission is 25%
  - Breast-feeding

Risk of HIV infection
- Most HIV-positive people do not know they are infected
- Long incubation period between infection and major illness
- Most people have no access to testing
- Stigma

Treating AIDS: Antiretroviral (ARV) therapy
- >30 drugs have been developed that suppress the virus
- Usually given in a “cocktail” of 3 - 4 pills
- Expensive, must be maintained for the rest of the patient’s life
  - Avoid developing resistance to drugs
  - Still no known cure or vaccine for HIV

ARV targets
- Drugs that inhibit viral enzymes
  - Reverse Transcriptase inhibitors
    - Inhibit conversion of viral RNA into DNA
  - Integrase inhibitors
    - Inhibit integration of viral genome into host genome
  - Protease inhibitors
    - Inhibit enzymes that cut viral proteins into pieces → protein coat of new HIV particles

With the use of ARVs, AIDS is now a chronic illness in industrialized nations

Prevention efforts have lagged
- New approaches
  - Condoms
  - ARV drugs – reduce viral load
  - Giving ARVs to HIV positive pregnant women
  - Routine testing
  - Male circumcision
    - reduces risk of female-to-male transmission by 60%
  - Needle exchanges
- Still in R&D stage
  - Vaginal microbicides
  - HIV Vaccine – the holy grail