Stem Cells in Life and Disease:

Immortality Inside You

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Splash! Fall 2012

What do you think a stem cell is?

(discuss with people around you)

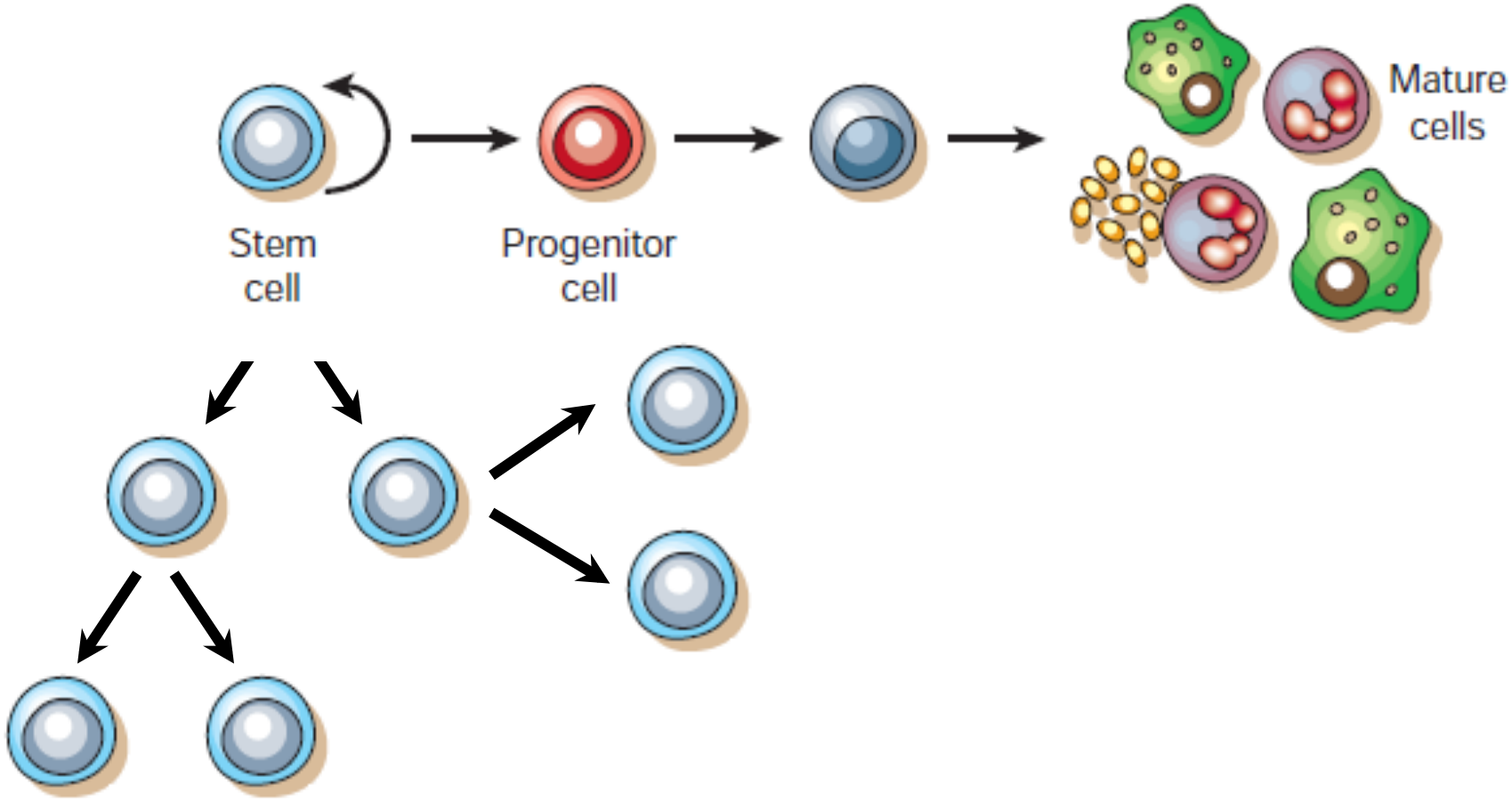
A stem cell is one that can BOTH:

(1) Self-Renew.
(2) Differentiate into other kinds of cells.

Stem Cells Are Immortal

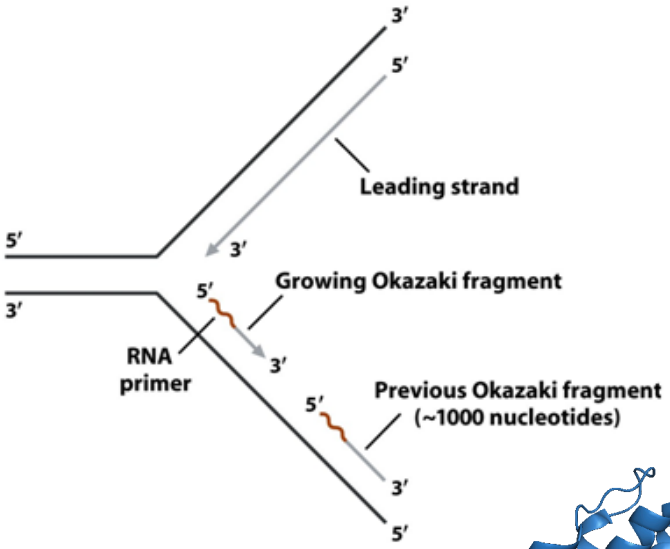
What makes a cell immortal?

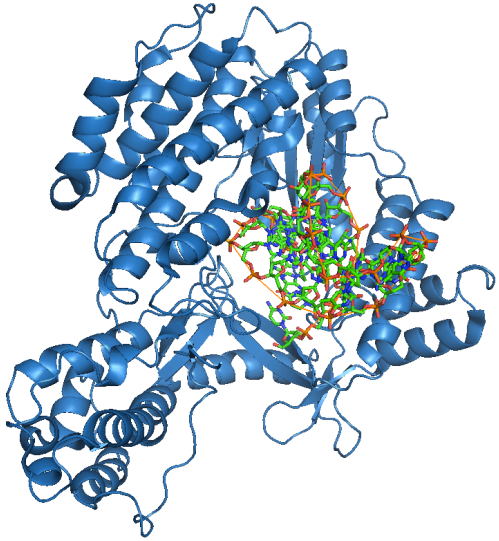
1. Self-renewal: the ability to make copies of yourself.

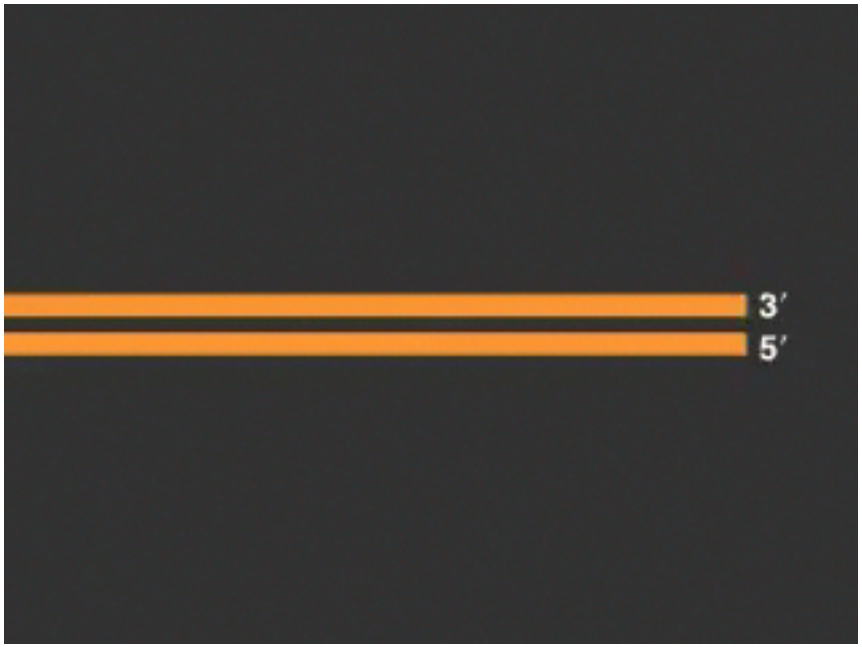


What else makes a cell immortal?

2. Unlimited Replication: the ability to divide forever.







http://www.youtube.com/watch?v=AJNoTmWsE0s

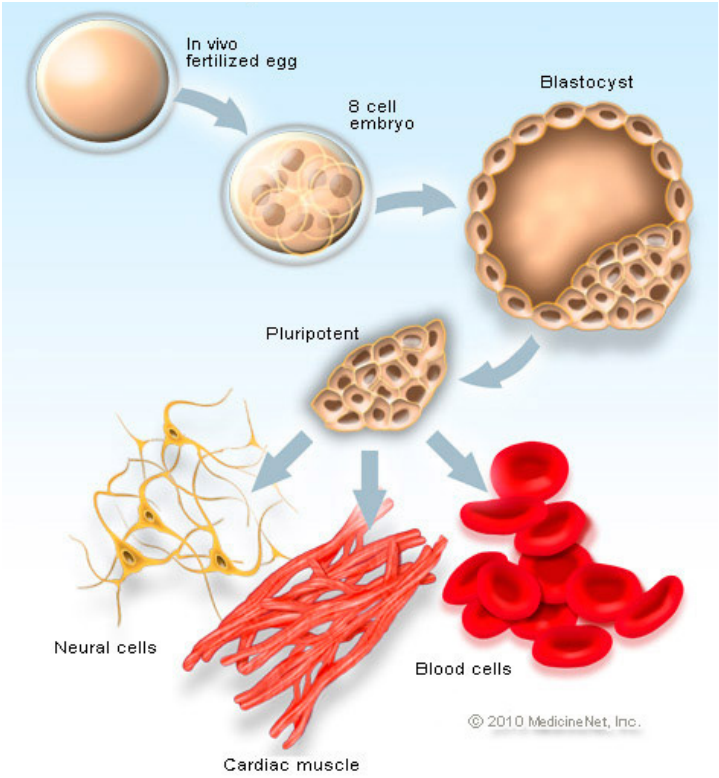
Is there more than one type of stem cell? If so, how many?

YES! There are many types of stem cells,
and we still haven’t even found them all…

Embryonic Stem Cells

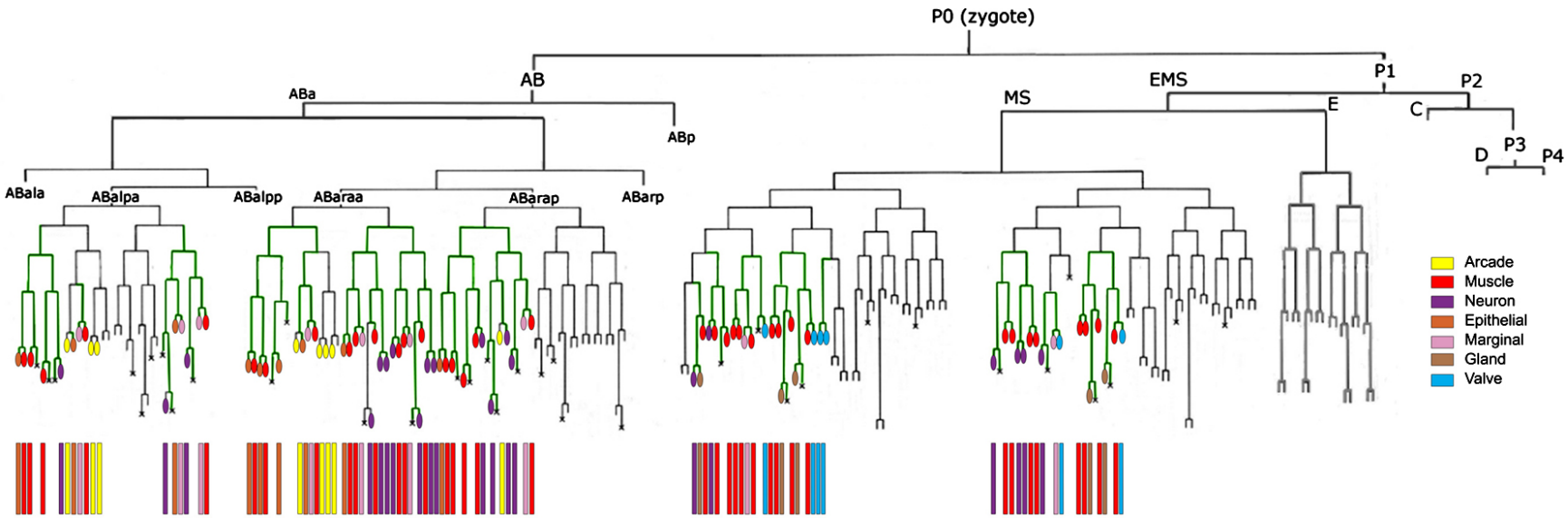
Embryonic stem cells are pluripotent stem cells first seen in the blastocyst that can give rise to the entire organism.

http://homepages.wmich.edu/~dkane1/flipbook/Flipbook%20Movie.mov

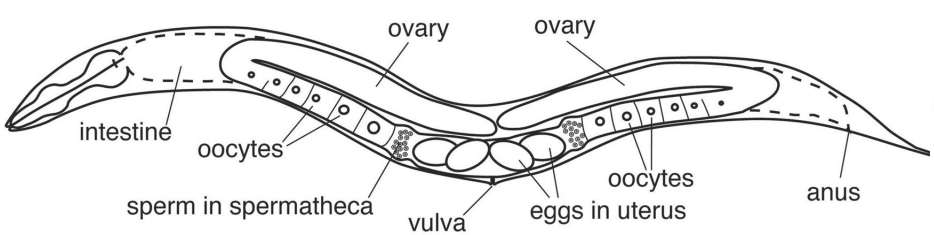


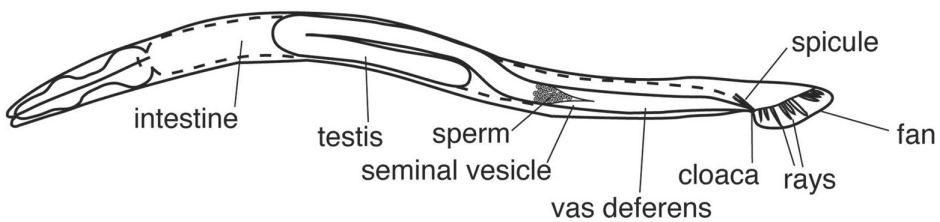
Danio Rario

The “Lineage” Concept



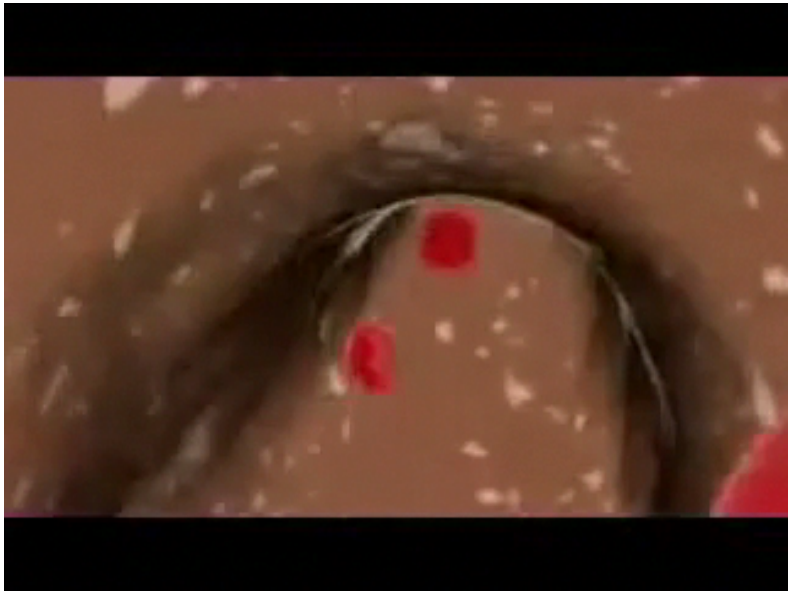
Caenorhabditis Elegans

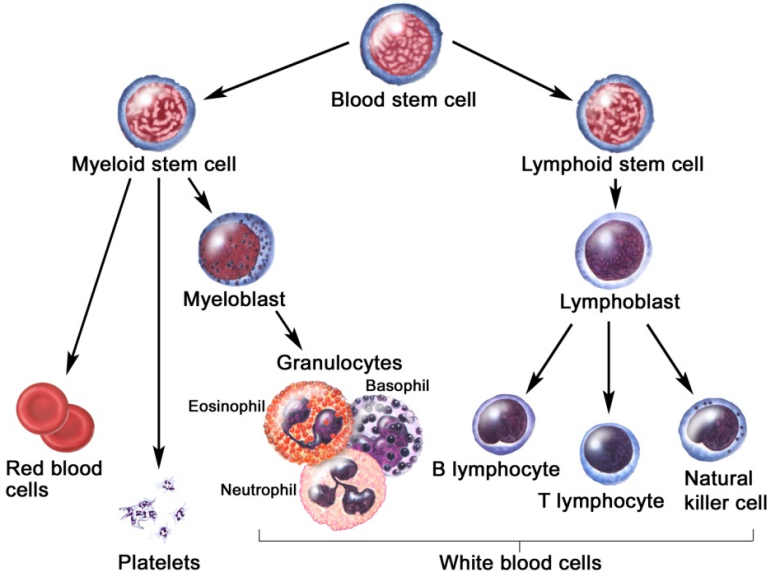




Adult Stem Cells in the Blood

Hematopoietic stem cells give rise to all red and white blood cells and platelets.

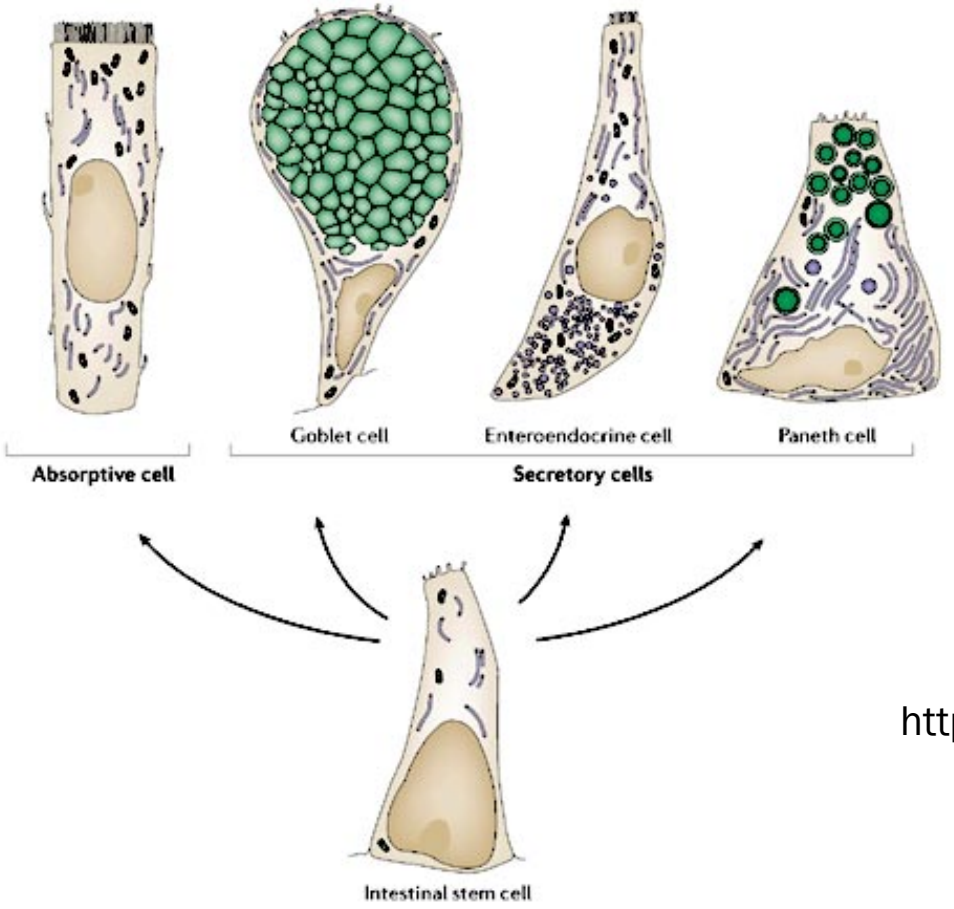




http://www.youtube.com/watch?v=mUcE1Y_bOQE

Adult Stem Cells in the Intestine

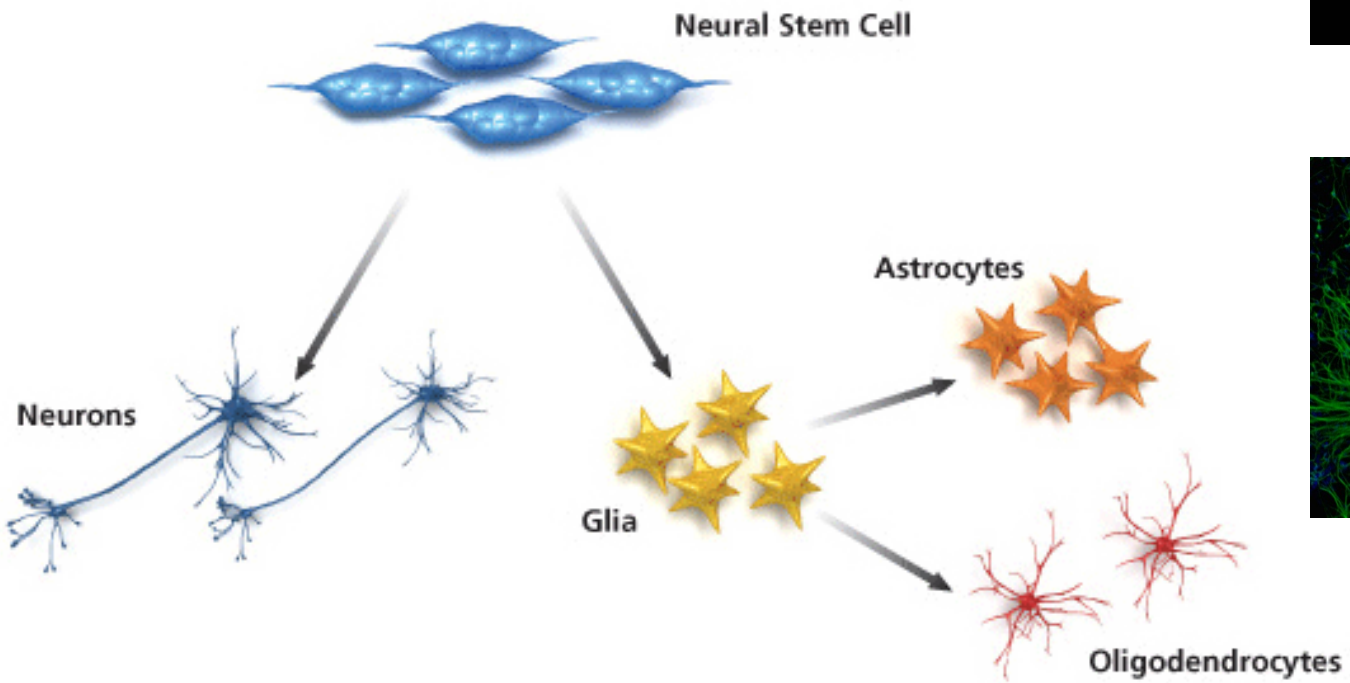
Intestinal stem cells maintain and repair intestinal tissue – they are the most rapidly dividing stem cells in the human body.

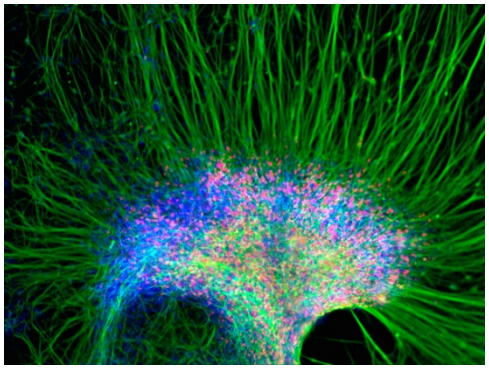


http://www.youtube.com/watch?v=mUcE1Y_bOQE

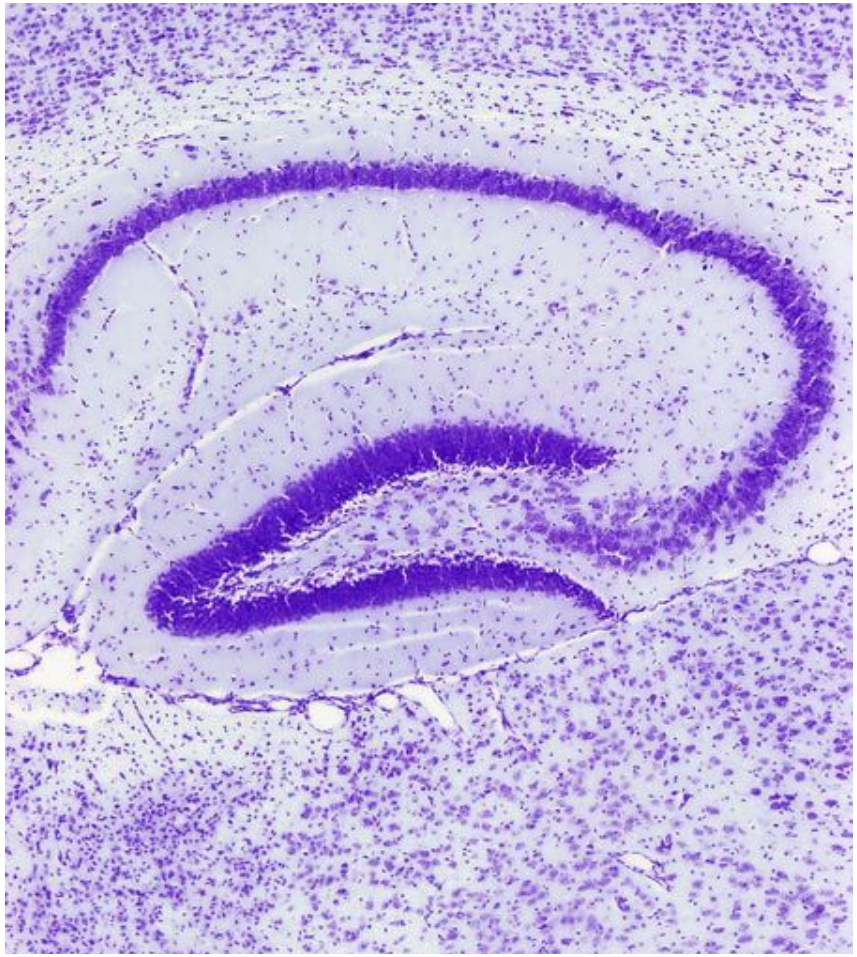
Adult Stem Cells in the Brain

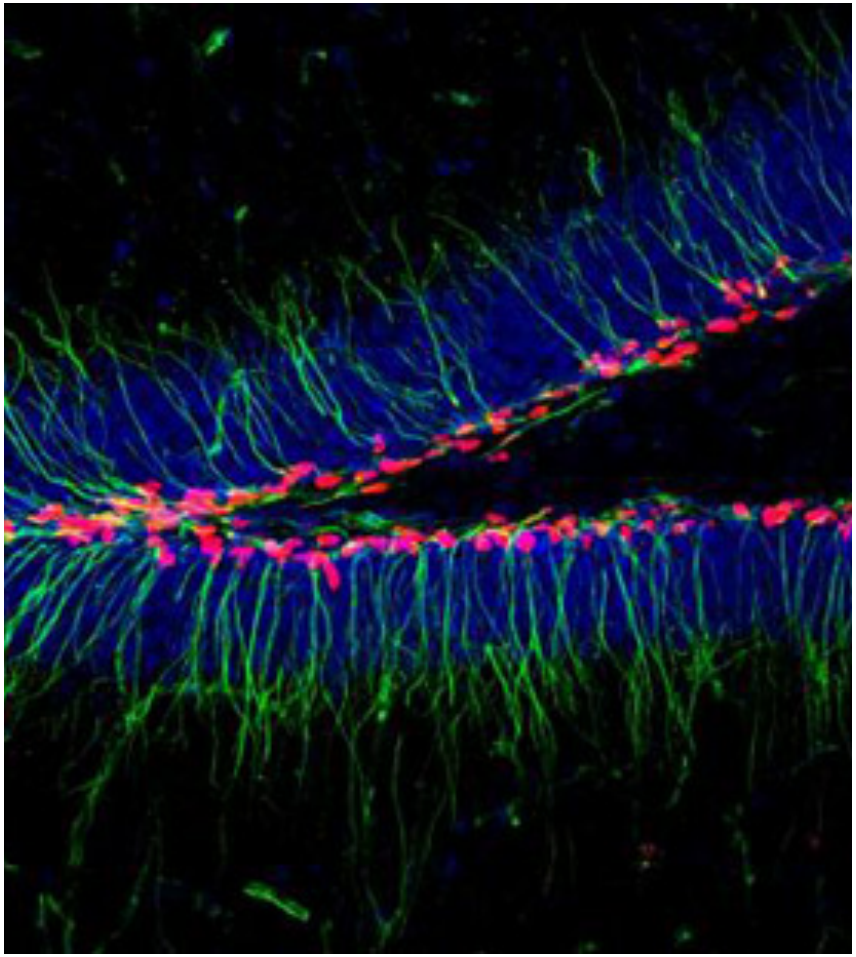
Neural stem cells build neurons, which allow learning and memory, and glial cells in the brain and spinal cord.



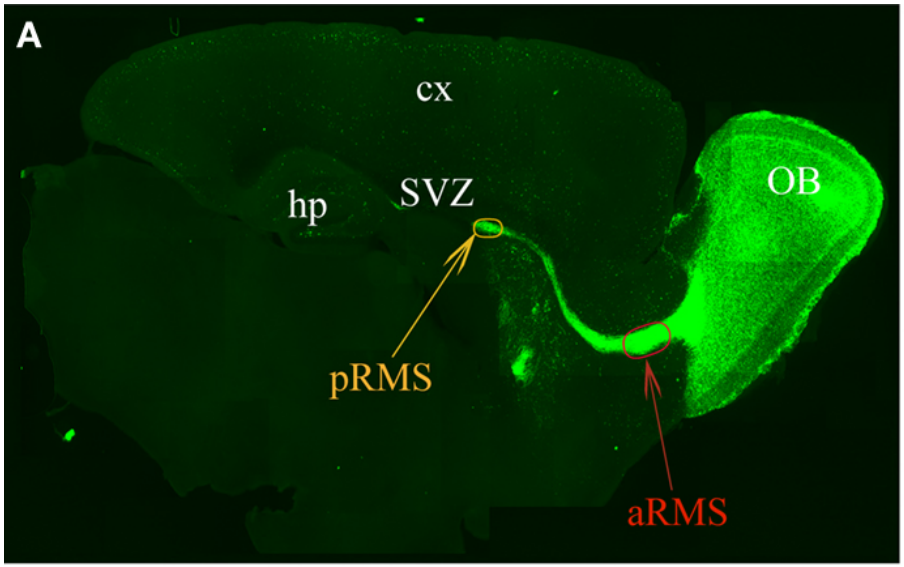


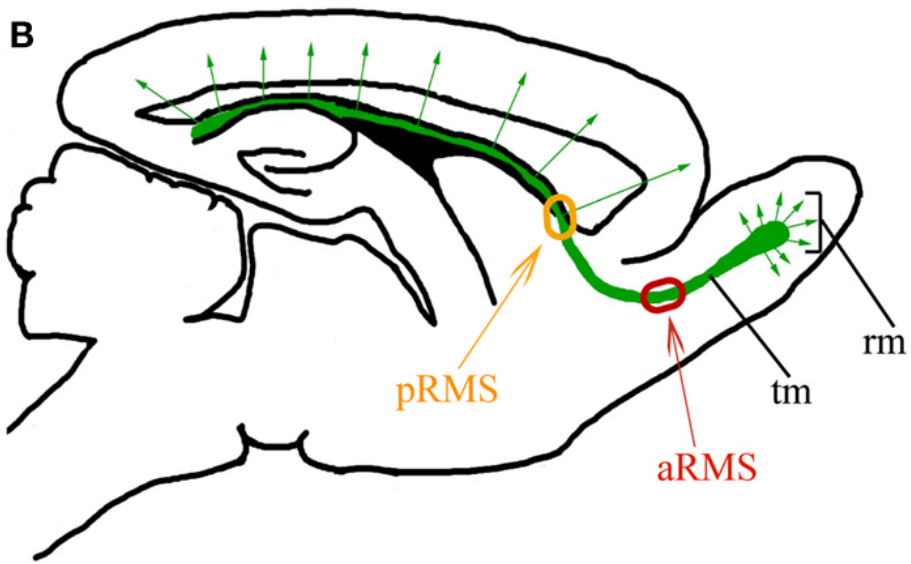
Neural Stem Cells Serve Memory Functions



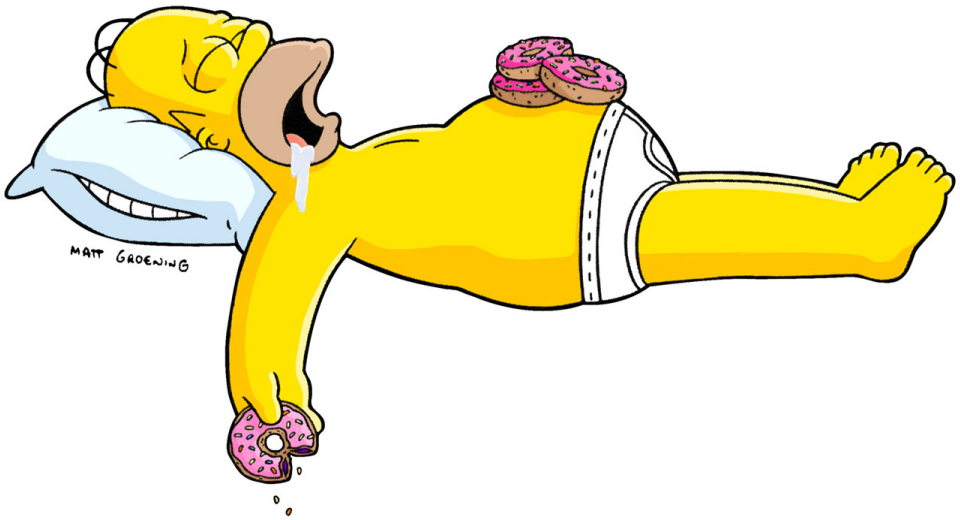


They Are Important in Olfaction (smell)

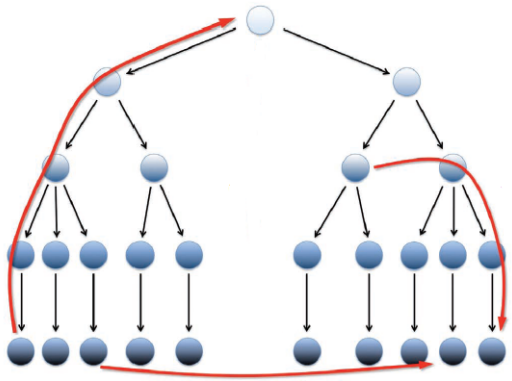




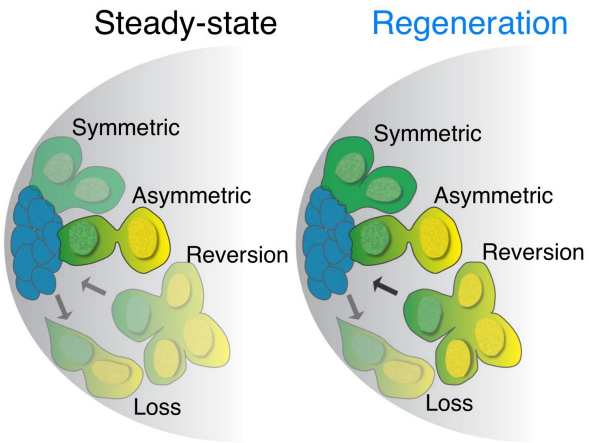
They Can be Influenced by Diet and Exercise

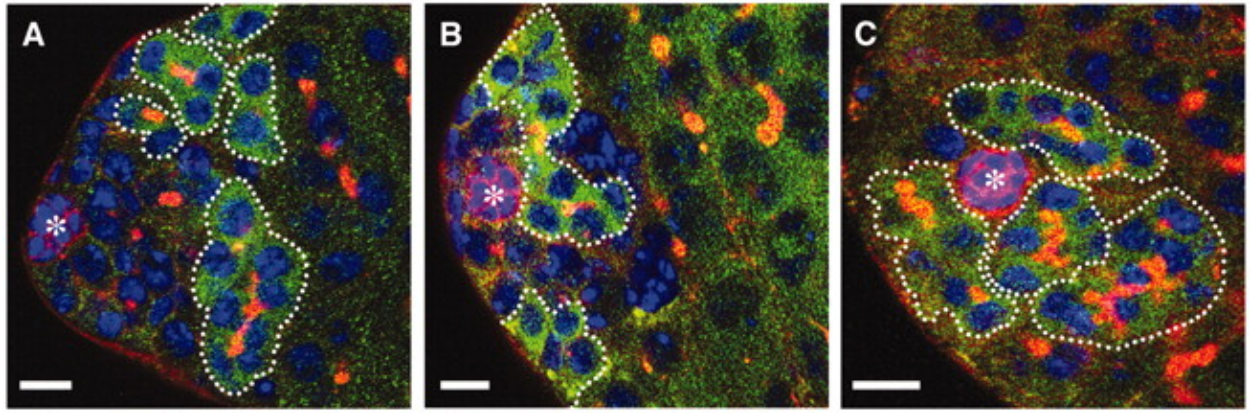


They can sometimes de- or trans-differentiate

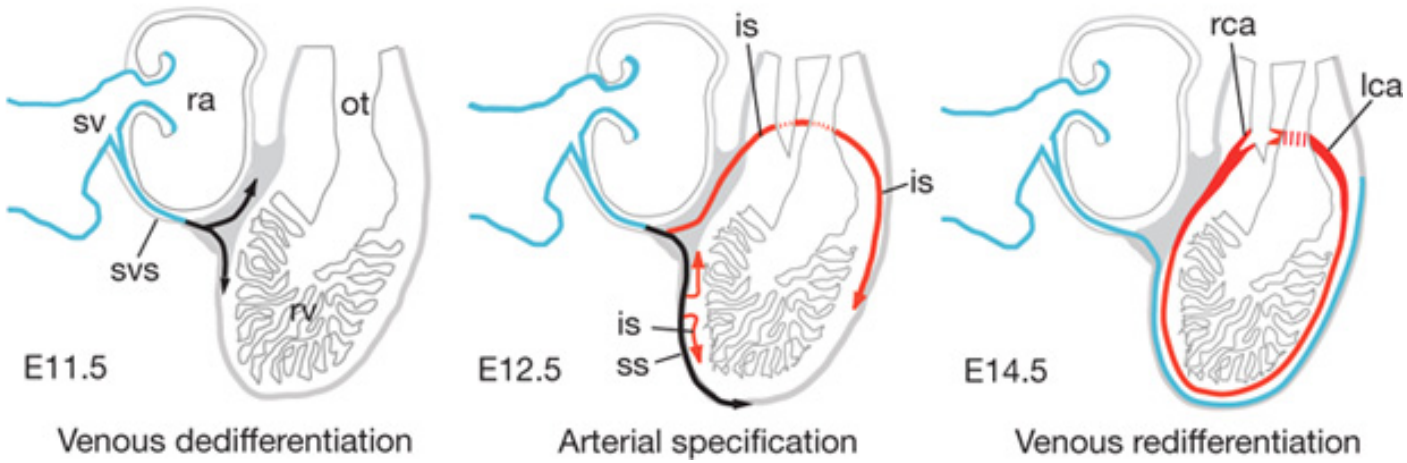


Drosophila Melanogaster





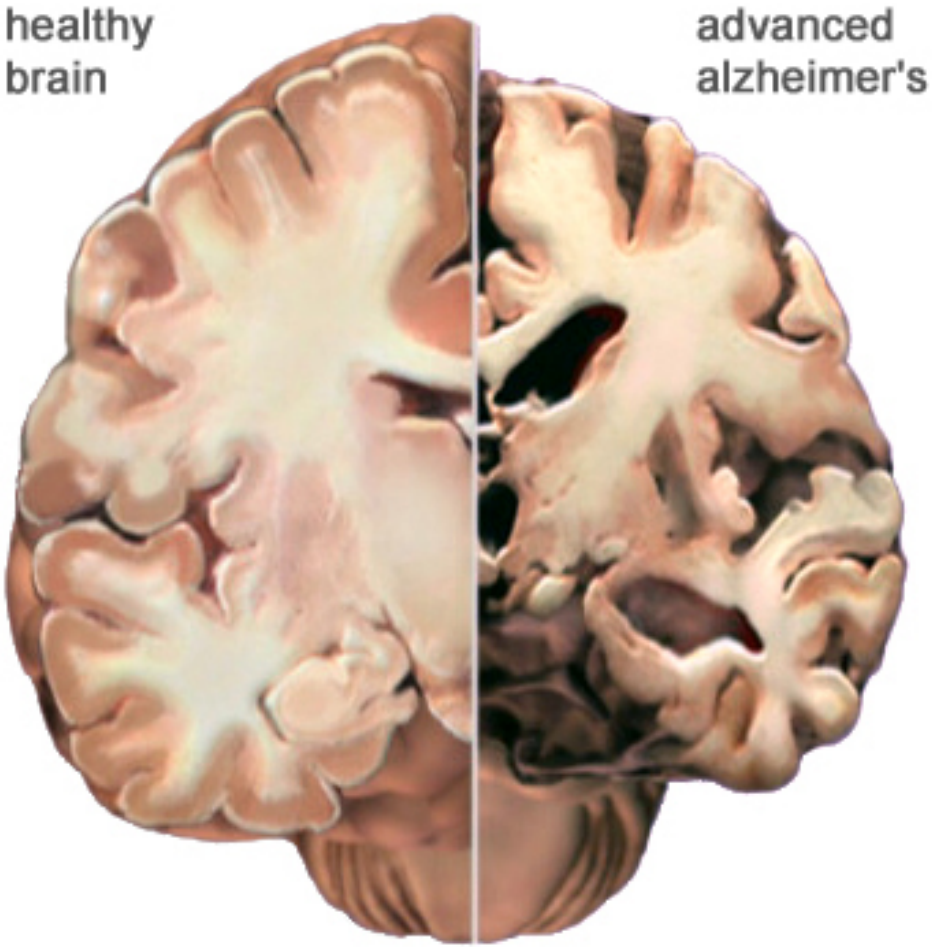
Mus Musculus



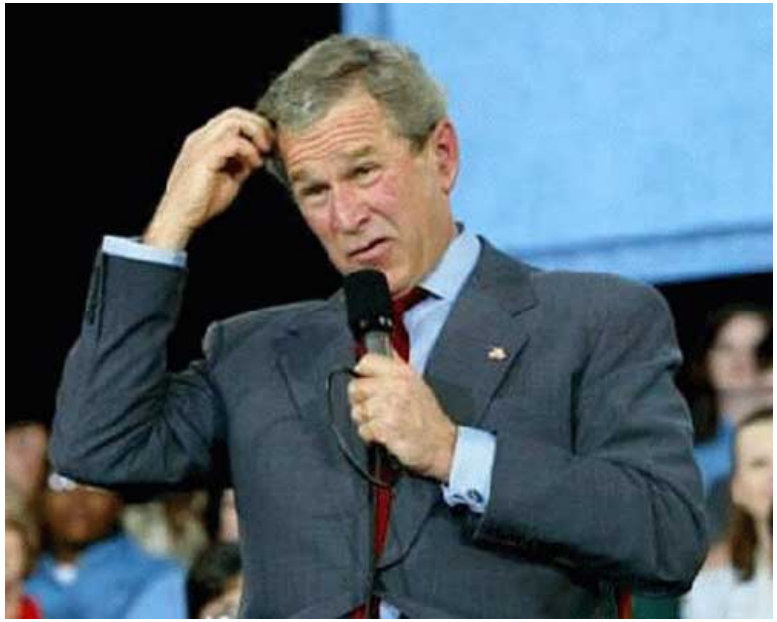
Degenerative Diseases

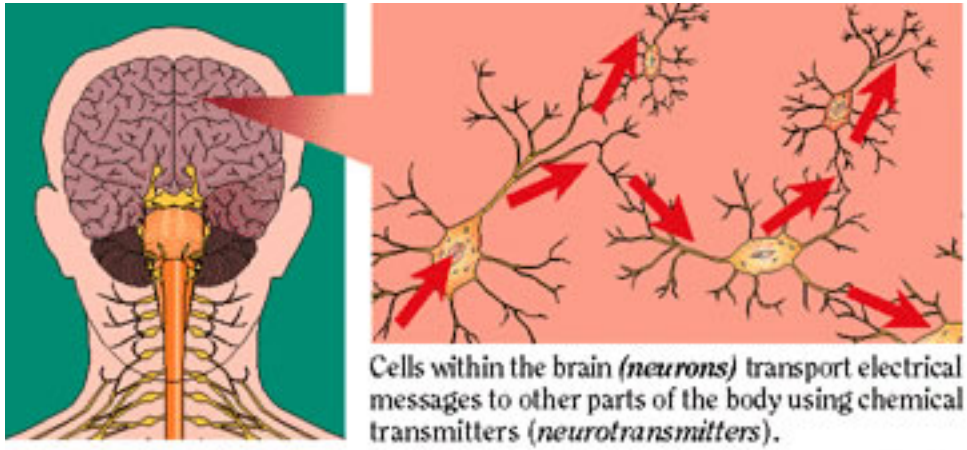
Alzheimer's disease
Parkinson's disease

Alzheimer’s Disease

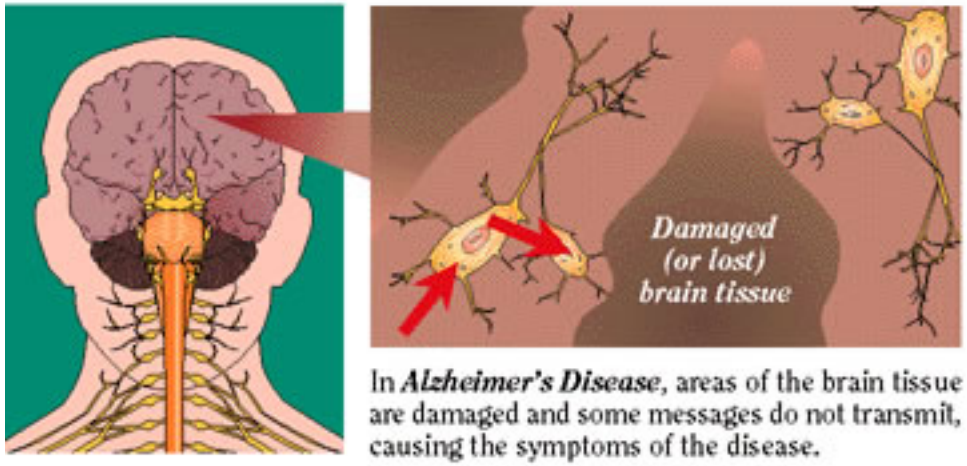


Symptoms



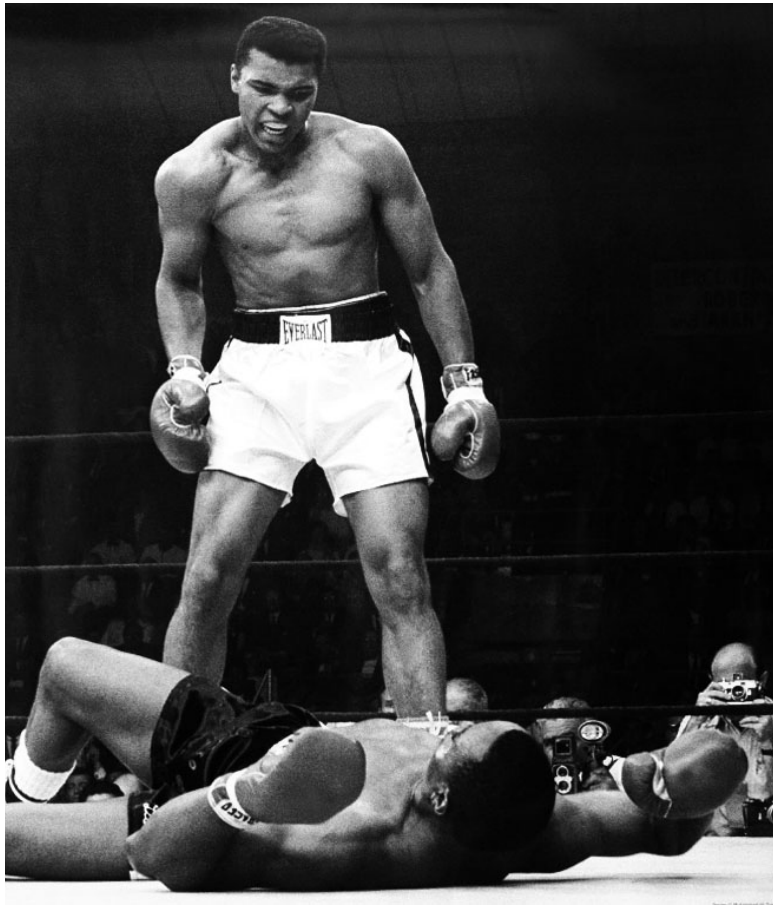


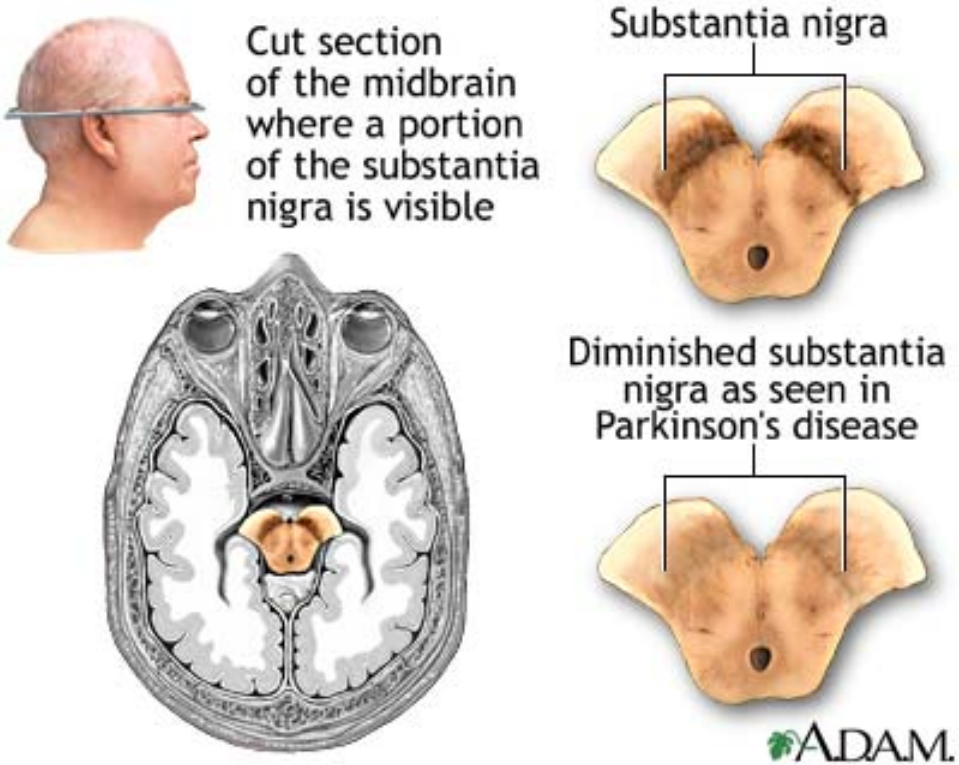
Cells within the brain *(neurons)* transport electrical messages to other parts of the body using chemical transmitters (*neurotransmitters*).



In ***Alzheimer's Disease***, areas of the brain tissue are damaged and some messages do not transmit, causing the symptoms of the disease.

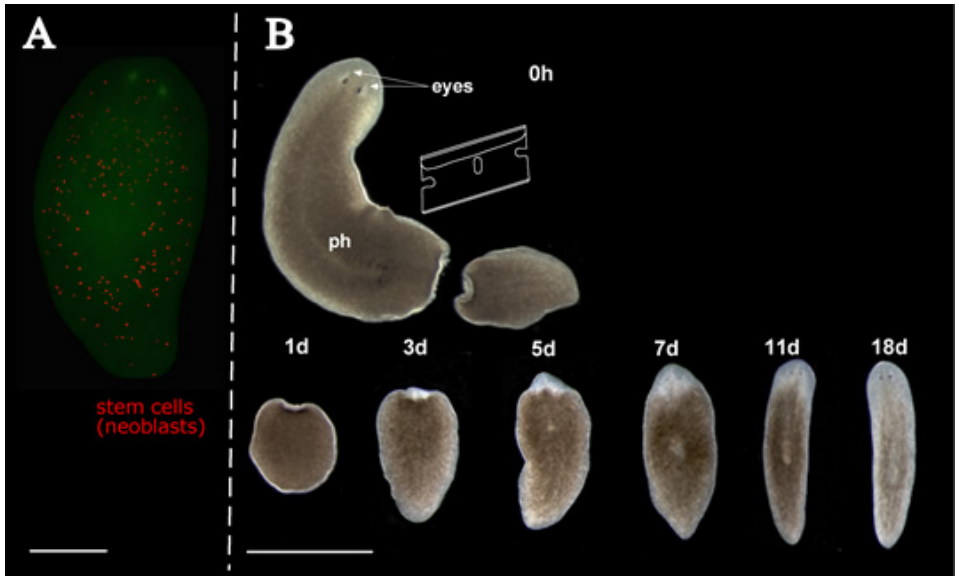
Parkinson’s Disease



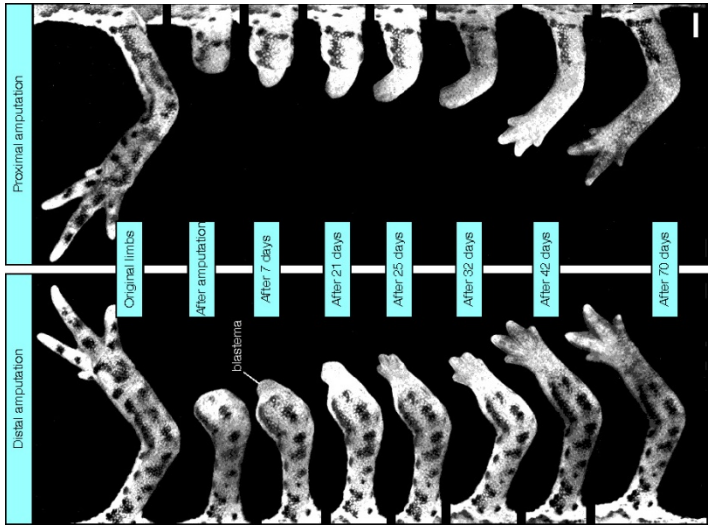


Regeneration: Non-Human Examples

<u>Planaria</u> (flatworms) can regrow their entire body! Someone even showed that 1/127 of a worm is sufficient to regrow the whole thing!



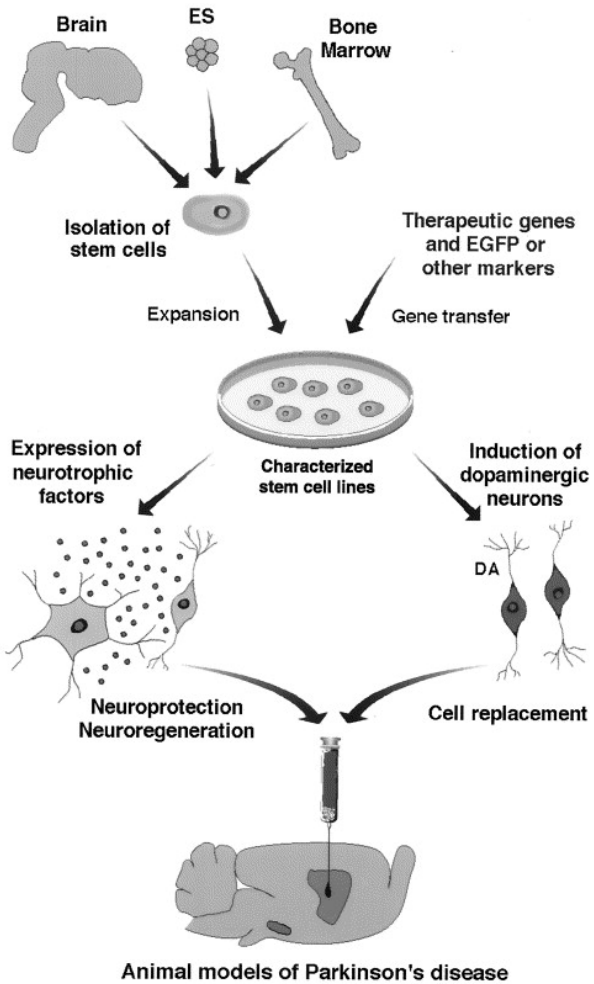
<u>Newts</u> (and salamanders) are vertebrates that can regrow whole limbs, tails, eyes, etc.



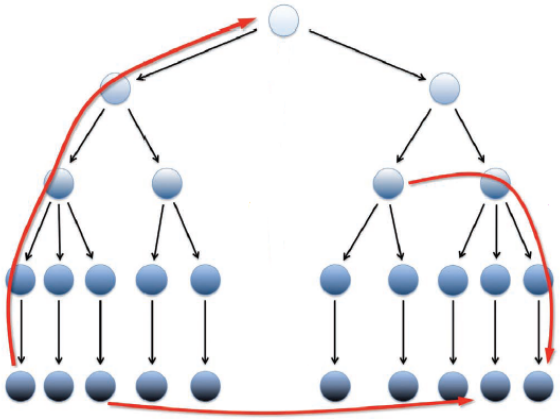
Humans can’t naturally regenerate as well as some animals can, so how would you design a regenerative therapy for degenerative diseases like Alzheimer’s and Parkinson’s?

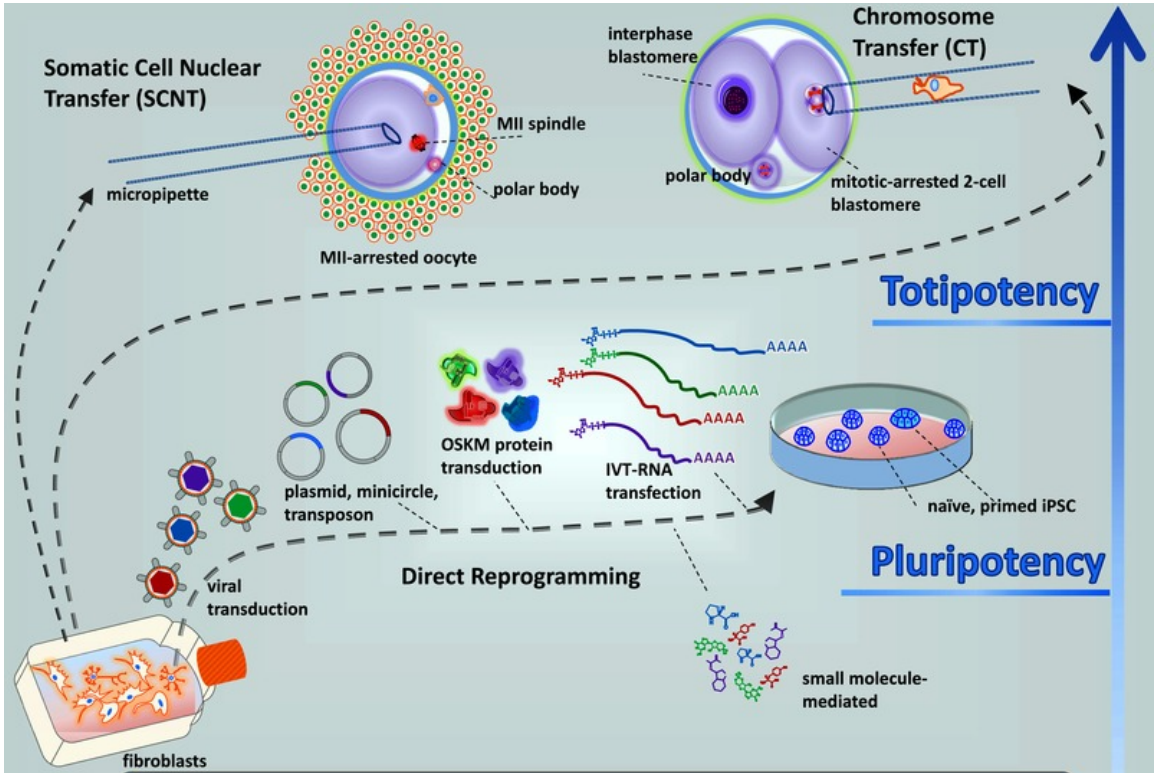
Many scientists are working on stem cell therapies for this exact purpose.

Treating Humans with Stem Cells

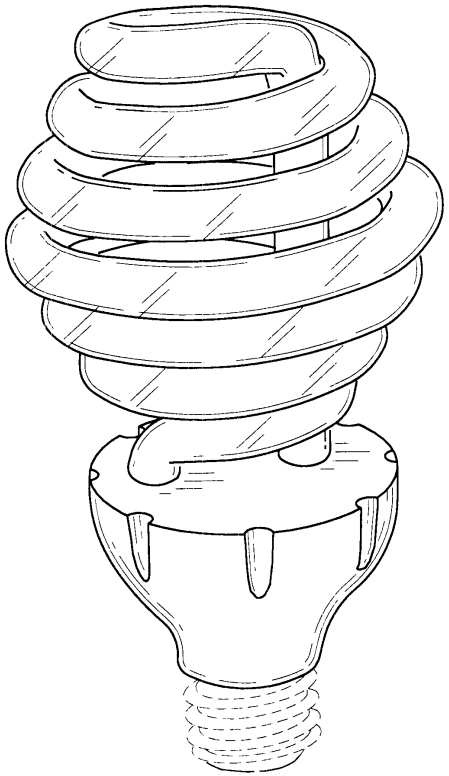


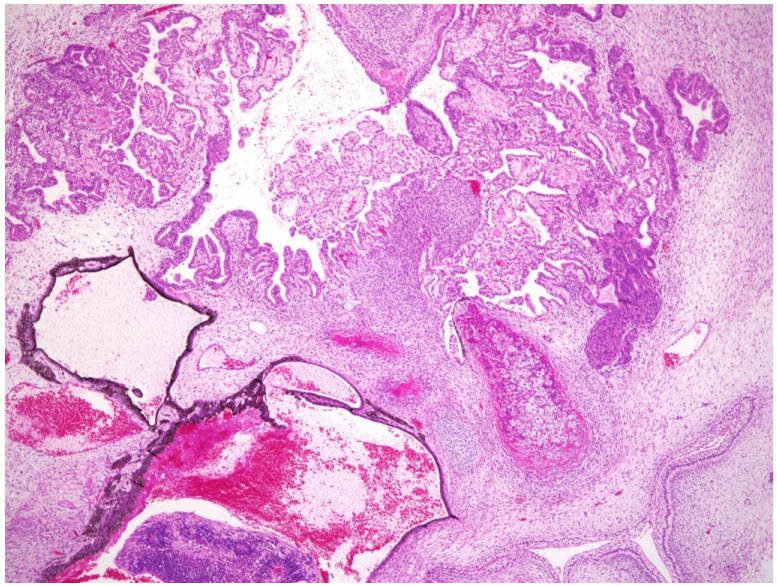
iPS Cells: an (unlimited?) source of stem cells

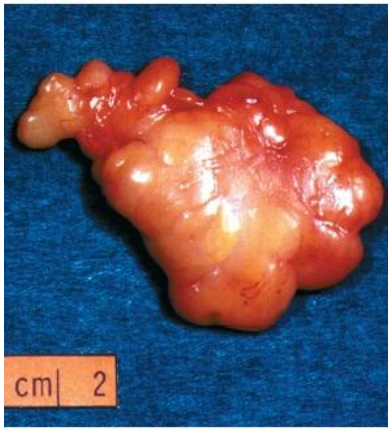




Problems with iPS Technology

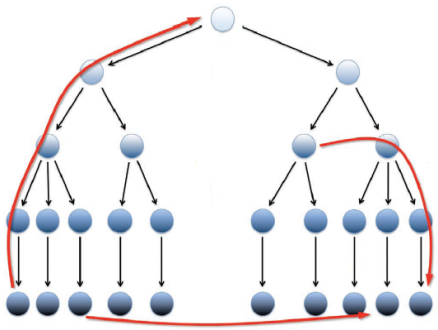




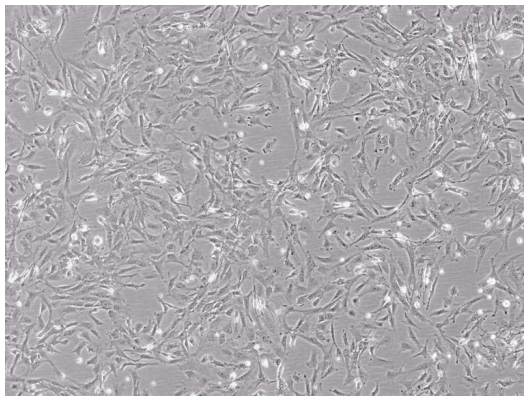


Direct Reprogramming

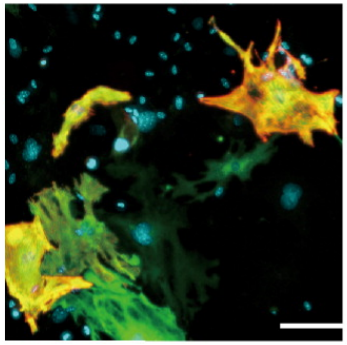
In addition to converting adult cells “back” into iPS, scientists can now also convert them directly into other cell types.



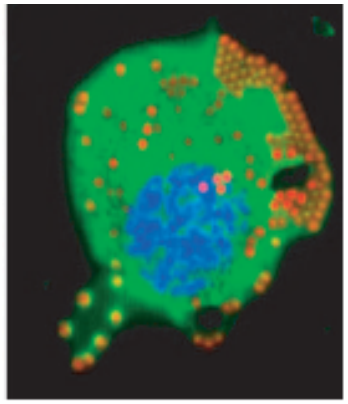
Fibroblasts



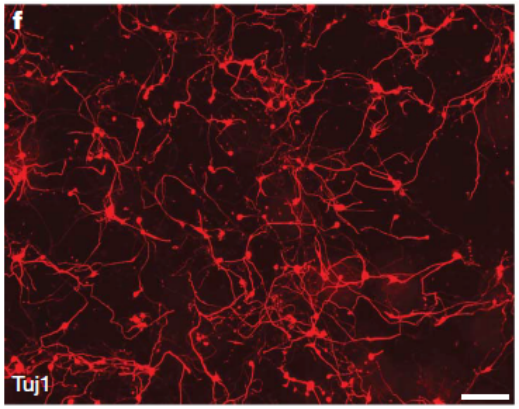
Cardiomyocytes



Macrophages



Neurons

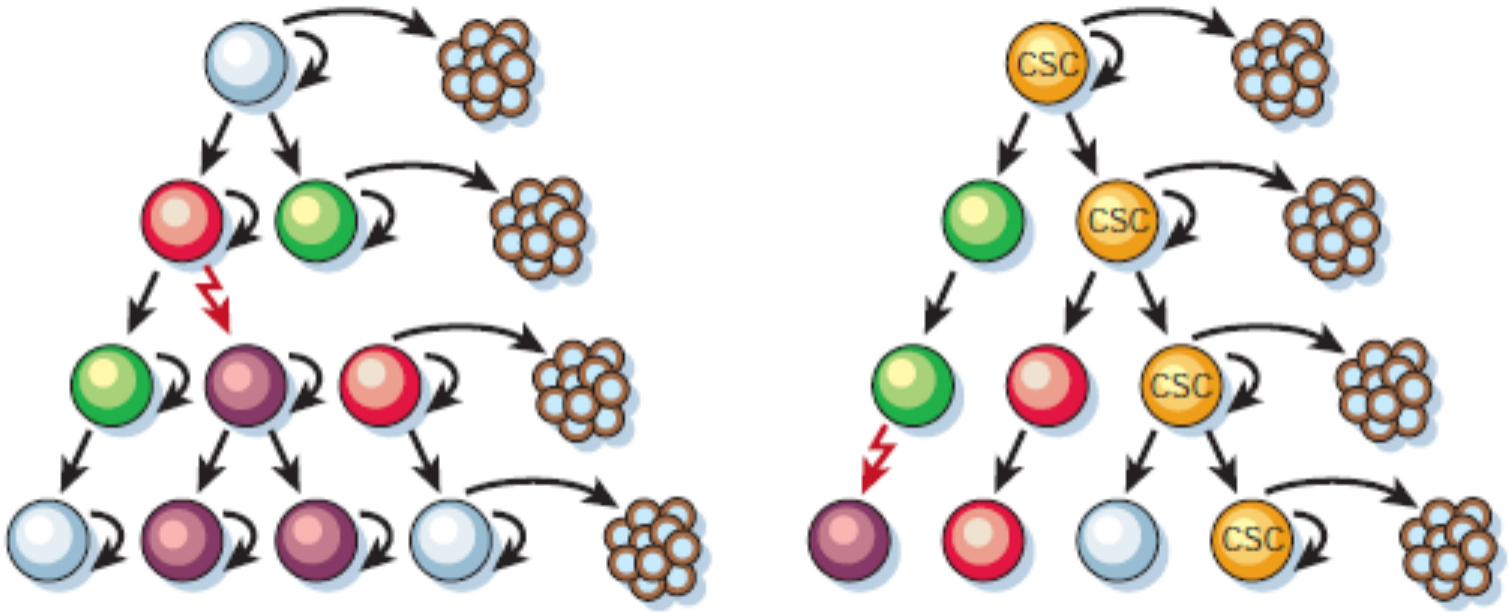


Overproliferative Diseases

Cancer

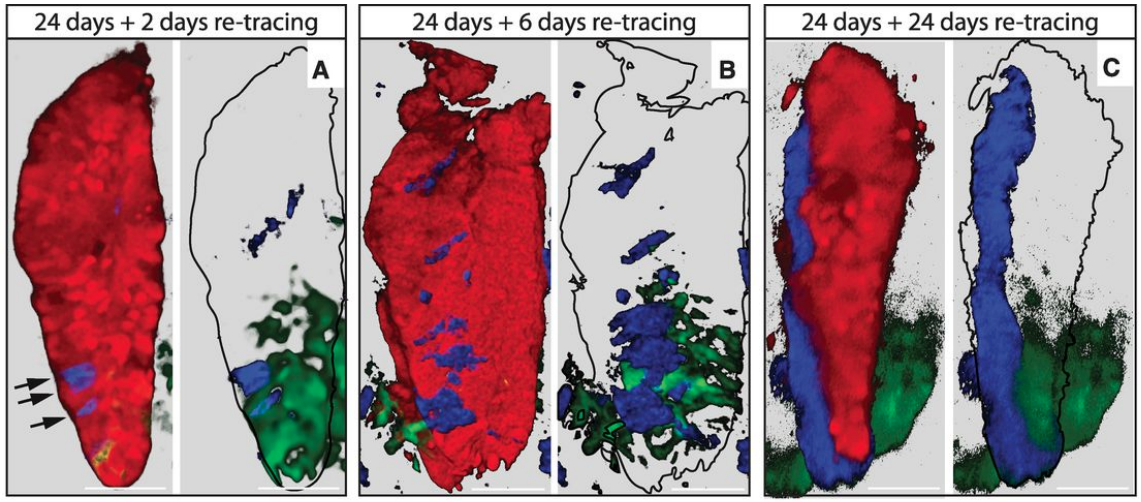
Stem Cells in Cancer

One major question in cancer therapy is, do cancers act like normal organs?

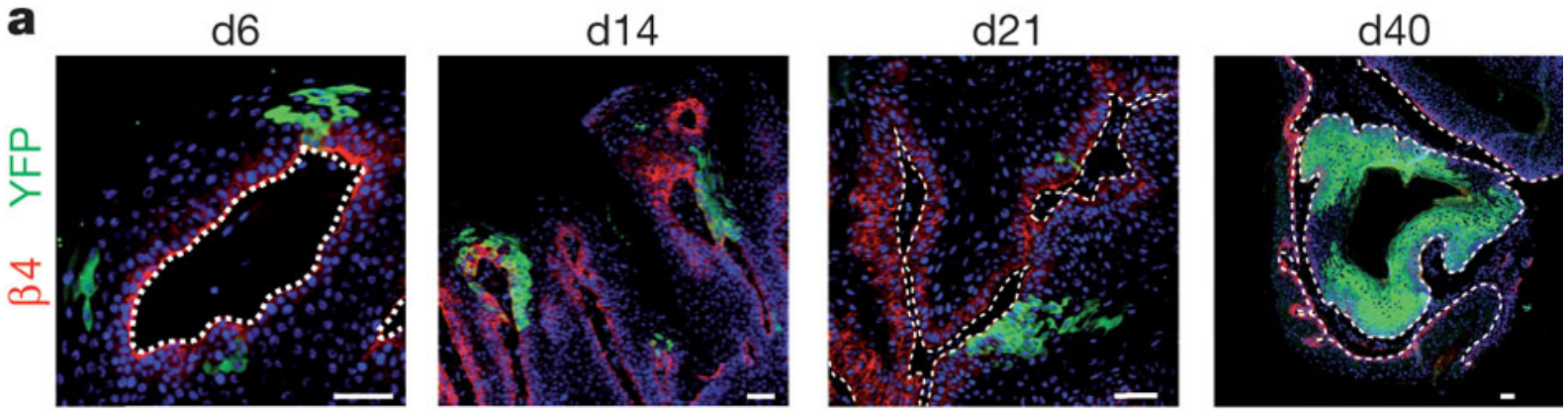


Direct evidence for Cancer Stem Cells

Mouse Intestinal Crypts (Intestinal Cancer)



Mouse Epidermis (Skin Cancer)



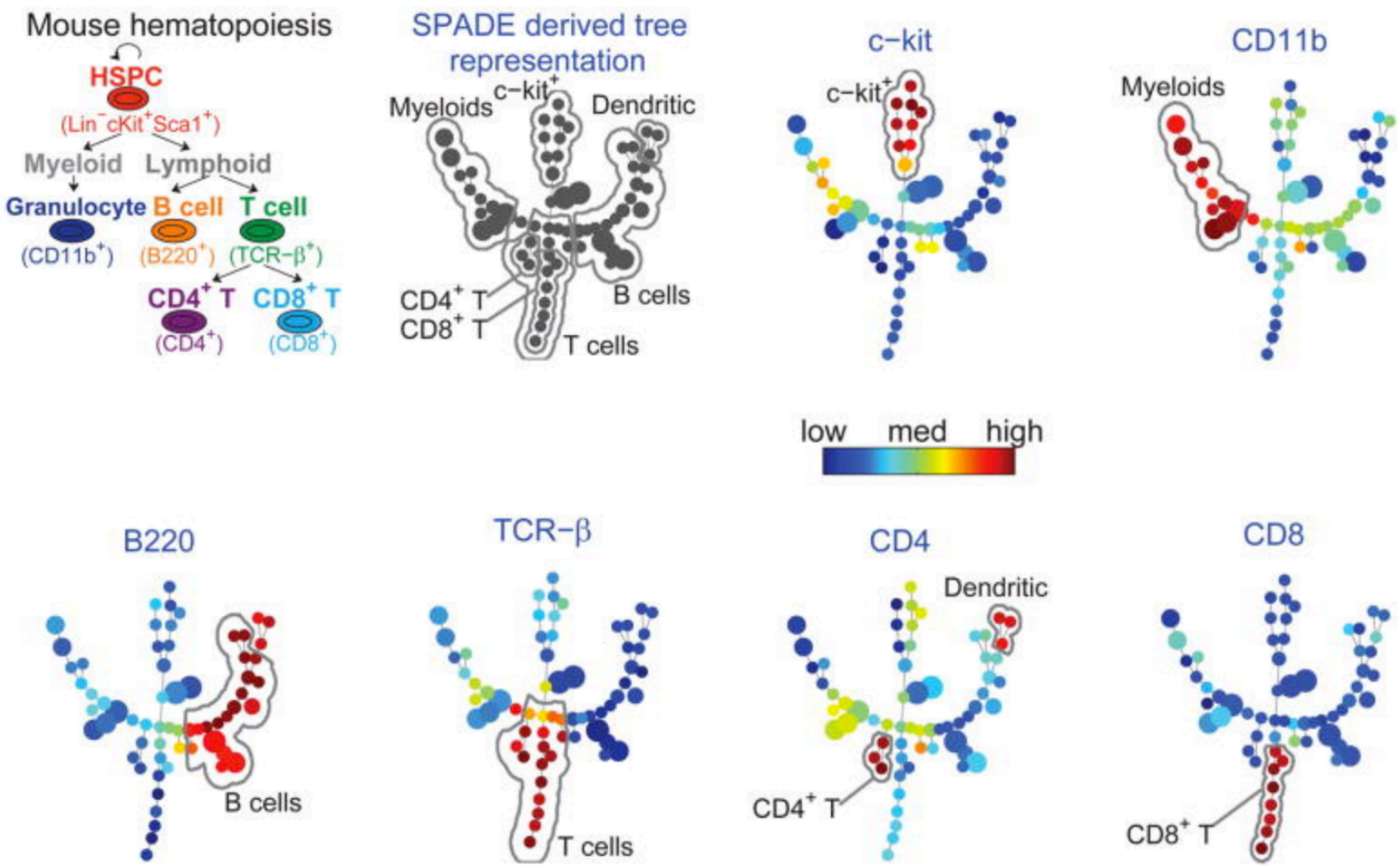
Finding Cancer Stem Cells

1. Surface Antigens – “flags” that cells express on their surface to identify themselves.
2. Transcription Factors – nuclear proteins that control what genes a cell expresses.

Why are they hard to find?

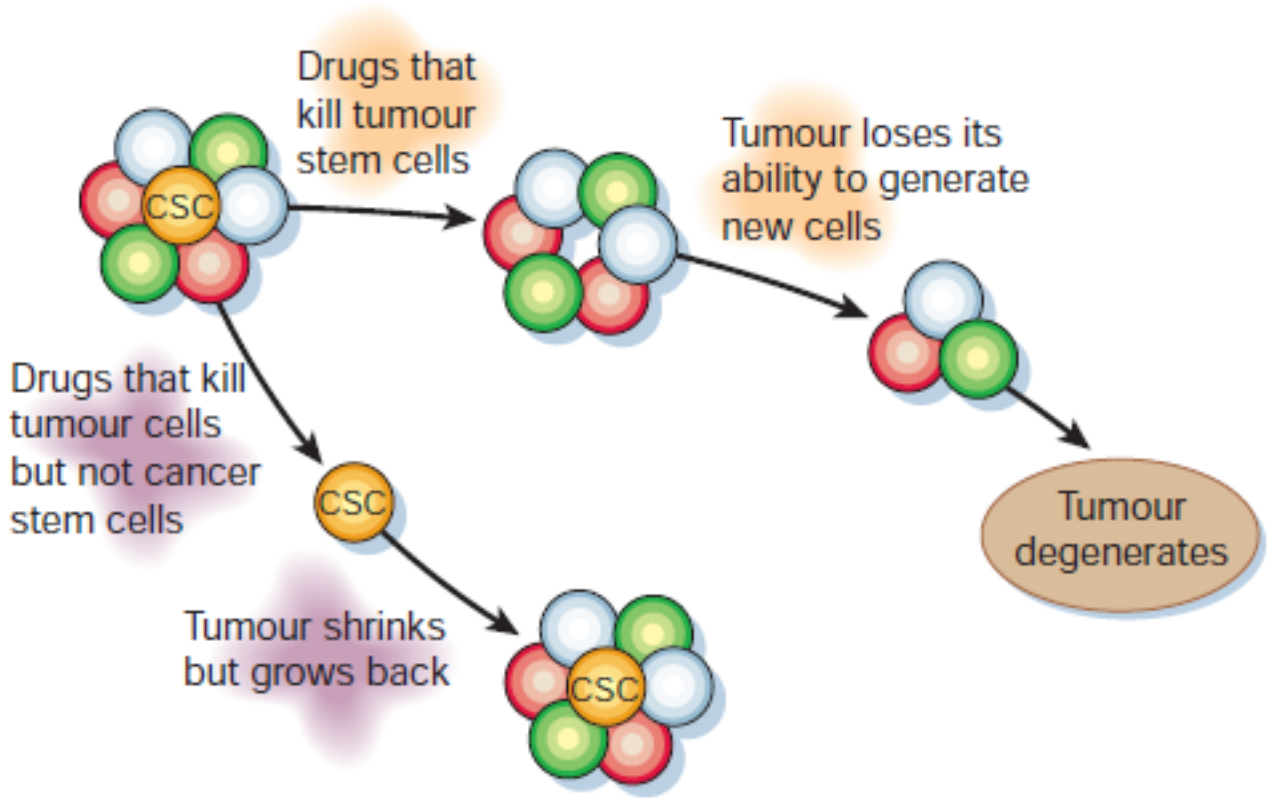
1. It is difficult to get human tumor samples.
2. Stem cells can be different in different tissues (especially in cancer) so it’s difficult to assign permanent CSC markers.
3. Cancer cells always have genetic mutations, so they can “choose” to follow some aspects of normal organogenesis and ignore others.

Finding cancer stem cells: Systems Biology



Why does the CSC model matter?

If cancers really do have their own stem cells, then we need to start designing smarter drugs to target them.



How would you design a drug that specifically targets cancer stem cells?

Antibodies that target CSC-specific markers can teach the immune system to consider those cells as an infection (immunotherapy).

Because stem cells tend to live in places with lots of blood vessels, anti-angiogenic drugs (like Avastin) might be good at targeting them.

Where is the stem cell field going?

Full genome sequencing now allows us to figure out entire gene networks that give stem cells their unique functions, as opposed to looking at one gene at a time.

Dedifferentiation and transdifferentiation have now been observed to occur naturally in both humans and other animals, so scientists are trying to figure out when, how, and why this happens.

Reprogramming (iPS or direct) tends to introduce mutations into the genome that can be damaging, so scientists are trying to find ways to reprogram cells less invasively for clinical use.

And much, much more…

The End!

Questions? (about anything)

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