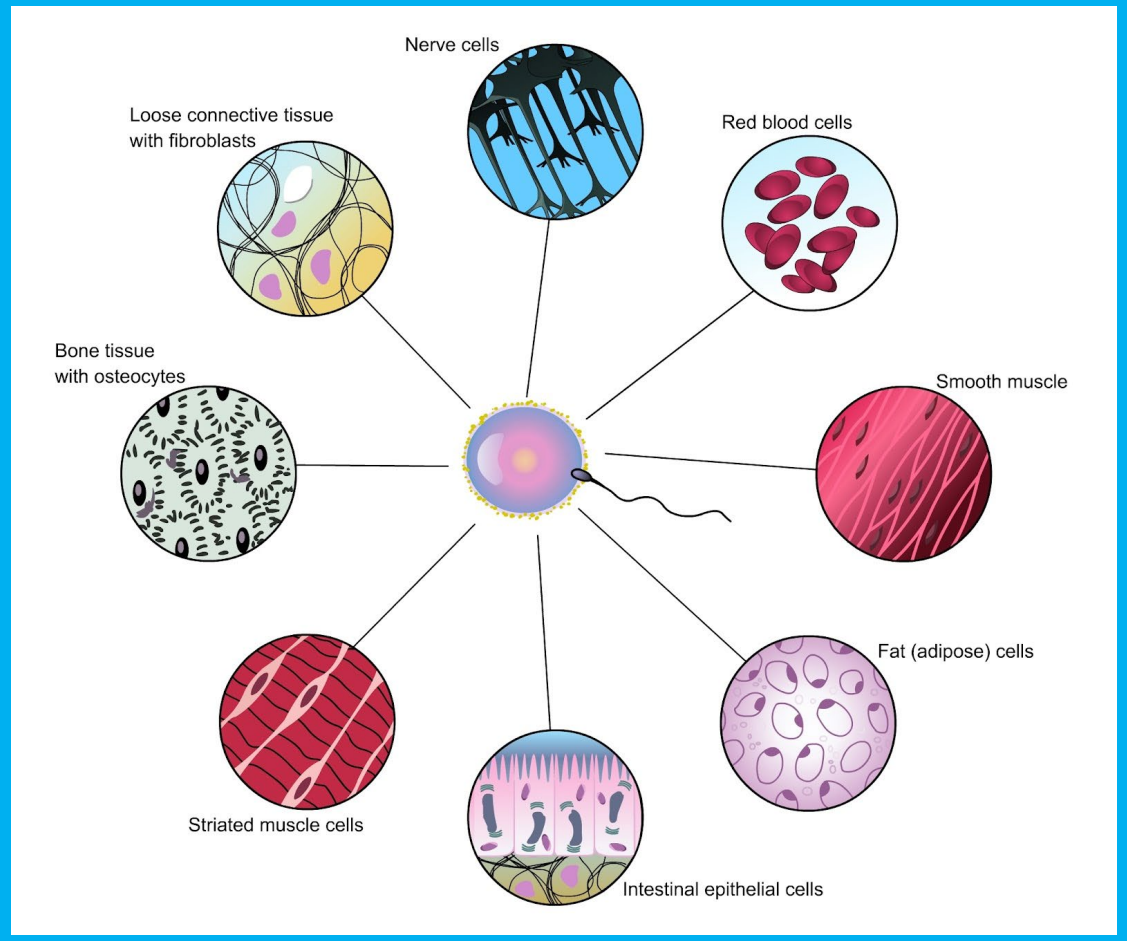


Cell Differentiation

Marjorie D. Shaw, Ph.D.

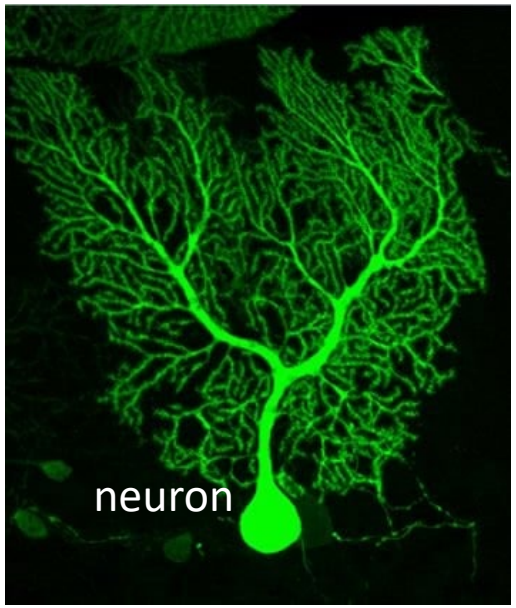
OLLI Spring 2024

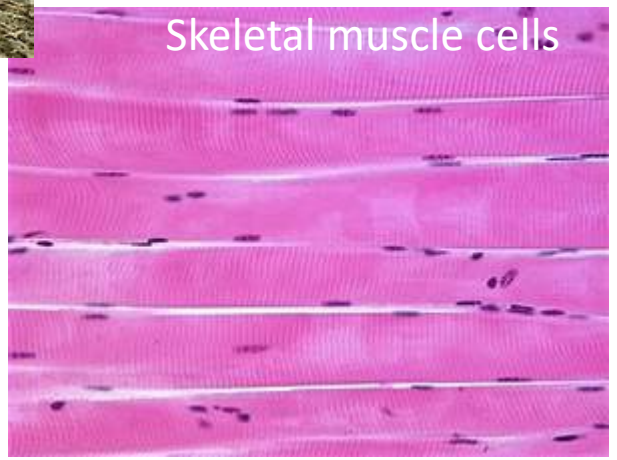
Study Group : 426

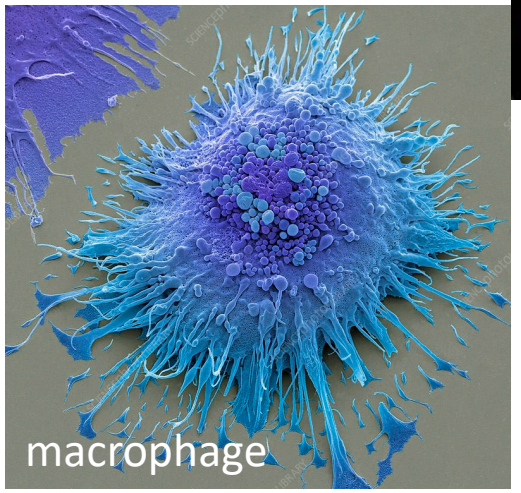
Differentiation

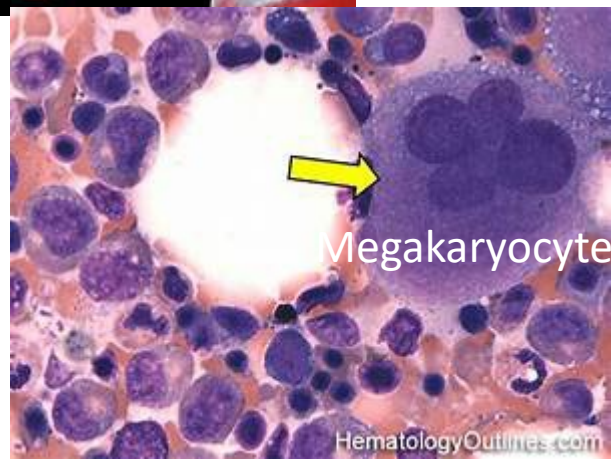
Now have a read-out of the entire human genome, but it's like having a list of all possible words and lots of nonsense besides. How can these be arranged to produce a Shakespeare?
All cells in one body have the same genome. How and when is each gene expressed (or inhibited), to create and operate a human body?

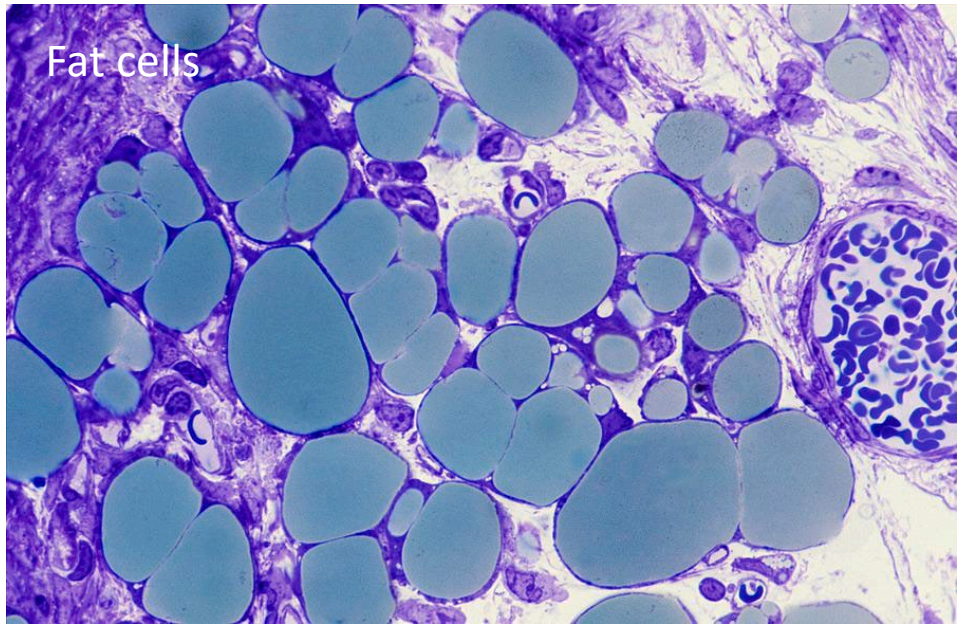
Specialized Cells





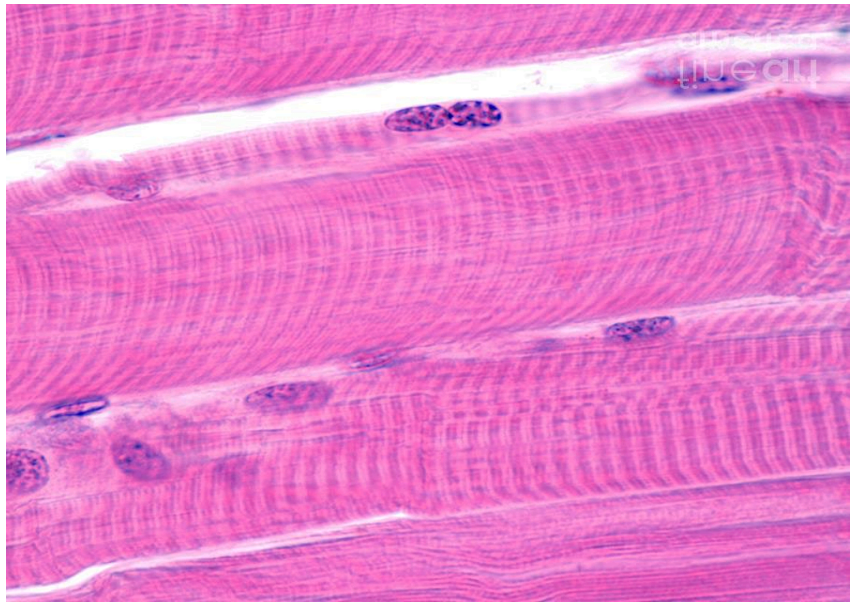


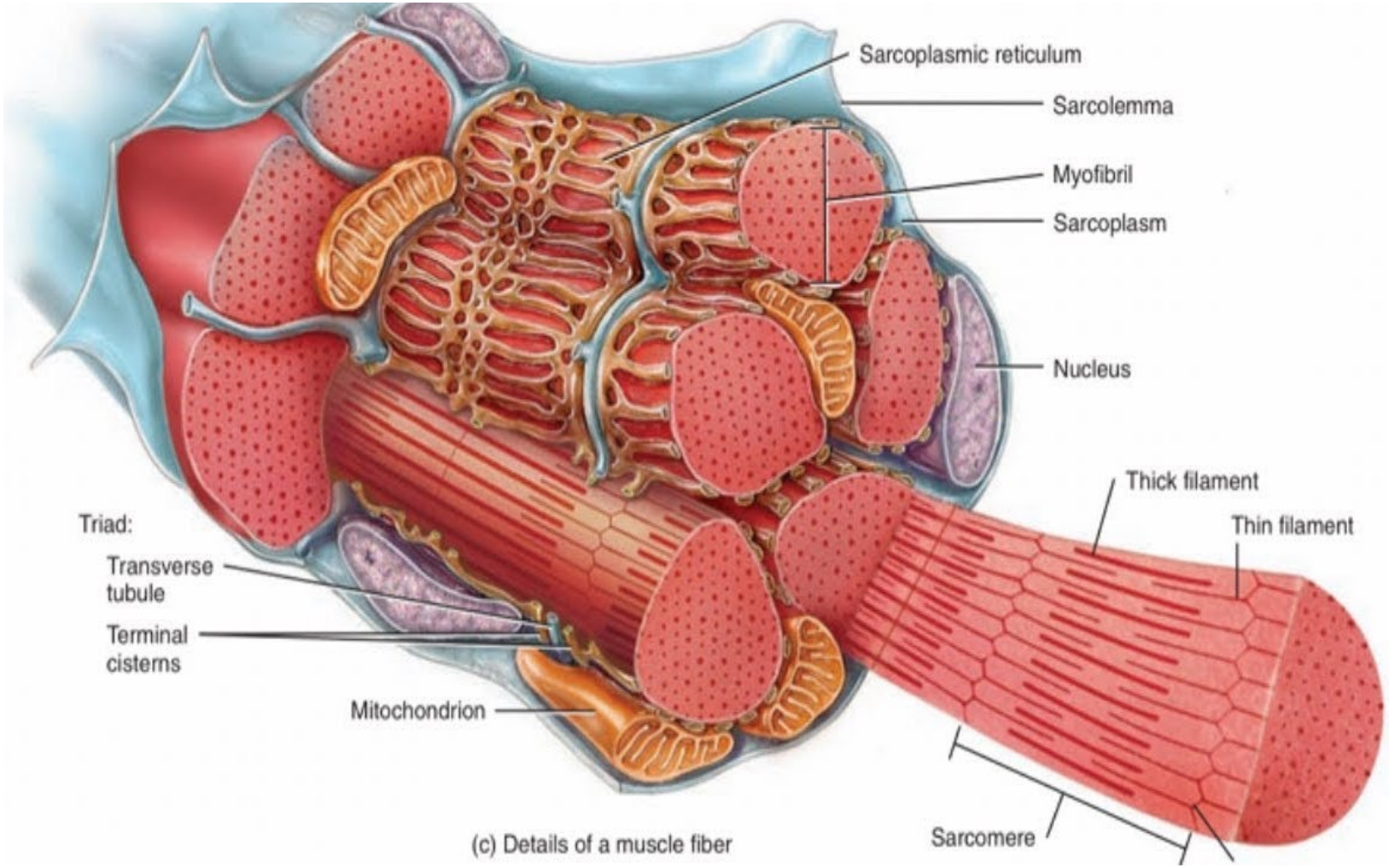




Skeletal Muscle: Actin + Myosin

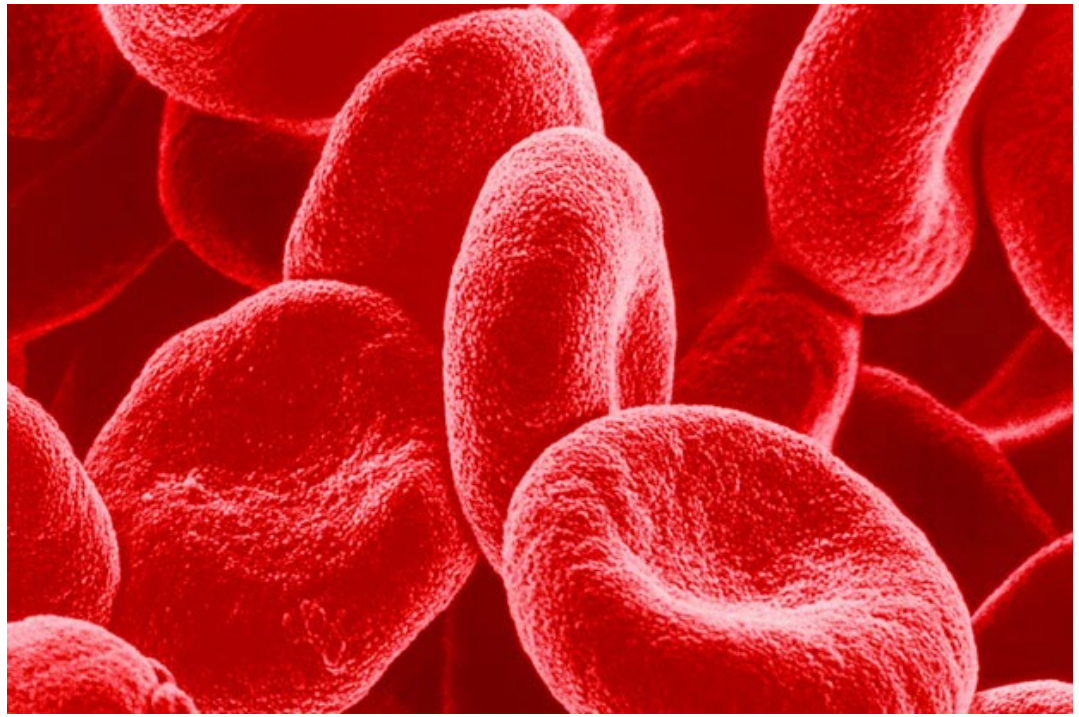
Microfilaments pack the cytoplasm; nuclei and sER forced to periphery. Many nuclei.



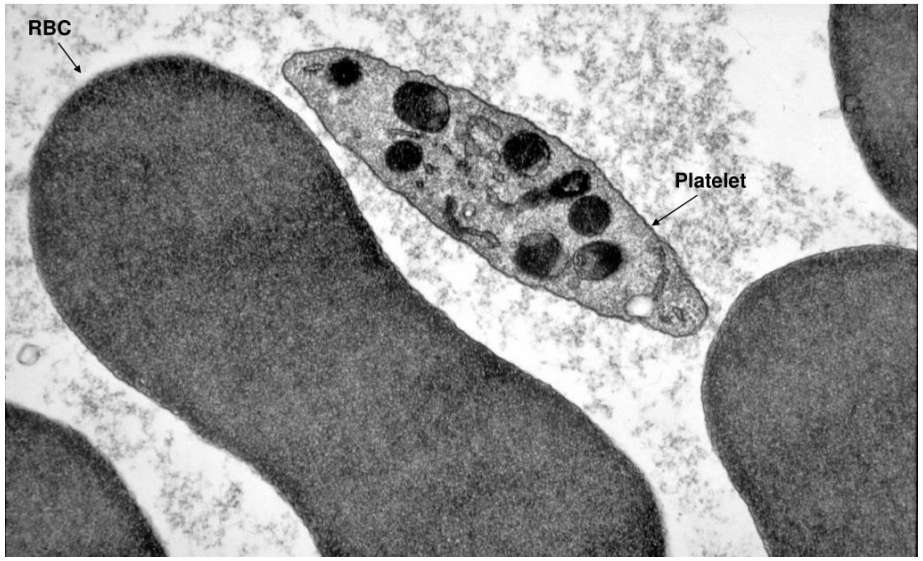


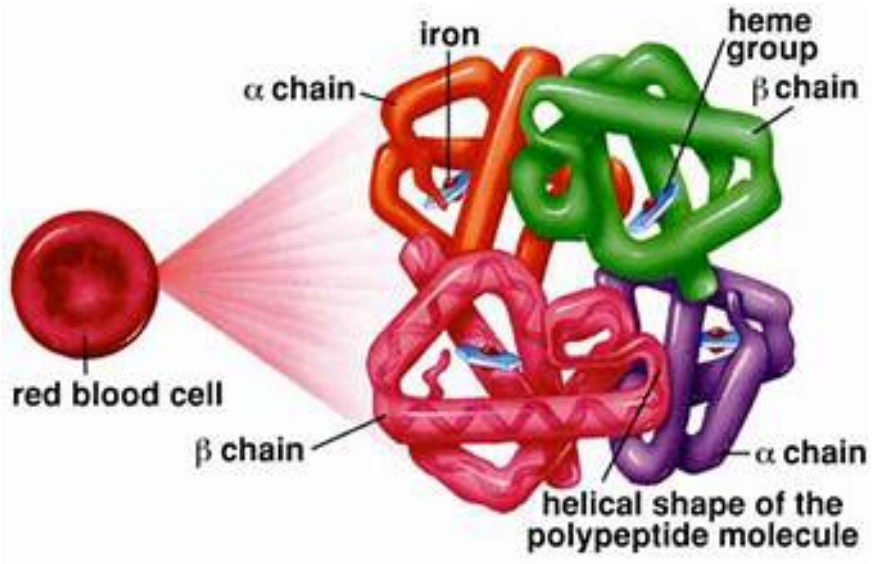
Red Blood Cells

Strong flexible membrane. Lack nuclei, mitochondria etc.. Packed with hemoglobin to bind oxygen. Make 2 million/sec; last 120 days.



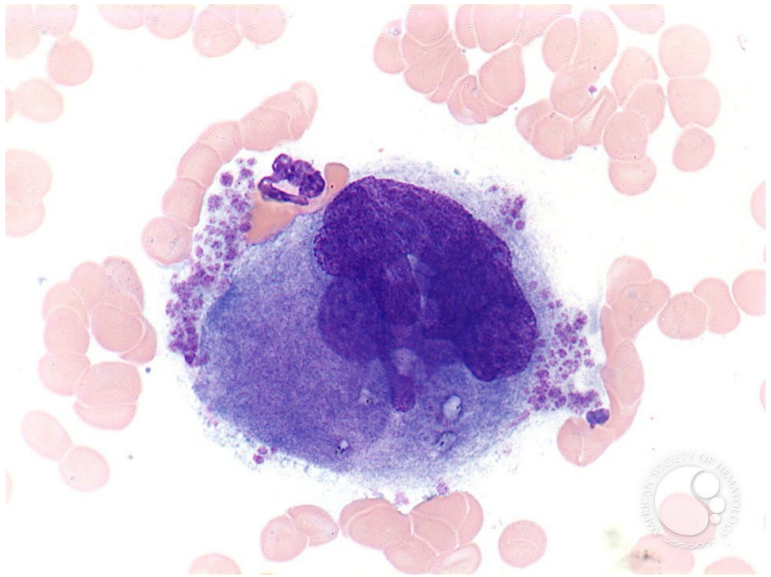
RBC & platelet, TEM

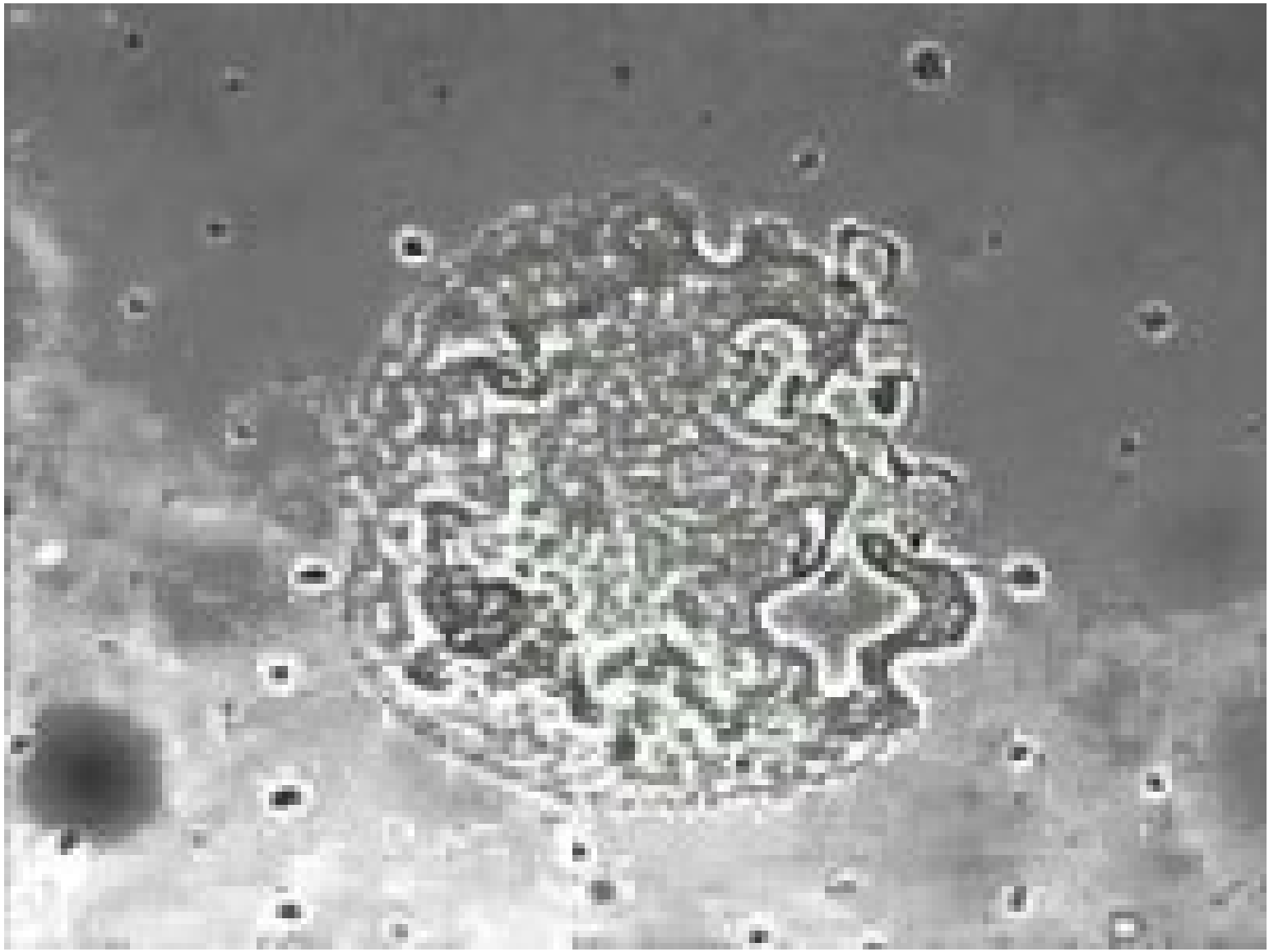




Megakaryocyte: Platelets

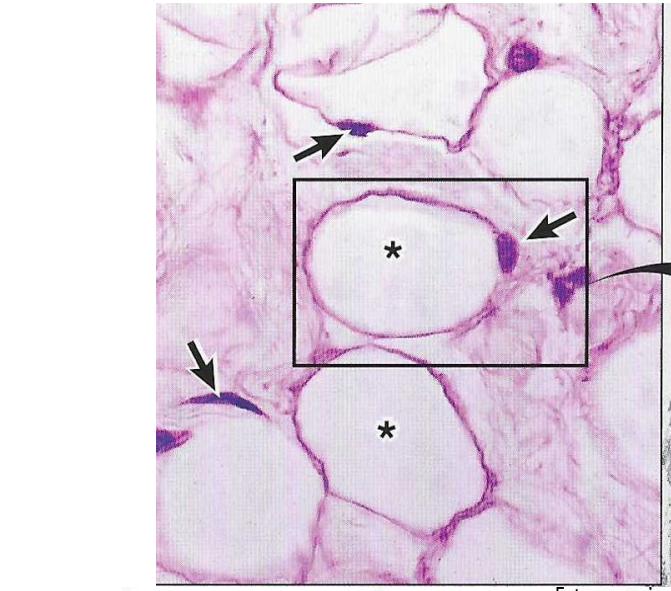
Multinucleated; in bone marrow; burst into 3,000 fragments called platelets, which promote blood clotting. Live 5-9 days.

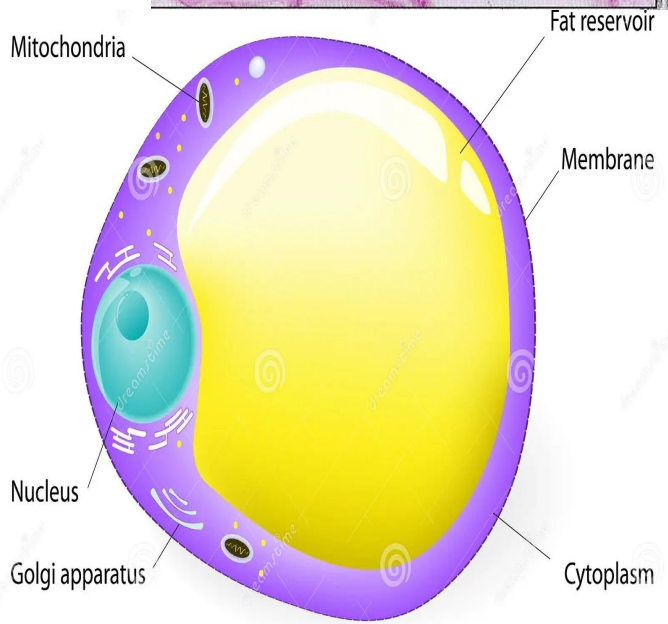


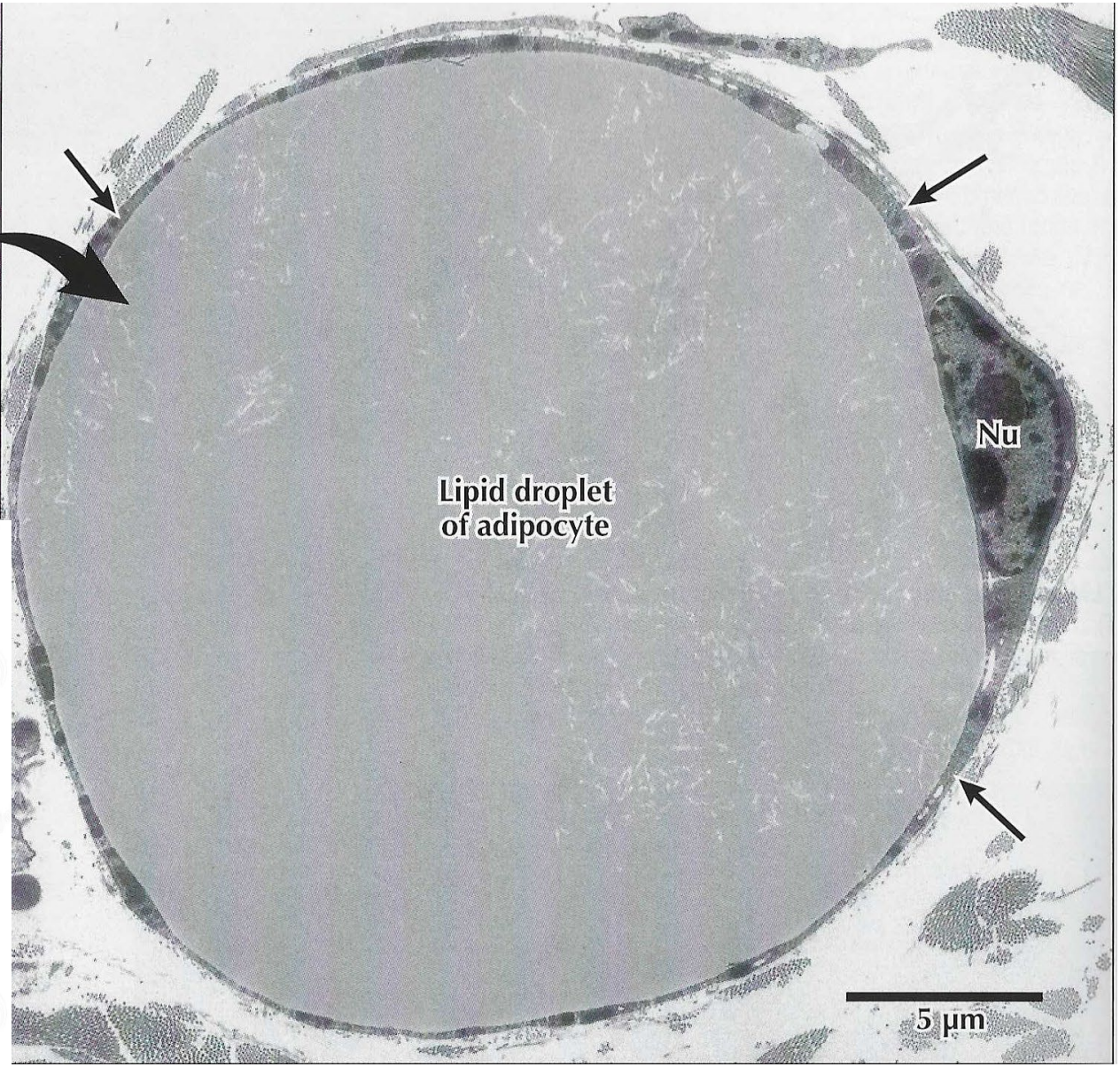


Fat Cells

Accumulation of lipid forces cytoplasm into a narrow ring. Childhood obesity results in more fat cells; adult in larger fat cells.

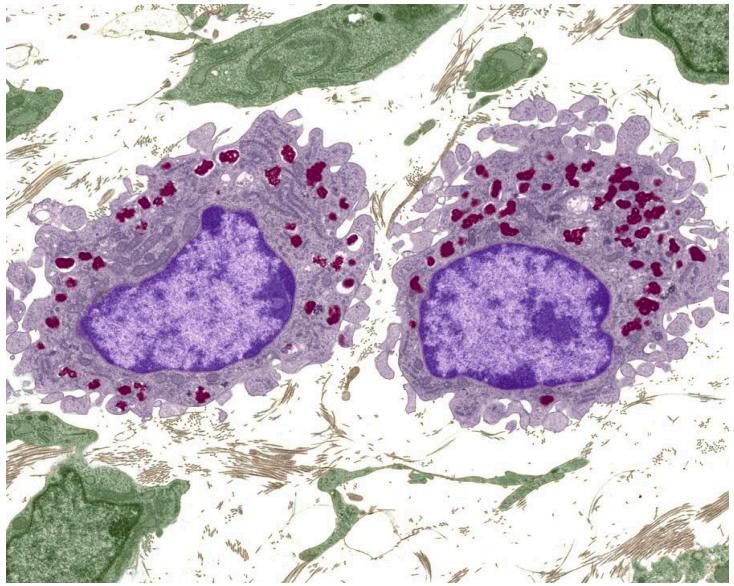


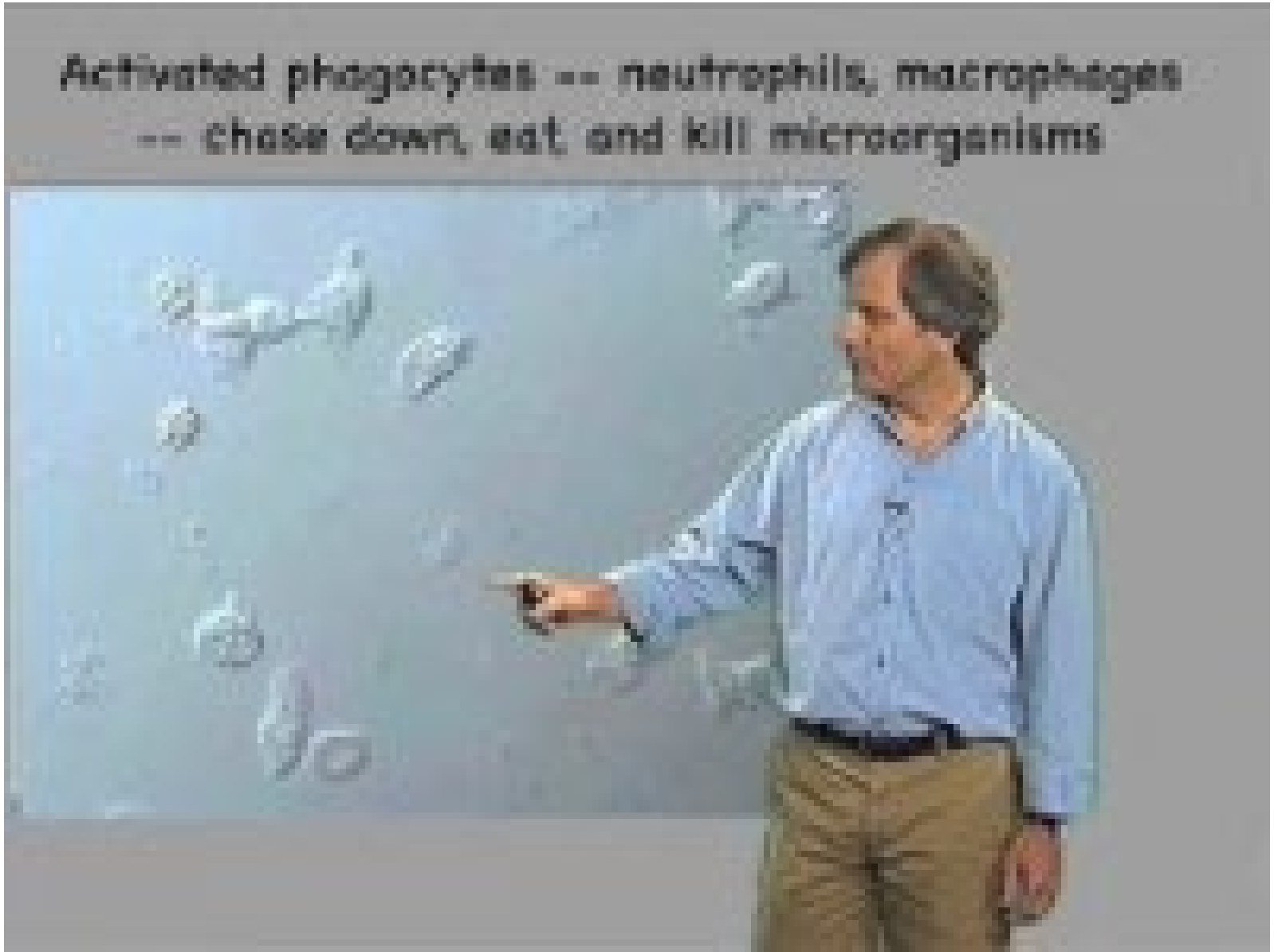




Macrophage: Phagocytosis

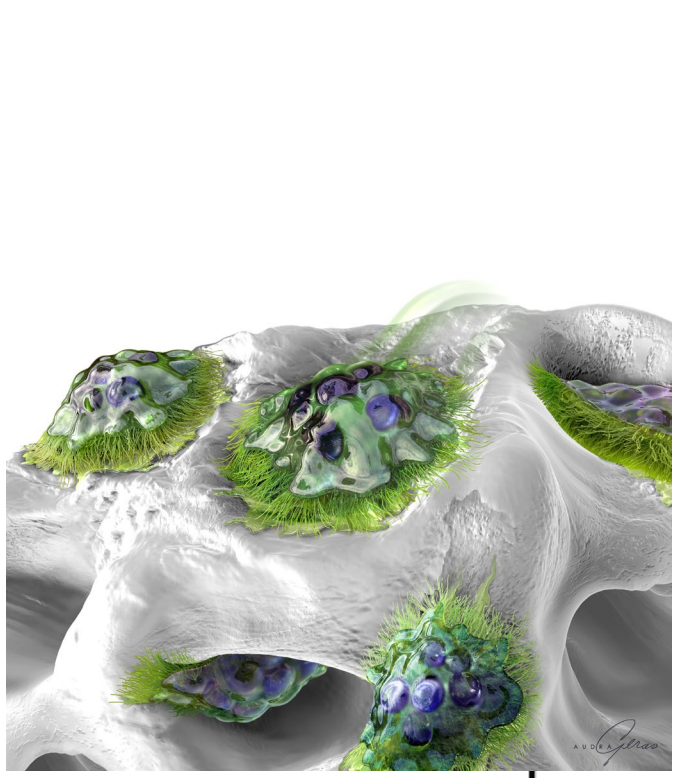
Use actin to engulf particles (bacteria, debris, diseased cells etc.); merge with lysosomes to digest. Present fragments on their membranes to lymph cells for possible immune reaction.

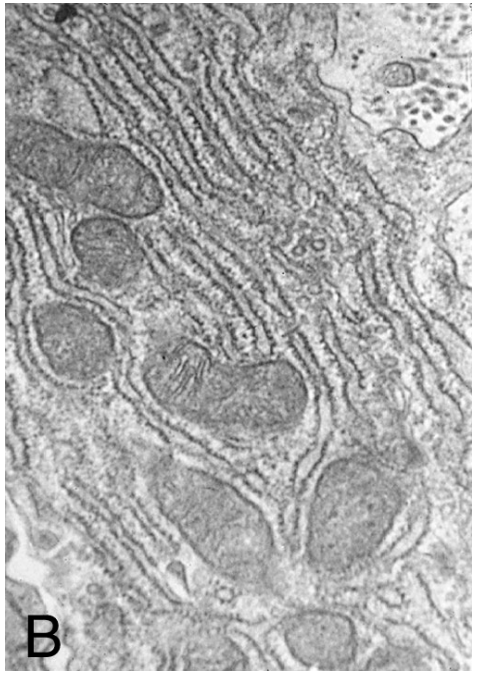


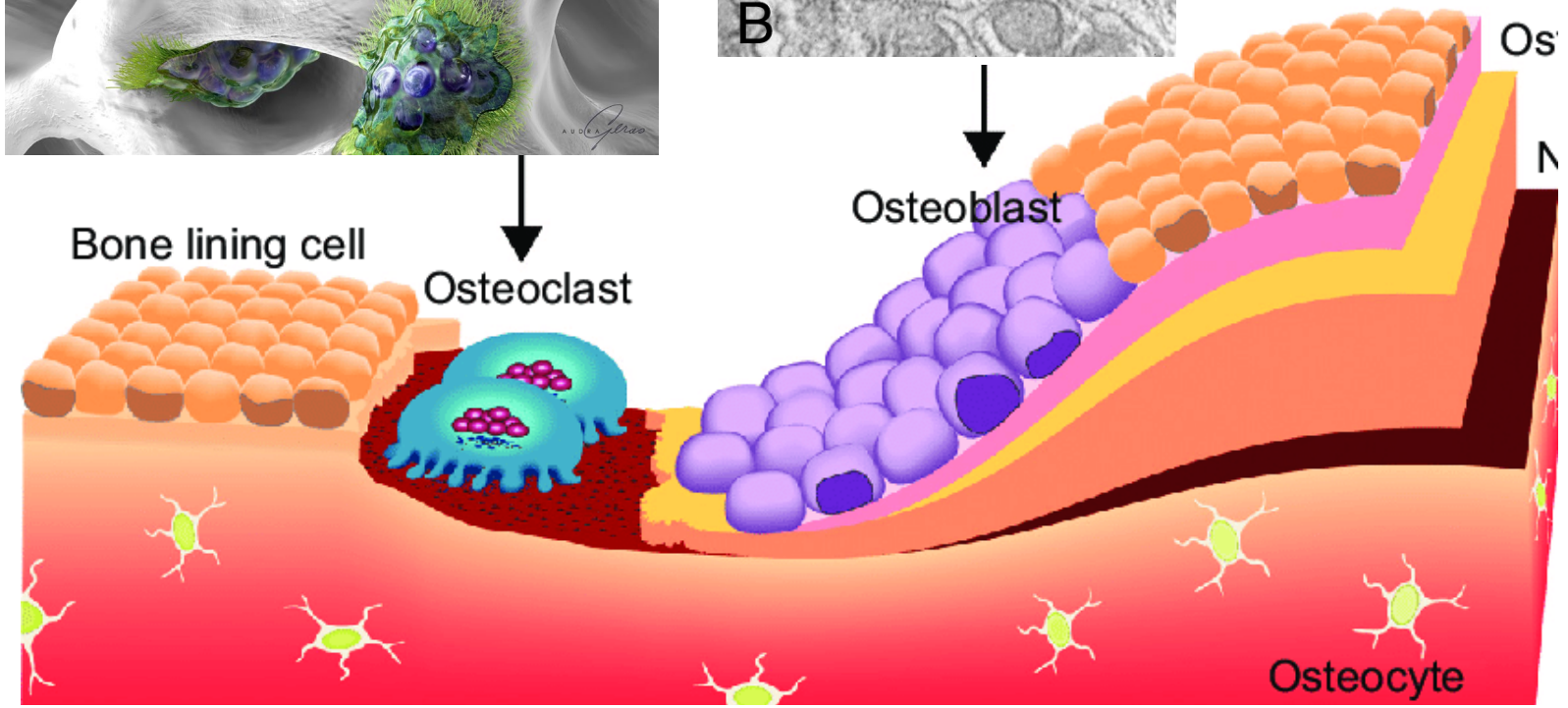


Bone Cells

Bone is constantly being remodeled. Old bone digested by **osteoclasts**. New bone is deposited by **osteoblasts.** Mature bone cells are **osteocytes**.

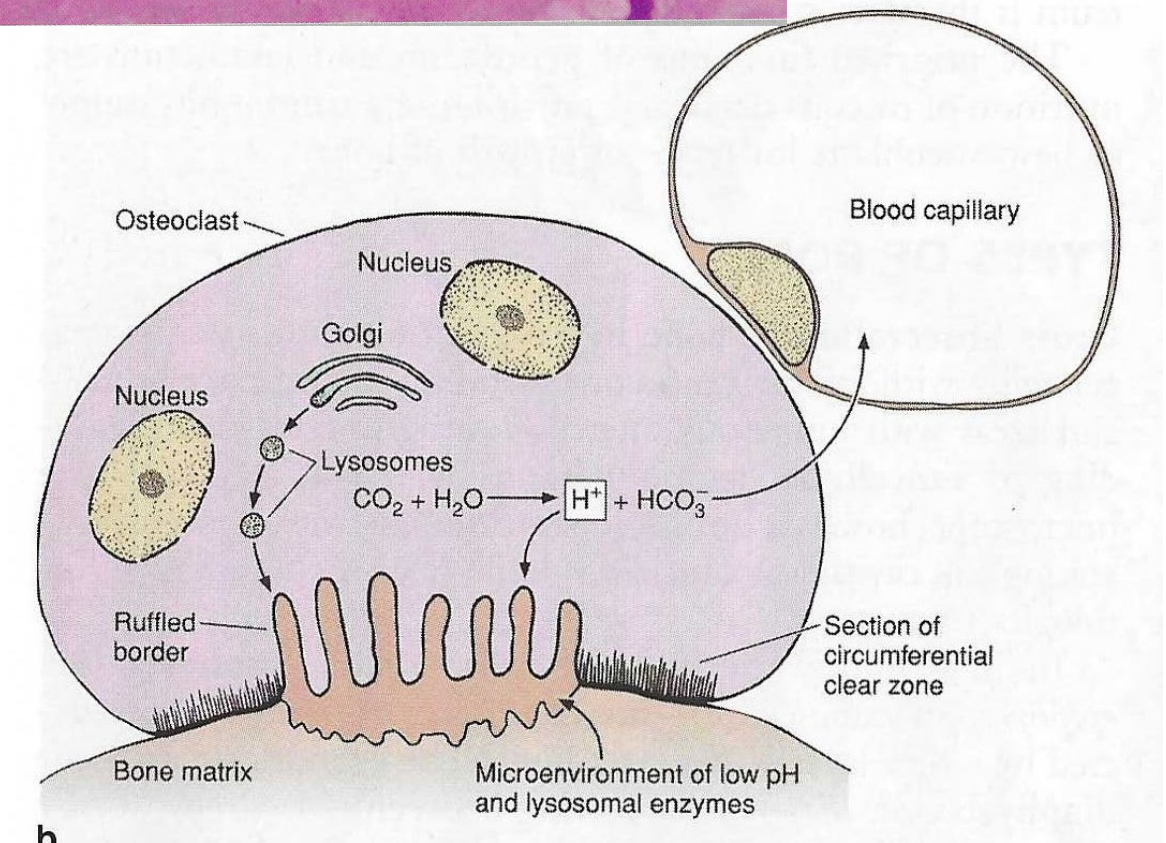






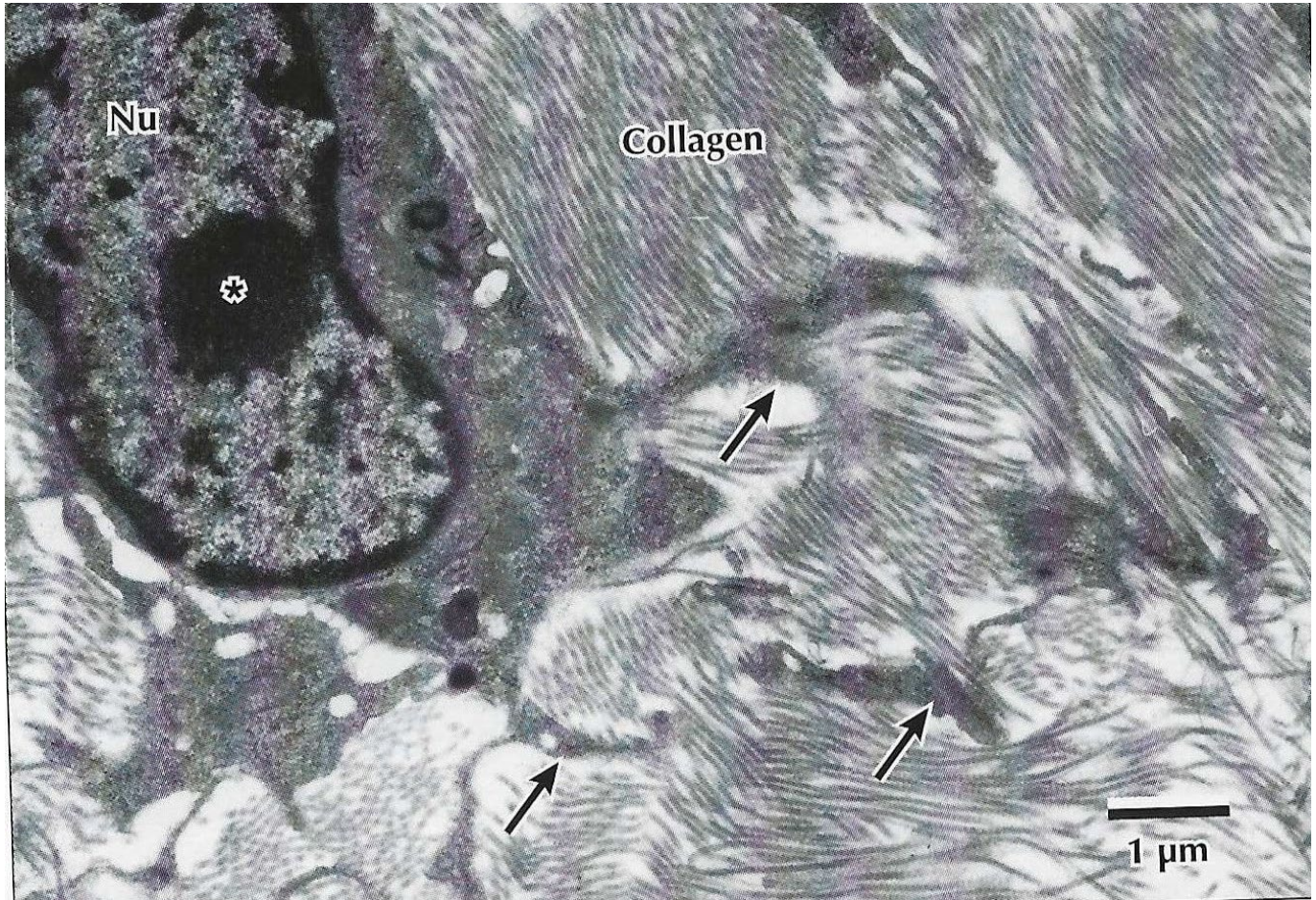
Osteoclasts: digestion

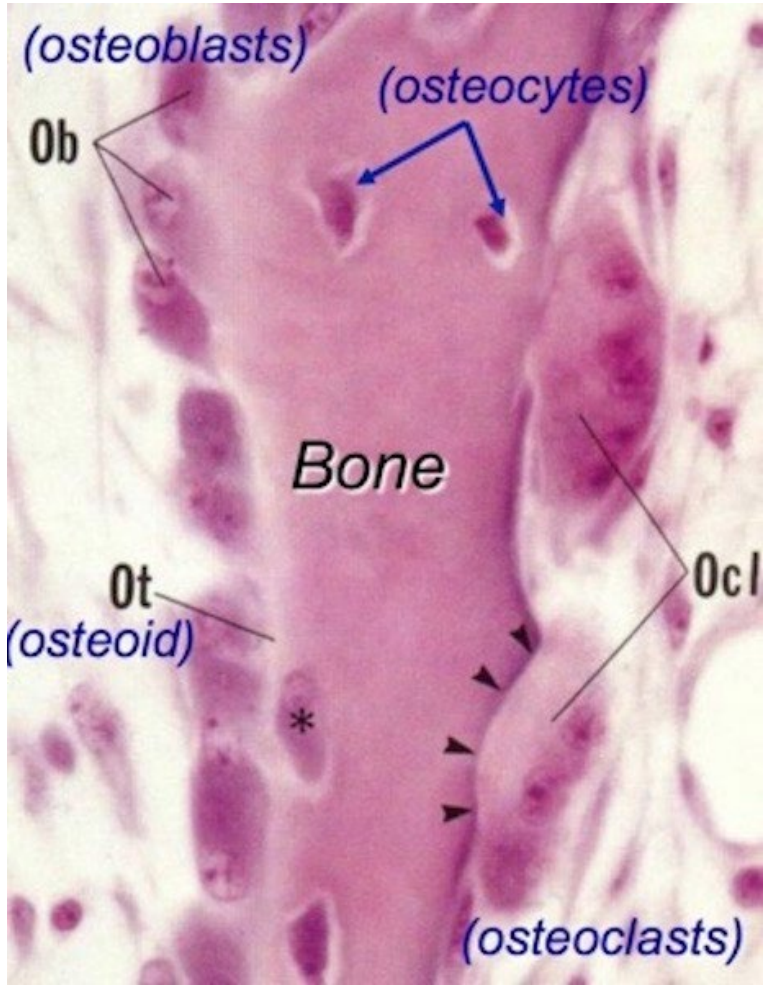
Osteoclasts pump out acid to dissolve bone minerals and release contents of lysosomes to digest protein scaffolding of bone (osteoid).



Osteoblasts: secretion

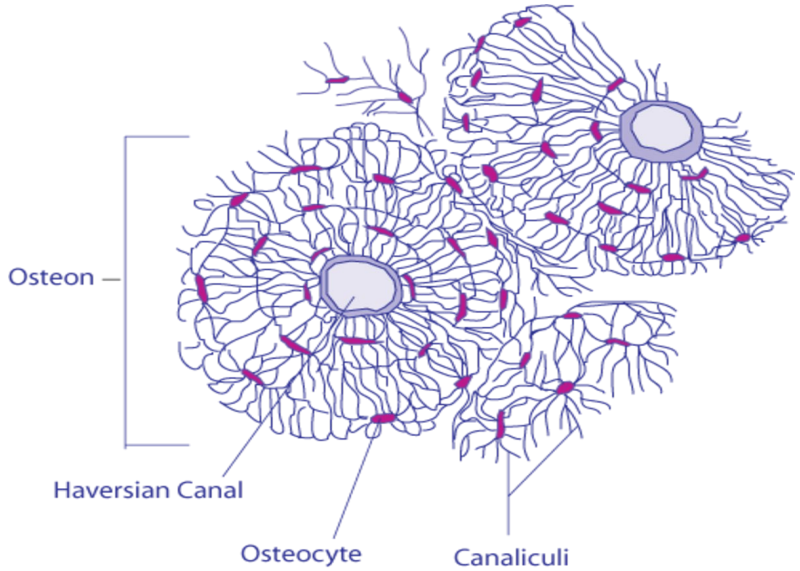
Osteoblasts make collagen precursors, so need lots of rER. Sent to Golgi for packaging in vesicles for exocytosis. Outside the cell, collagen is assembled into **collagen fibers** (using Vitamin C) = **osteoid**. Mineralized osteoid = bone matrix.

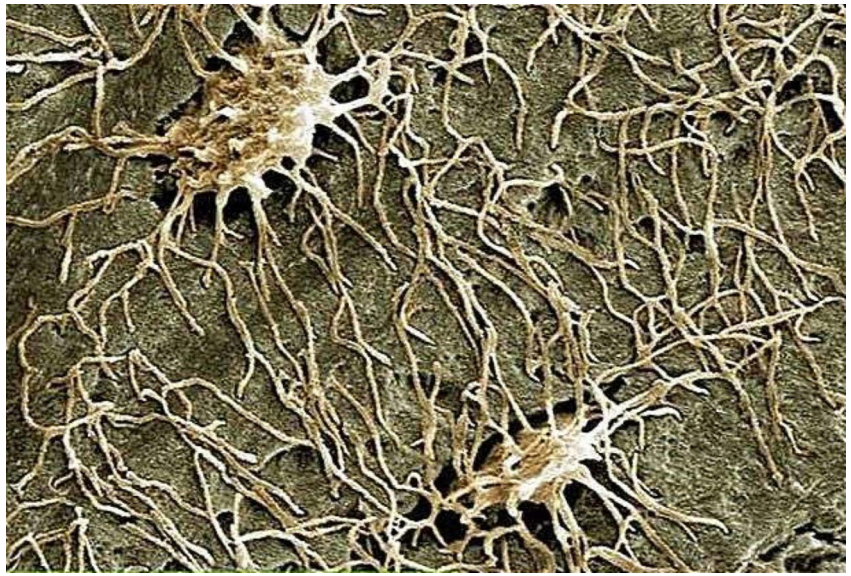


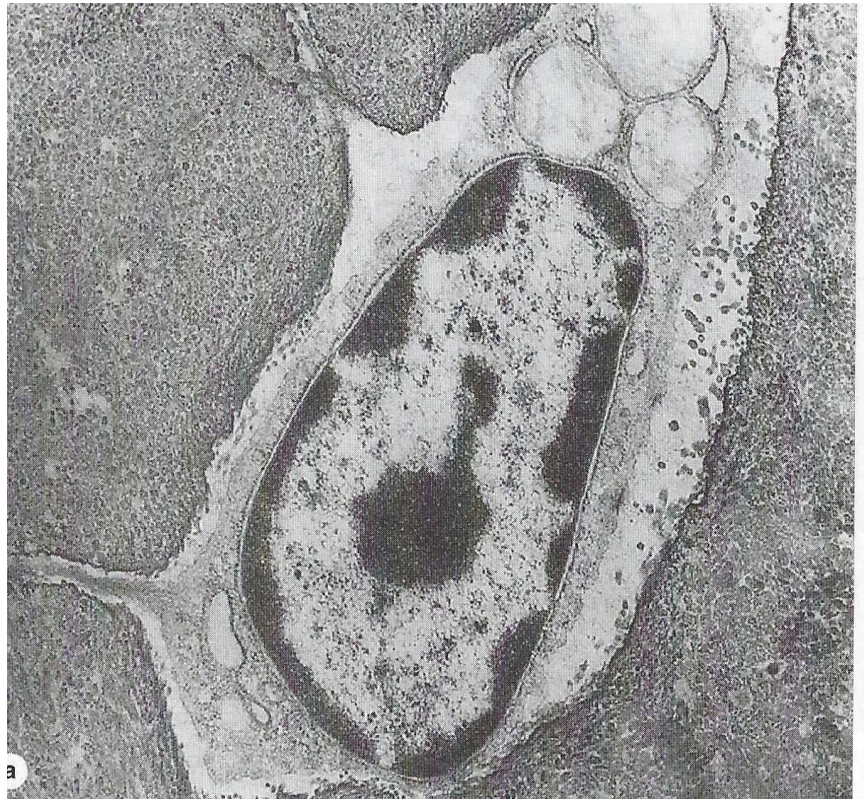


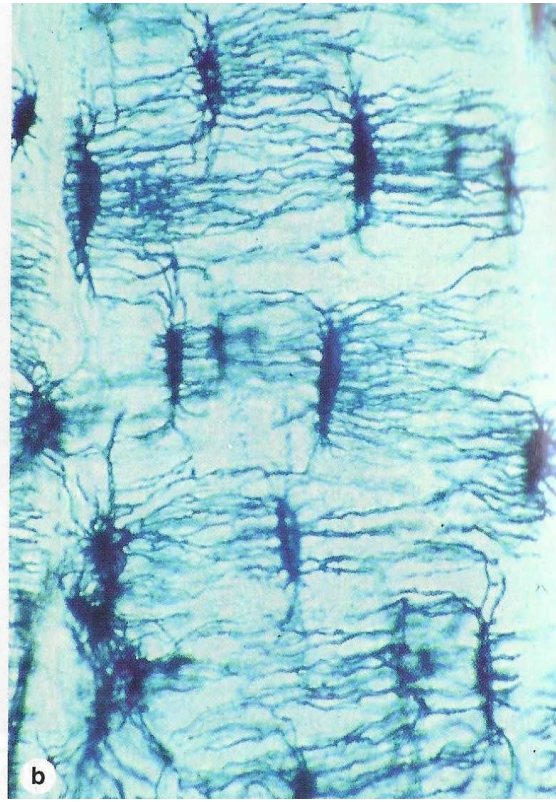
Osteocytes: maintenance

Surround blood vessels. Nutrients and minerals transferred thru osteocytes, connected to each other by canaliculi, to maintain bone matrix. If OC die, bone is reabsorbed.





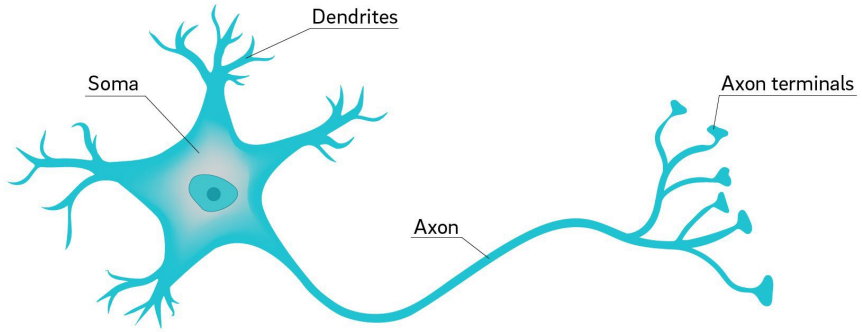


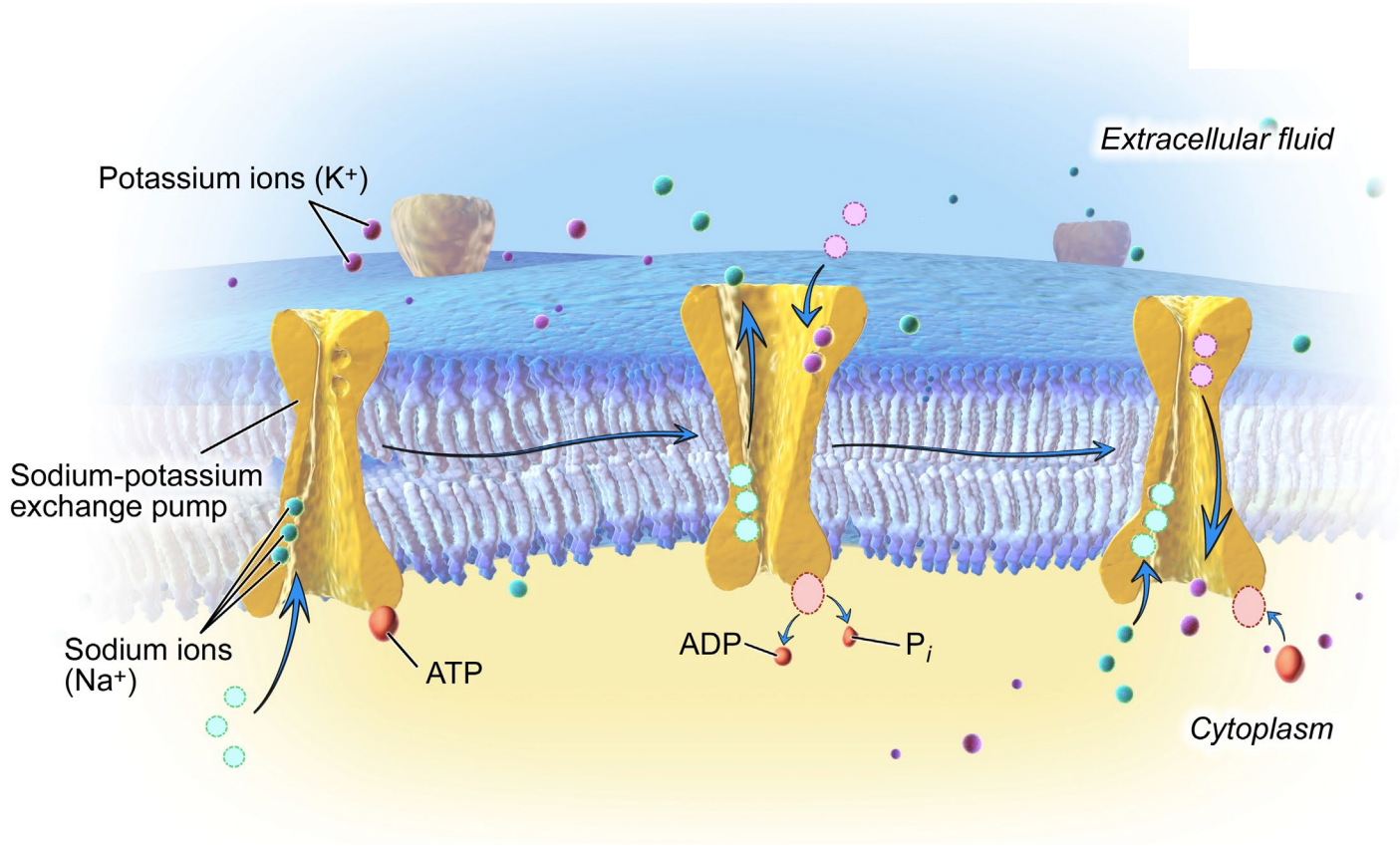


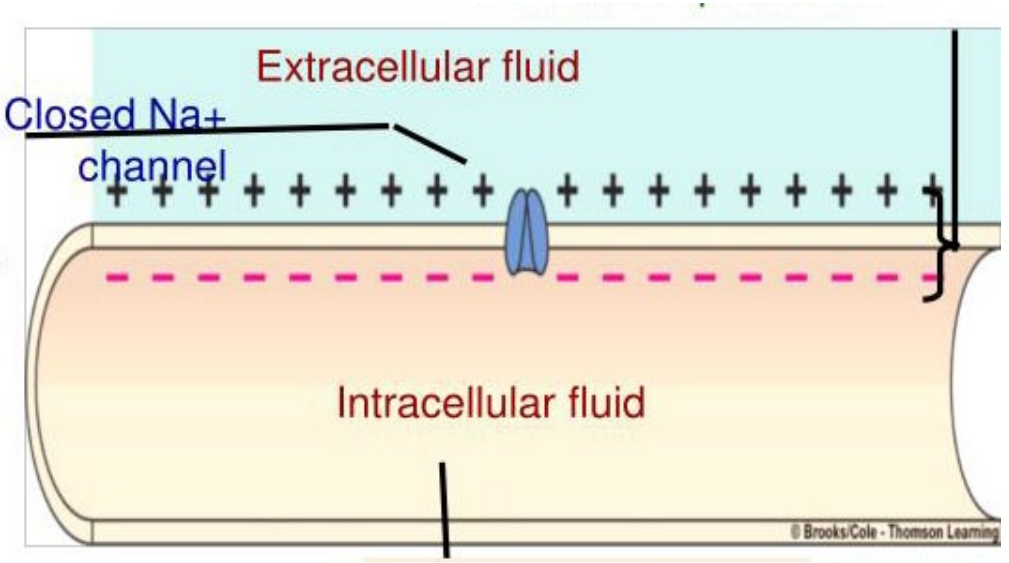
Neuron: signaling

Resting potential: ATP powered pumps set up a resting voltage by pumping $3Na^+$ out and $2K^+$ in.

Neuron

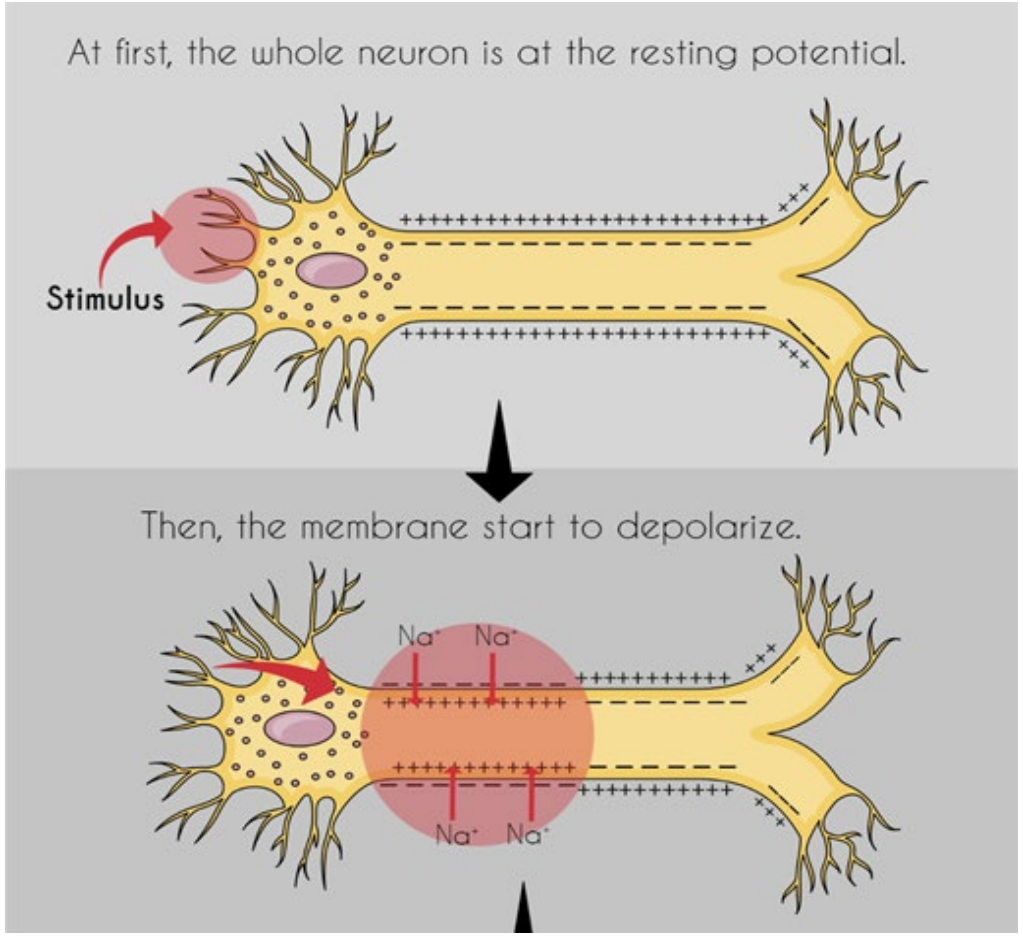






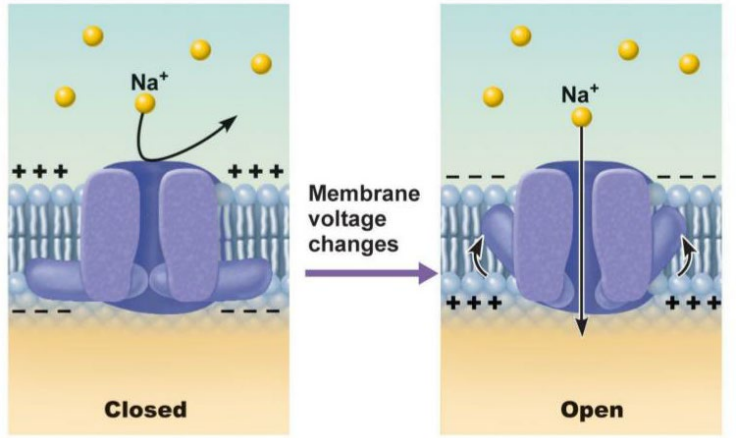
Axon membrane

Signal Propagation

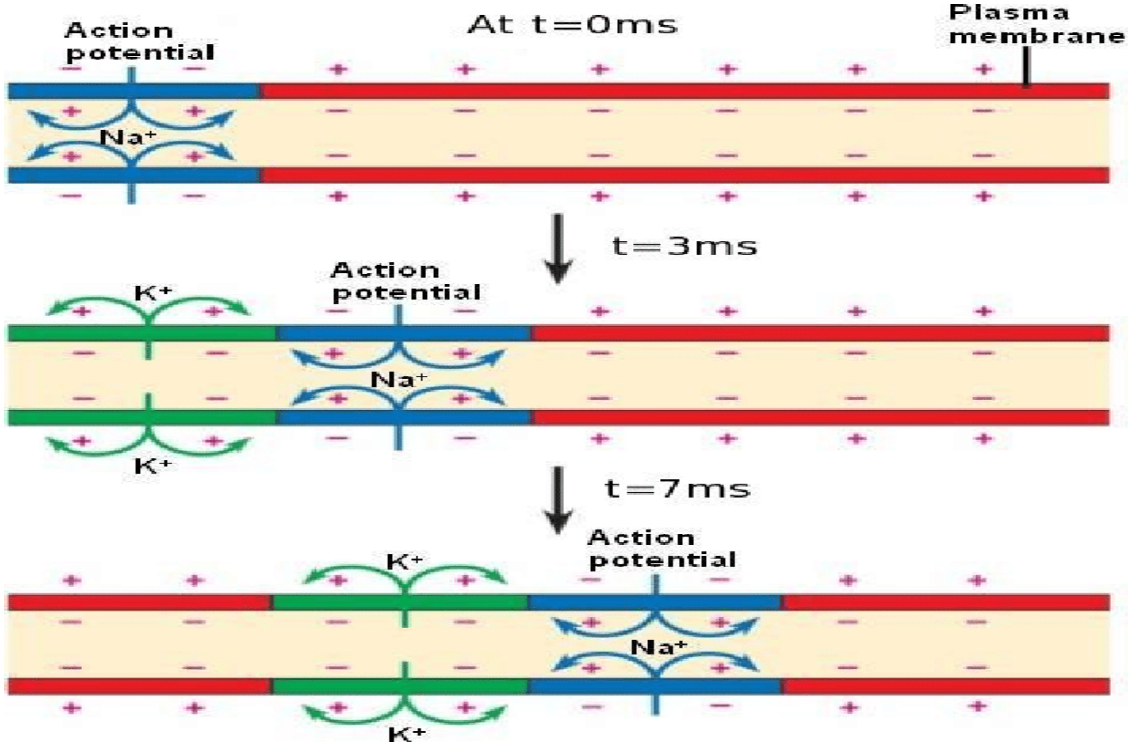


Voltage-gated channels allow self-regenerating signal to travel long distance.

Voltage Gated Channels

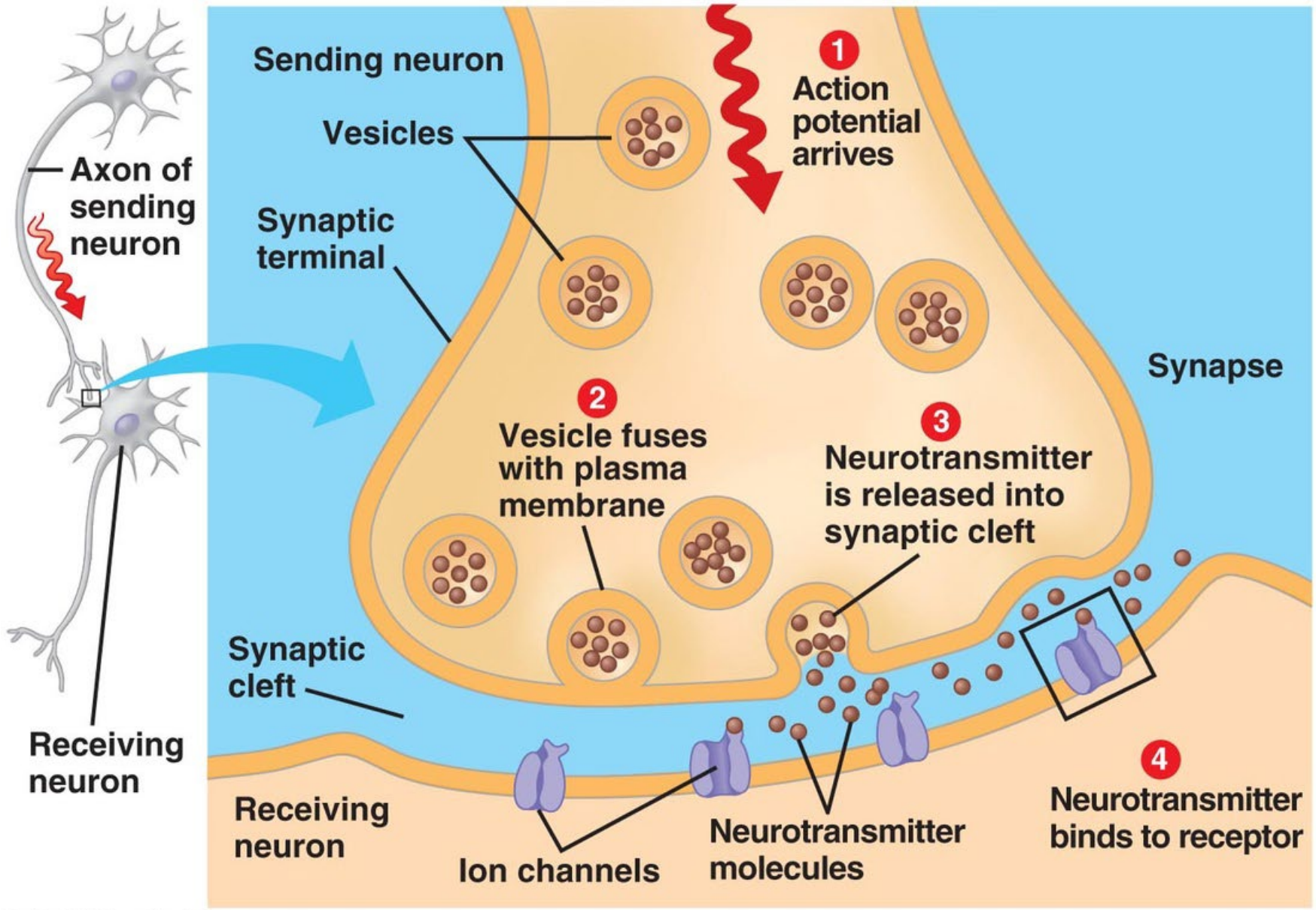


(b) Voltage-gated ion channels open and close in response to changes in membrane voltage.

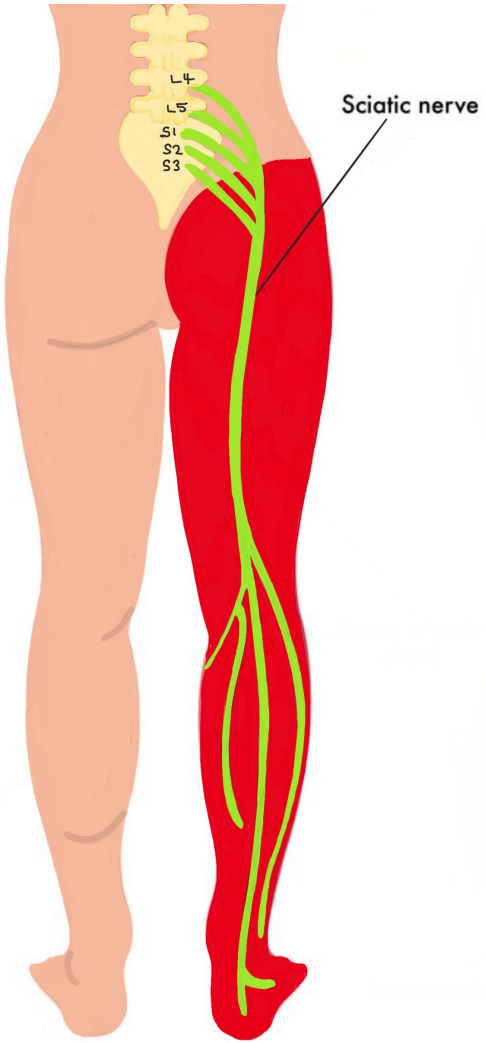


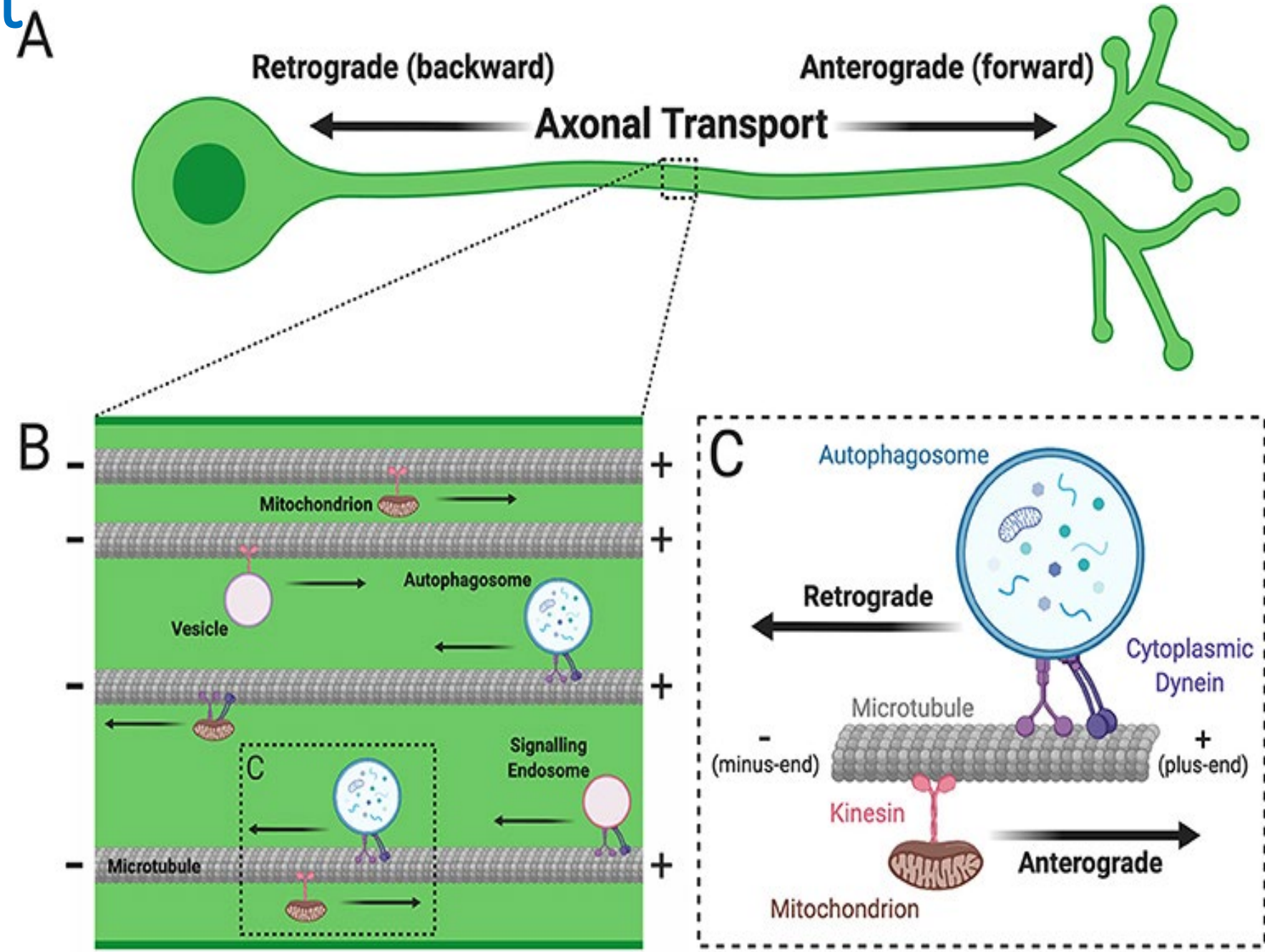
Synaptic transmission

Voltage-triggered exocytosis (using voltage-gated Ca++ channels). Receptor-gated channels.



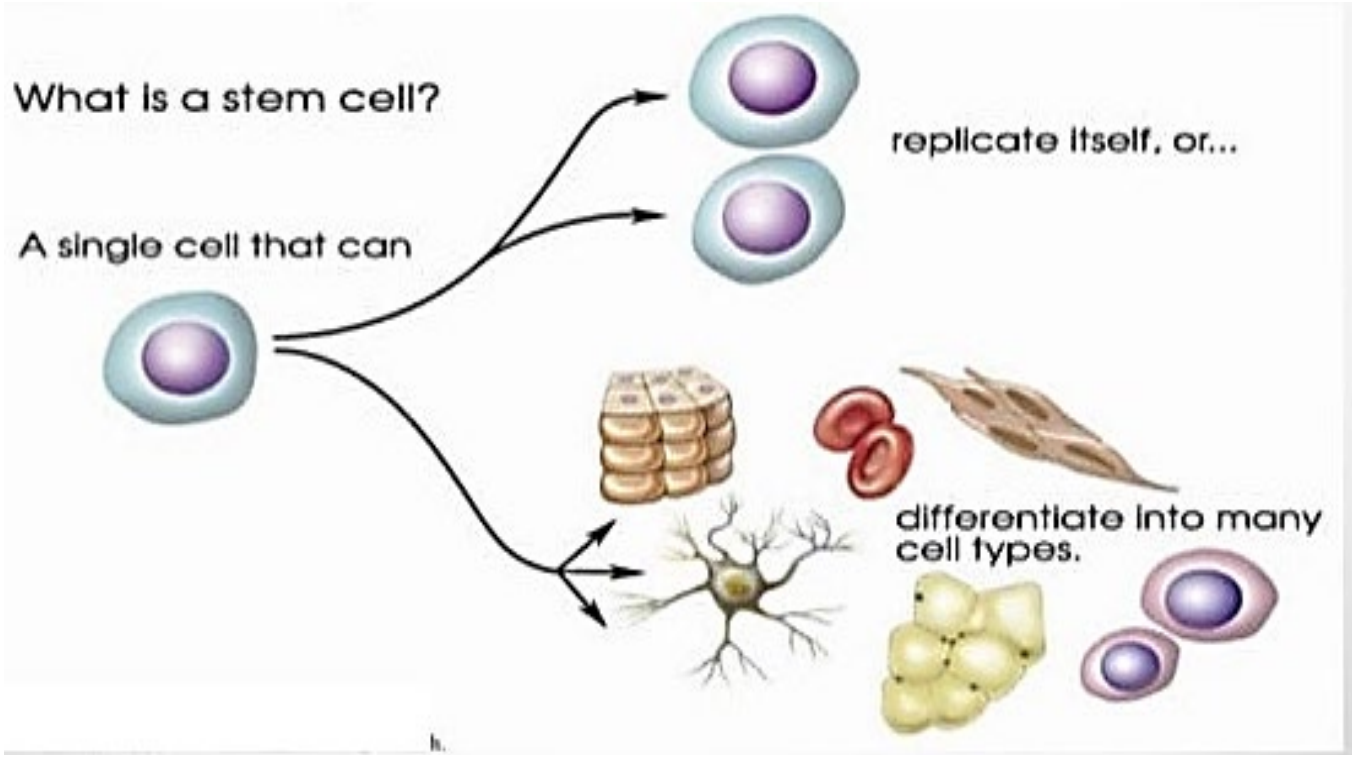
Axonal Transport





Stem Cells

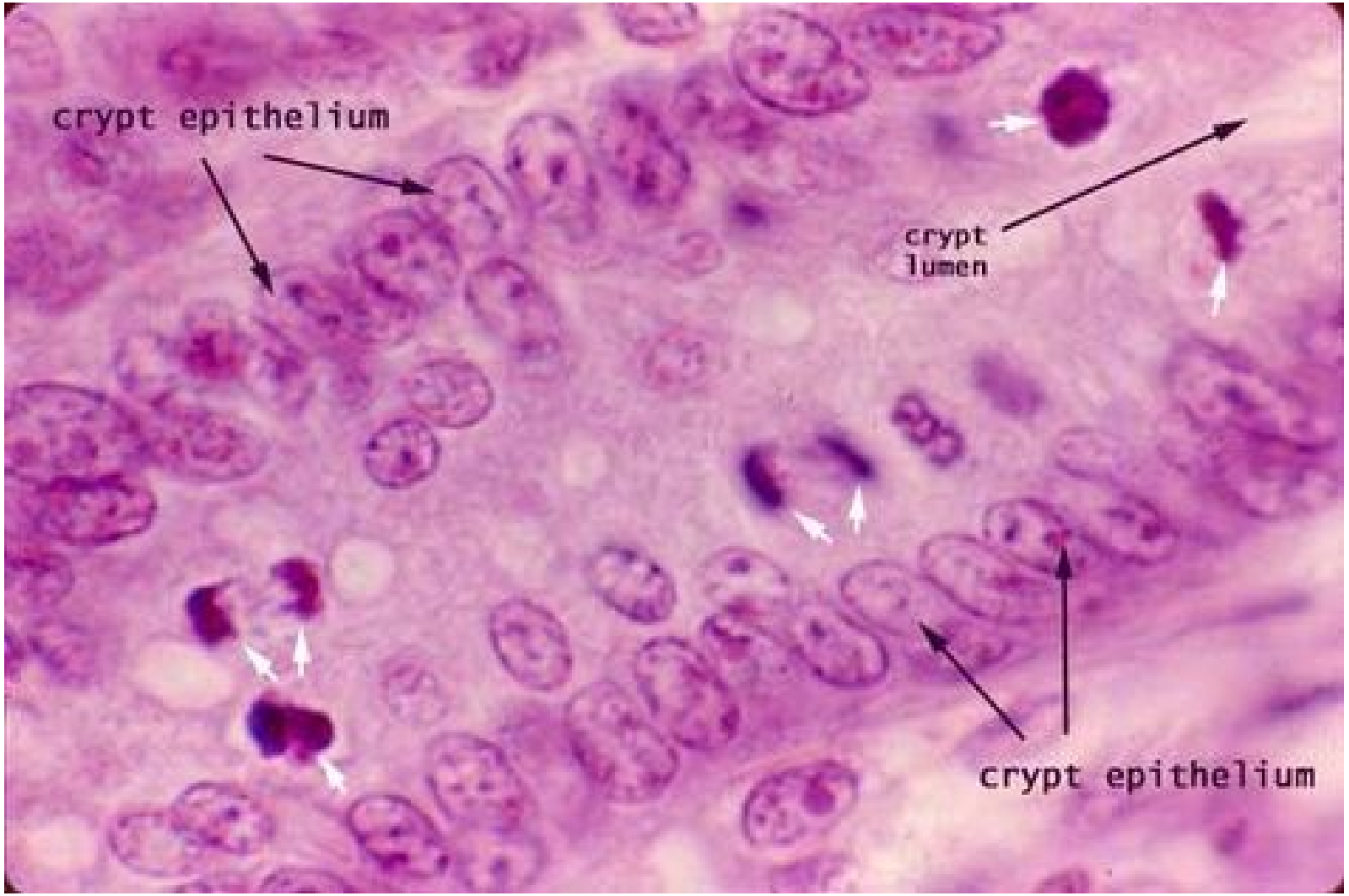
A stem cell is an unspecialized cell capable of perpetuating itself through cell division **and** having the potential to give rise to differentiated cells with specialized functions.
Most organs have their own populations of stem cells.



Embryonic vs Adult Stem Cells

Embryonic stem cells capable of forming all cell types of the adult.

Adult stem cells are found in particular tissues to replenish cell populations as needed: intestinal lining, blood cells, hair follicles, skin etc.

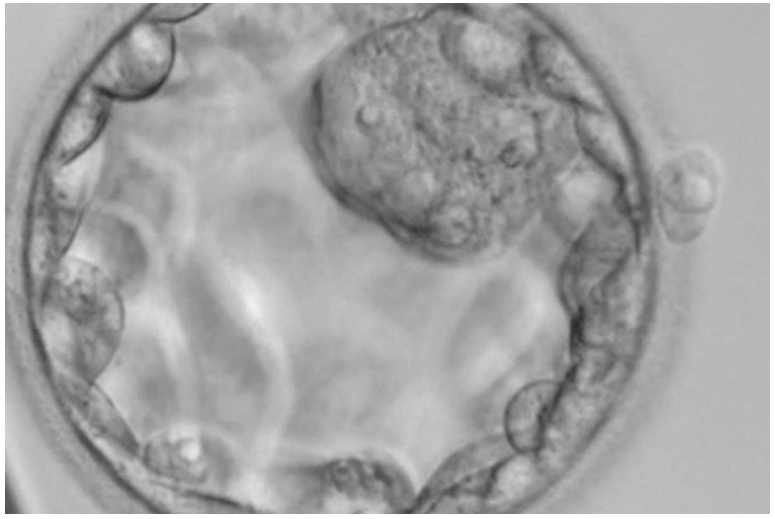


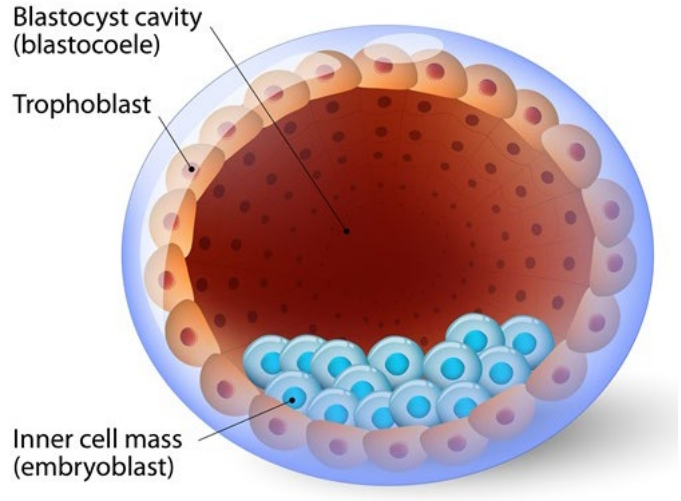
Stem cells dividing in intestine

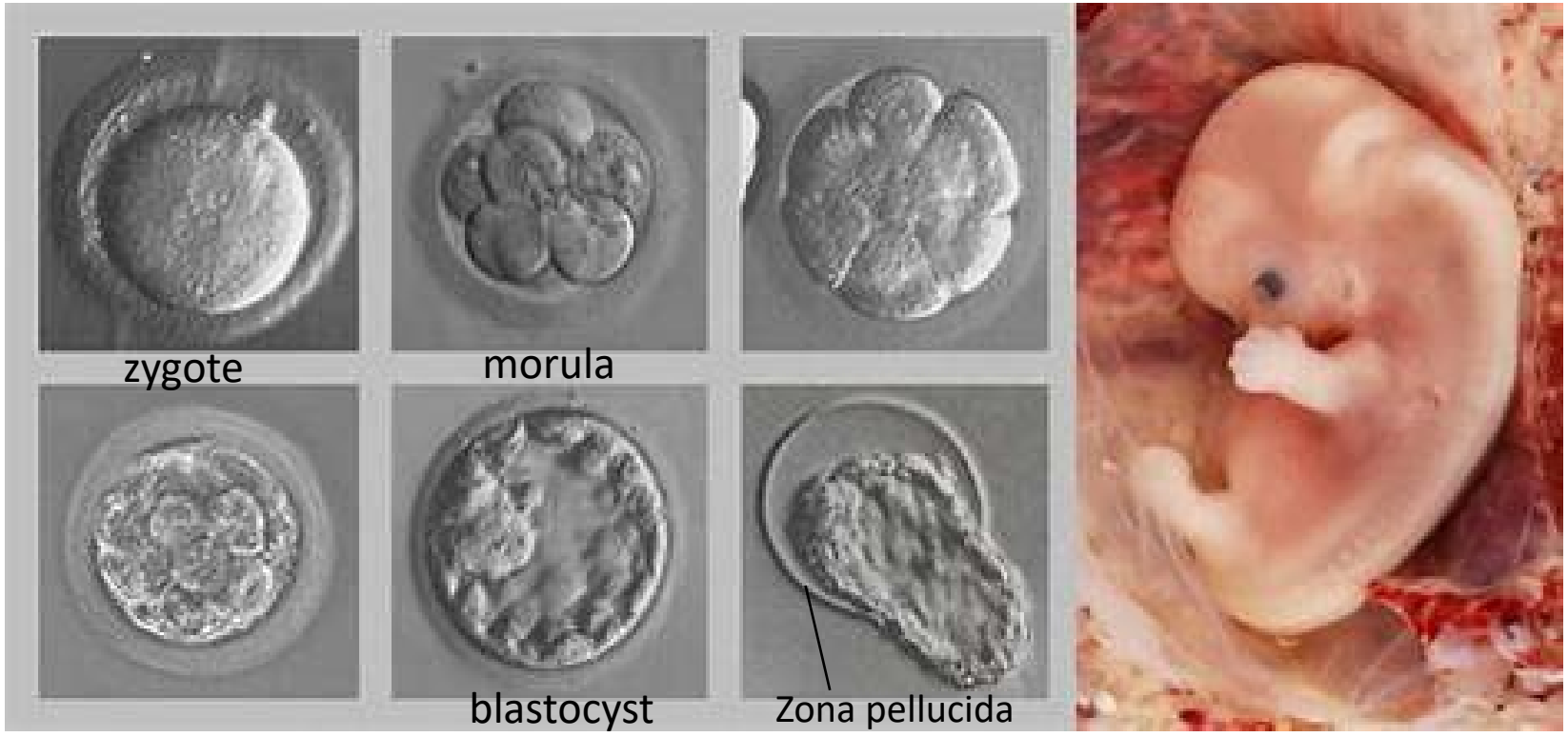
Differentiation: Early Embryo

Early cells = **totipotent**: can become any cell in the body or placenta.

Morula: **pluripotent**: inner cells can become any body cell; outer cells become placenta.

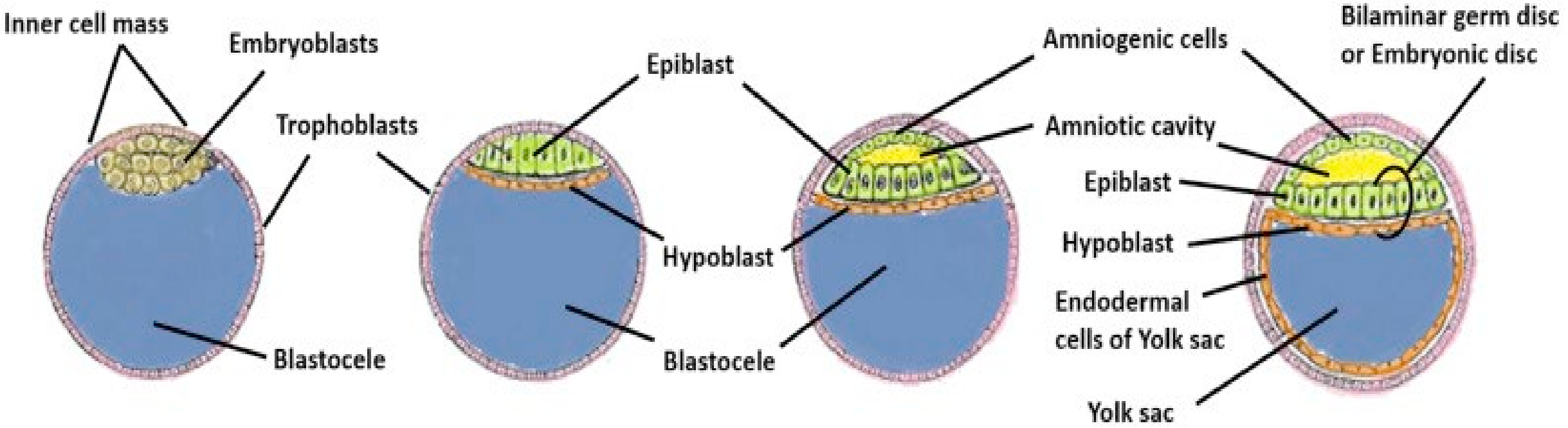






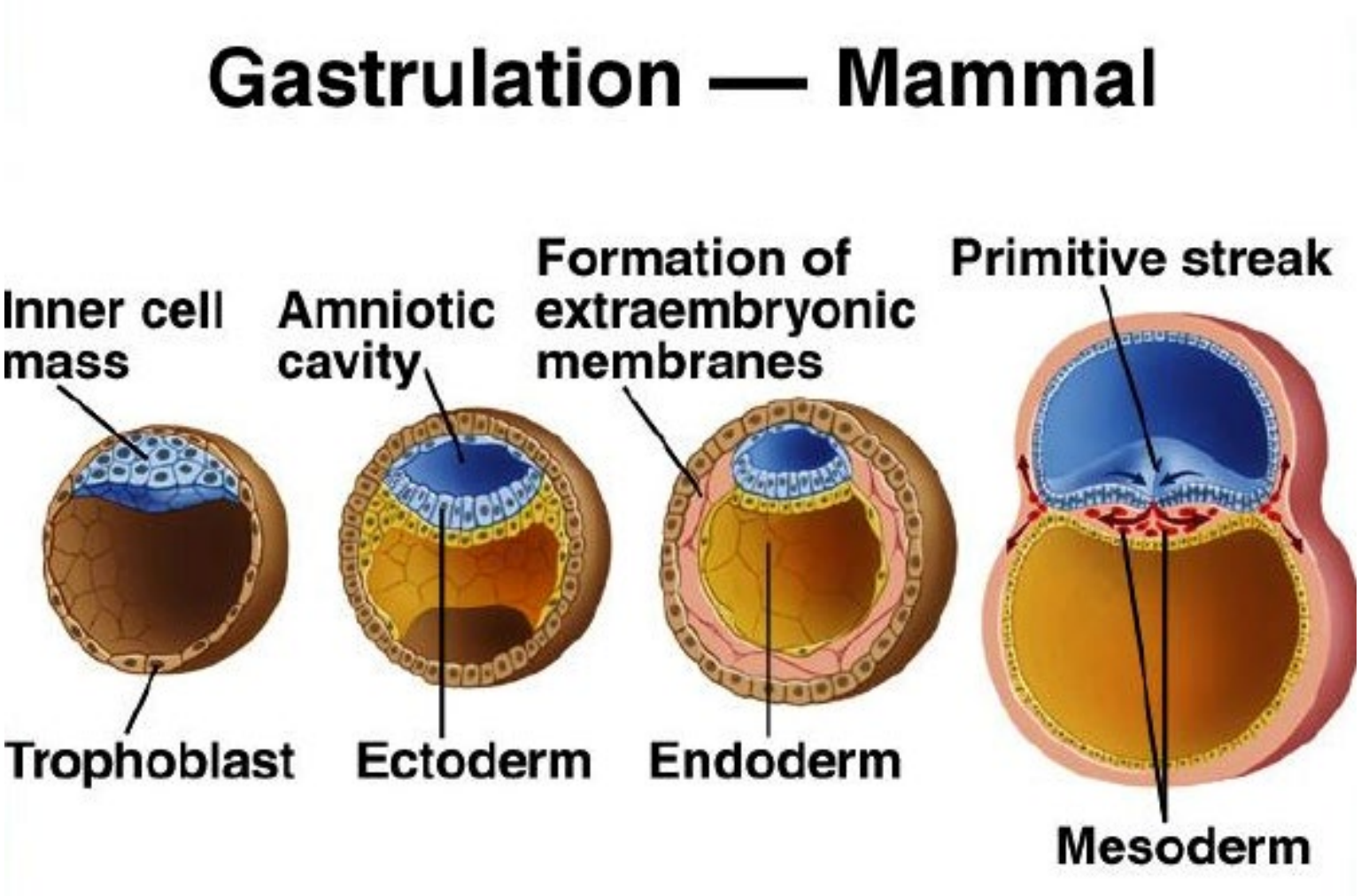
Bilaminar Disc

*Differential cell adhesion
*Secretion of extracellular matrix (basement membrane)
*Pumping of fluid to create a new cavity



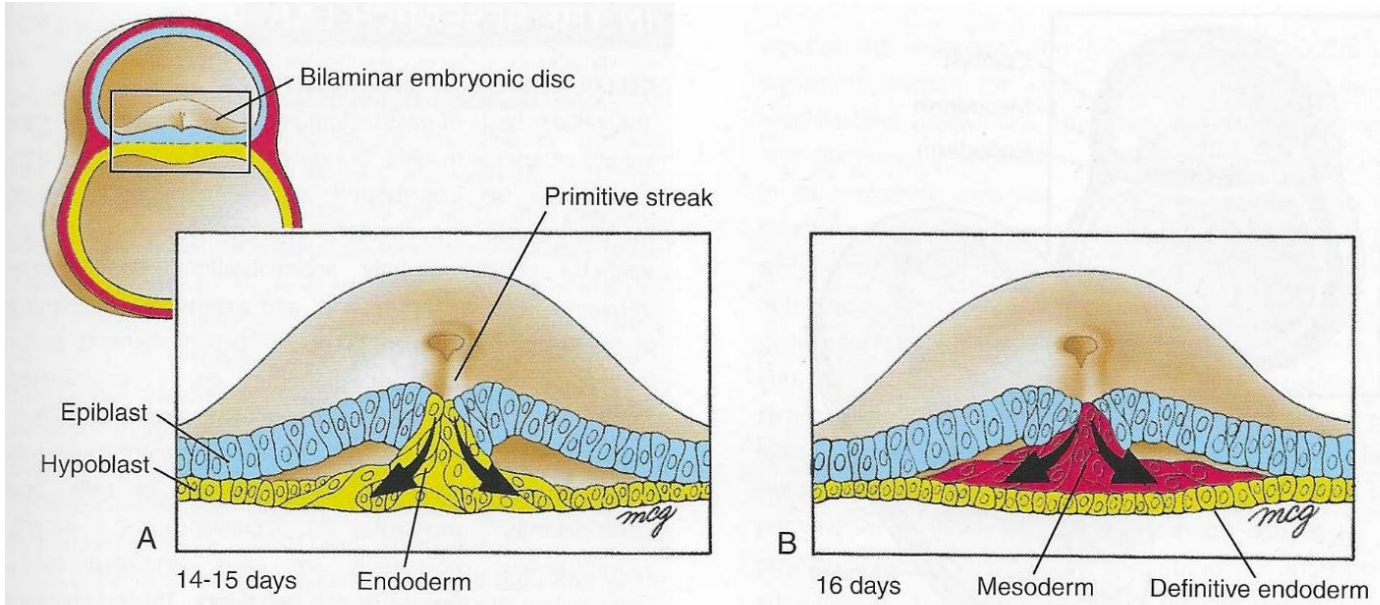
Gastrulation: 3 layers

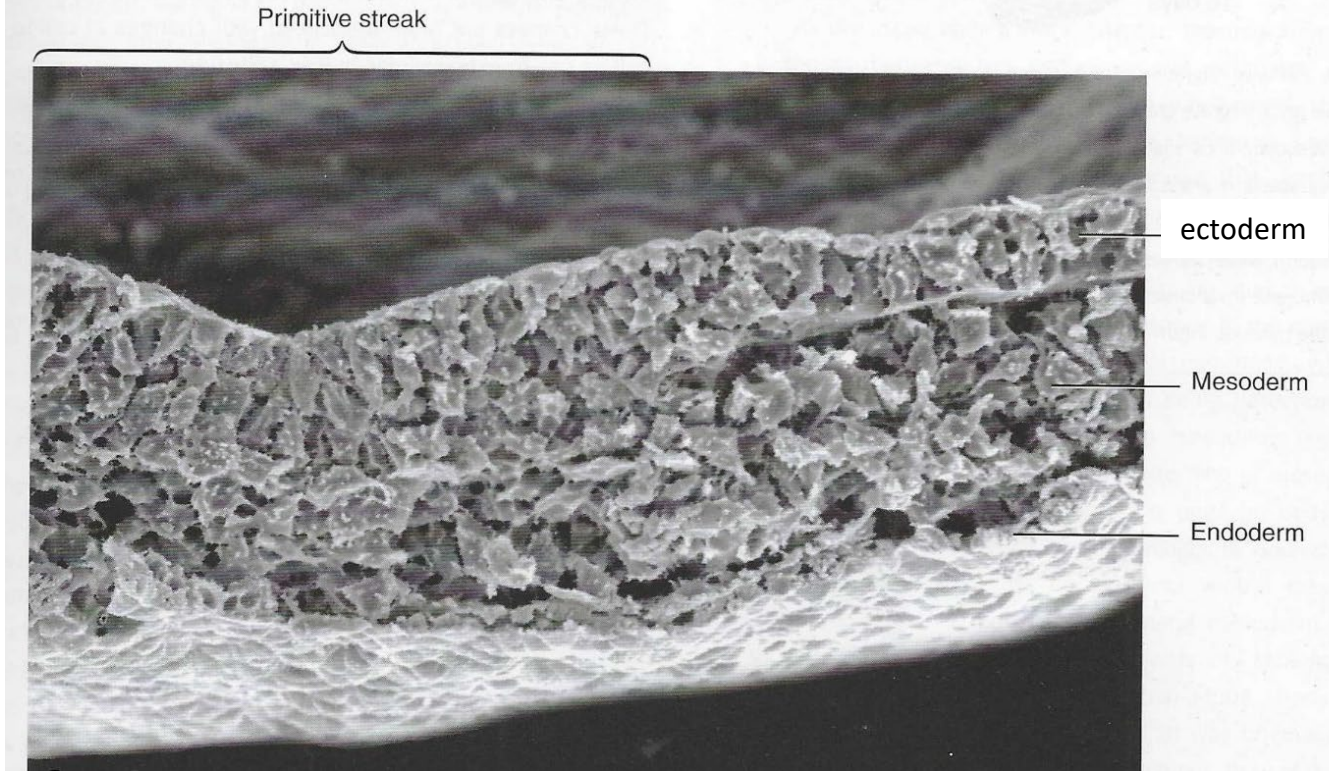
Migration, involving loss of adhesion molecules and activation of actin networks, forms middle layer (mesoderm), migrating on basement membrane.



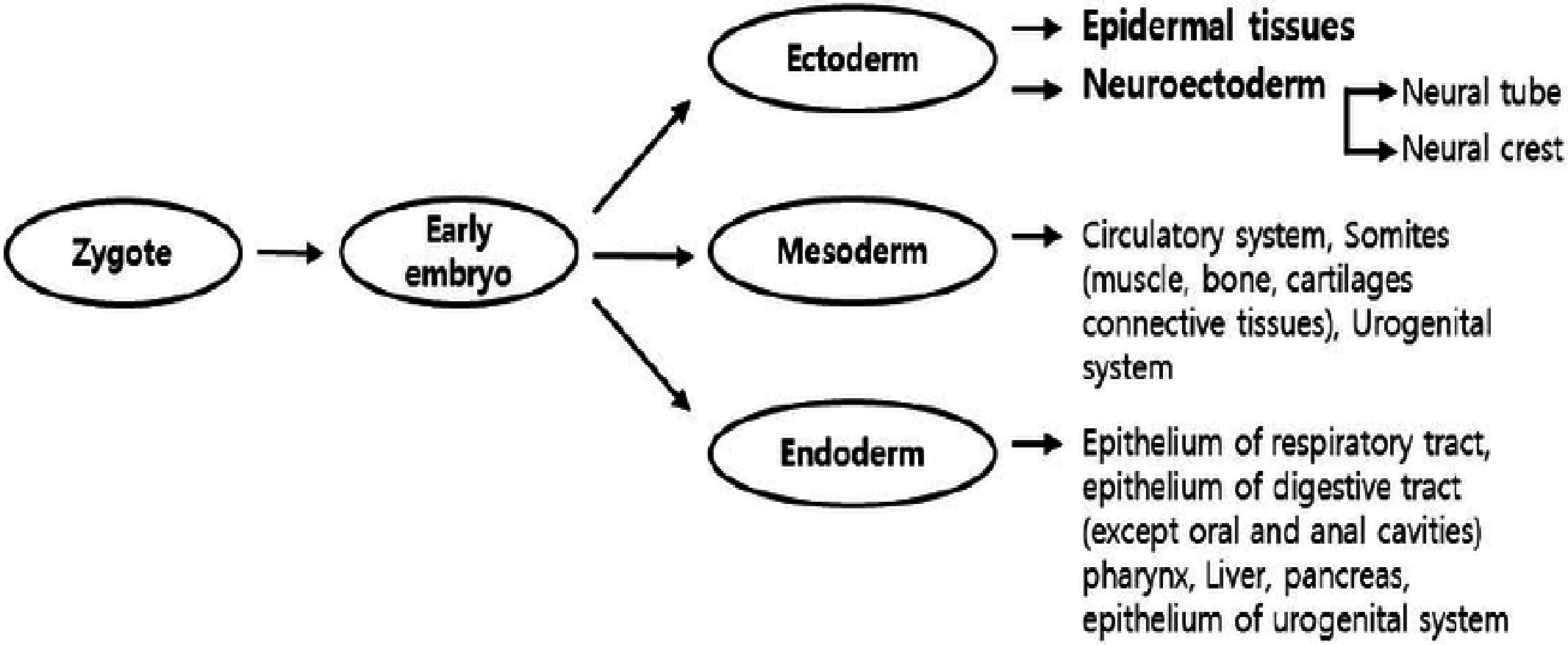
3 Primary Germ Layers

Become the outside, middle and inside layers of the embryo: **ectoderm, mesoderm and endoderm**.



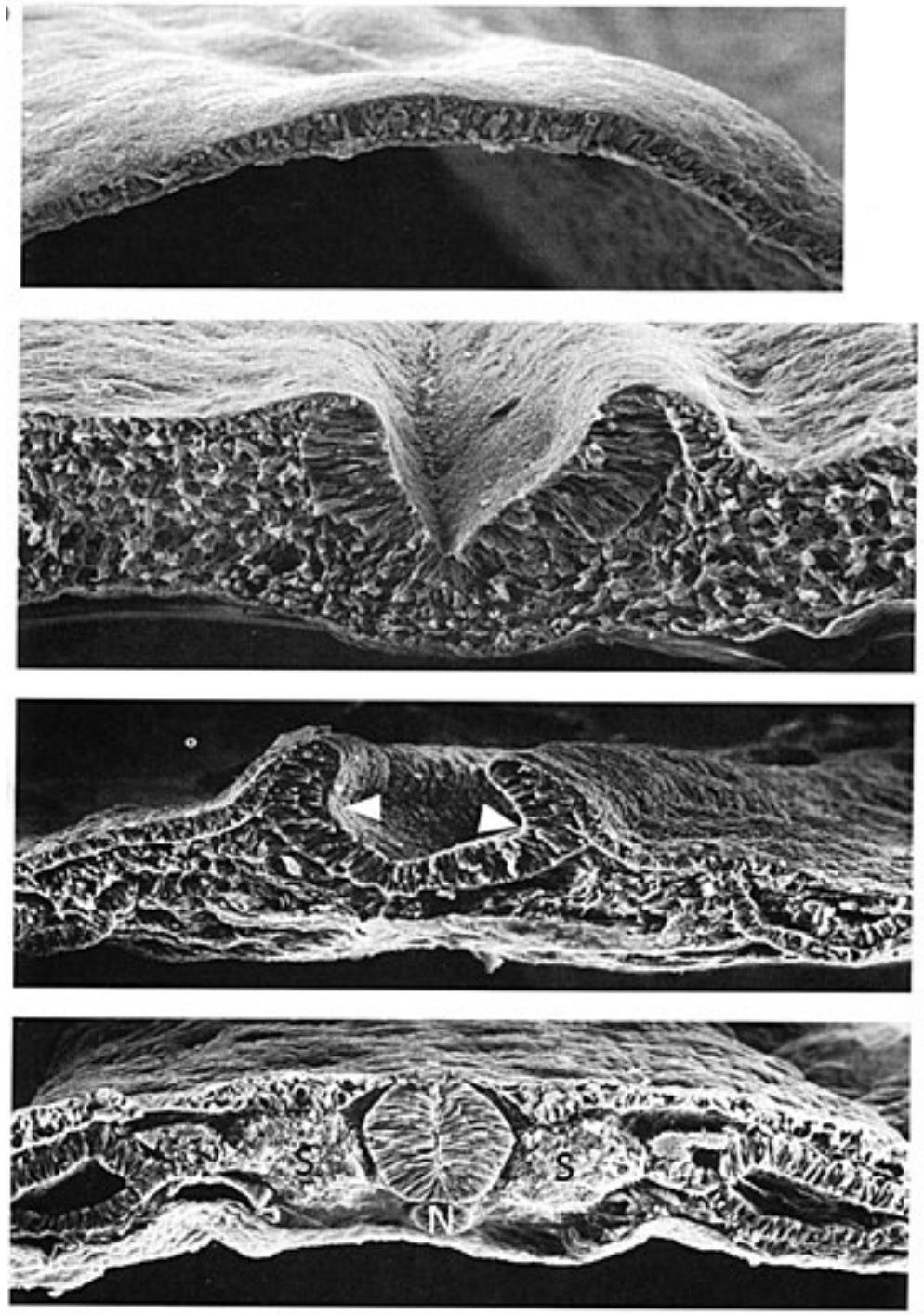


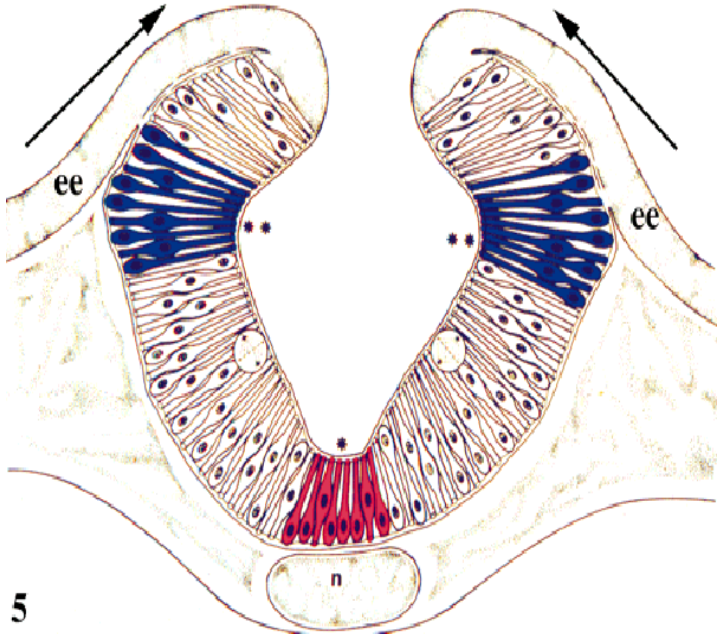
Fates


Zygote
Early embryo
Ectoderm
Epidermal tissues
Neuroectoderm
Neural tube
Neural crest
Mesoderm
Circulatory system, Somites (muscle, bone, cartilages connective tissues), Urogenital system
Endoderm
Epithelium of respiratory tract, epithelium of digestive tract (except oral and anal cavities) pharynx, Liver, pancreas, epithelium of urogenital system

Neurulation

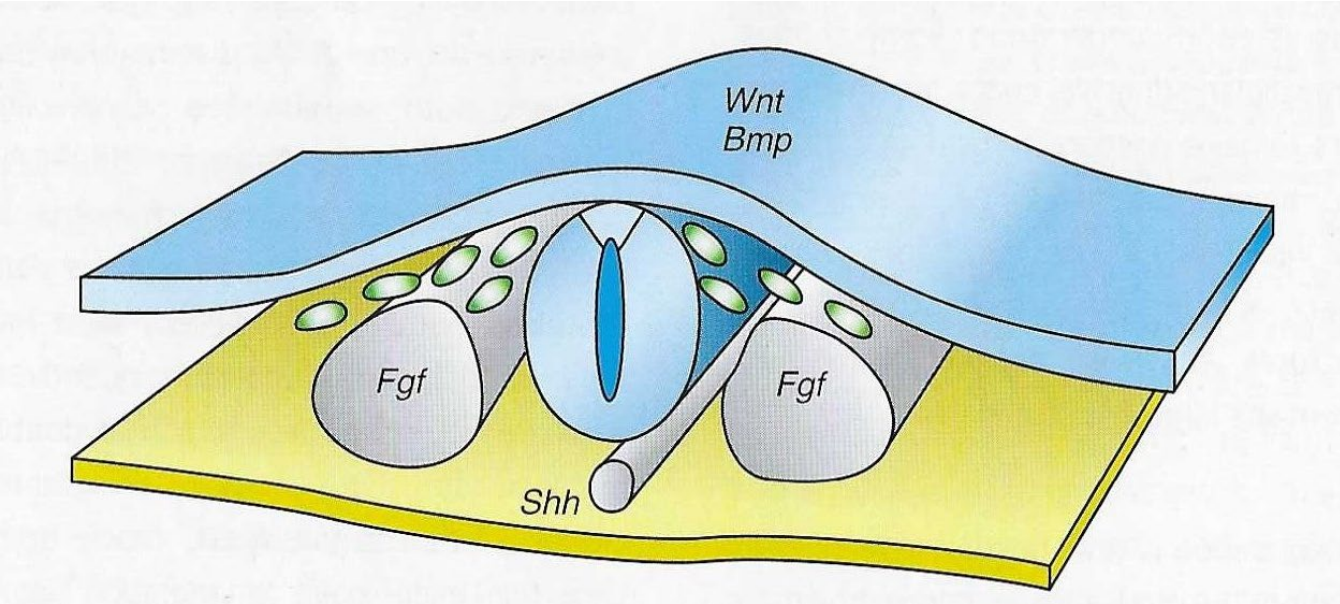
At hinge points, cells change shape (actin network constricts at apex) and nucleus is forced down)





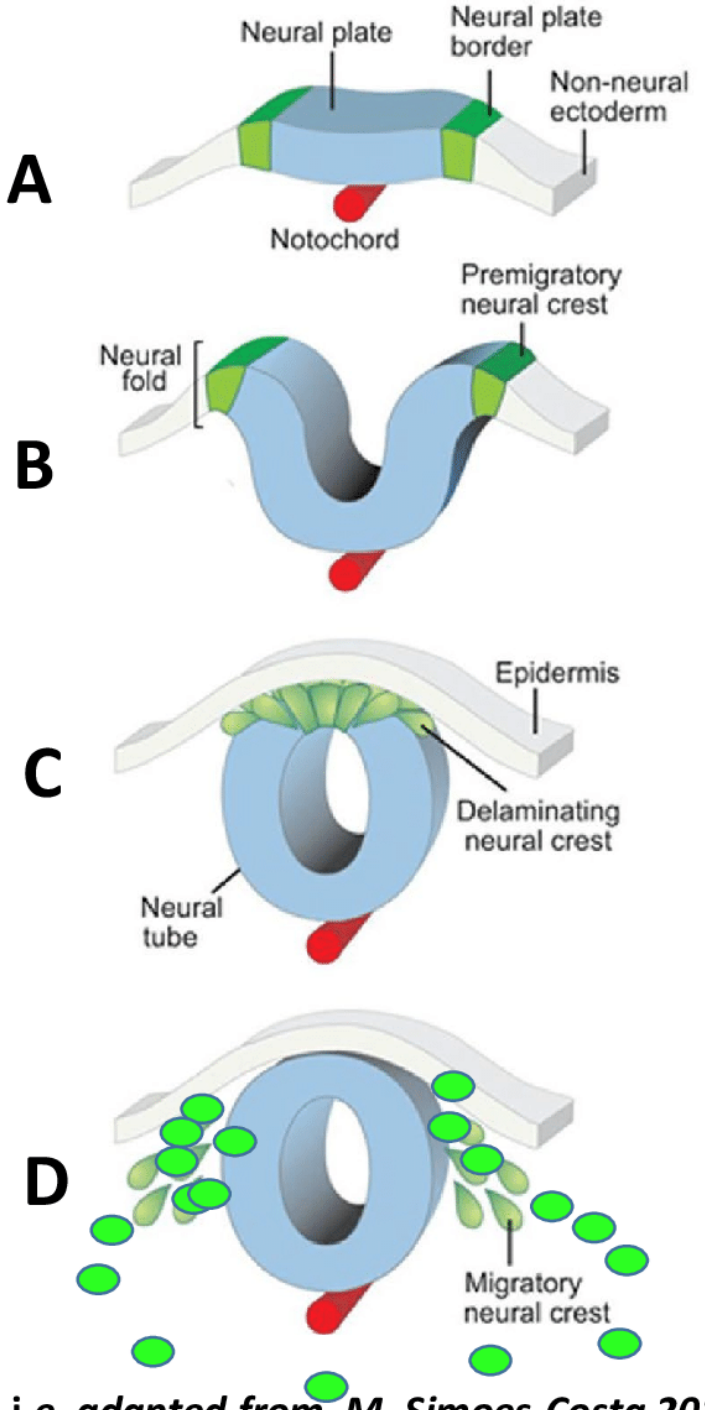
Induction

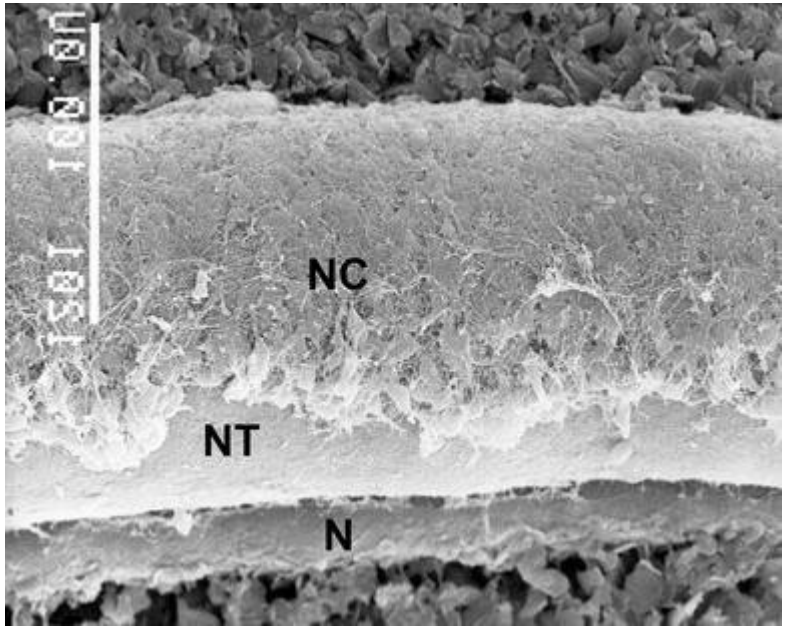
Induction: one cell group secretes an **inducer** that the neighboring group has receptors for. Endocytosis or activation of an internal cell signaling system results in gene activation and differentiation.



Neural Crest

4th germ layer.
Migrate to many different sites; *new neighborhood determines what they will become.*



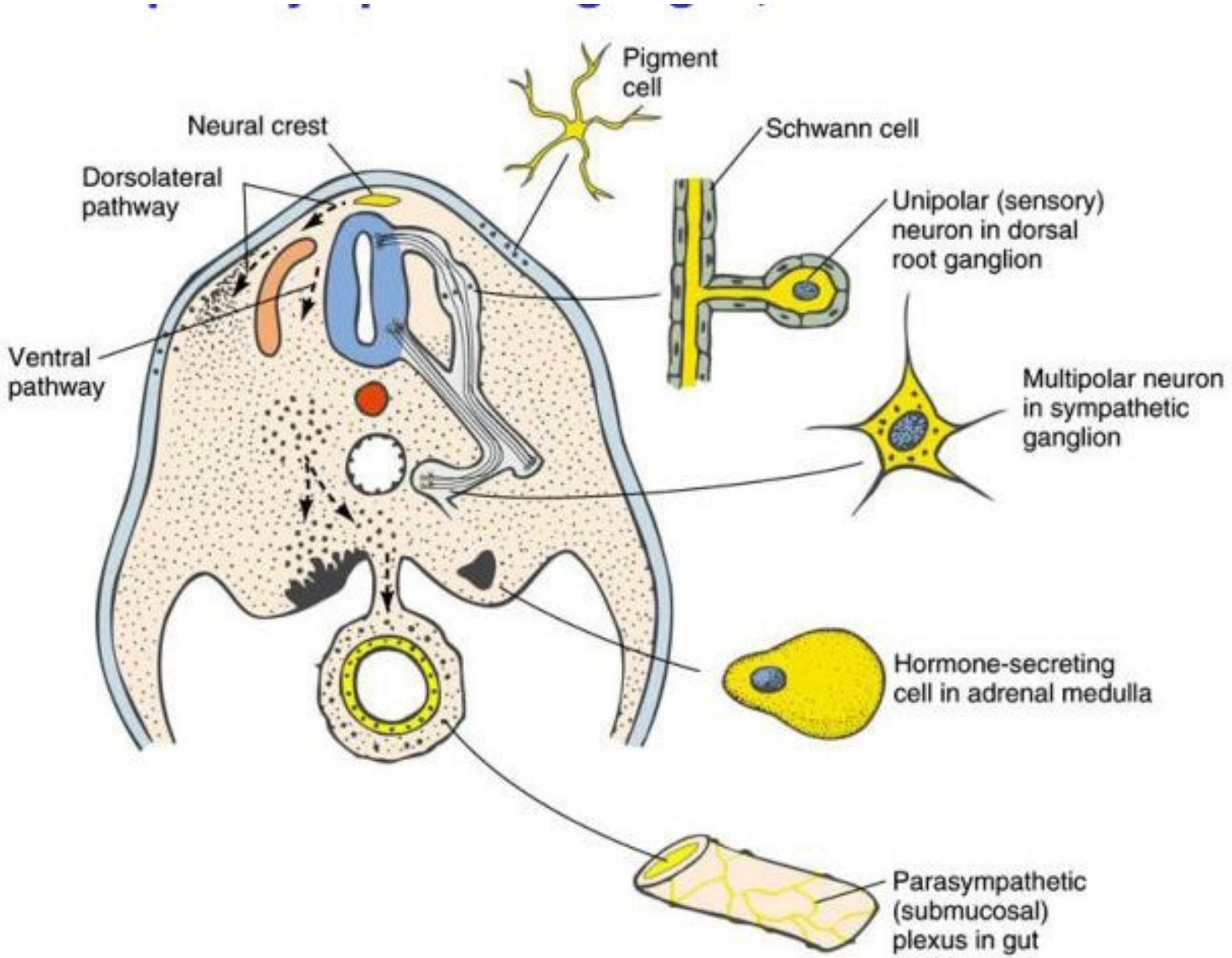


i.*e. adapted from M. Simoes-Costa 2014*

Derivatives

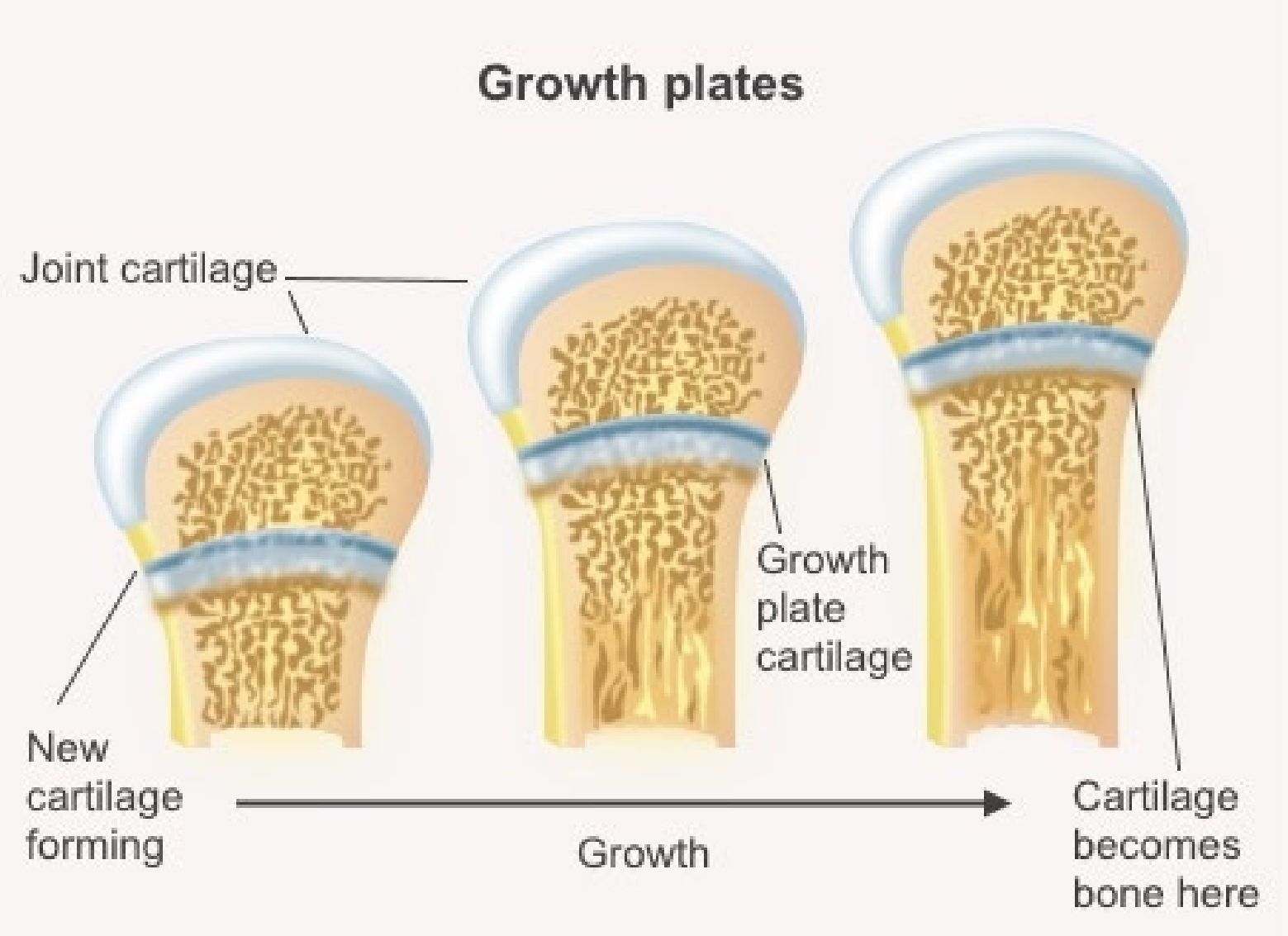
If enter skin: melanocytes.
If enter area around spinal cord: neurons.
If enter posterior abdomen: adrenal gland.
NC from head form most structures of face .
If enter heart: create major vessels.

The environment it travels to determines its fate.



Stem Cells and Osteoarthritis

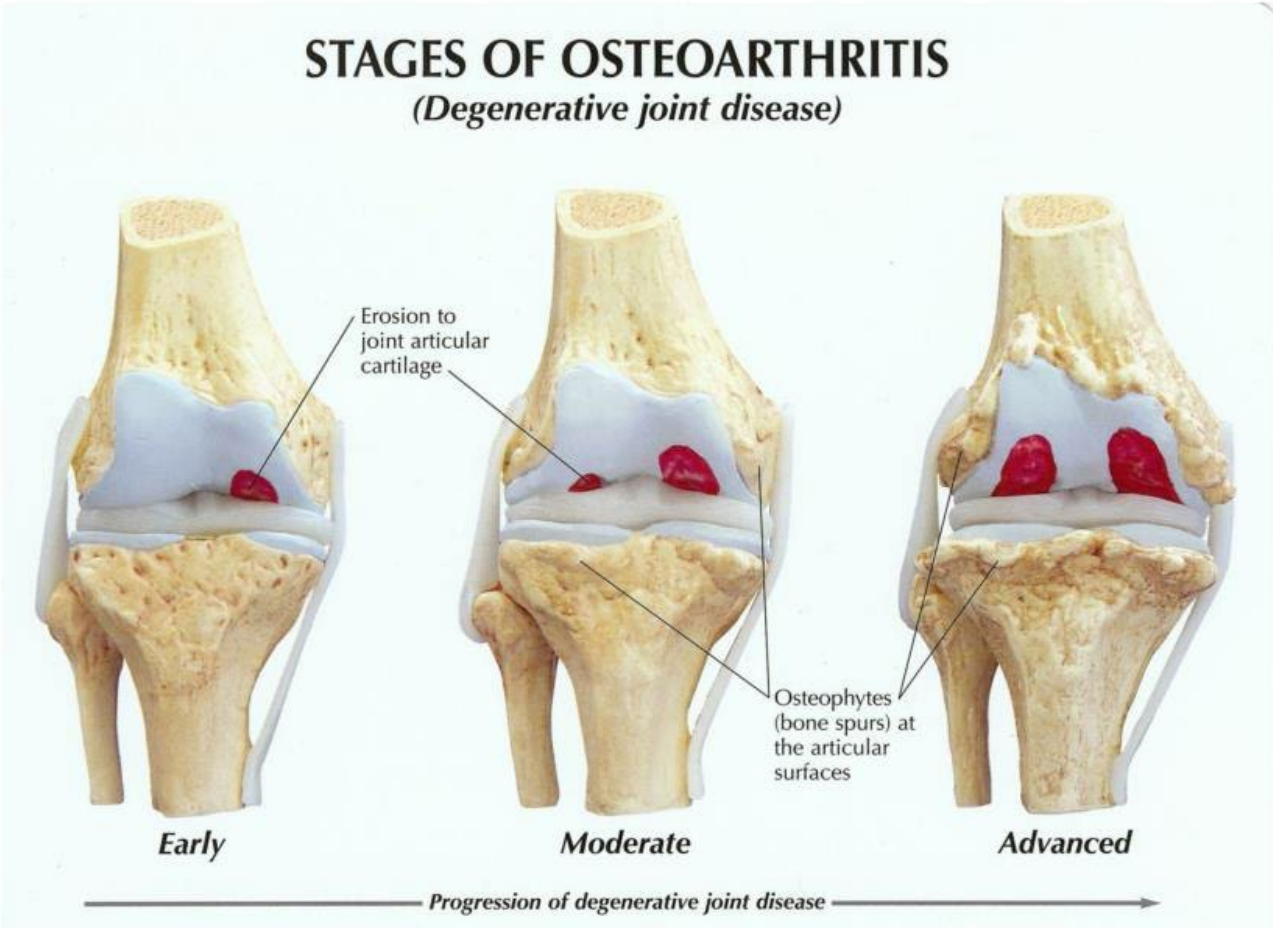
Bone grows in length at growth plates, which ossify around puberty. But cartilage stem cells have recently been found at joints too, in articular cartilage.



Cartilage Degeneration

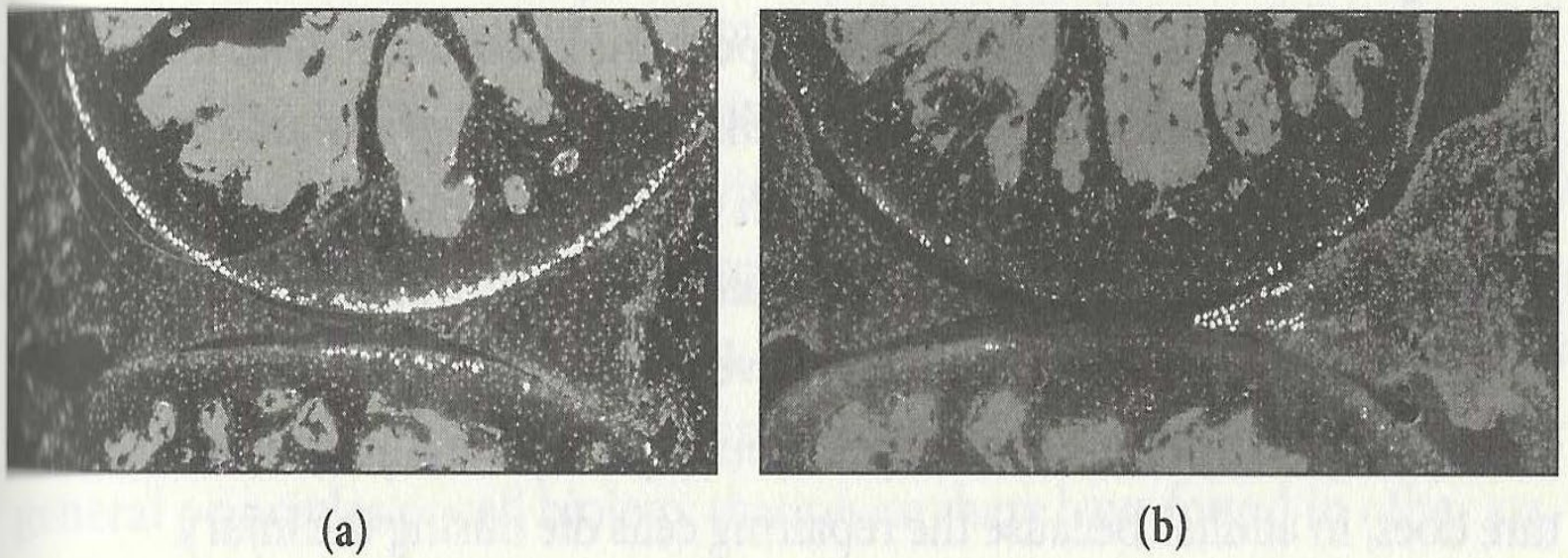
Had been thought that articular cartilage cannot repair itself. Once worn away, bone is exposed. Although cartilage has no pain nerves, bone does.

Stages of Osteoarthritis



Cartilage Stem Cells

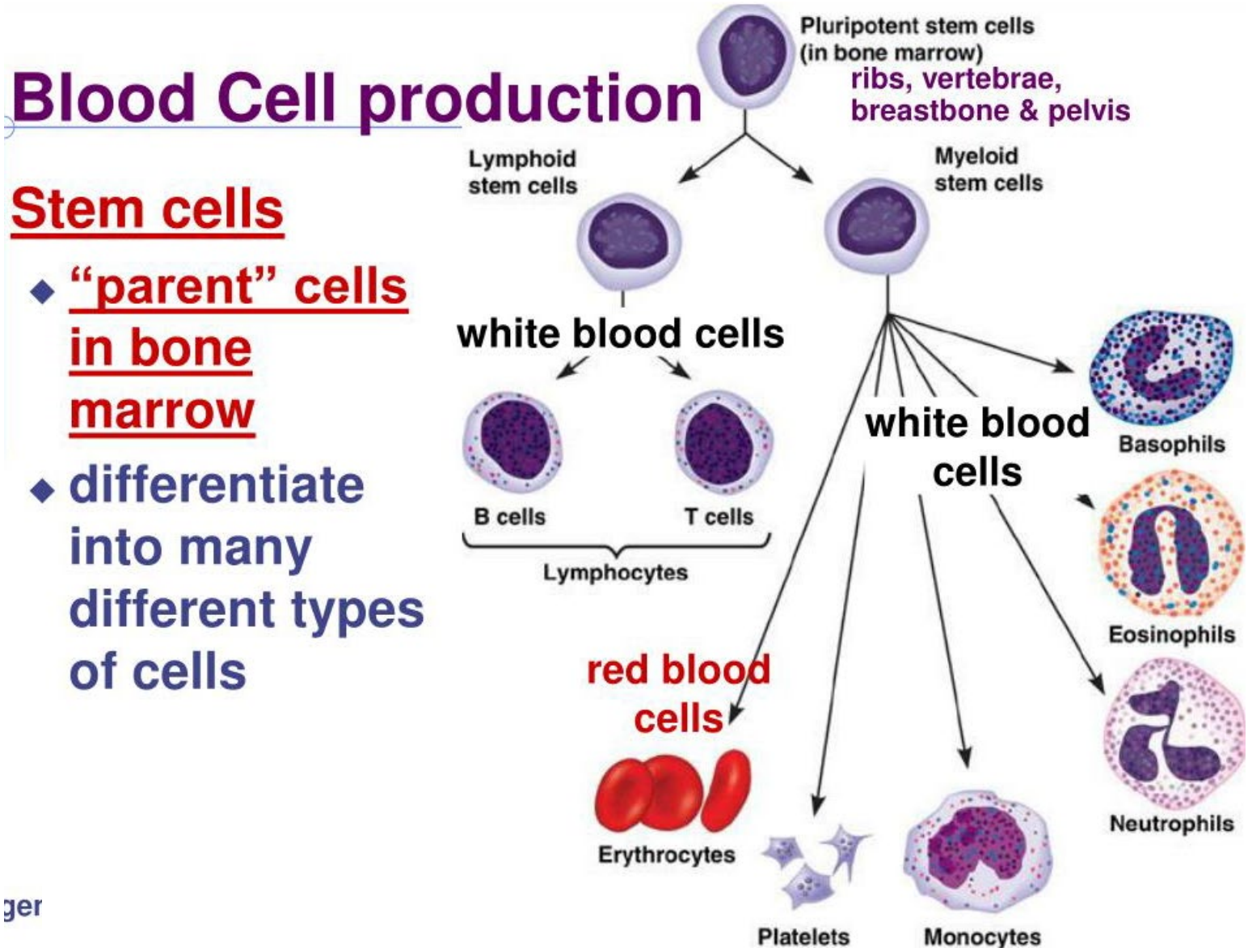
Stem cells now shown in articular cartilage, which normally replace tissue over time. But if cause osteoarthritis-inducing injuries (in mice), the stem cells die. Osteoarthritis may be a disease caused by death of stem cells, by age or injury. If a drug is injected that increases the stem cells, the mice are protected from osteoarthritis.



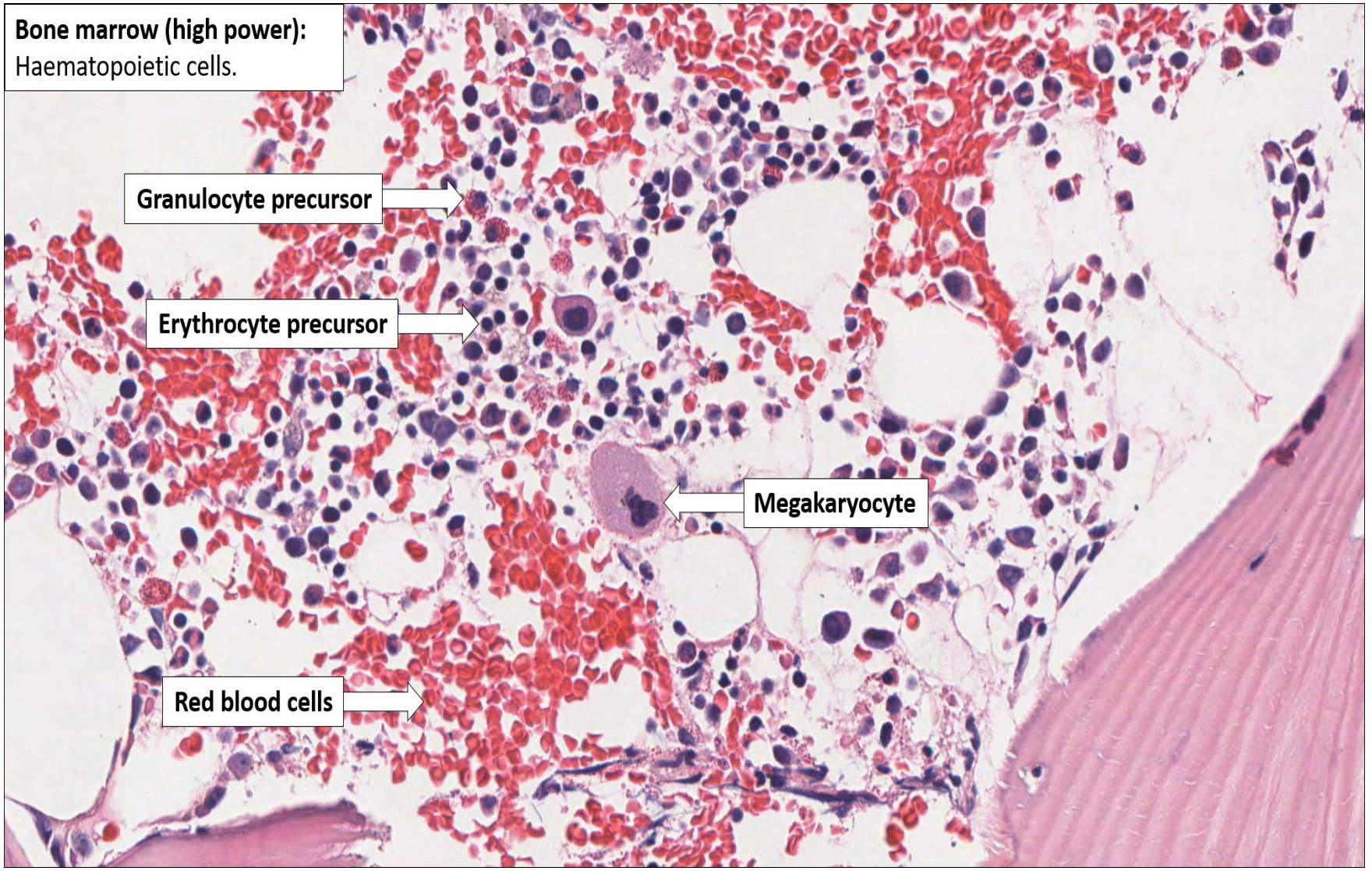
(a) A young mouse showing the cells marked with Gremlin lit up by the fluorescent protein. (b) The same joint after an arthritis-inducing injury, with the gradual death and disappearance of the Gremlin-expressing cells. The images are from Jia Ng's work.

Bone Marrow

All blood cells arise from a single type of stem cell in the bone marrow. (10 ^{9} blood cells/kg/day). Rate adjusted to meet needs; growth factors may be used therapeutically.

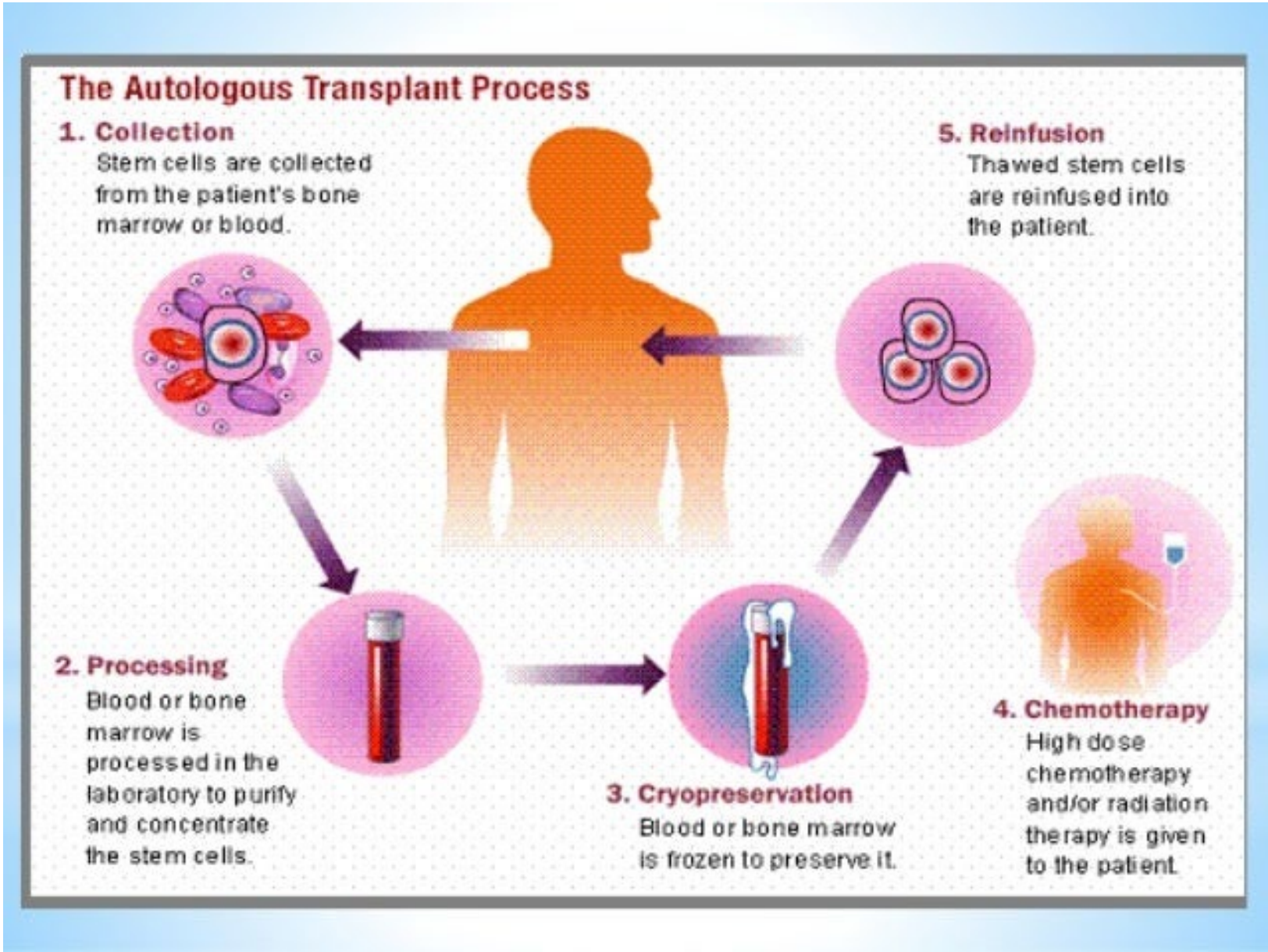


Bone Marrow


Bone marrow (high power):
Haematopoietic cells.
Granulocyte precursor
Erythrocyte precursor
Megakaryocyte
Red blood cells

Bone Marrow Transplants

Stem cells can be removed and stored, then used to repopulate patient's own blood forming tissues. Or given to another person (well matched) to correct for faulty genes in their marrow.
Stem cells may be genetically altered and replaced.



Induced Stem Cells

Somatic cells (eg skin) can be reprogrammed in a number of ways to become toti- or pluripotent, then directed in a particular differentiation path. In experimental animals, can colonize and incorporate into adult tissues.