Lecture 22 Stem cells and Nerve cells

Outline

I. Stem cell introduction
II. Early metazoan development and embryonic stem cells
III. Stem cells and niches in multicellular organisms
IV. Neurons and Glia: Building blocks of the nervous system

I. Definition of Stem cell

Cells that exist in embryo or adult that have the proliferation potential, self-renewal and differentiation into different type of cells.

can be divided into : totipotent stem cells
pluripotent stem cells
multipotent stem cells
monopotent stem cells

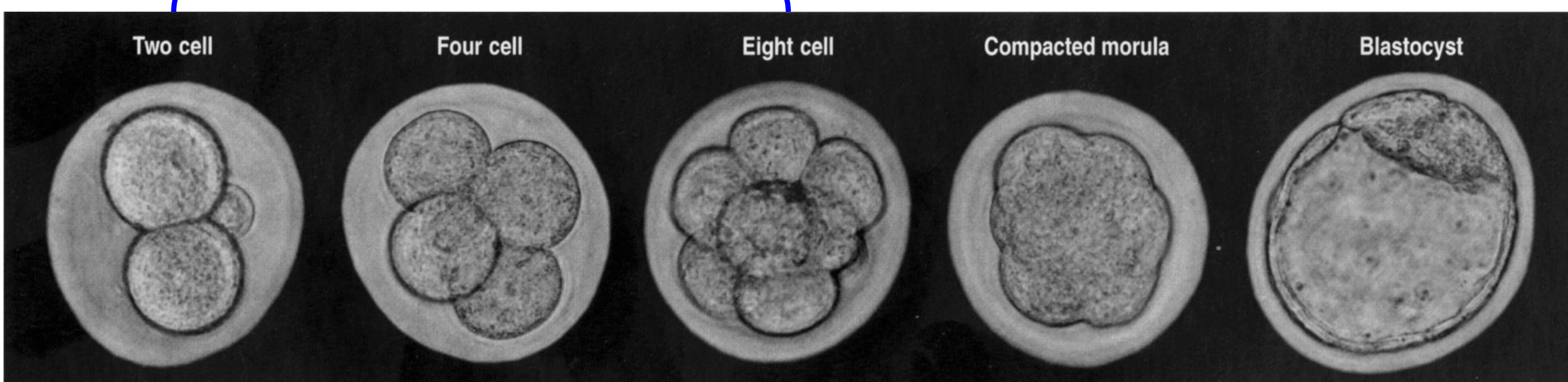
By differentiation capability

embryonic stem cells
tissue stem cells

By origin

Totipotent cells

- Be able to differentiate into a whole organism
- Examples: fertilized egg
- every single cell at development stage from zygote to 8-cell stage



Pluripotent stem cells

Be able to differentiate into a wide variety of cells, but not the whole organism

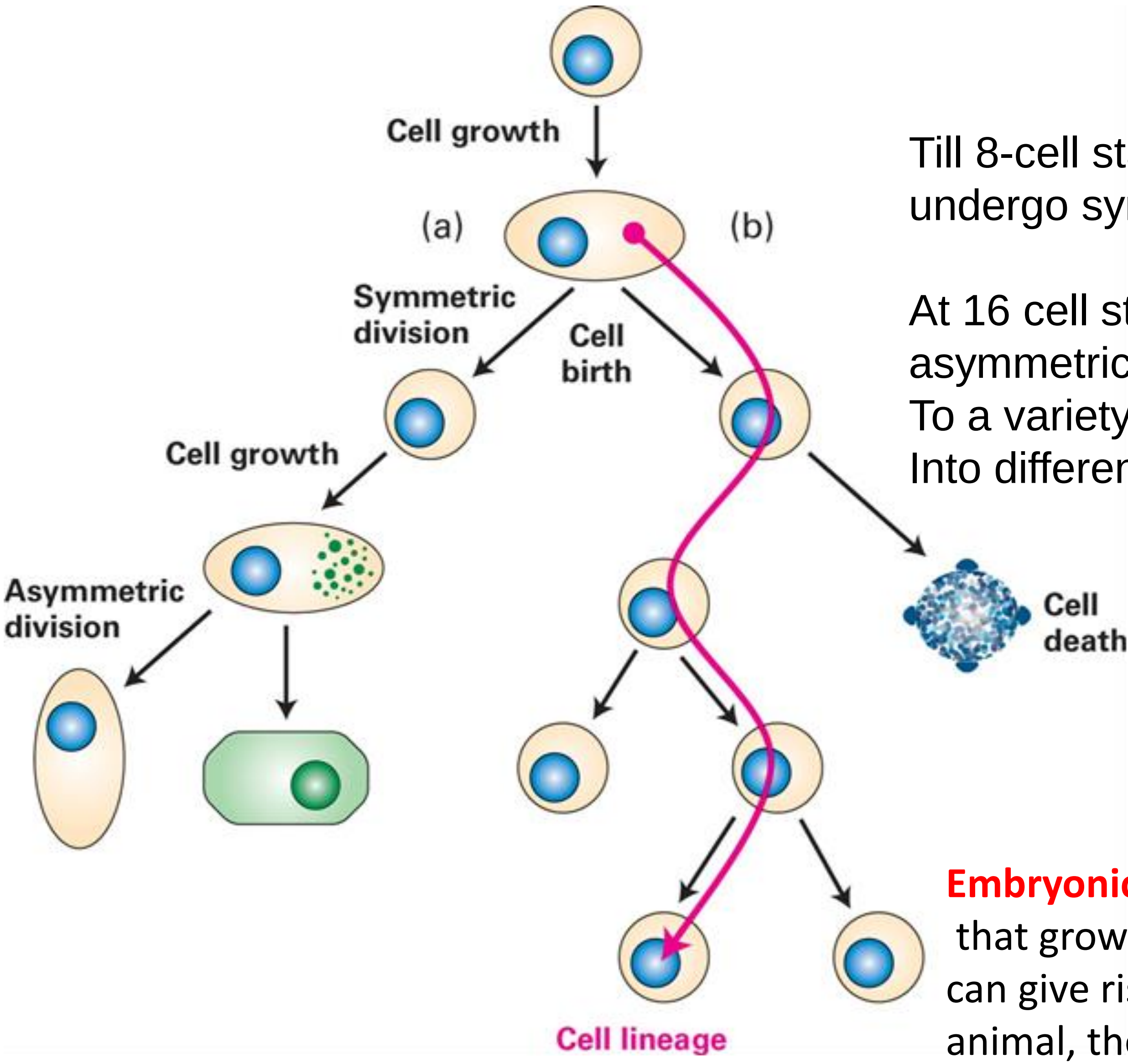
Examples: embryonic stem cells
bone marrow stromal stem cells
nerve stem cells
embryonic germ cells.

Multi- and mono-potent stem cells

Differentiation into a few types of cells or special type of cells.

Examples: neuroglial cells
nerve stem cells
satellite cells
epithelial stem cells
hematopoietic stem cells

II. Starting from a fertilized egg…



Till 8-cell stage, all cells are equal, undergo symmetrical division.

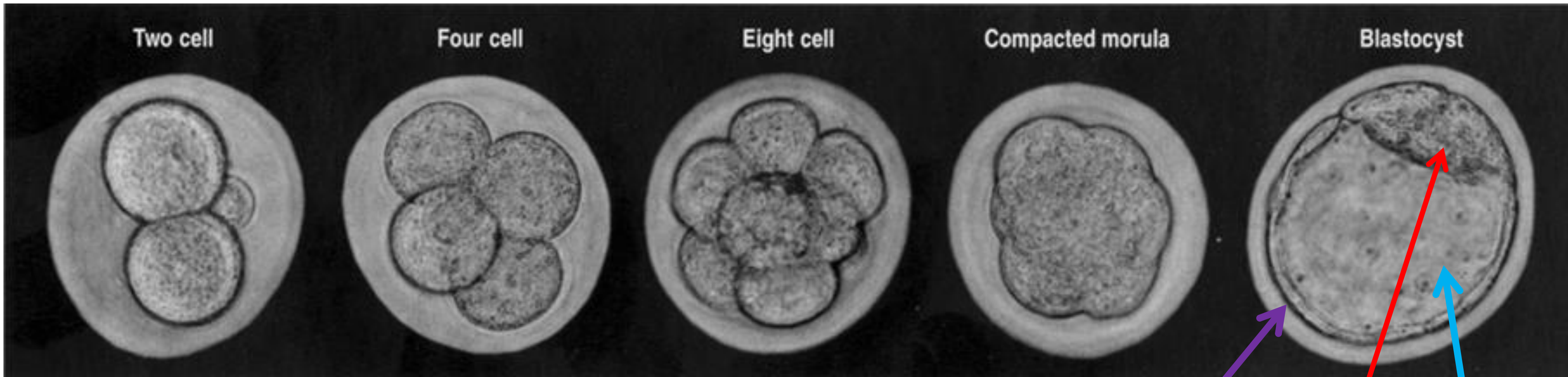
At 16 cell stage, cells start to undergo asymmetrical division, which gives rise To a variety of cells which differentiate Into different cells.

Embryonic stem cells: lineage of cells that grow indefinitely in culture and can give rise to different tissues of an animal, they are pluripotent.

Different stages in early embryo development

16-cell morula
E-cadherin mediates
cell compaction

64 cells blastocyst



blastocoel

Inner cell mass

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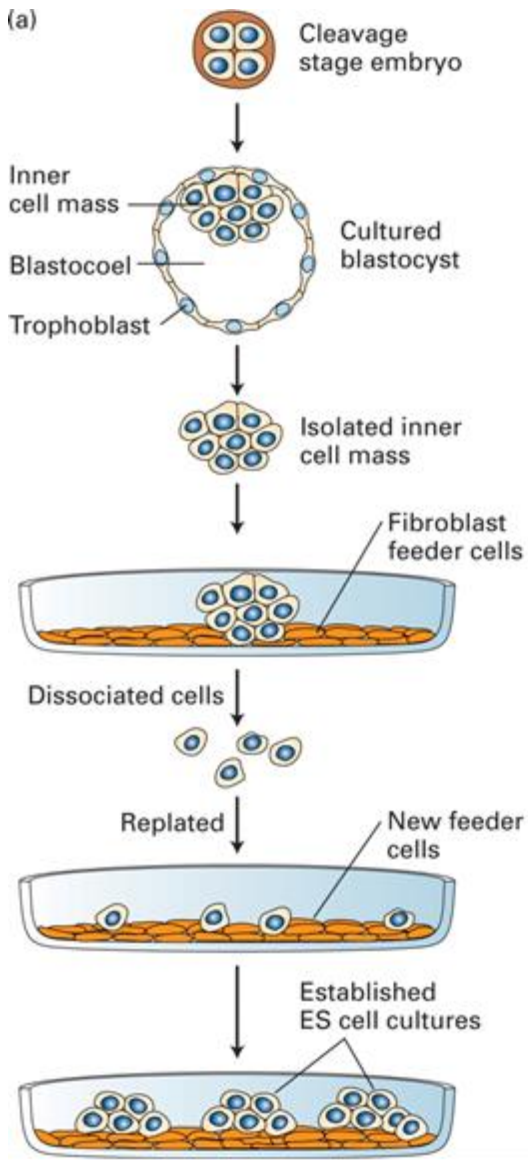
Trophectoderm (TE)

Inner Cell Mass is the source of pluripotent ES cells



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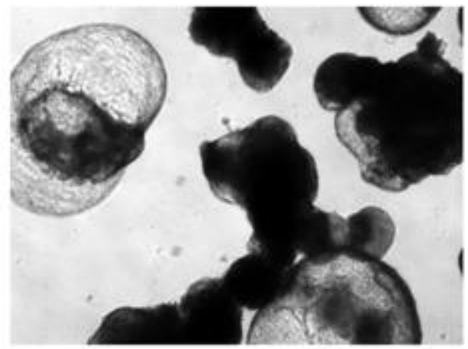

Embryoid bodies

ES cells in suspension can develop into embryoid bodies upon stimulation by STAT3

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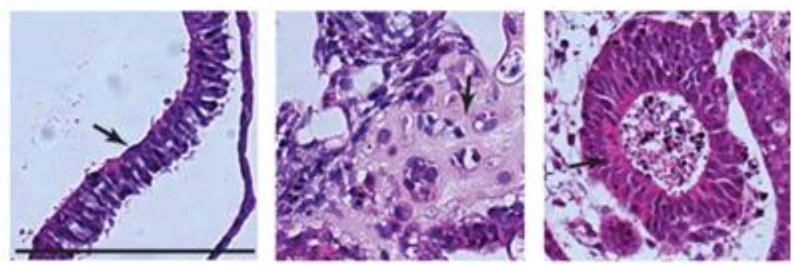


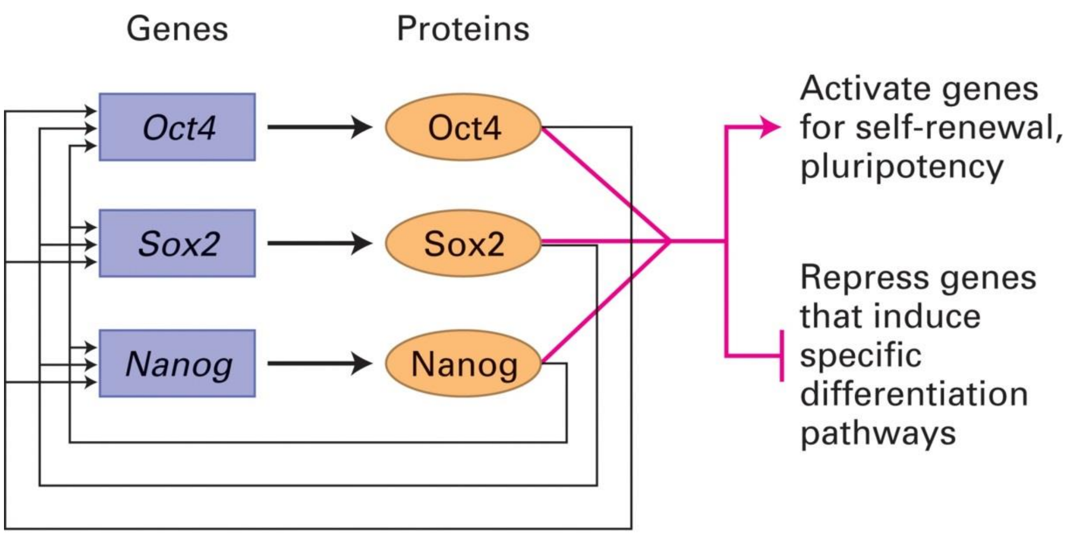
Endoderm Mesoderm Ectoderm

Tissue staining of embryoid bodies show cell layers resembling that of true embryo.

Multiple factors control/maintain the pluripotency of ES cells

- DNA demethylation (at early stage of development, a wide-spread DNA demethylation occurs)
- Transcription factors Oct 4, Sox2, Nanog
- Chromatin regulators
- miRNAs

Each of these transcription factors has been found to regulate over 1000 different genes



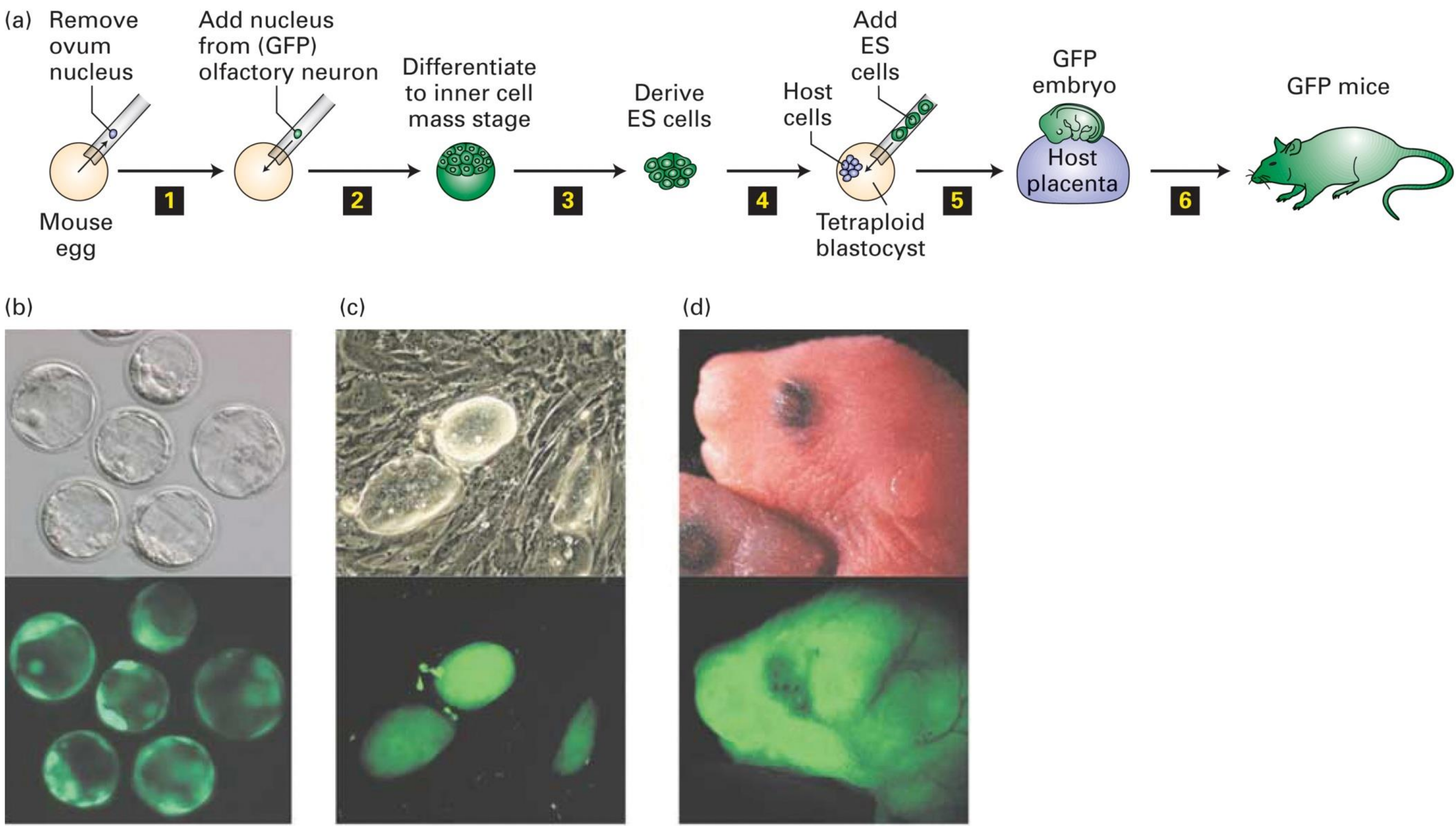
ES cells to restore and replace damaged tissue

- Diabetes--- ES cells were induced to differentiate into pancreatic endoderm, which were then transplanted into mice. These mice will produce functional beta islet cells to produce insulin.
- Danger in introducing undifferentiated ES cells, because they will produce tumor like mass containing large amount of poorly differentiated ES cells.

Animal cell differentiation can be reversed

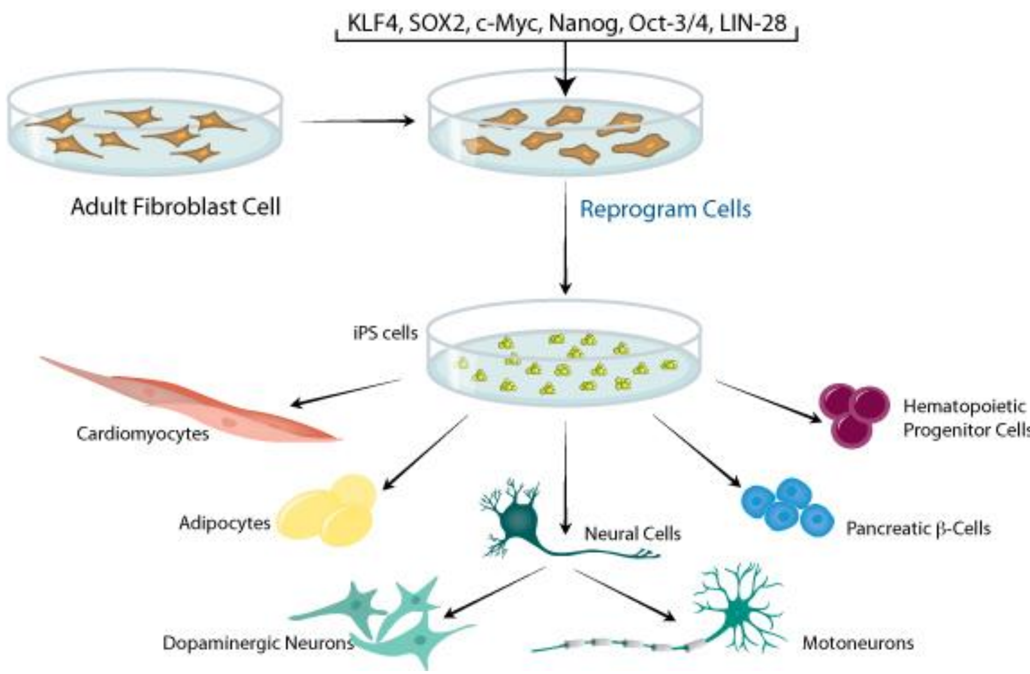
- Clone animal by somatic cell nuclear transfer
- Induced pluripotent stem cell (iPS)

Somatic cell nuclear transfer



Induced Pluripotent stem cells

- By introducing four different transcription factors, Klf4, Sox2, Oct4, c-Myc (they are also called Yamanaka transcription factors)

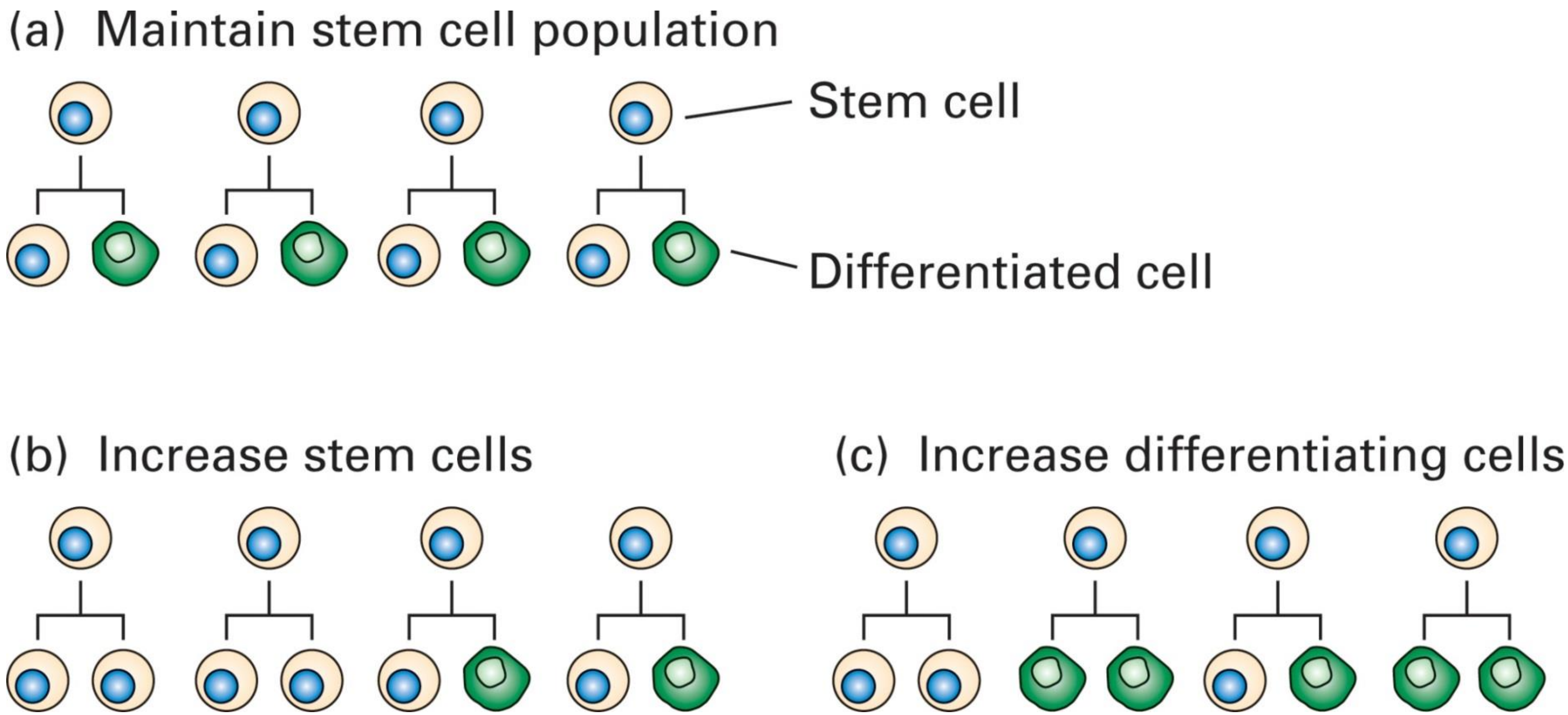


III. Stem cell and Niches in multicellular organisms

- Stem cells for many tissues: blood, intestine, skin, ovaries and testes and muscle, to replace old differentiated cells and for tissue regeneration; while for liver and pancreatic beta-islet, cells renewal maybe from existing differentiated cells

1. germ-line stem cells
2. intestinal stem cells
3. neural stem cells
4. hematopoietic cells

Patterns of stem-cell differentiation



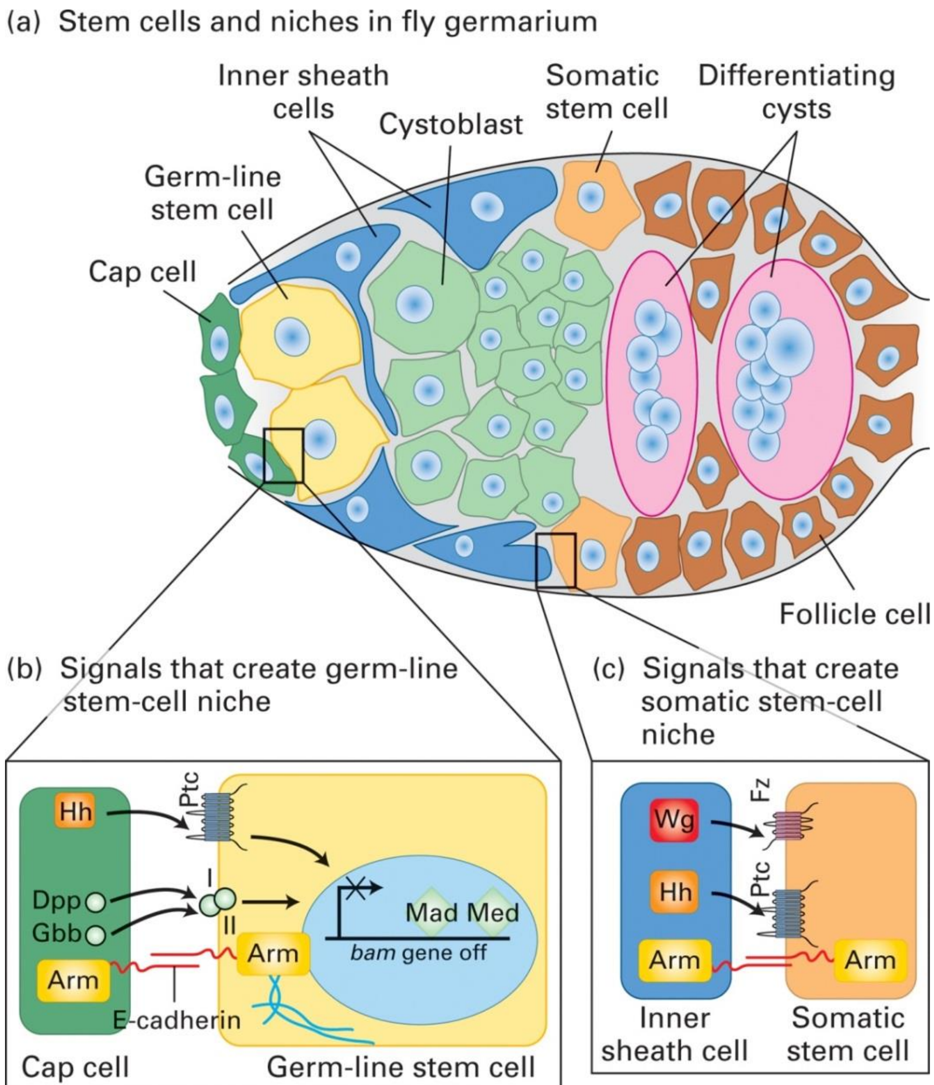
Self-renewal and differentiation both occur,
depending on which one predominates,
three different outcomes occur

Stem cells stay in certain places --- Niche

- Both intrinsic and extrinsic factors control stem cell status.
- Extrinsic factors refer to hormonal and regulatory signals from surrounding cells

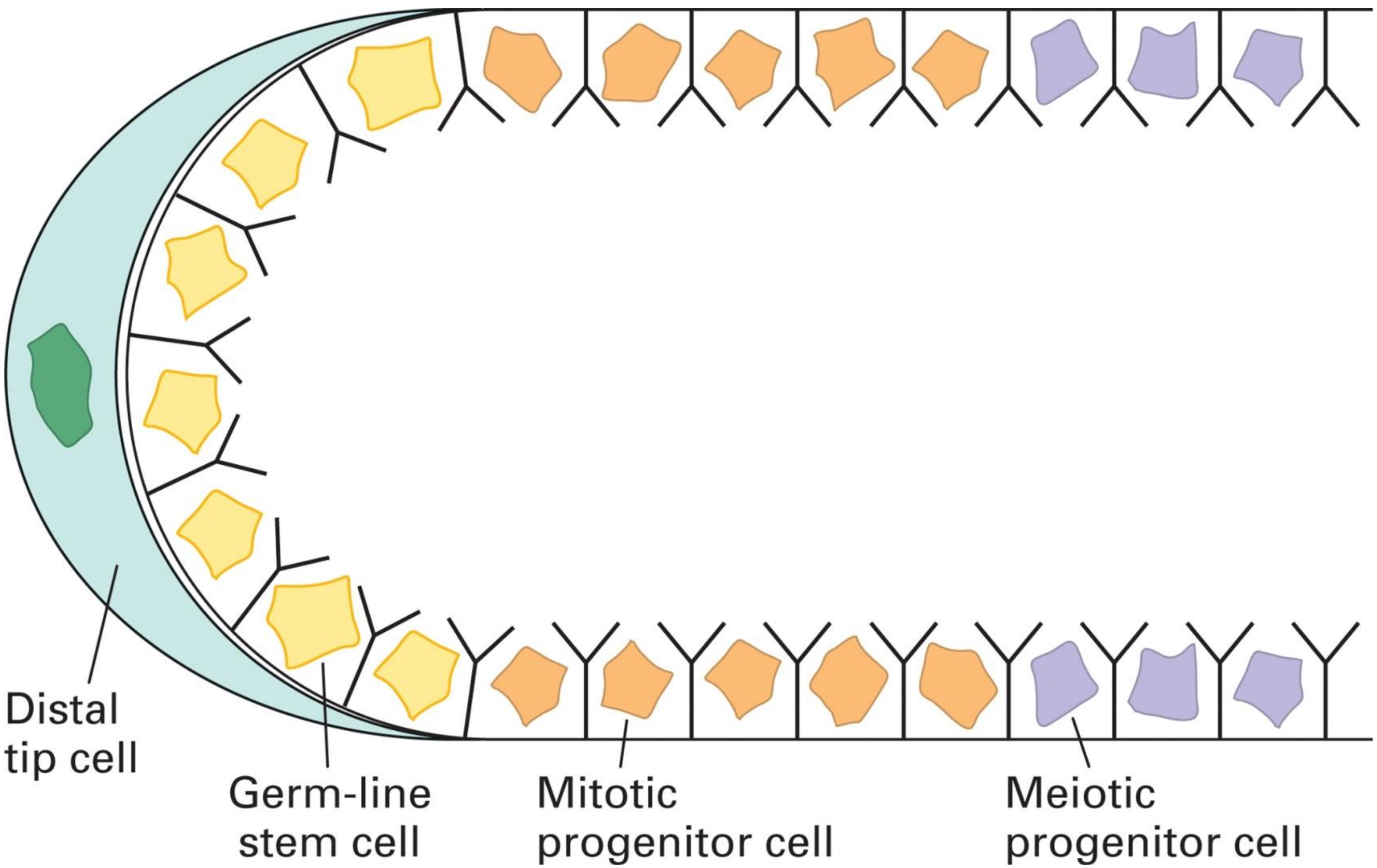
1. Germ-line stem cells

- Germ-line: cell lineage that produce sperm and oocyte



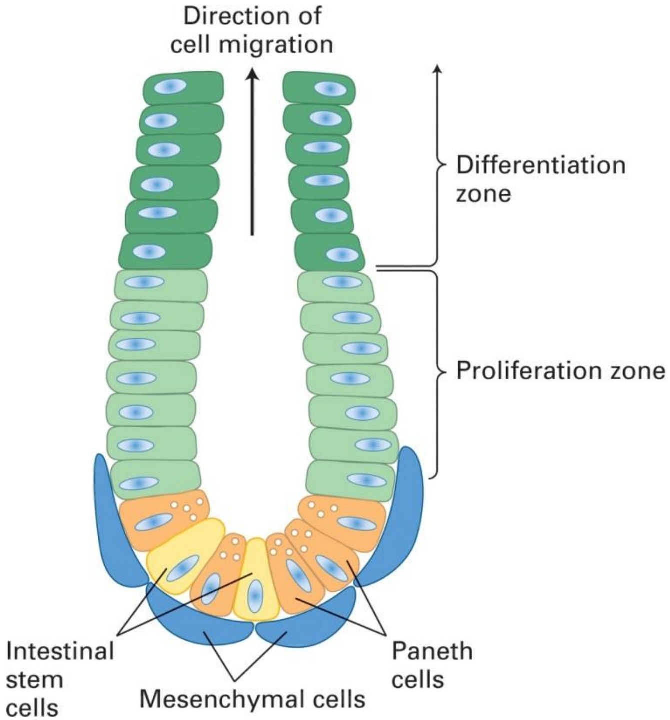
TGF-beta
Notch
Wnt
Hedgehog
play roles
In maintaining
Germ-line stem
cell status

Germ-line stem cells in C. elegans



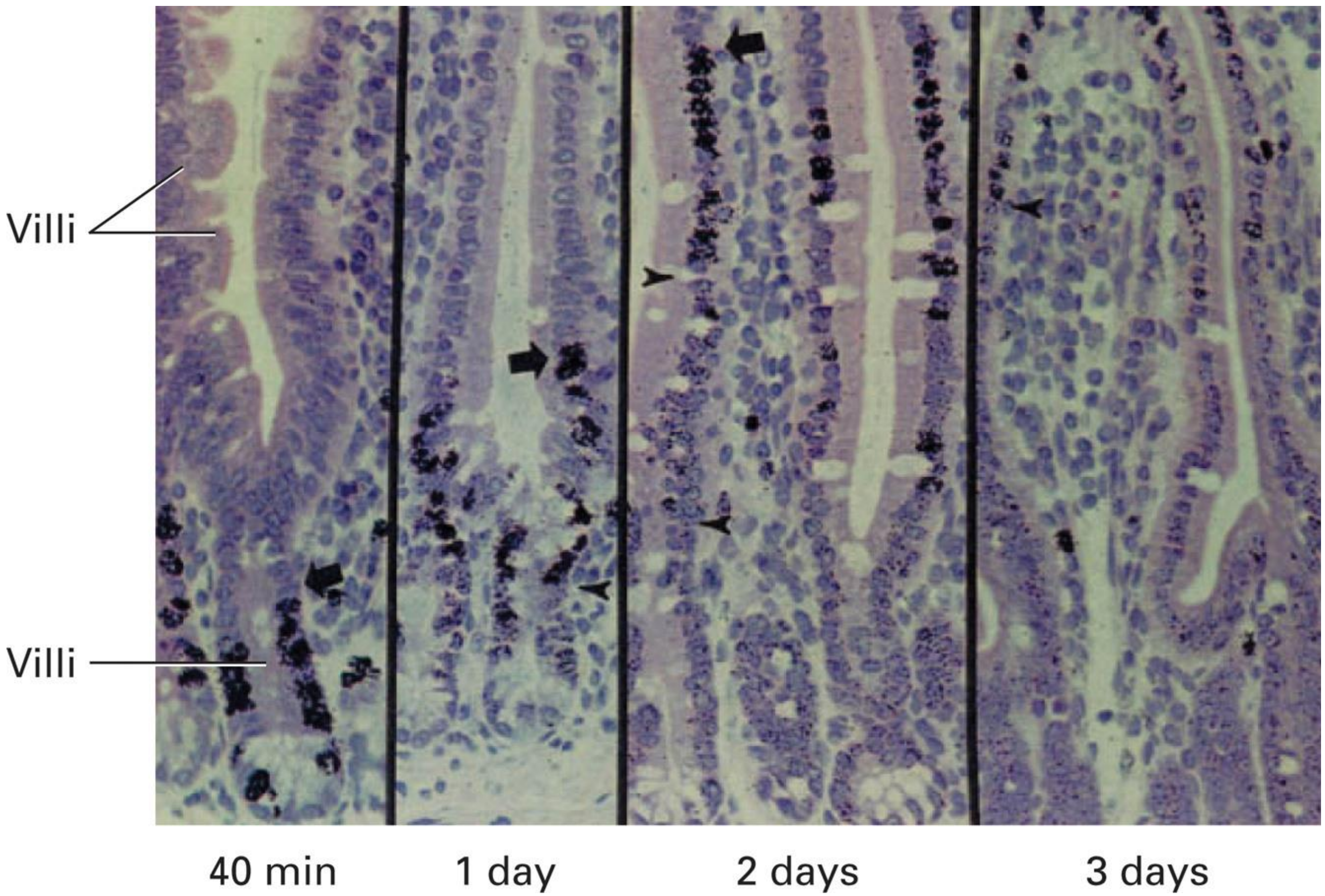
2. Intestinal stem cells

- Intestinal epithelial cells renew every 5 days, through stem cells beneath the crypts



How to prove this?

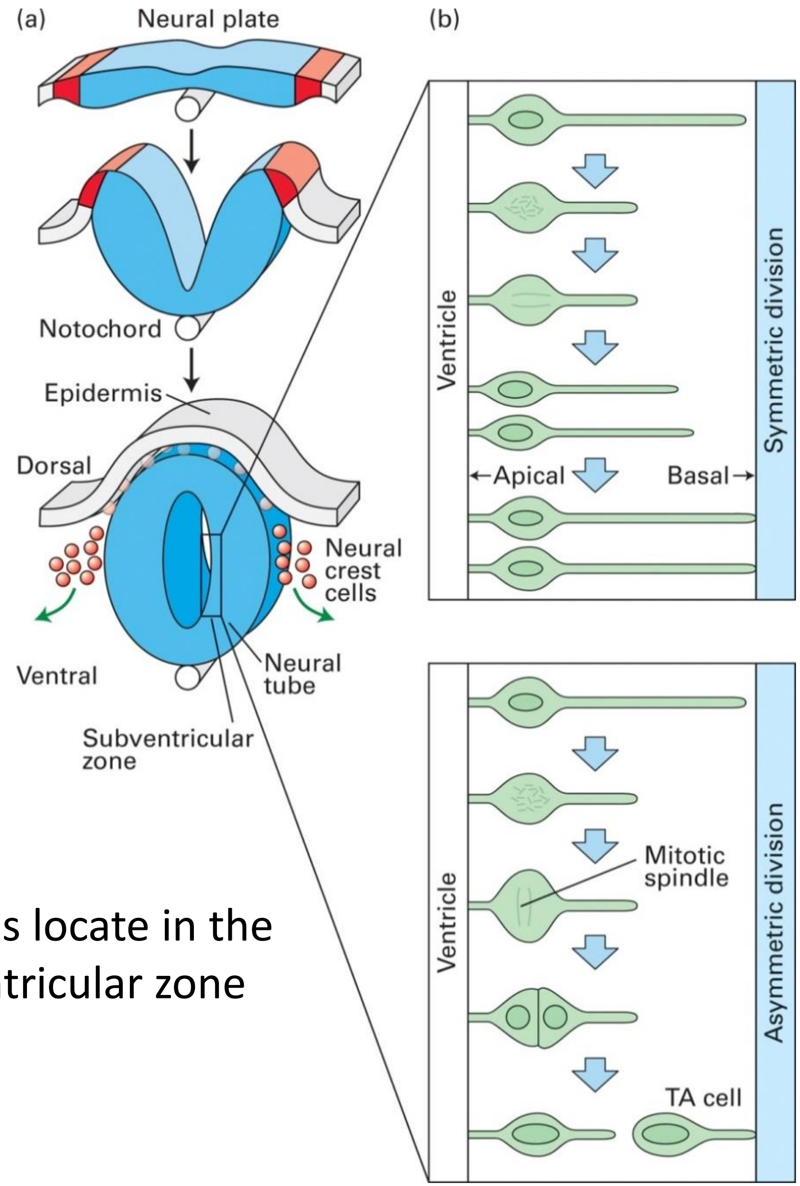
- Pulse-chase experiments by radiolabeled Thymidine



3. Neural stem cells

- Neural stem cells form nerve and glial cells in the central nervous system
- It is promising to use neural stem cells to find a cure for neurodegenerative disease.

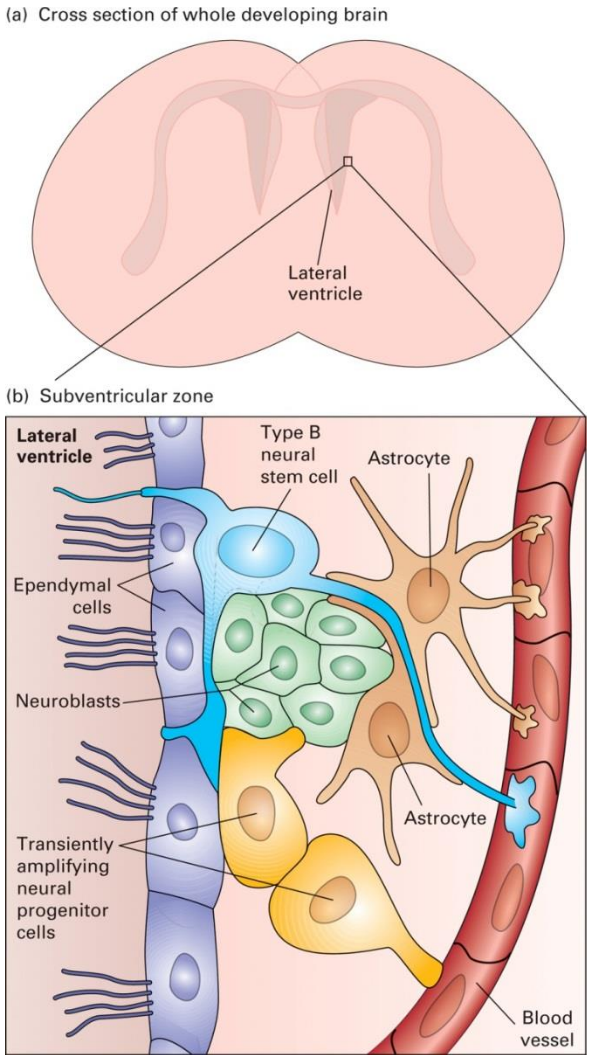
Formation of the neural tube and division of the neural stem cells



Stem cells locate in the subventricular zone

Spindle poles orient differently

Does adult brain produce new nerve cells?

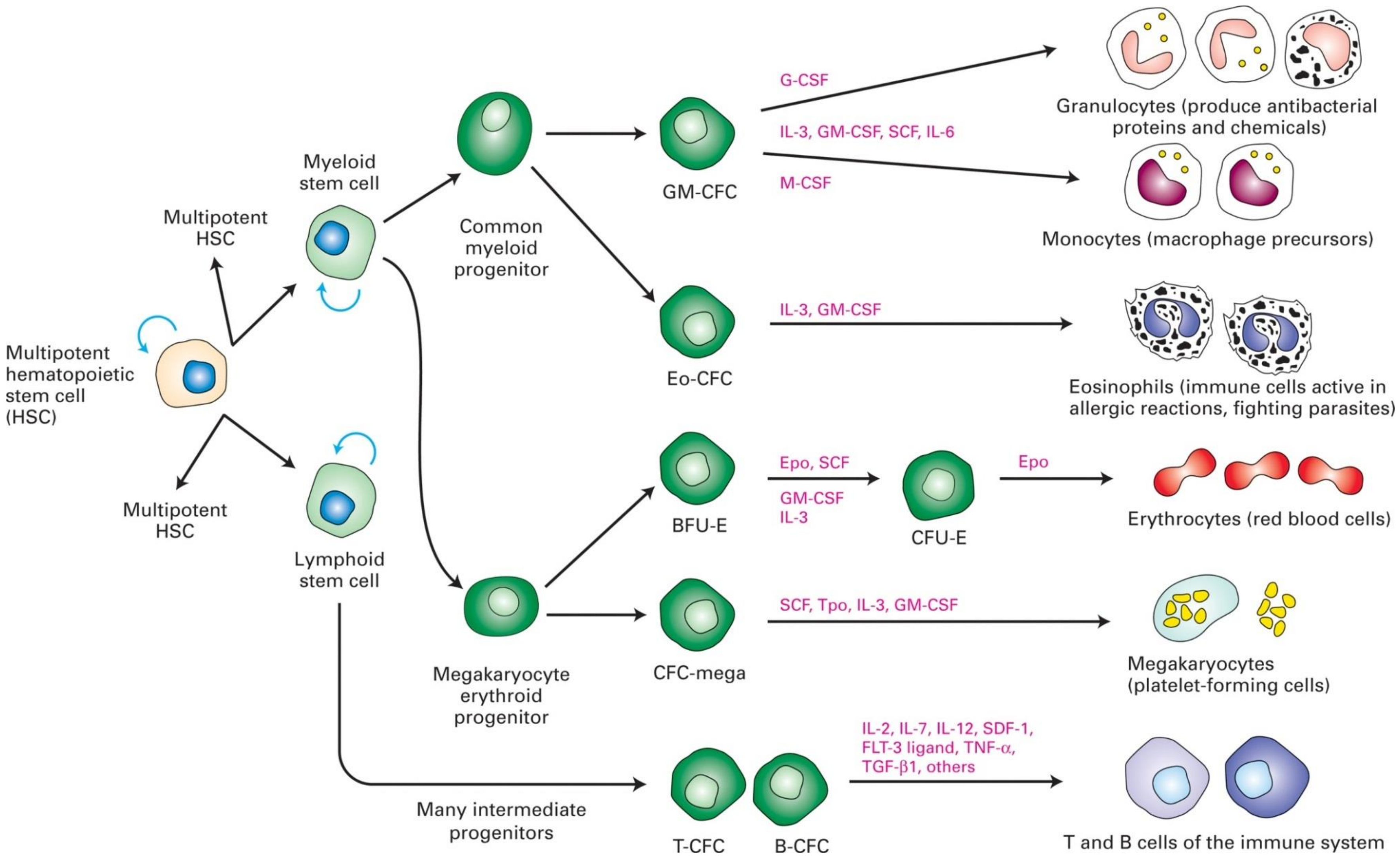


Yes: nerve stem cells exist in Hippocampus zone, subventricular region

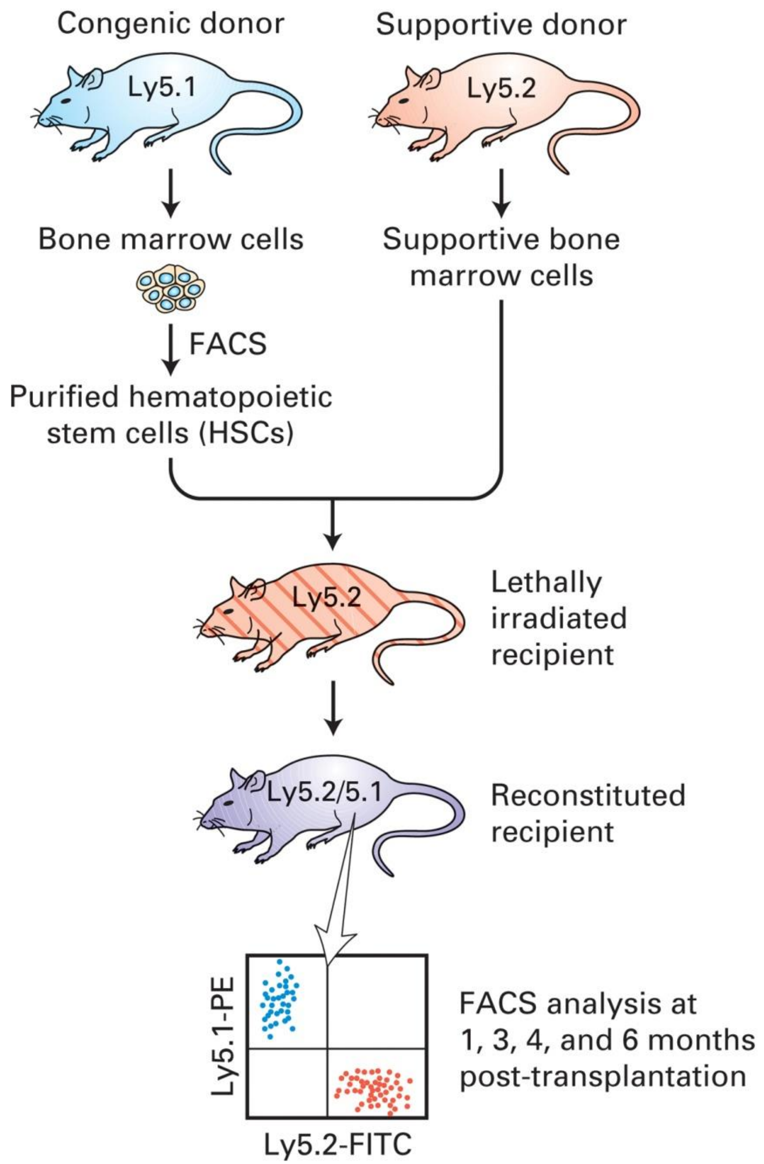
4. Hematopoietic stem cells

- Exists in embryonic liver and adult bone marrow.
- Form all blood cells

Formation of blood cells from hematopoietic stem cells in the bone marrow

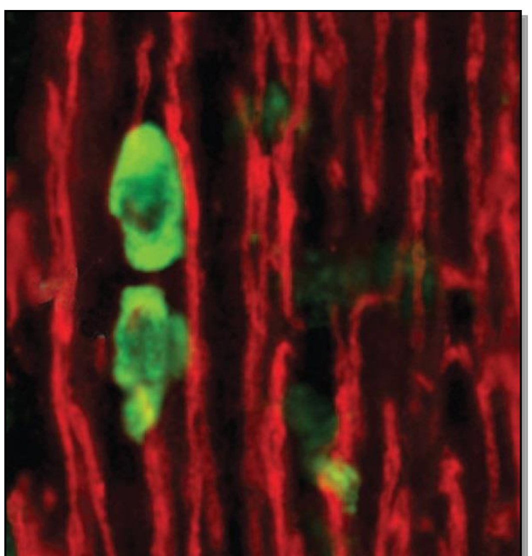


Bone marrow transplantation has been effective to treat many blood disease including leukemia



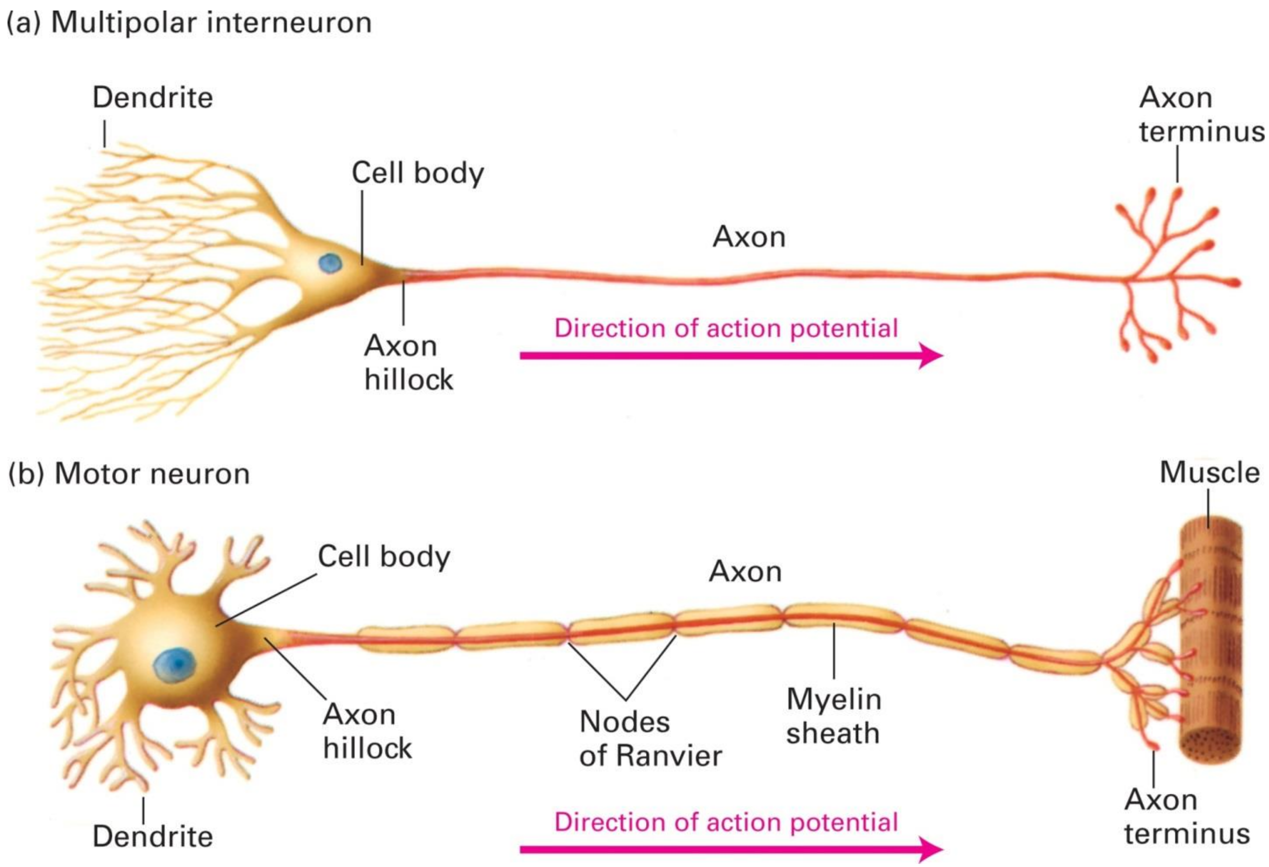
IV. Neurons and glia

- Human brain has 10^11 neurons, 10^14 synapses.
- Glial cells occupy the space between neurons and modulate neuron function.



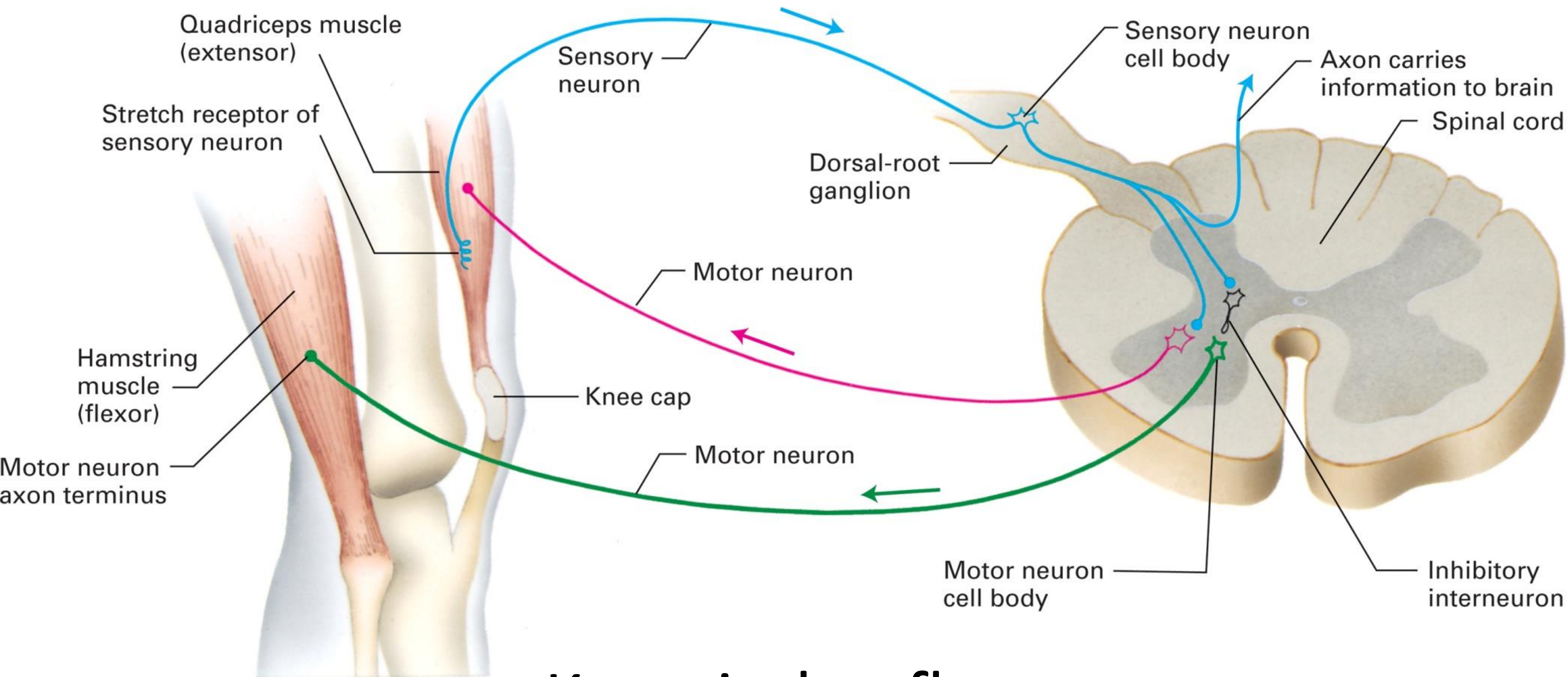
Red: neuron axon
Green: glial cells

- Two types of neurons: multipolar interneuron and motor neuron



- Myelin sheath is composed of glia cells on motor neurons, but not on multipolar interneuron
- Motor neurons function to transmit signals to effector cells such as muscle cells
- Multipolar interneurons have a lot more dendrites , they function to receive signals and transmit the signal to central nervous system.

Multiple neurons in signaling circuits



Knee-jerk reflex

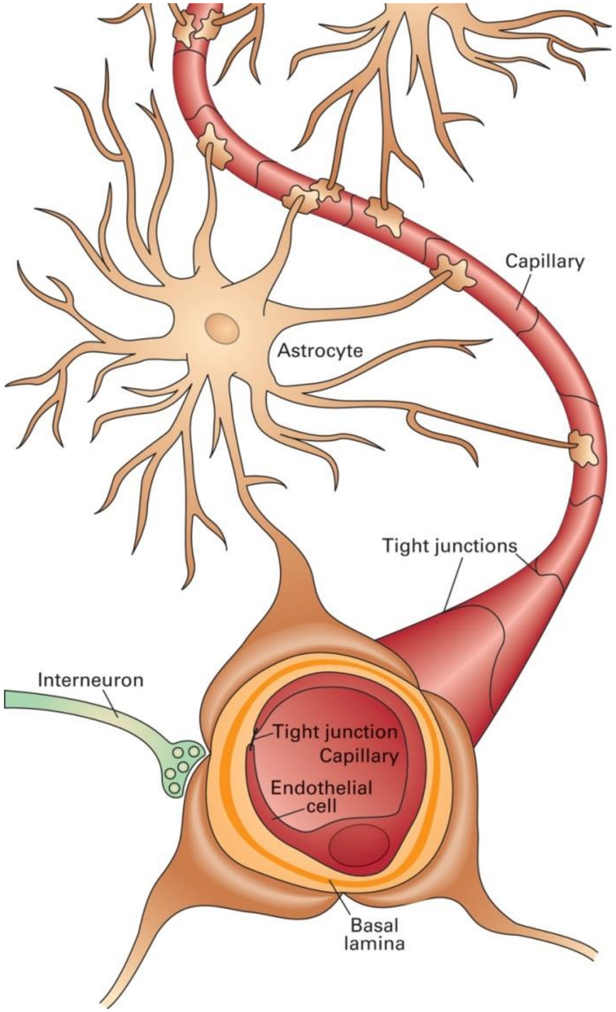
Sensory neurons
Effector neurons
Interneurons: the largest group

Glia cells

- Form myelin sheaths and support neurons, can be divided into three categories:

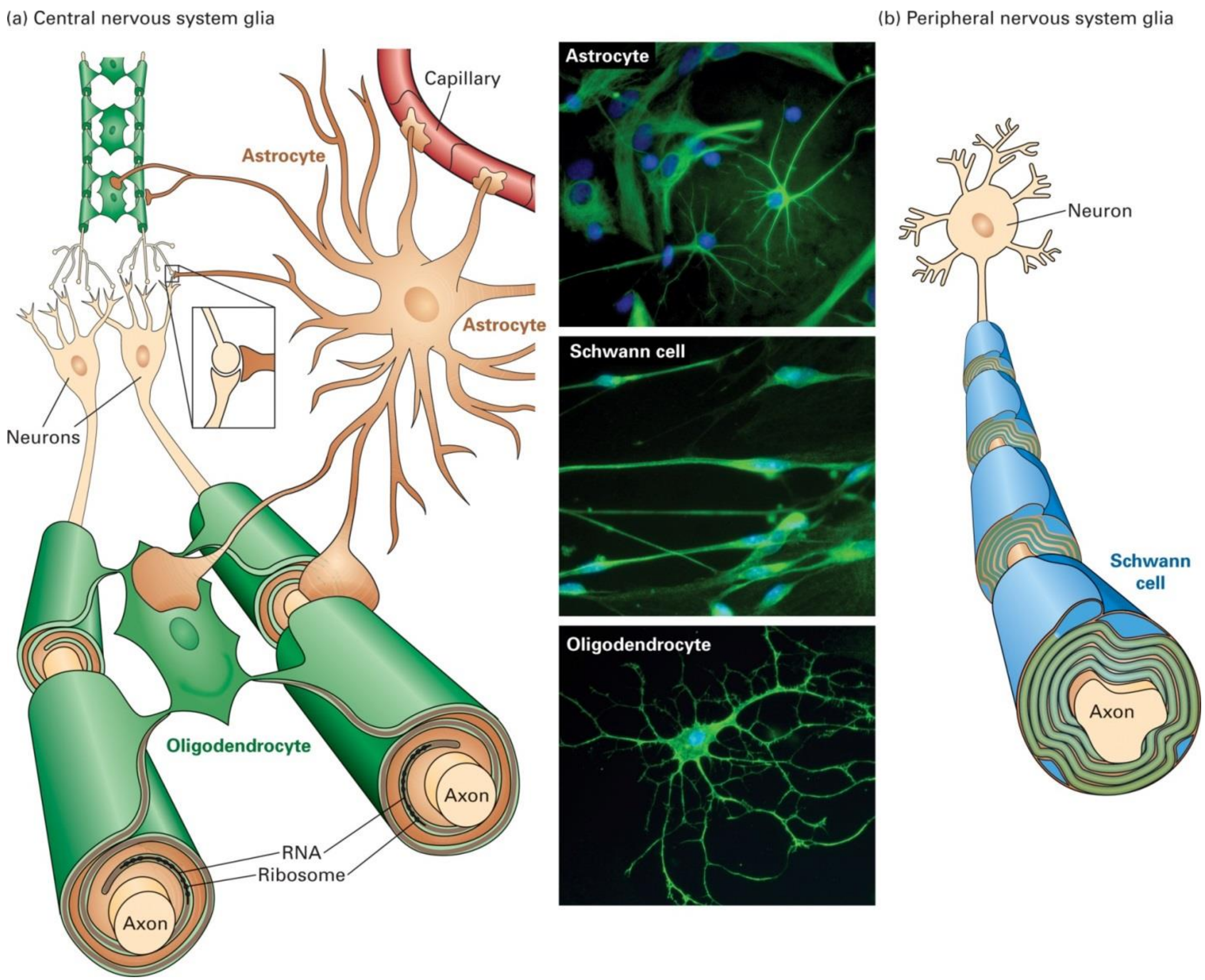
1. Oligodendrocytes: make sheaths for the central nervous system
2. Schwann cells: make sheaths for the peripheral nervous system.
3. Astrocytes: starlike shape, provide growth factors and other signals to neurons, receive signals from neurons and induce synapse formation between neurons.

Astrocytes

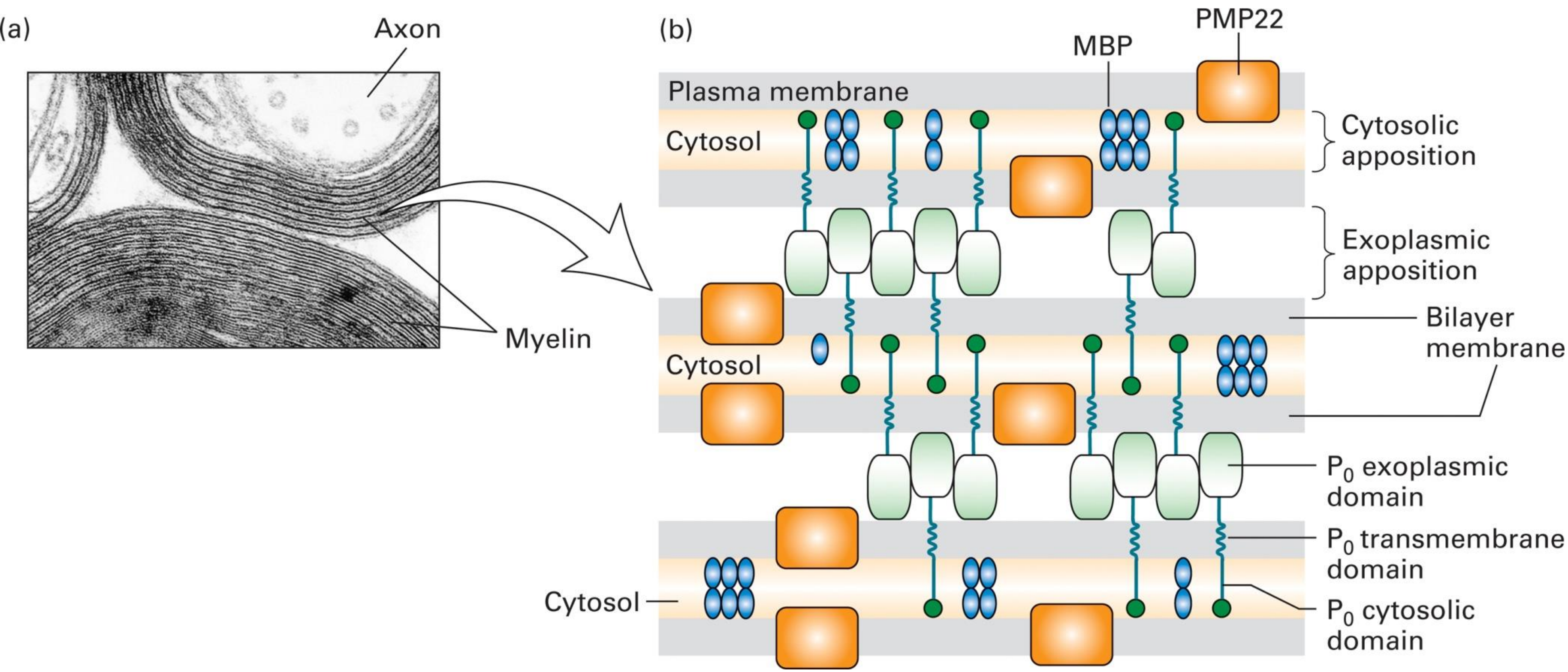


take 1/3 of brain mass and
1/2 of total brain cells.
Produce ECM proteins.
Joined together by gap junctions

The three types of glia cells

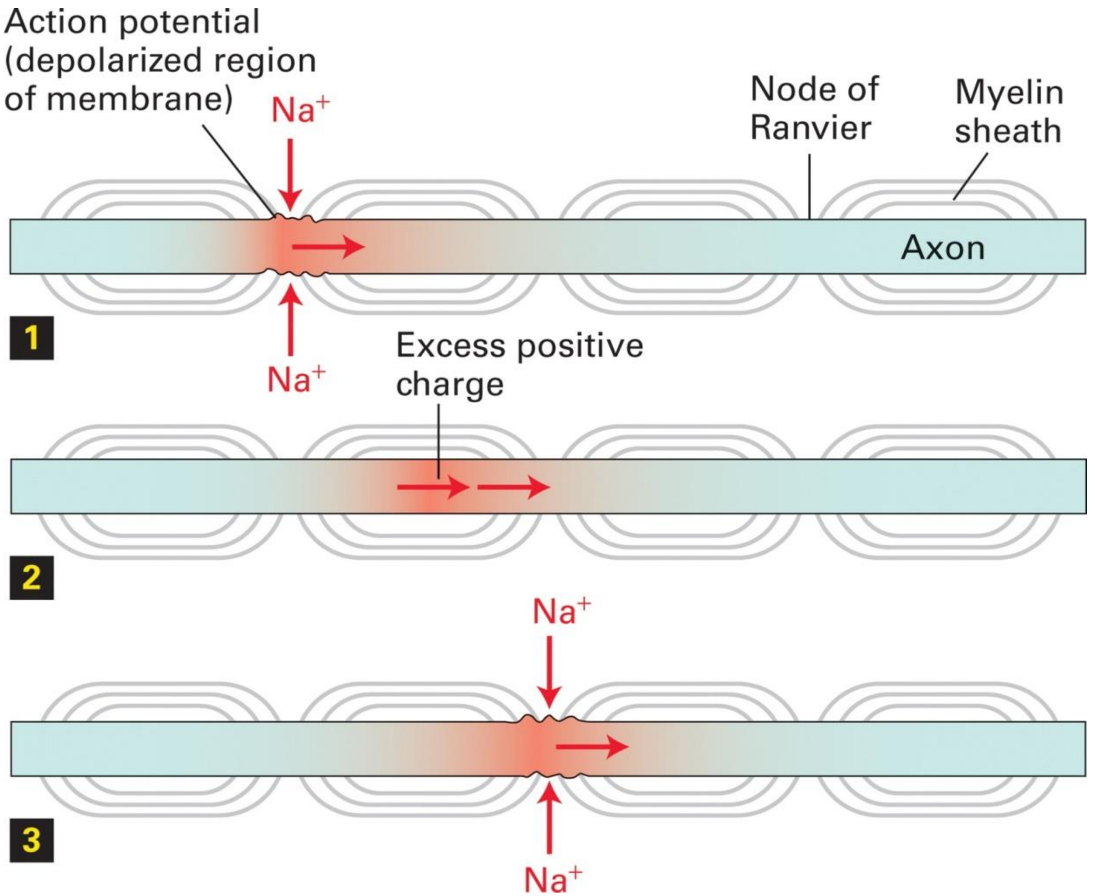


The structure of myelin sheath



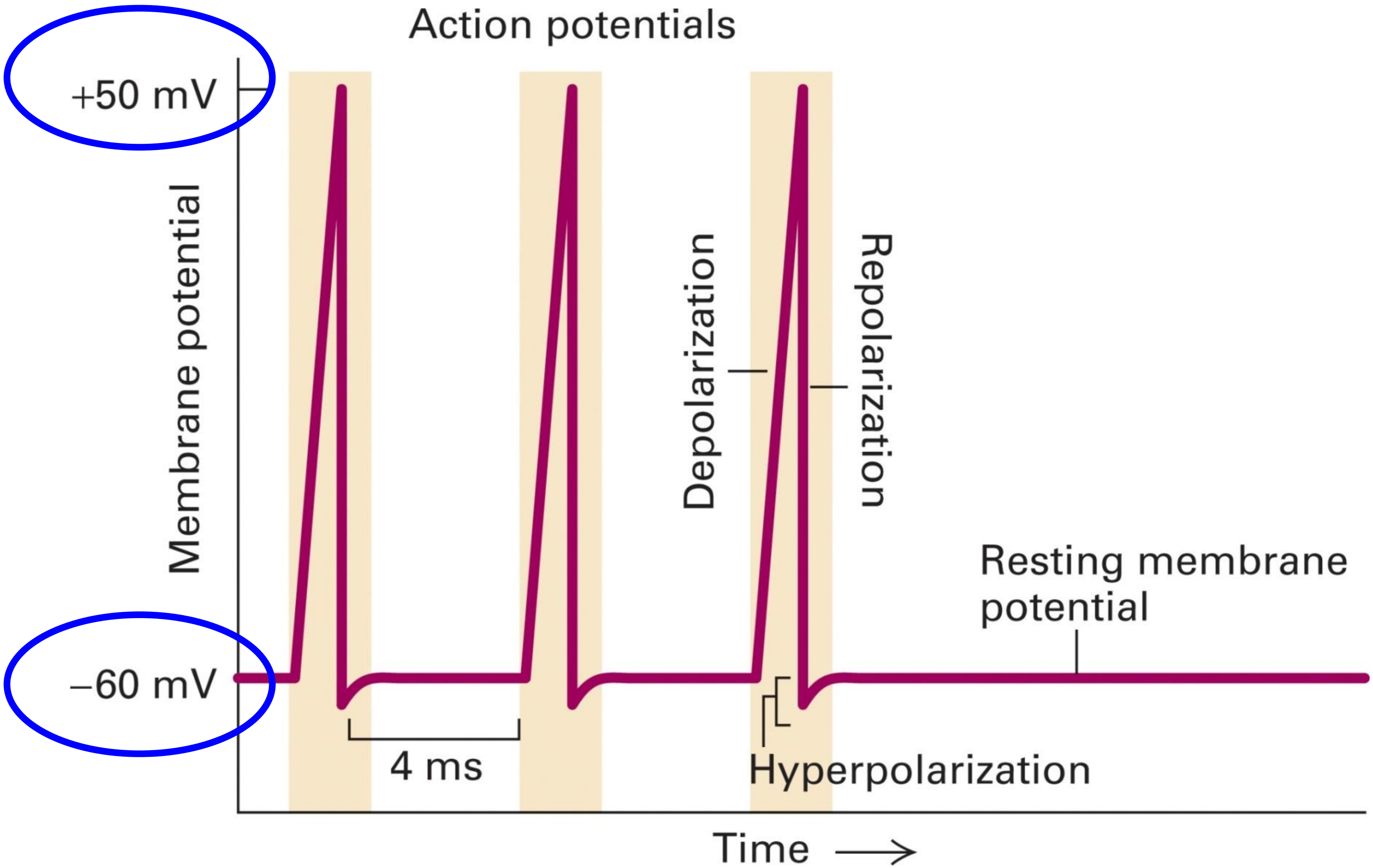
Functions of myelin sheath

- Increases the velocity of impulse conduction

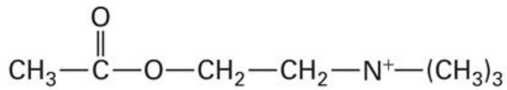


Action potential
Jumps from node
To node

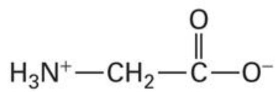
Nerve resting potential and action potential



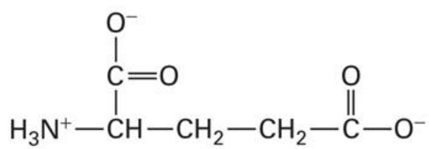
Several neurotransmitters



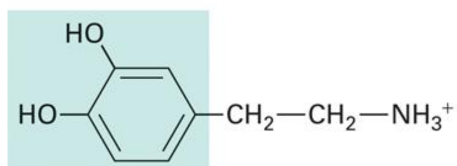
Acetylcholine



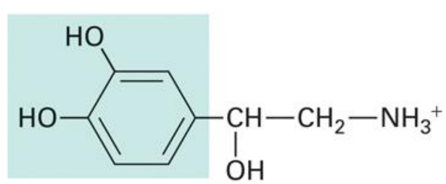
Glycine



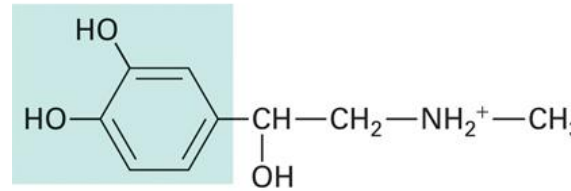
Glutamate



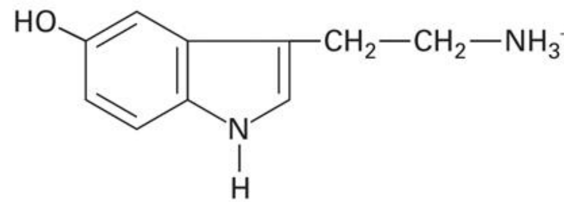
Dopamine
(derived from tyrosine)



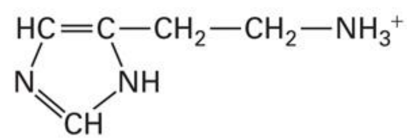
Norepinephrine
(derived from tyrosine)



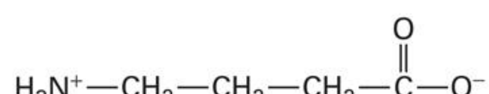
Epinephrine
(derived from tyrosine)



Serotonin, or **5-hydroxytryptamine**
(derived from tryptophan)

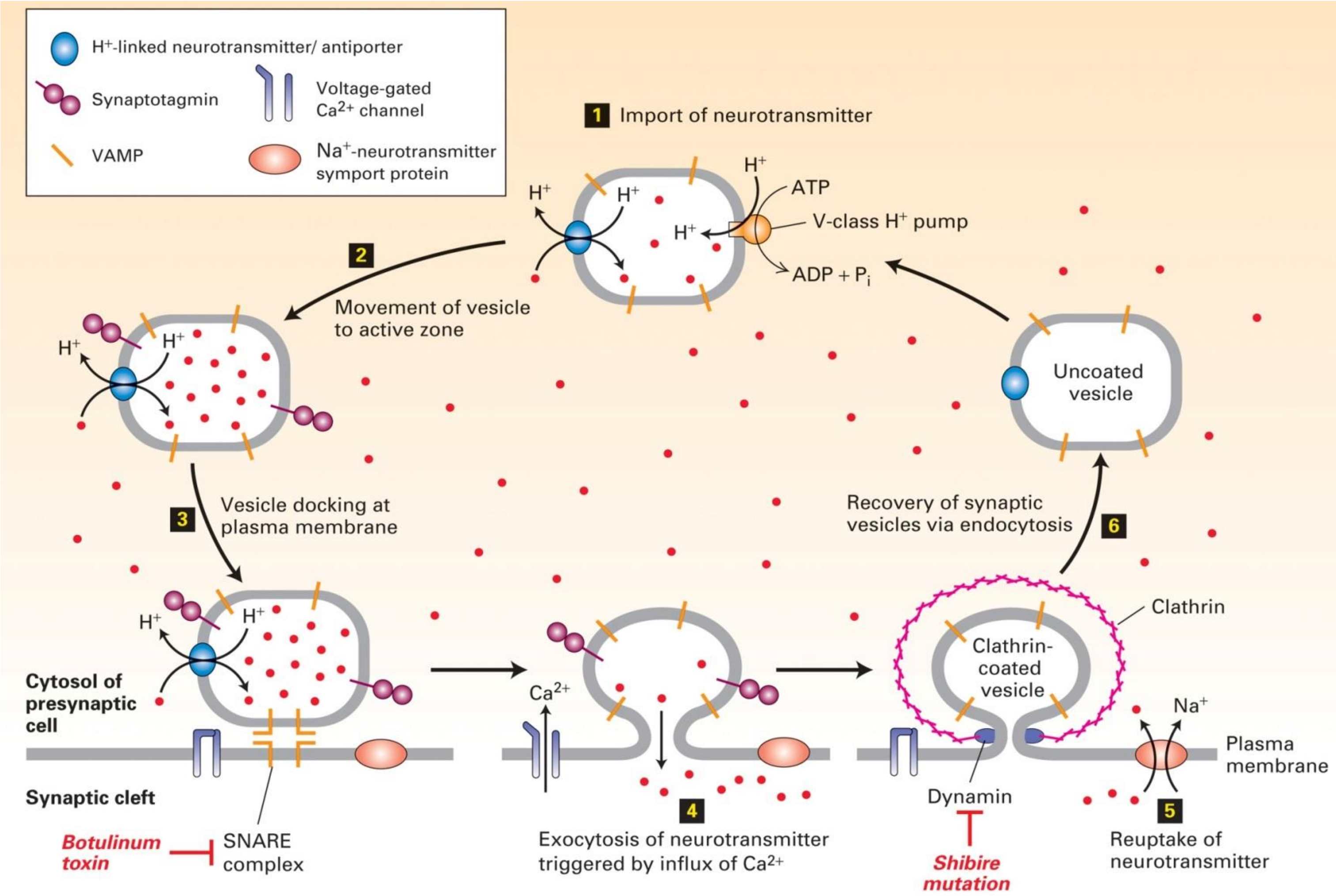


Histamine
(derived from histidine)

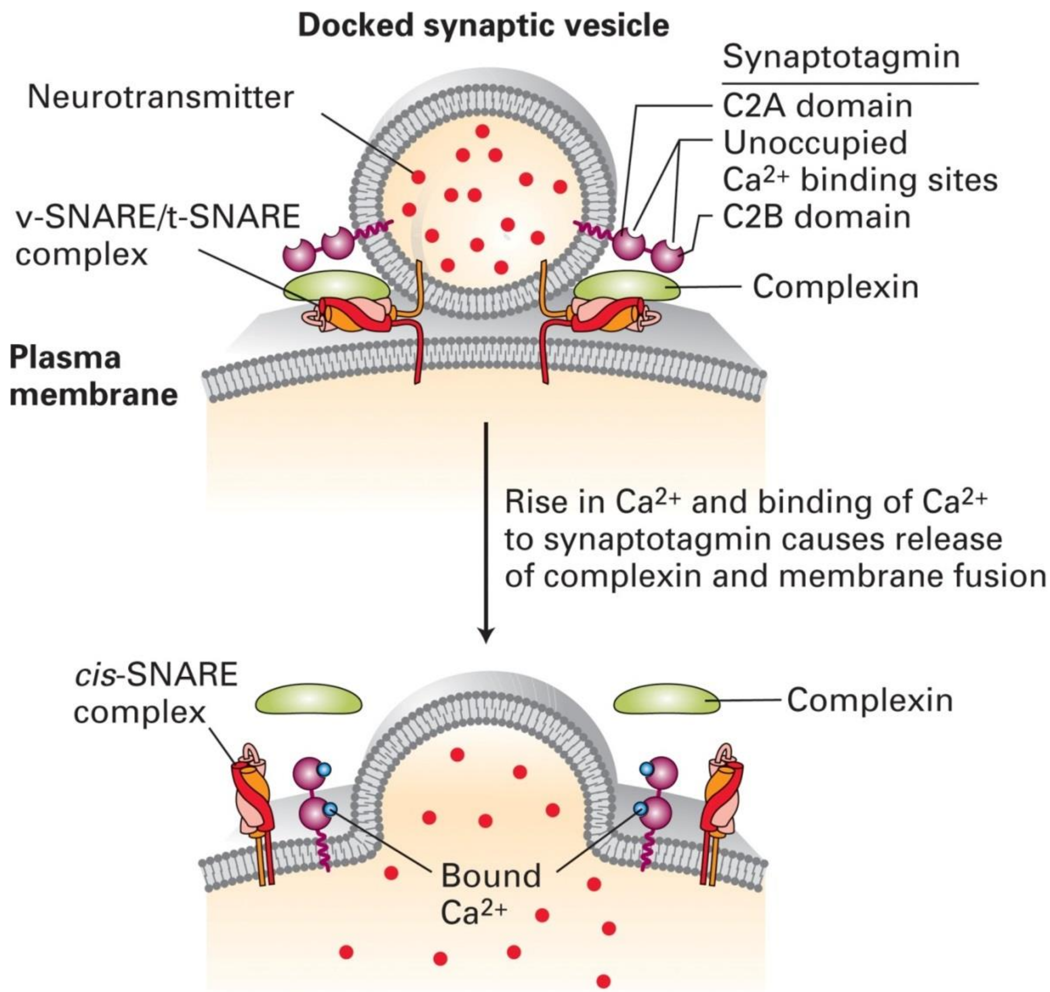


γ-**Aminobutyric acid**, or **GABA**
(derived from glutamate)

The cycling of neurotransmitters and of synaptic vesicles in axon termini



Fusion of synaptic vesicles with the plasma membrane



- Signaling at synapses is terminated by degradation or reuptake of neurotransmitters