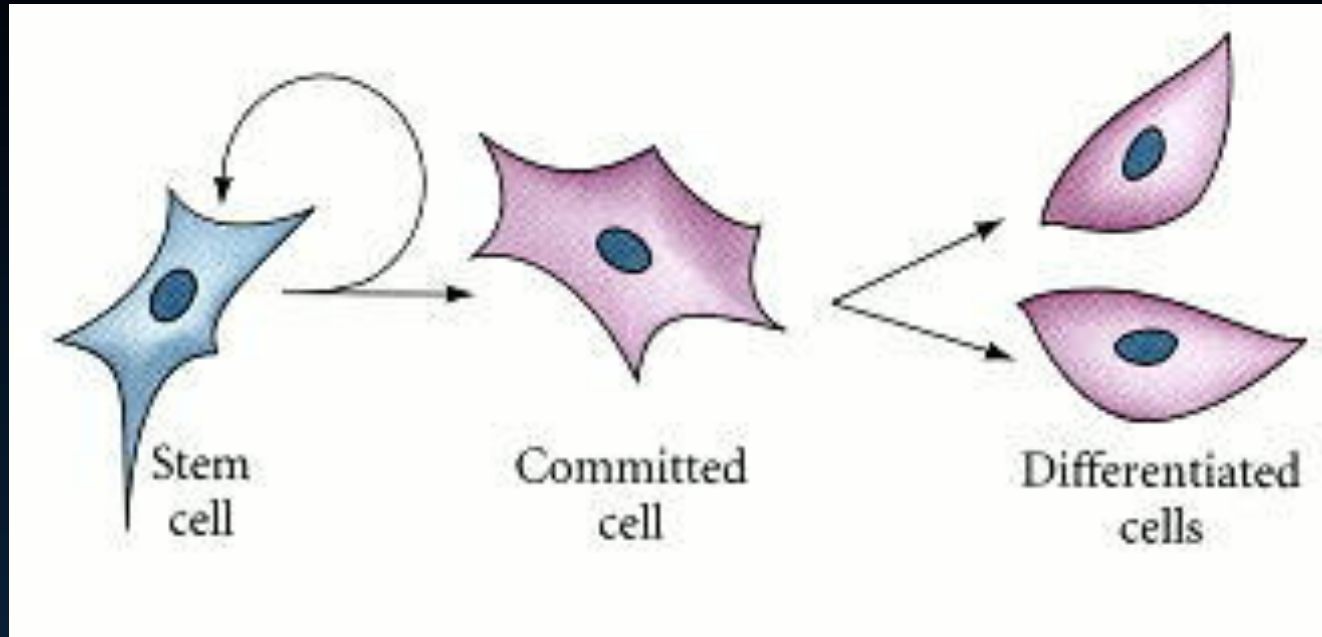


A **stem cell** is a cell that is capable of extensive proliferation, creating more stem cells (*self-renewal*) as well as more differentiated cellular progeny

A stem cell divides to produce another stem cell and a committed cell.



A stem cell can also produce two stem cells or two committed cells

Each day we replace about 1,5 grams of skin cells and about 10^{11} red blood cells

Stem cells are categorized by their potential to differentiate into other types of cells. **Embryonic stem cells** are the most potent since they must become every type of cell in the body.

The full classification includes:

Totipotent - the ability to differentiate into all possible cell types. Examples are the zygote formed at egg fertilization and the first few cells that result from the division of the zygote.

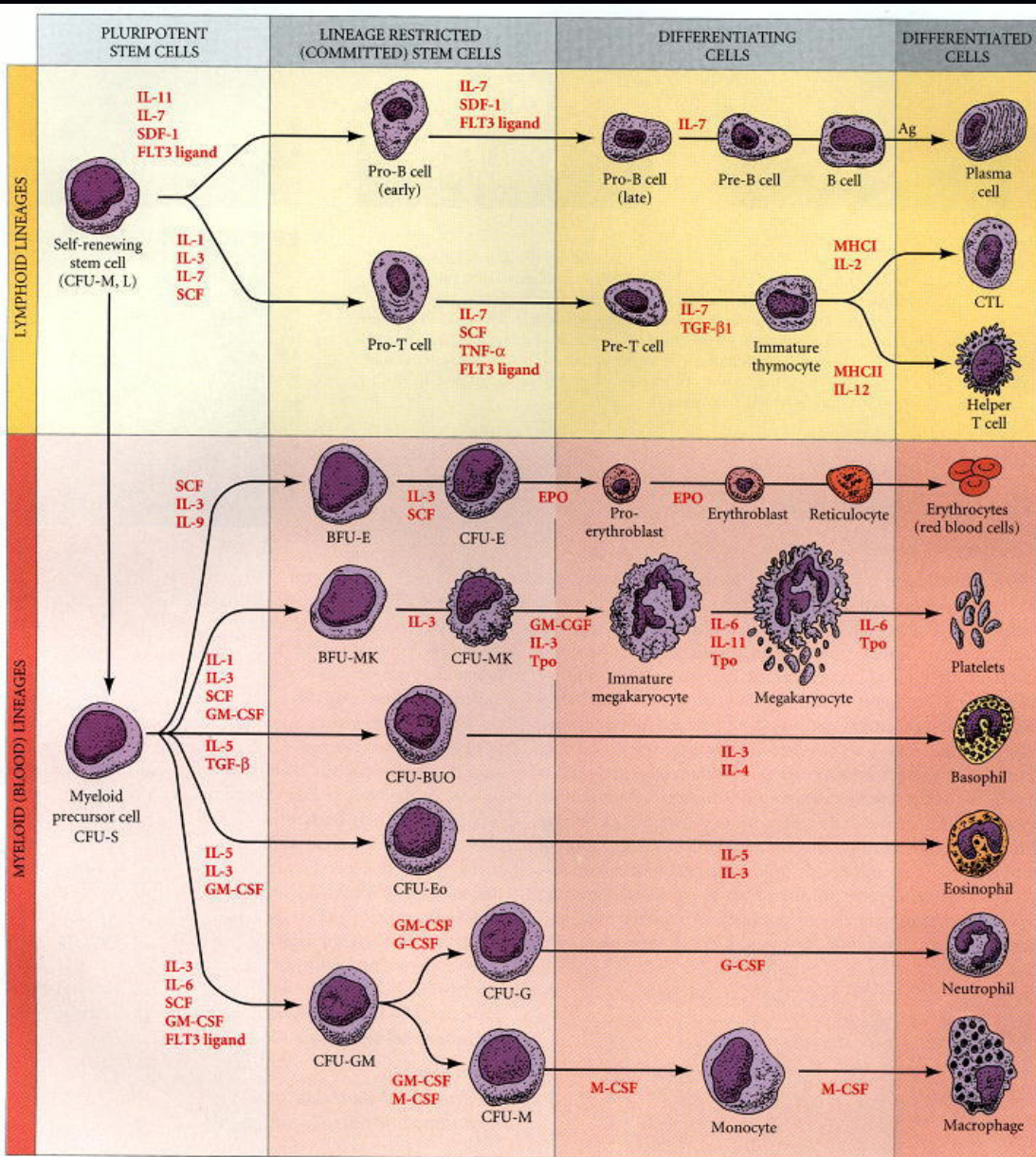
Pluripotent - the ability to differentiate into almost all cell types (except trophoblast). Examples include embryonic stem cells and cells that are derived from the mesoderm, endoderm, and ectoderm germ layers that are formed in the beginning stages of embryonic stem cell differentiation.

Multipotent - the ability to differentiate into a closely related family of cells. Examples include hematopoietic (adult) stem cells that can become red and white blood cells or platelets.

[Oligopotent - the ability to differentiate into a few cells. Examples include (adult) lymphoid or myeloid stem cells.]

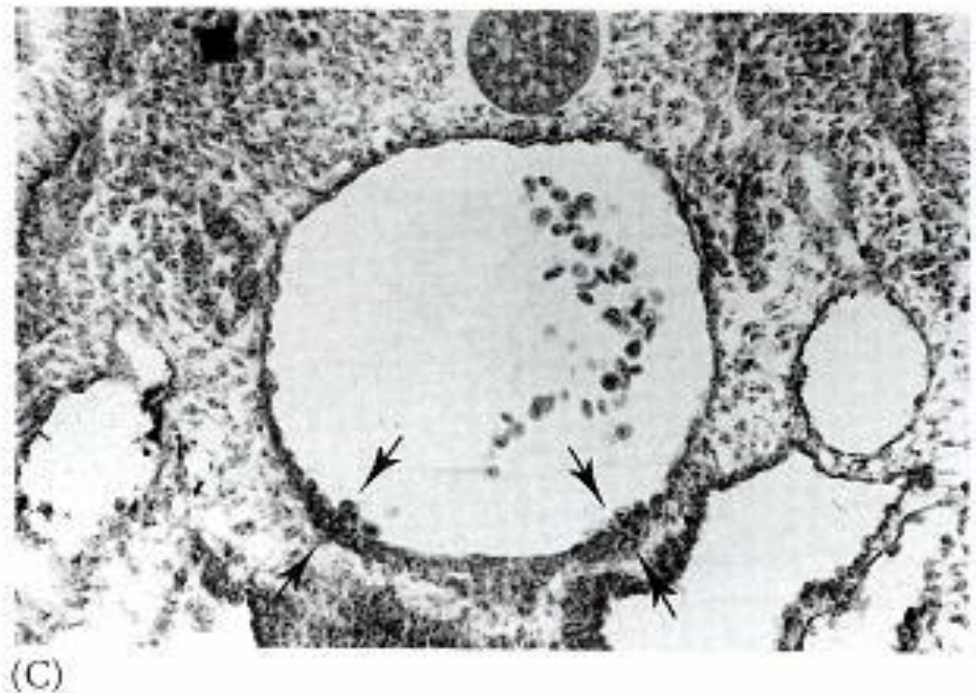
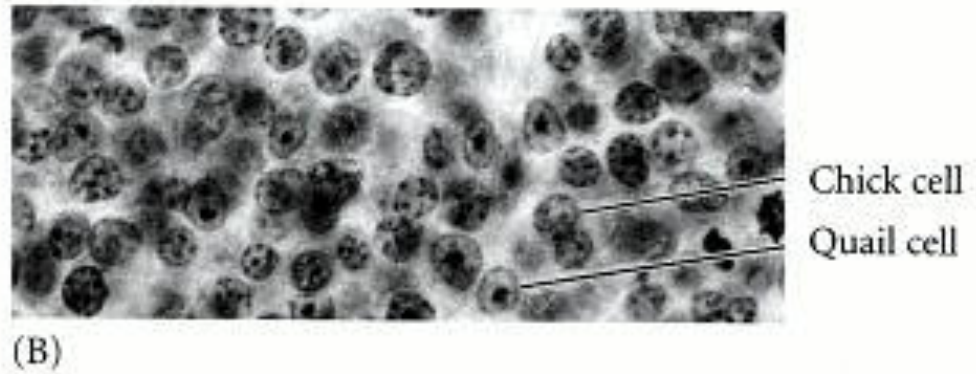
Unipotent - the ability to only produce cells of their own type, but have the property of self-renewal required to be labeled a stem cell. Examples include (adult) neuronal stem cells.

A model for the origin of mammalian blood and lymphoid cells

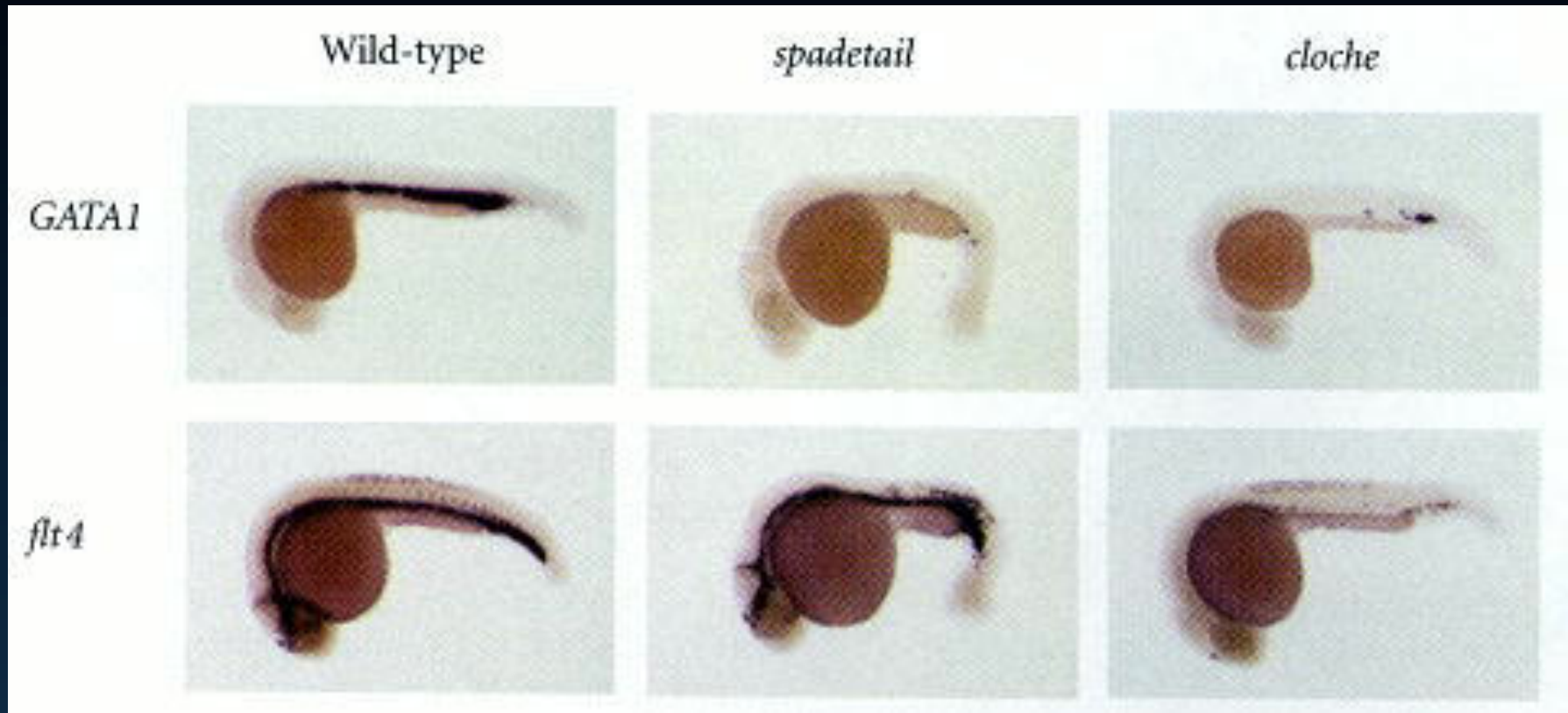


Isolated blood-forming colonies

Blood cell mapping using chick-quail chimeras



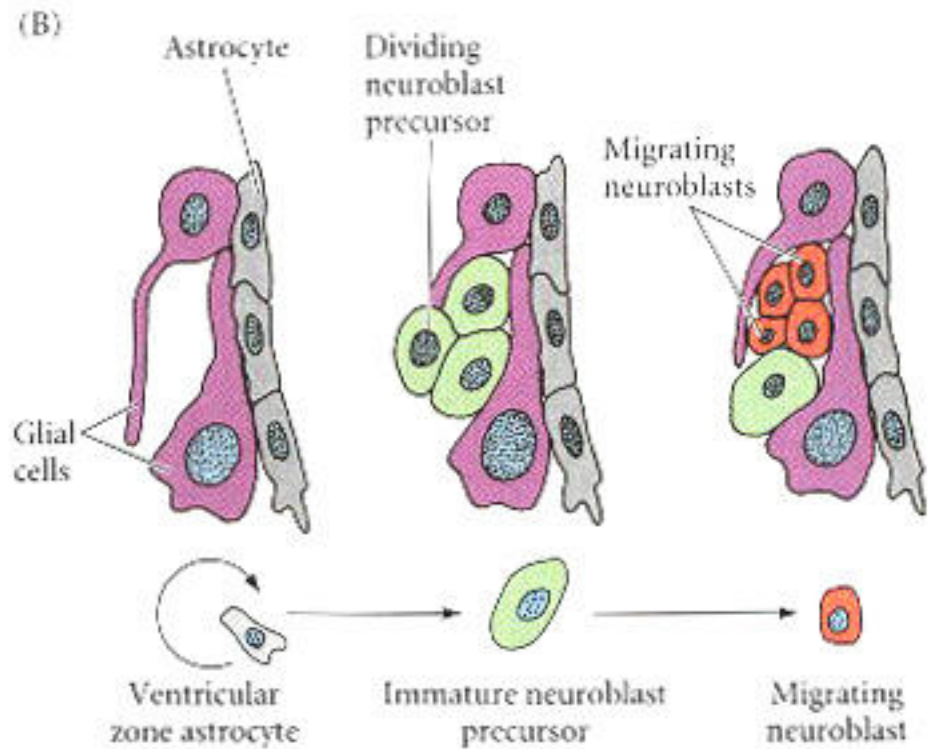
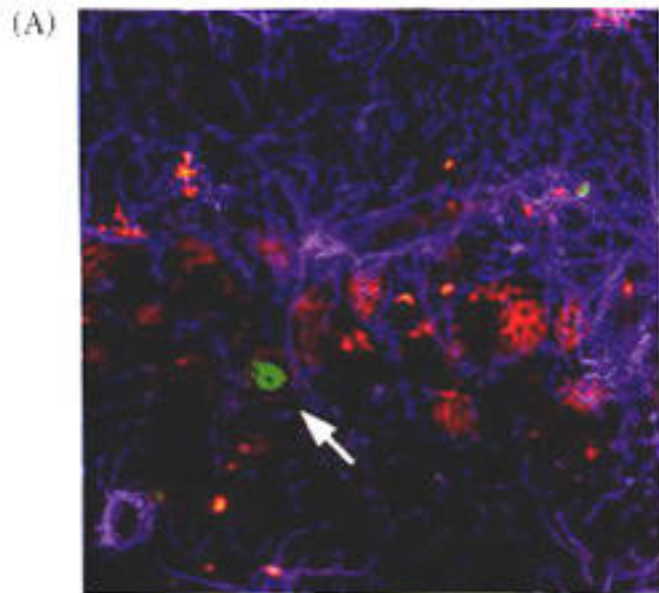
Expression of the *flt4* and *GATA1* genes (dark areas) in wild-type and mutant zebrafish embryos

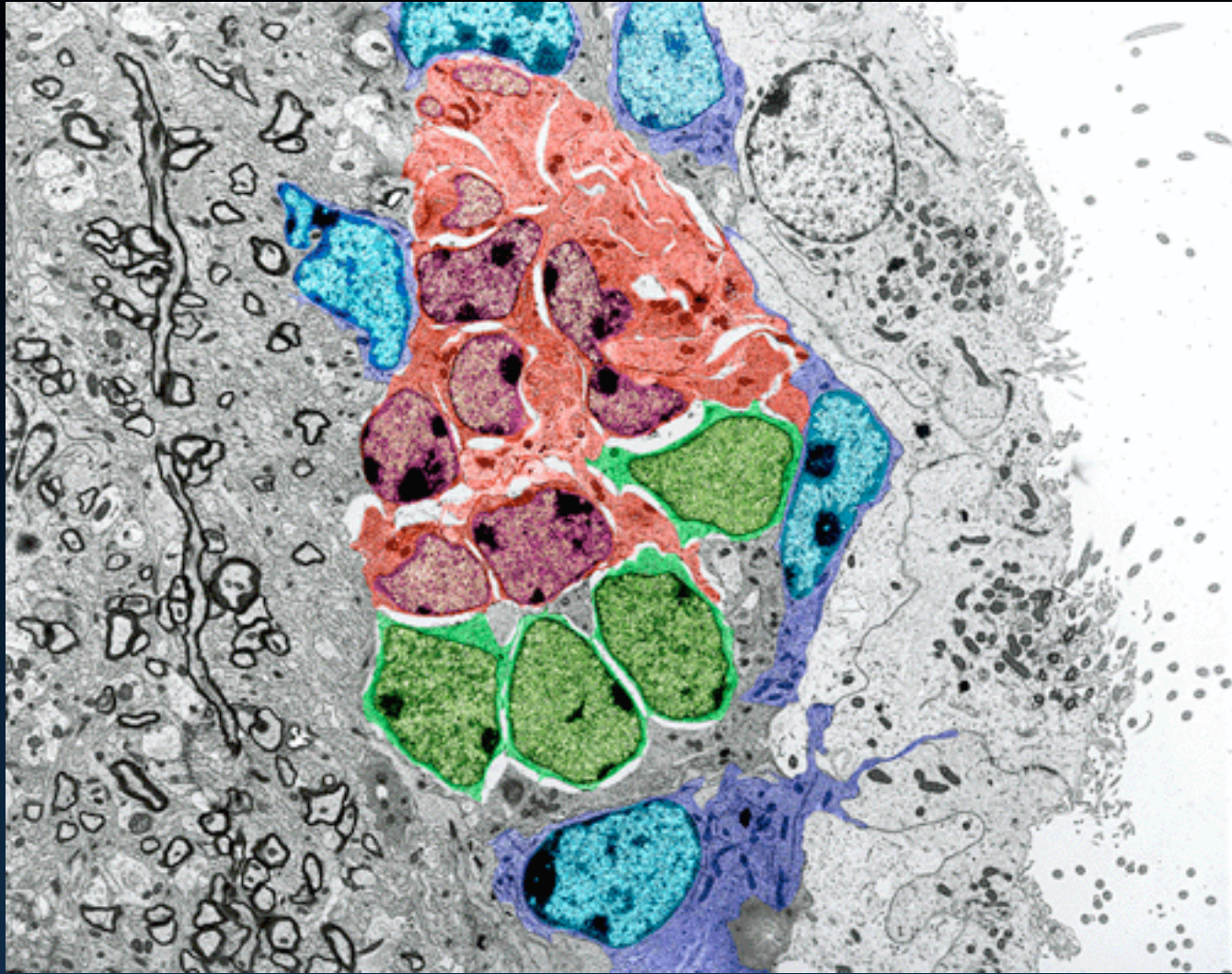


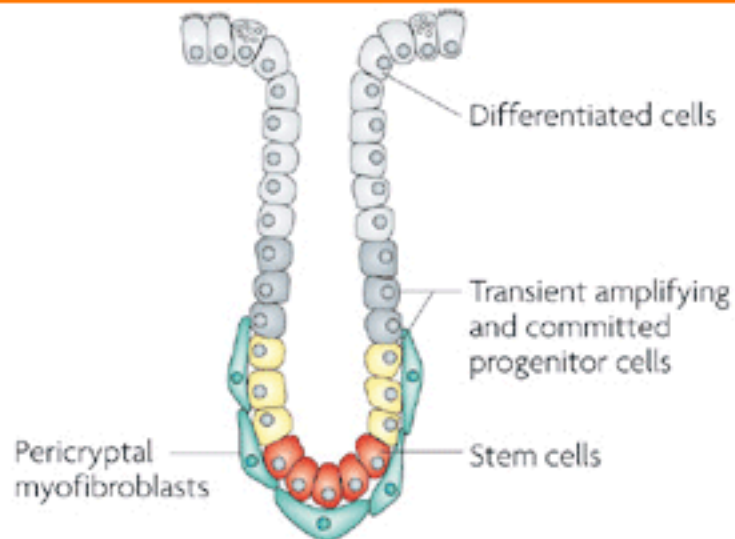
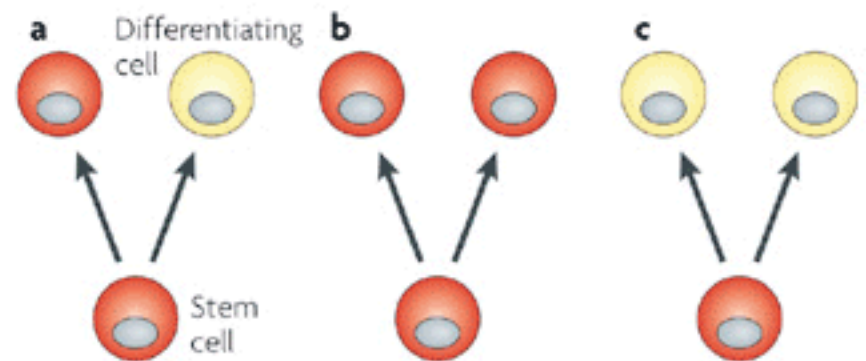
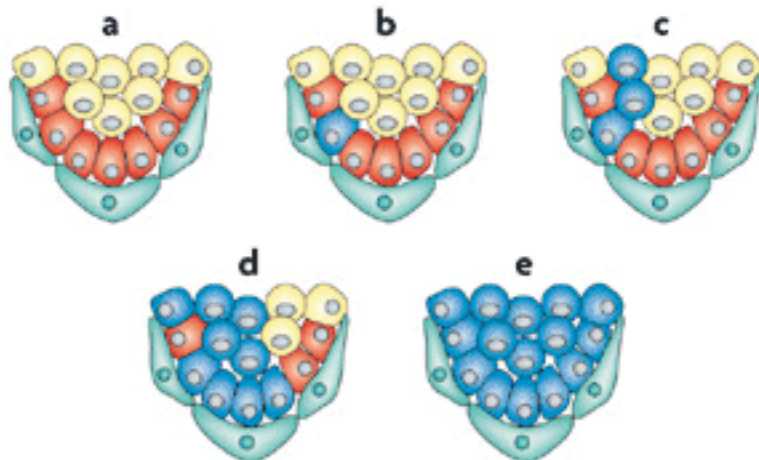
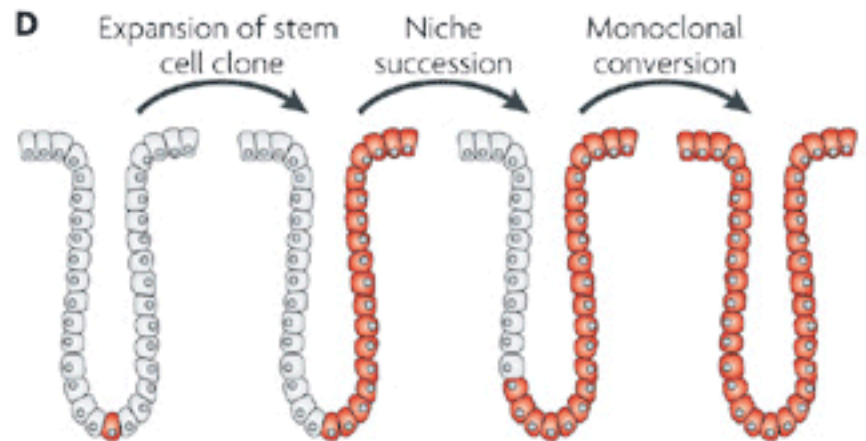
STEM CELL NICHE: the microenvironment in which stem cells are found, which interacts with stem cells to regulate stem cell fate.

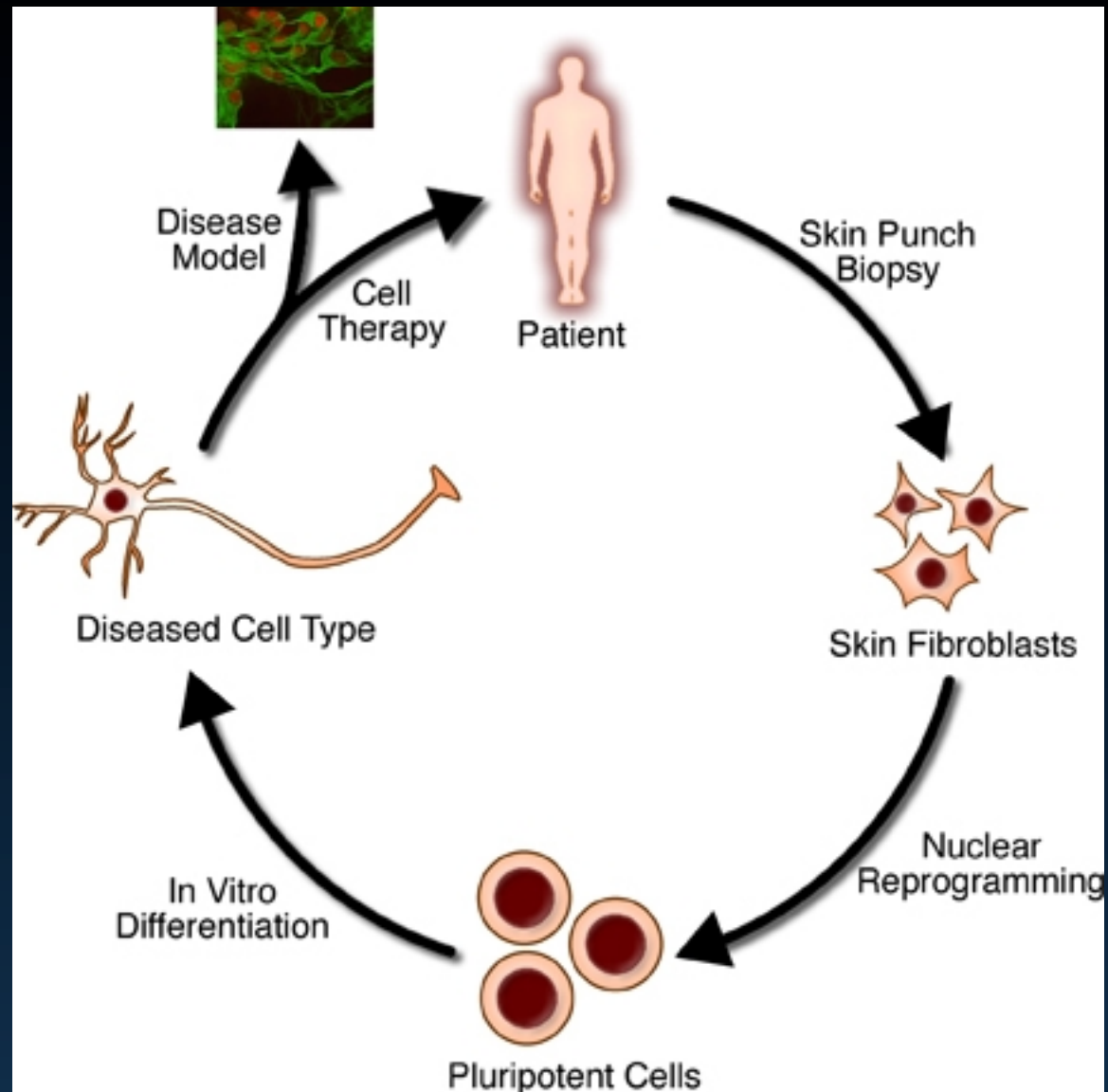
The word 'niche' can be in reference to the in vivo or in vitro stem cell microenvironment. During embryonic development, various niche factors act on embryonic stem cells to alter gene expression, and induce their proliferation or differentiation for the development of the fetus. Within the human body, stem cell niches maintain adult stem cells in a quiescent state, but after tissue injury, the surrounding micro-environment actively signals to stem cells to either promote self renewal or differentiation to form new tissues.

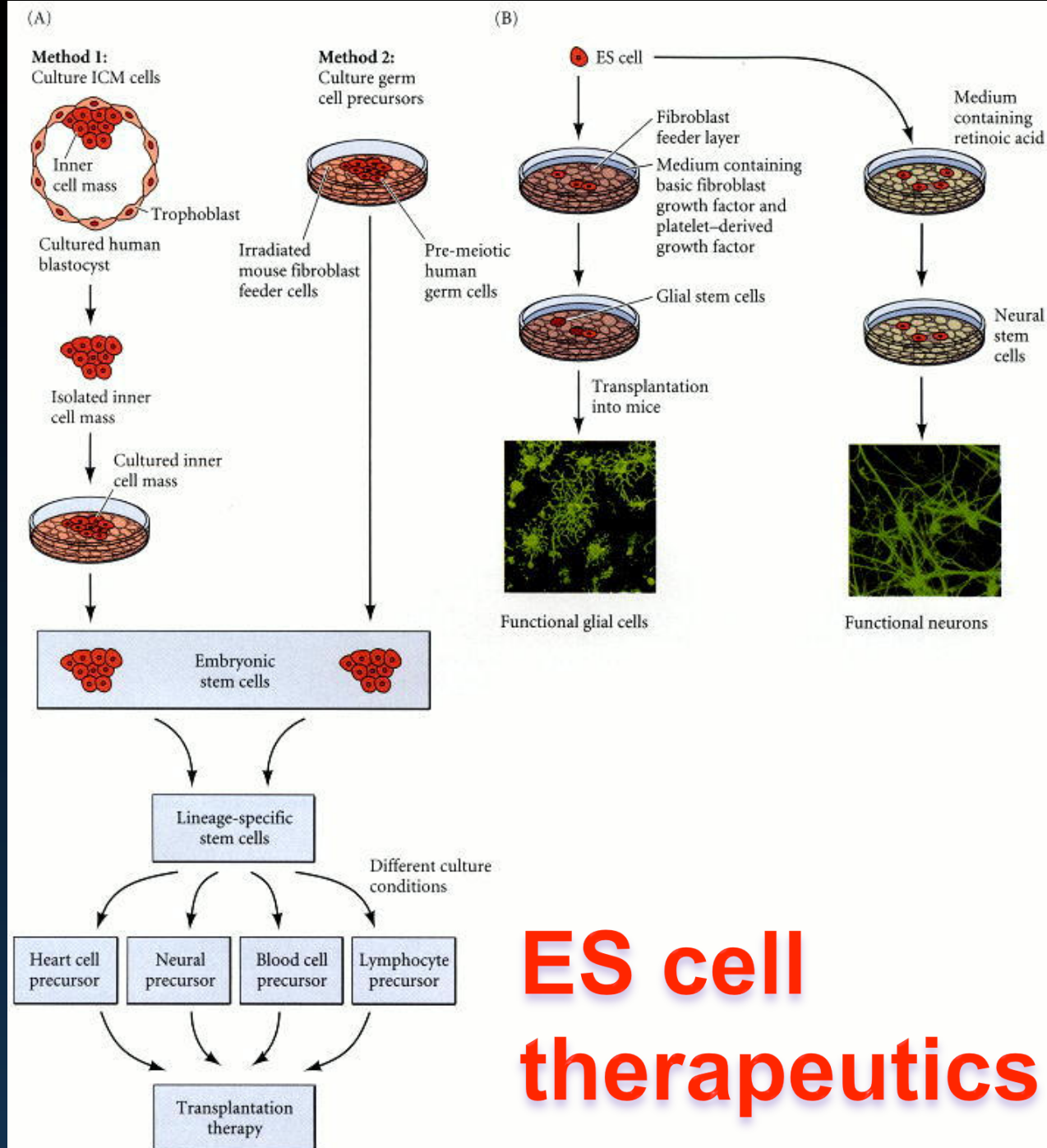
Evidence of adult neural stem cells

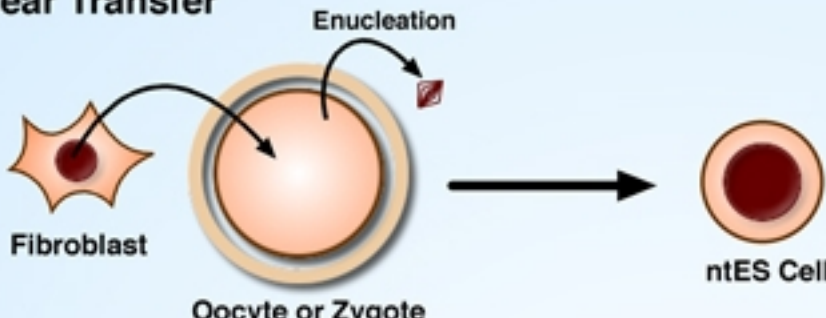
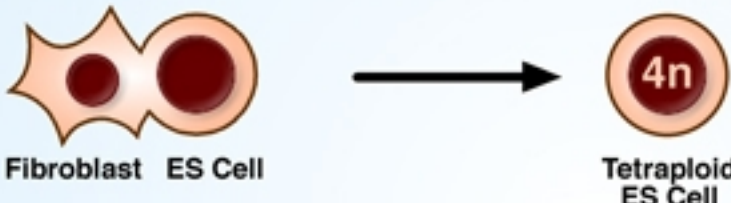
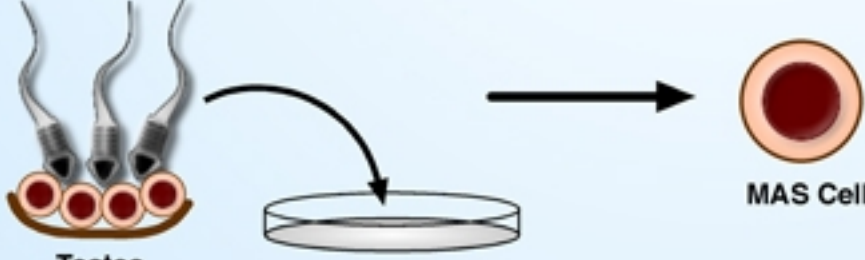


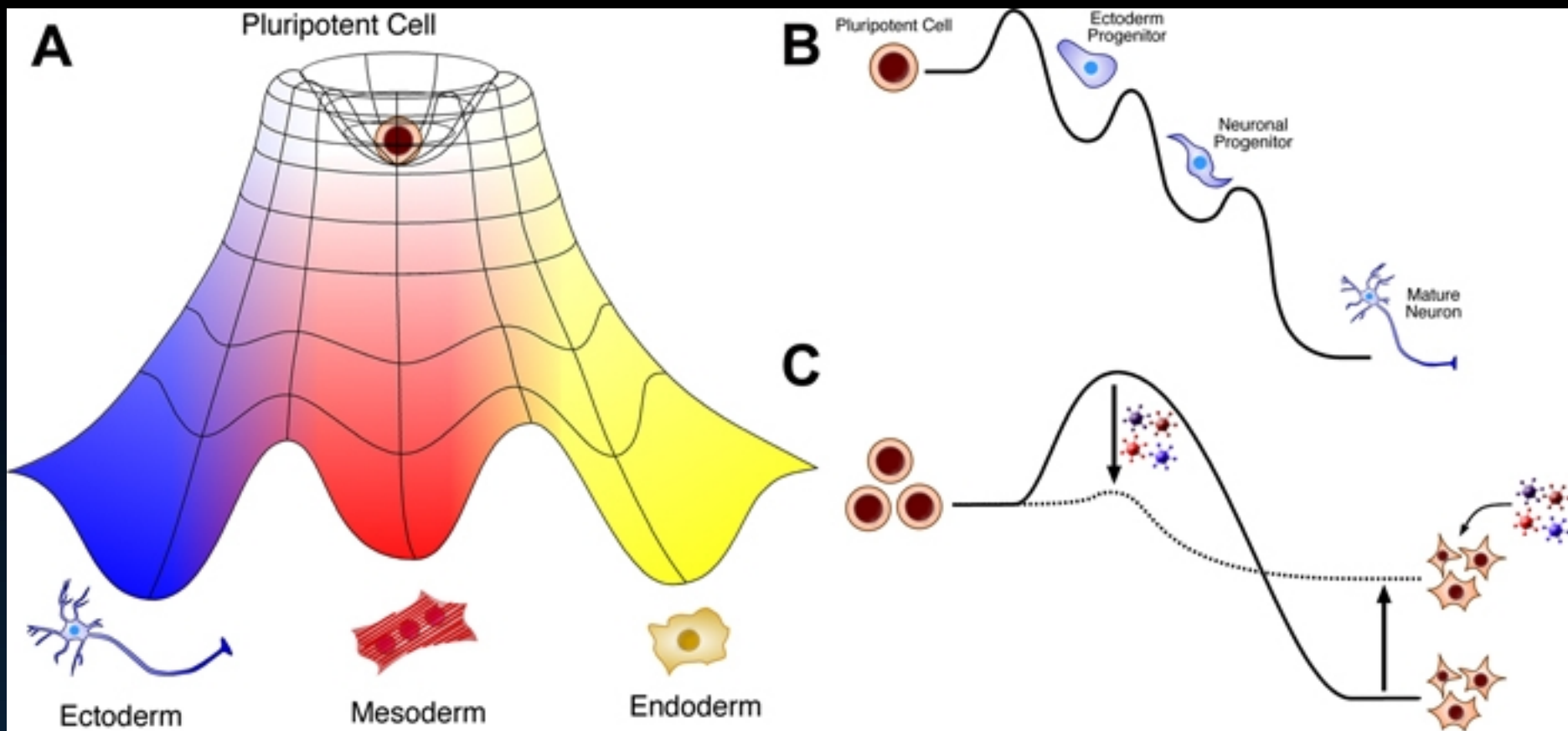


A**B****C****D**





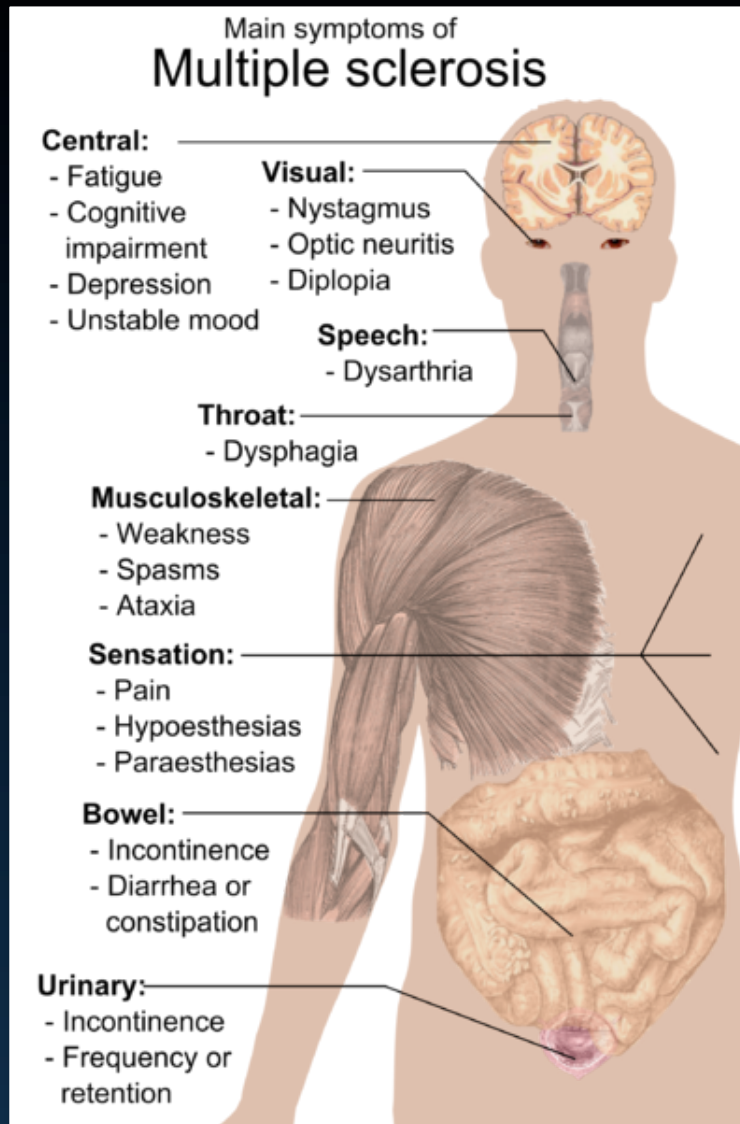
Nuclear Transfer  Fibroblast Oocyte or Zygote ntES Cell	Advantages Indistinguishable from Embryo-Derived ES Cells	Disadvantages Technically Challenging Sources for Oocytes and Zygotes
Cell Fusion  Fibroblast ES Cell Tetraploid ES Cell	Technically Straightforward	Fusion is Inefficient Reprogrammed Cells are Tetraploid
Direct Reprogramming  Fibroblast iPS Cell	Technically Straightforward Autologous to Fibroblast Donor	Uses Oncogenic Retroviruses and Transgenes
Cell Explantation  Testes MAS Cell	Technically Straightforward Fully Autologous to Donor	Limited Sources and Therapeutic Utility Carry Male Germ Cell Imprints



Klf4,
Sox2,
Oct4,
cMyc

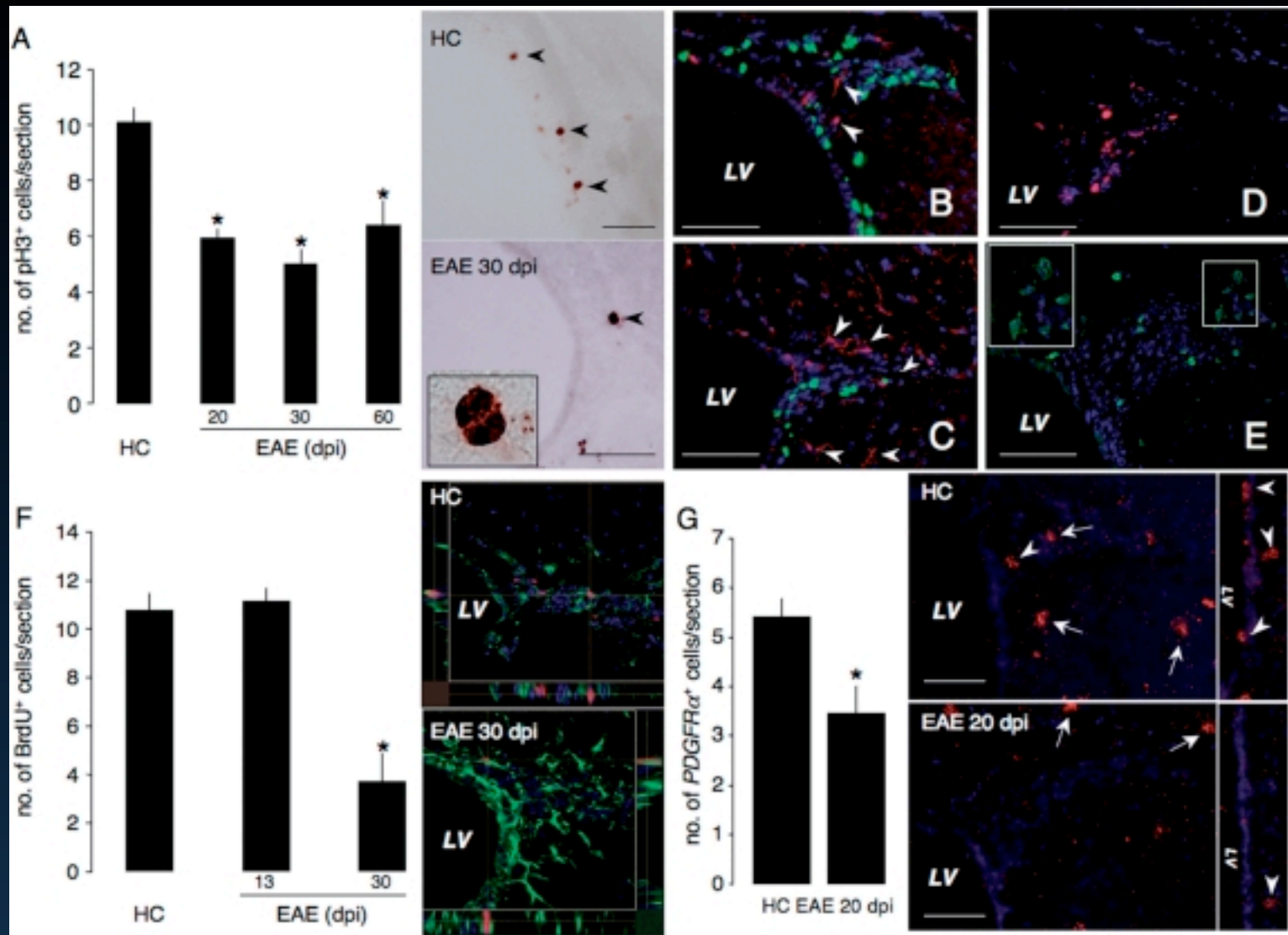
Takahashi e Yamanaka, *Cell* 126, 663-676

Problem solving 2.



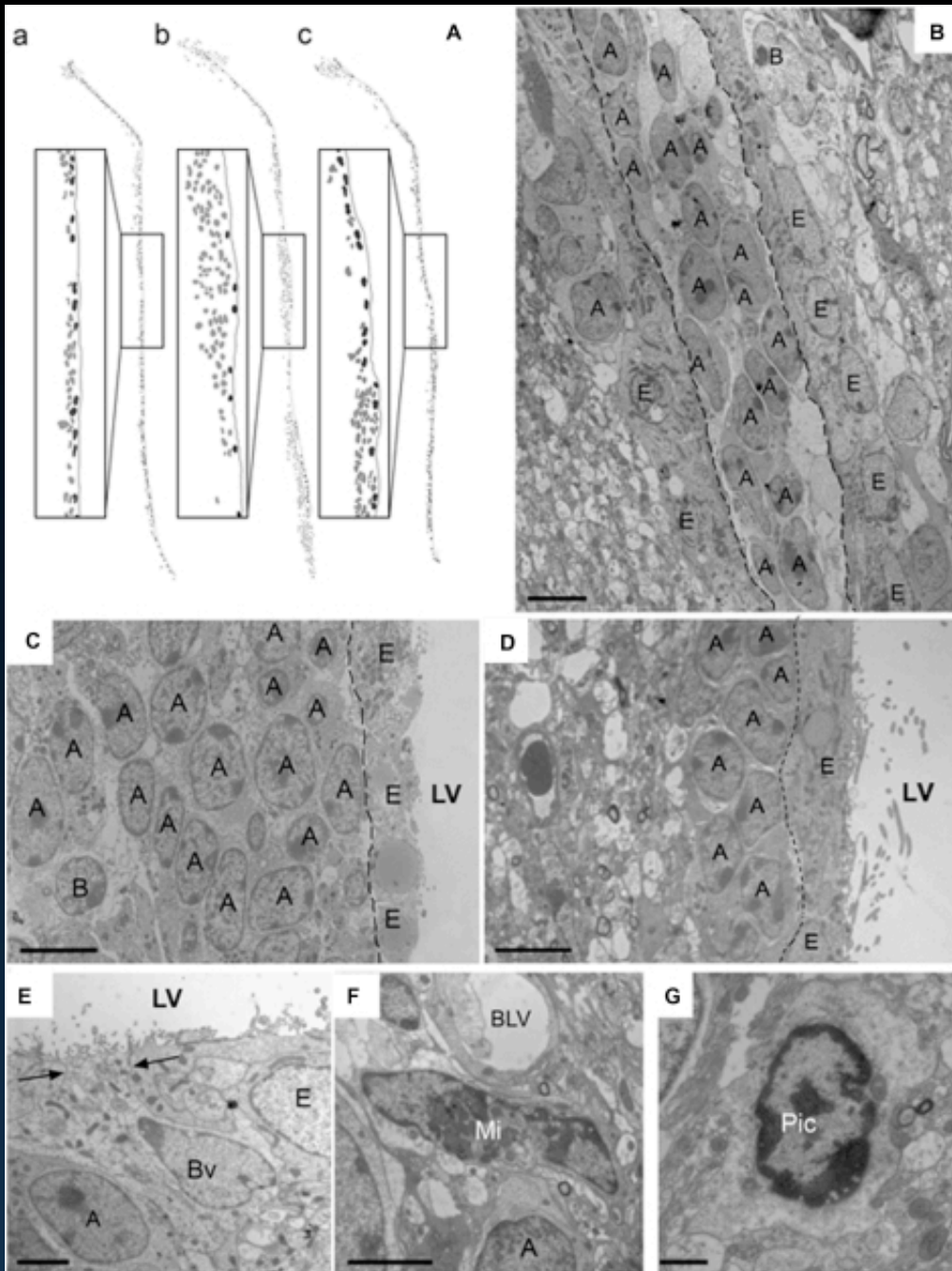
- a. In a given disease, neurons are affected
- b. The disease is not neuron-specific

Is the neuronal impairment involving degeneration or lack of adult neurogenesis?



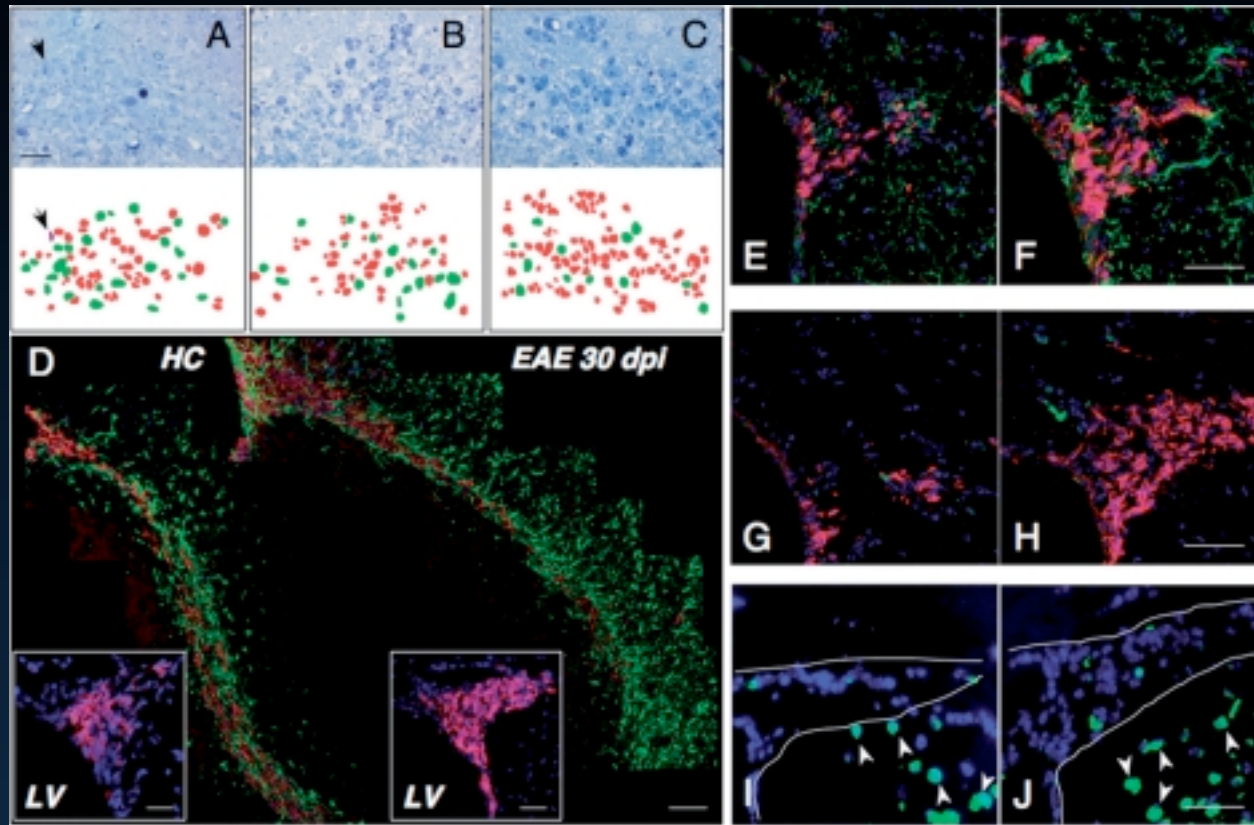
1. Proliferation check

2. Niche check



3. Migration Check

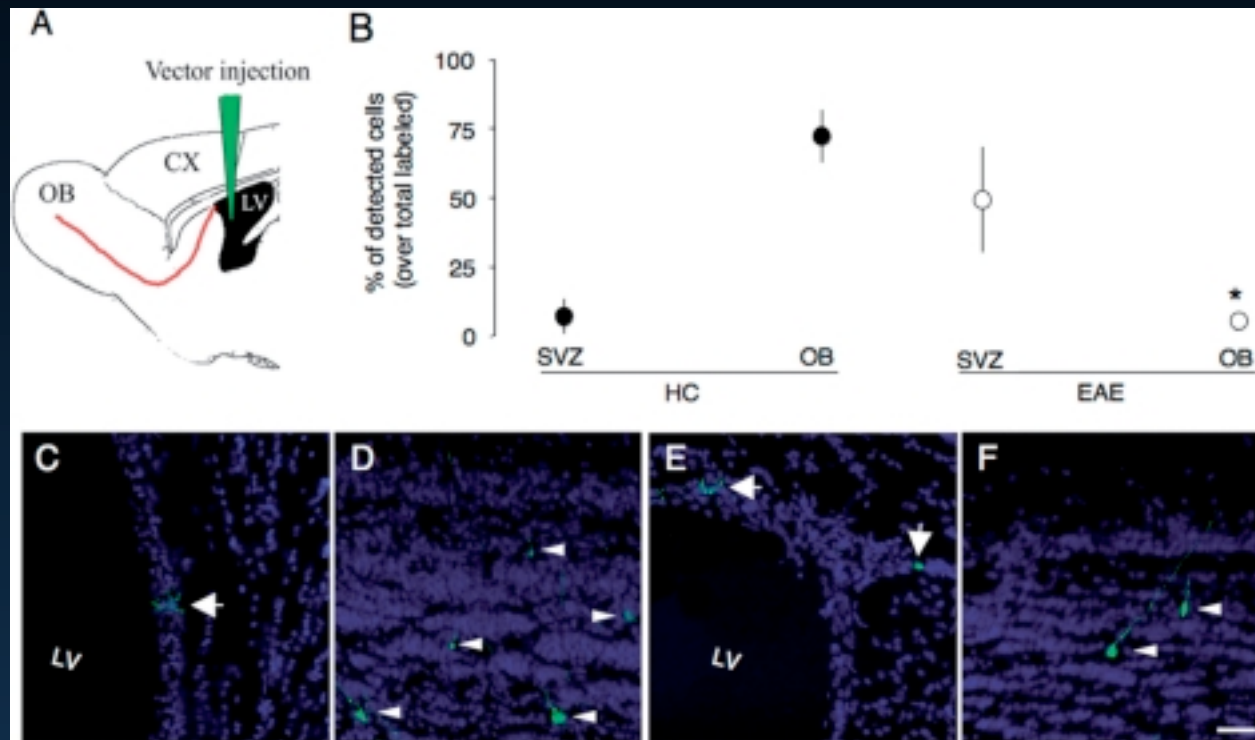
3.A Departure



PSA-NCAM: migratory cells (green)
GFAP: astrocytes (red)

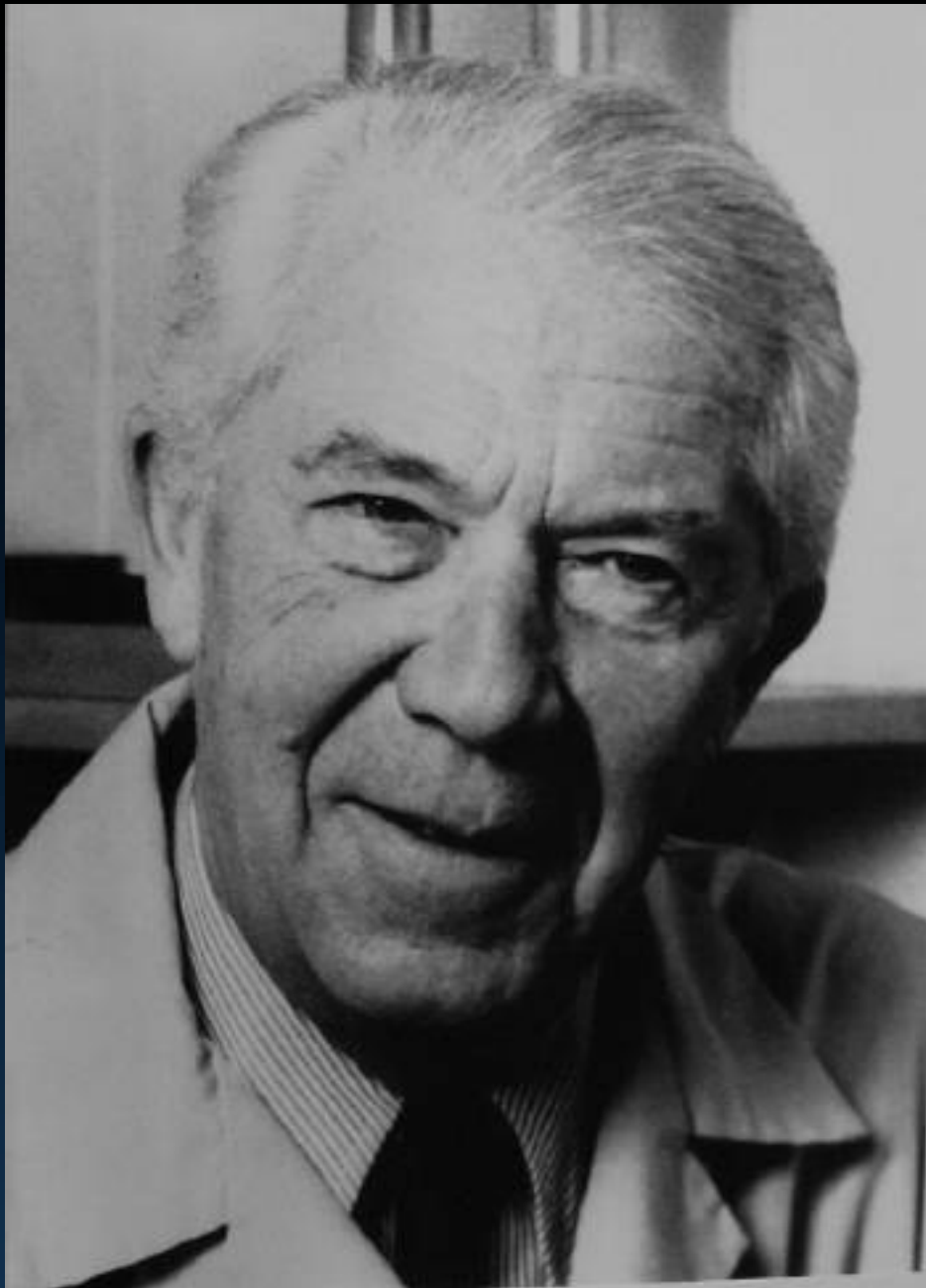
3. Migration Check

3.B Arrival



What is “Autophagy”?

Autophagy is a cellular pathway mediating degradation of bulk cytoplasm, long-lived proteins and entire organelles. In this process, double-membraned vesicles, termed autophagosomes, wrap around portions of cytosolic content and transport them to the lysosome for their degradation.





Roles of autophagy in disease

Myopathies

Pro: Autophagy prevents aggregate-prone protein accumulation that leads to physiological dysfunction.

Con: Autophagy may contribute to muscle wasting and defective autophagosome clearance may interfere with cellular function.

Ageing

Pro: Autophagy removes damaged organelles and can limit production of reactive oxygen species.

Liver disease

Pro: Autophagy can alleviate endoplasmic reticulum stress by degrading portions of the organelle containing misfolded proteins.

Con: Excessive autophagy may cause liver damage.

Neurodegeneration

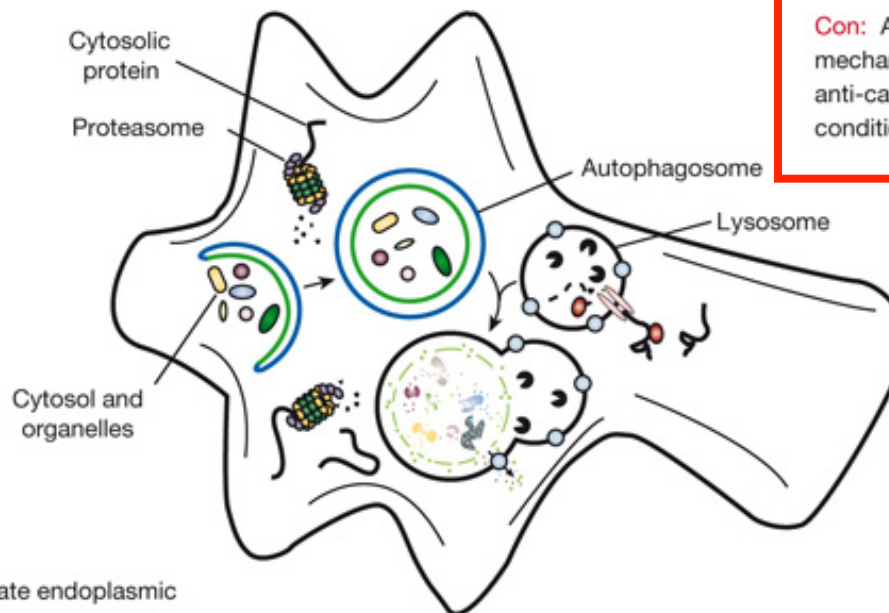
Pro: Basal autophagy is a homeostatic process that prevents intracellular proteins from accumulating to toxic levels.

Con: Inefficient lysosomal clearance results in intracellular accumulation of autophagosomes, which may process the amyloid precursor protein into toxic forms.

Cancer

Pro: Autophagy acts in tumour suppression by removing damaged organelles and possibly growth factors, and reduces chromosome instability.

Con: Autophagy acts as a cytoprotective mechanism that helps cancer cells resist anti-cancer treatments and survive in conditions of low nutrient supply.



Infection and immunity

Pro: Intracellular bacteria, viruses and protozoans are removed from host removed from host cells by autophagy, and antigens are processed for MHC class II presentation. Autophagy may prevent auto-immune and inflammatory diseases.

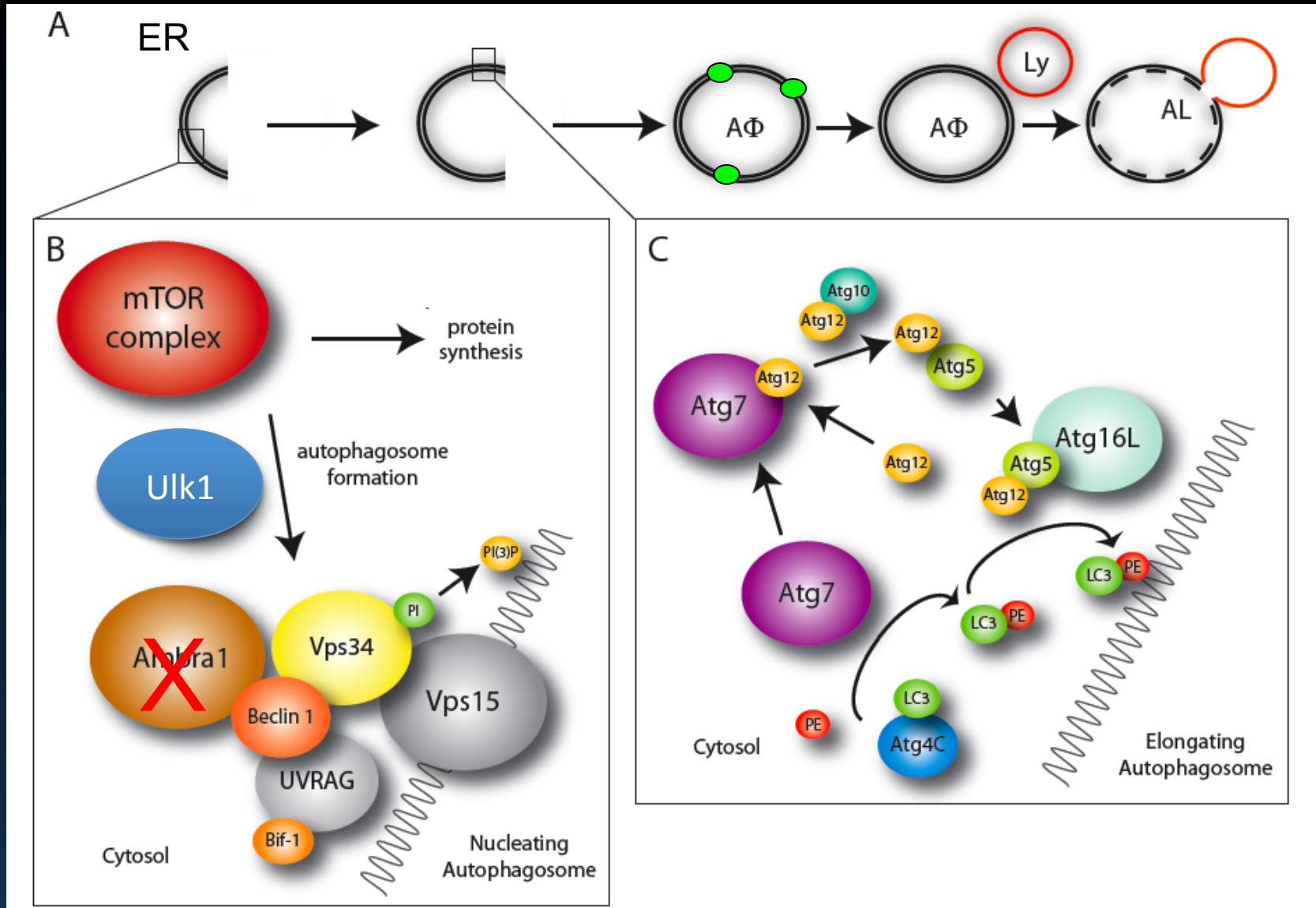
Con: Some microbes have evolved to subvert autophagy to establish a replicative niche.

Heart disease

Pro: Autophagy may be protective during ischaemia and pressure overload.

Con: Autophagy is harmful during reperfusion.

The process of autophagosome formation



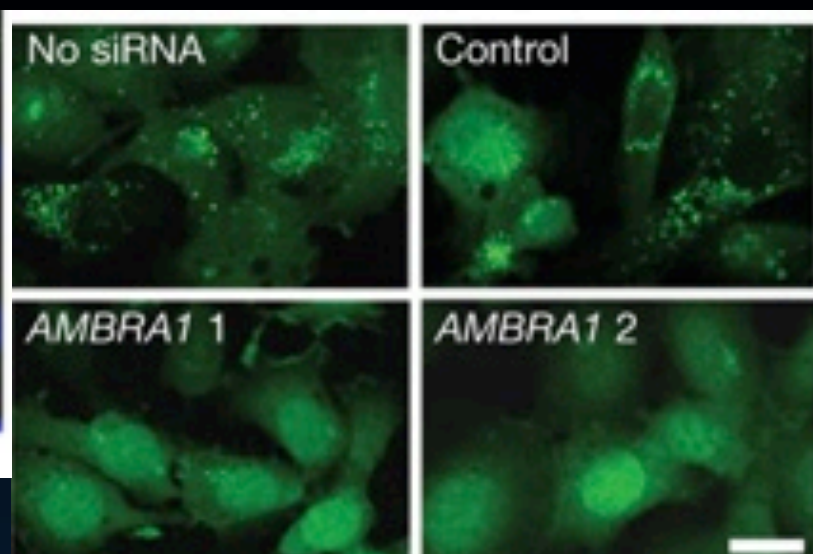
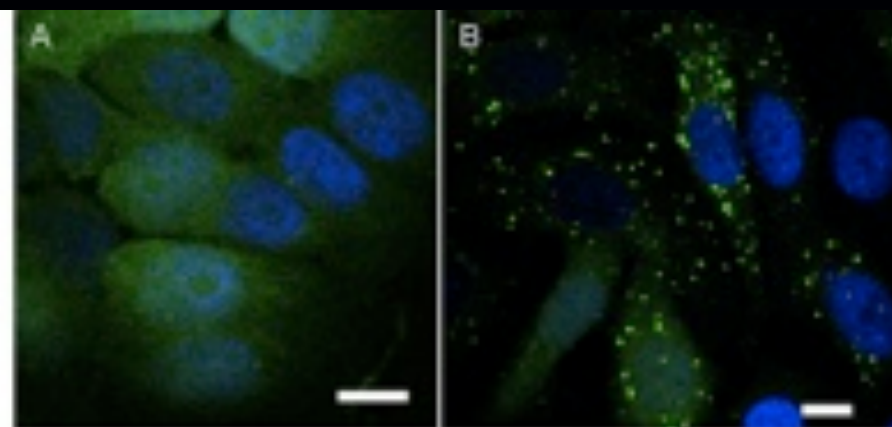


Figure 2
F. Cecconi, TOP

