

Differenziamento Cellulare

Concetti di staminalità, impegno (determinazione) e differenziamento cellulare

Basi molecolari, biochimiche e ultrastrutturali del differenziamento

Destino cellulare durante l'embriogenesi e nell'individuo adulto

Epigenetica e differenziamento

Regolazione della proliferazione cellulare

Apoptosi

Autofagia

Differenziamento delle cellule cutanee

Differenziamento dei linfociti

Differenziamento delle cellule muscolari

Differenziamento neuronale

Esempi di differenziamento terminale

Riprogrammazione cellulare e medicina rigenerativa

Cell type	Differentiated cell product	Specialized function of cell
Keratinocyte (epidermal cell)	Keratin	Protection against abrasion, desiccation
Erythrocyte (red blood cell)	Hemoglobin	Transport of oxygen
Lens cell	Crystallins	Transmission of light
B lymphocyte	Immunoglobulins	Antibody synthesis
T lymphocyte	Cell-surface antigens (lymphokines)	Destruction of foreign cells; regulation of immune response
Melanocyte	Melanin	Pigment production
Pancreatic islet cells	Insulin	Regulation of carbohydrate metabolism
Leydig cell (♂)	Testosterone	Male sexual characteristics
Chondrocyte (cartilage cell)	Chondroitin sulfate; type II collagen	Tendons and ligaments
Osteoblast (bone-forming cell)	Bone matrix	Skeletal support
Myocyte (muscle cell)	Muscle actin and myosin	Contraction
Hepatocyte (liver cell)	Serum albumin; numerous enzymes	Production of serum proteins and numerous enzymatic functions
Neurons	Neurotransmitters (acetylcholine epinephrine, etc.)	Transmission of electrical impulses
Tubule cell (♀) of hen oviduct	Ovalbumin	Egg white proteins for nutrition and protection of embryo
Follicle cell (♀) of insect ovary	Chorion proteins	Eggshell proteins for protection of embryo

The development of specialized cell types is called **differentiation** (Table). These overt changes in cellular biochemistry and function are preceded by a process involving the **commitment** of the cell to a certain fate. At this point, even though the cell or tissue does not appear phenotypically different from its uncommitted state, its developmental fate has become restricted. The process of commitment can be divided into two stages.

The first stage is a labile phase called **specification**. The fate of a cell or a tissue is said to be *specified* when it is capable of differentiating autonomously when placed in a neutral environment such as a petri dish or test tube. (The environment is neutral with respect to the developmental pathway.) At this stage, the commitment is still capable of being reversed.

The second stage of commitment is **determination**. A cell or tissue is said to be *determined* when it is capable of differentiating autonomously even when placed into another region of the embryo. If it is able to differentiate according to its original fate even under these circumstances, it is assumed that the commitment is irreversible.

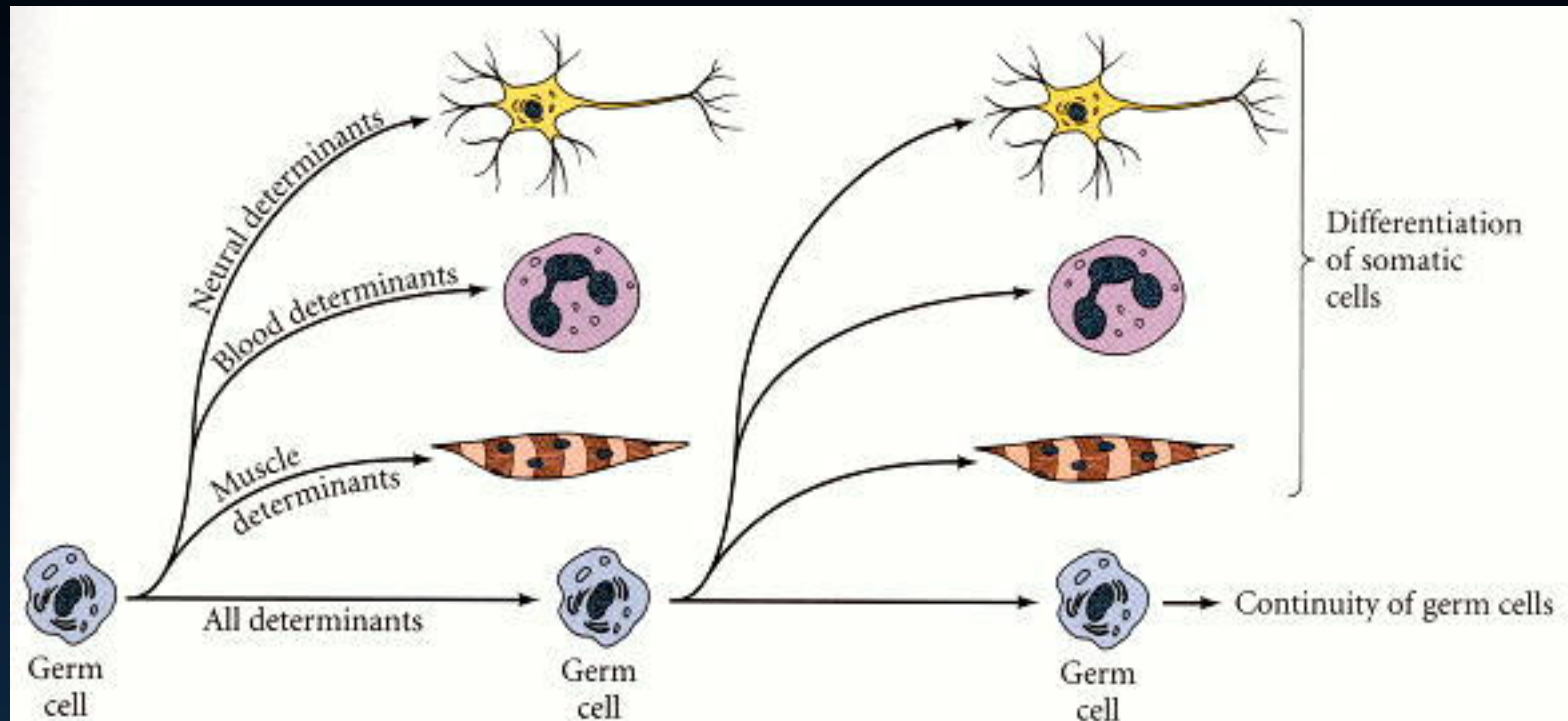
The defect experiment, wherein one destroys a portion of the embryo and then observes the development of the impaired embryo.

The isolation experiment, wherein one removes a portion of the embryo and then observes the development of the partial embryo and the isolated part.

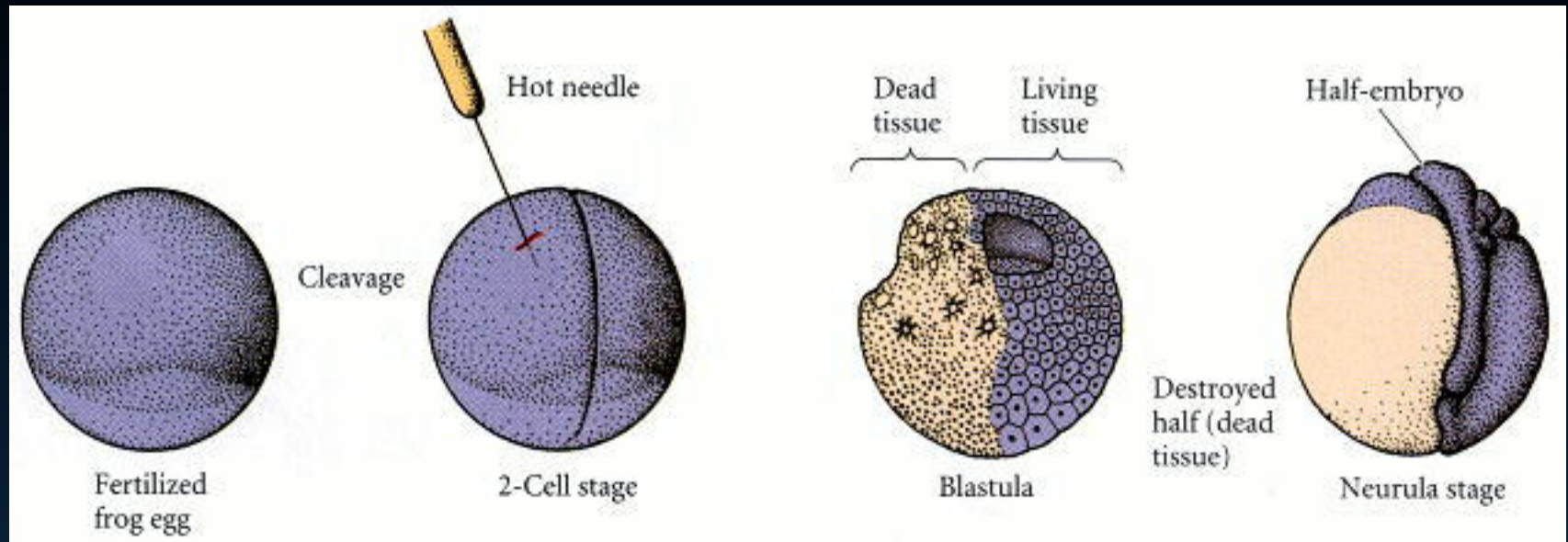
The recombination experiment, wherein one observes the development of the embryo after replacing an original part with a part from a different region of the embryo.

The transplantation experiment, wherein one portion of the embryo is replaced by a portion from a different embryo. This fourth technique was used by some of the same scientists when they first constructed fate maps of early embryos (see Mangold and Spemann).

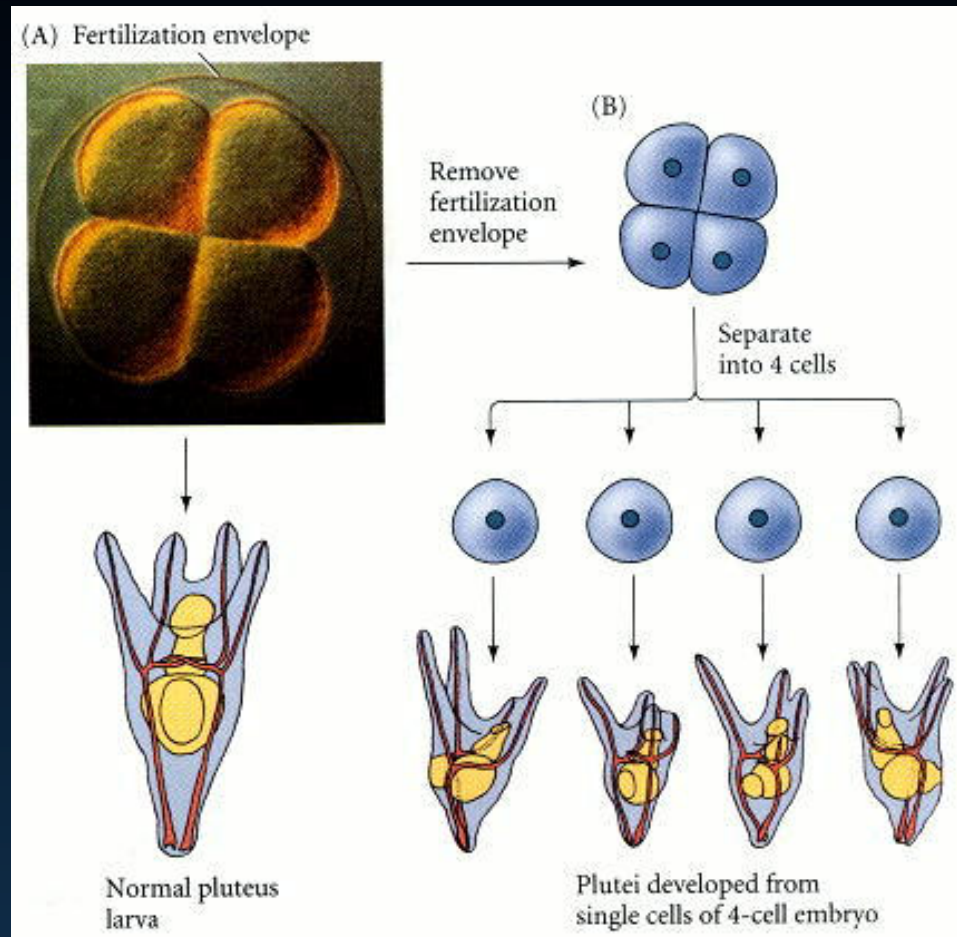
Weismann's theory of inheritance (1883)



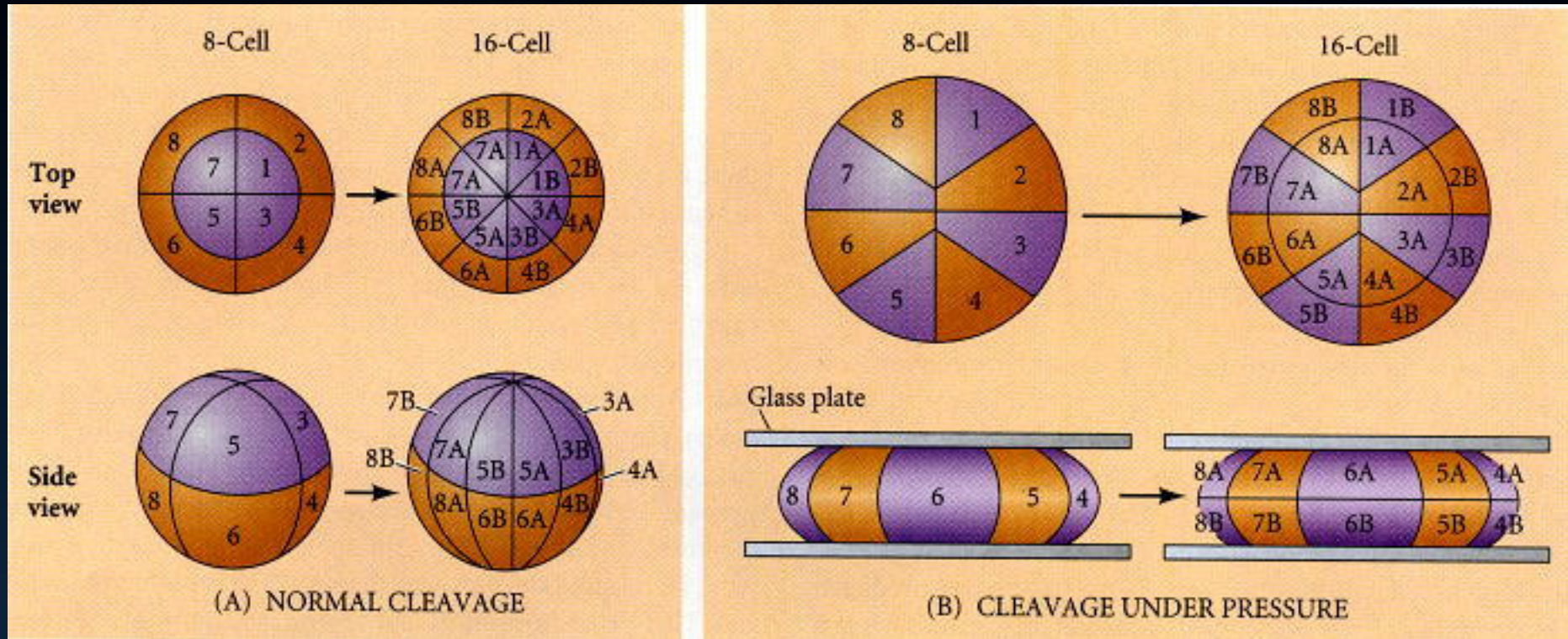
1. Defect experiment (Roux, 1888)



2. Isolation experiment (Driesch, 1892)



3. Recombination experiment (Driesch, 1893)

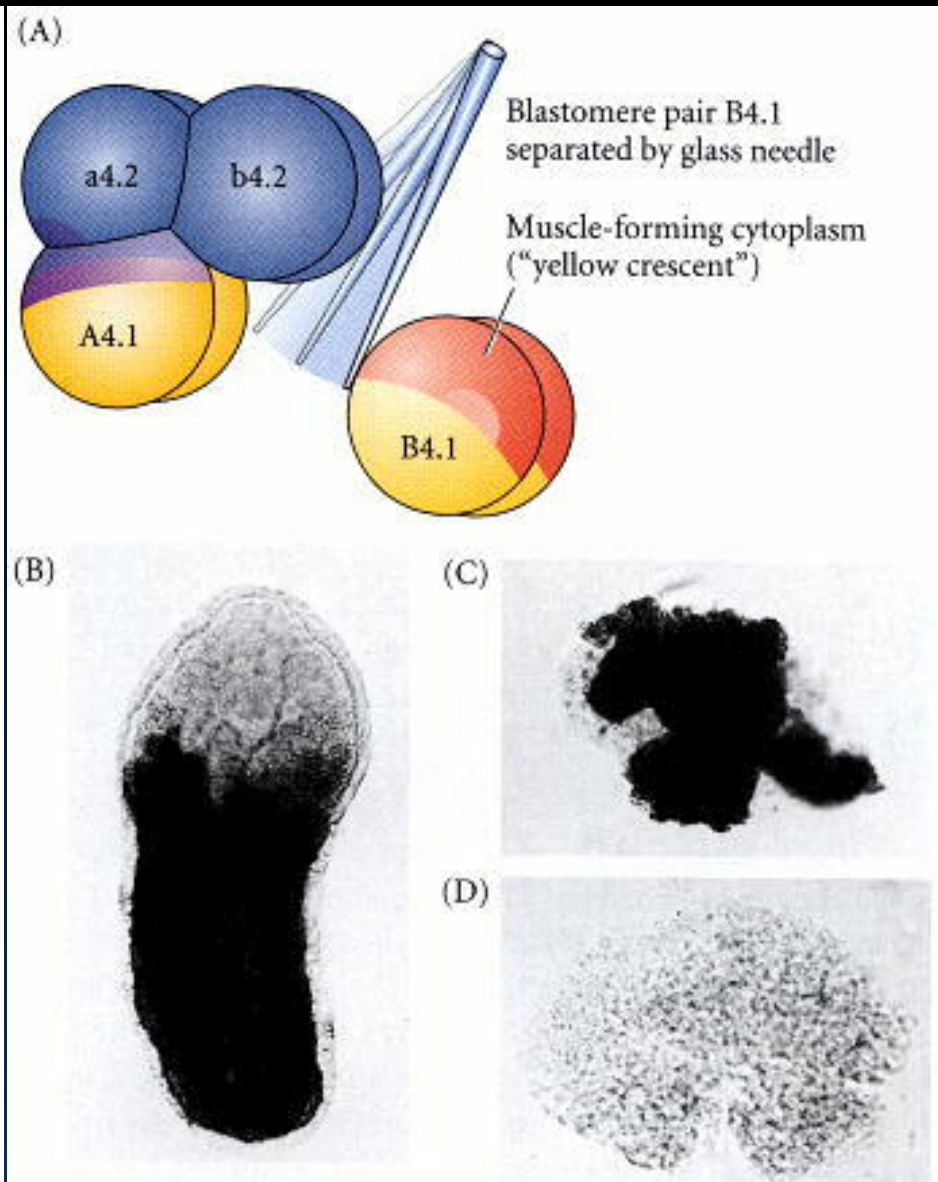
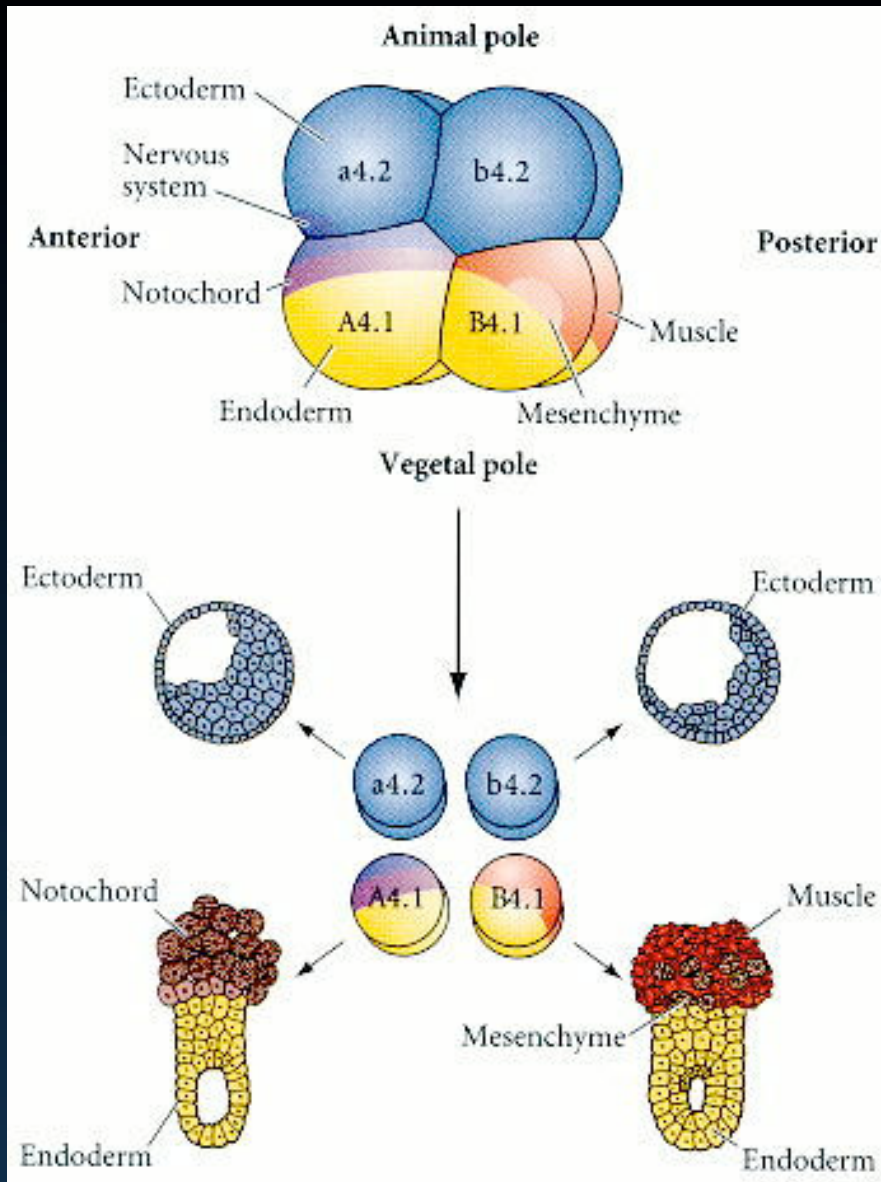


First, Driesch had demonstrated that the prospective potency of an isolated blastomere (those cell types it was possible for it to form) is greater than its prospective fate (those cell types it would normally give rise to over the unaltered course of its development).

Second, Driesch concluded that the sea urchin embryo is a “harmonious equipotential system” because all of its potentially independent parts functioned together to form a single organism.

Third, he concluded that the fate of a nucleus depended solely on its location in the embryo.

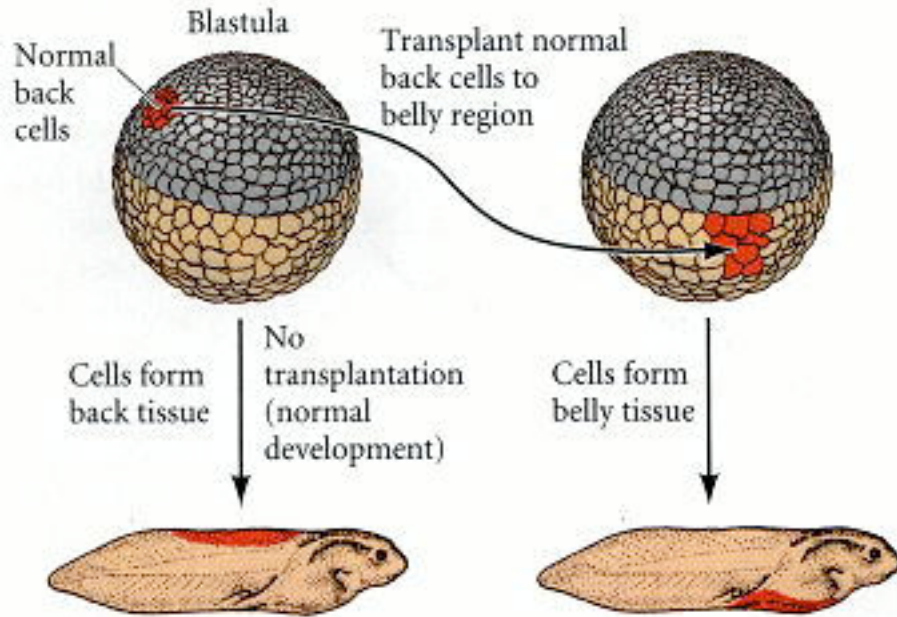
Investigator	Organism	Type of experiment	Conclusion	Interpretation concerning potency and fate
Roux (1888)	Frog (<i>Rana fusca</i>)	Defect	Mosaic development (autonomous)	Prospective potency equals prospective fate
Driesch (1892)	Sea urchin (<i>Echinus microtuberculatus</i>)	Isolation	Regulative development (conditional)	Prospective potency is greater than prospective fate
Driesch (1893)	Sea urchin (<i>Echinus</i> and <i>Paracentrotus</i>)	Recombination	Regulative development (conditional)	Prospective potency is greater than prospective fate



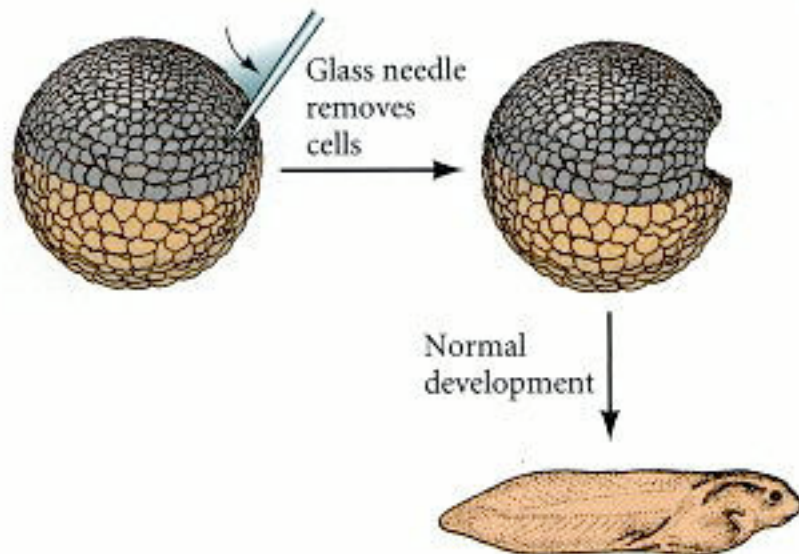
Laurent Chabry, 1887

Acetilcolinesterasi

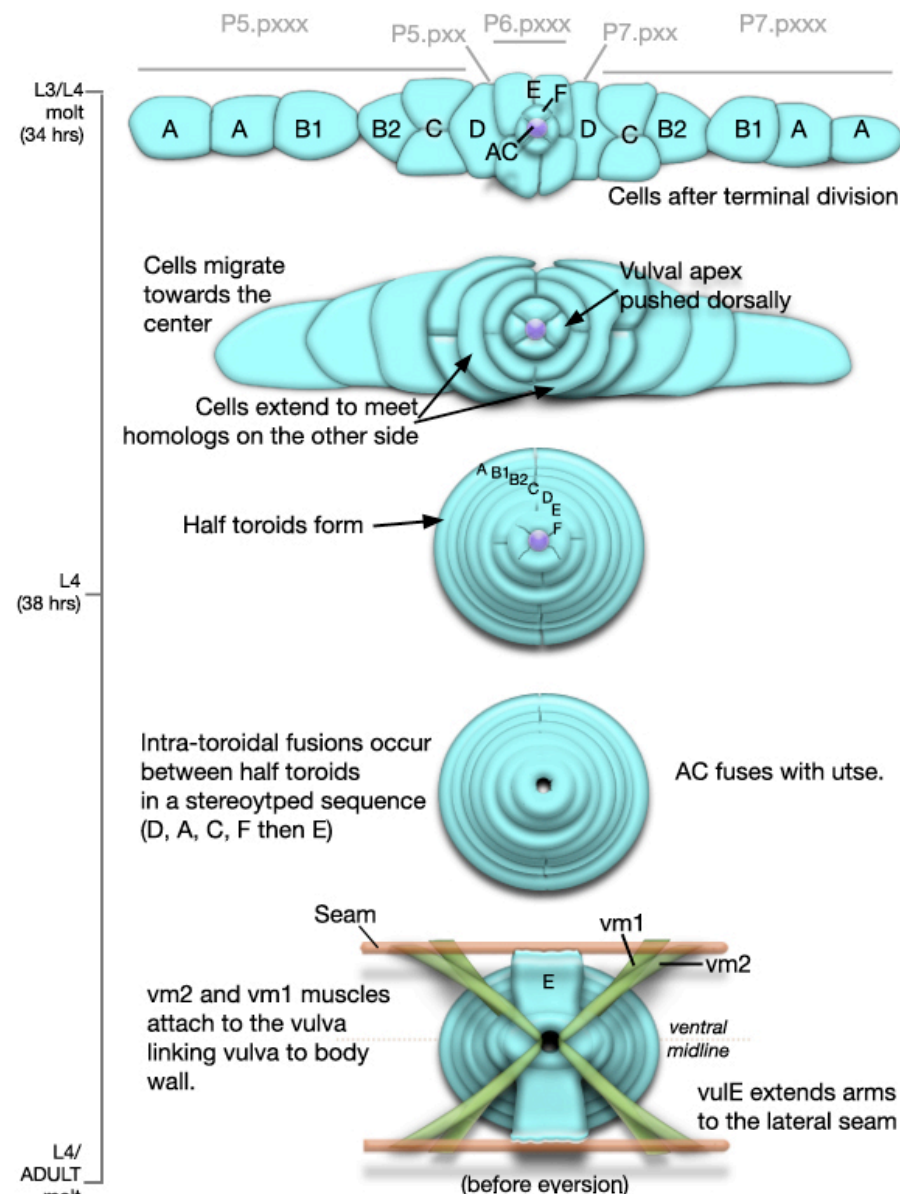
(A)



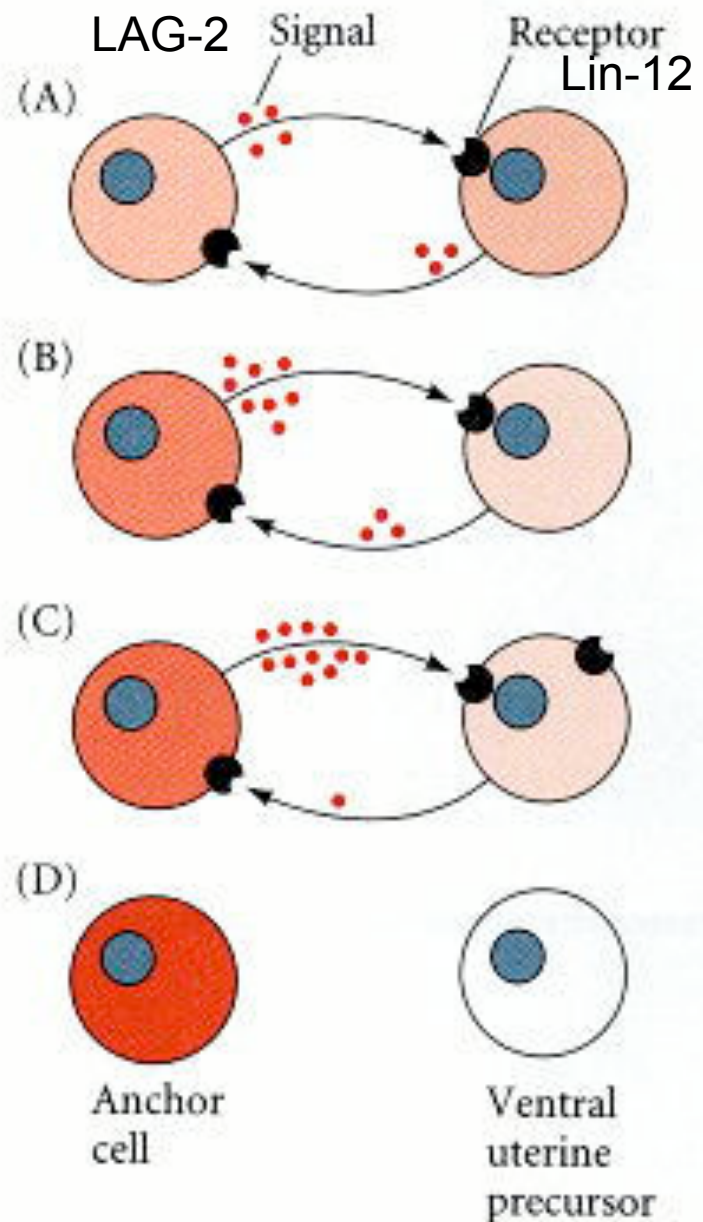
(B)

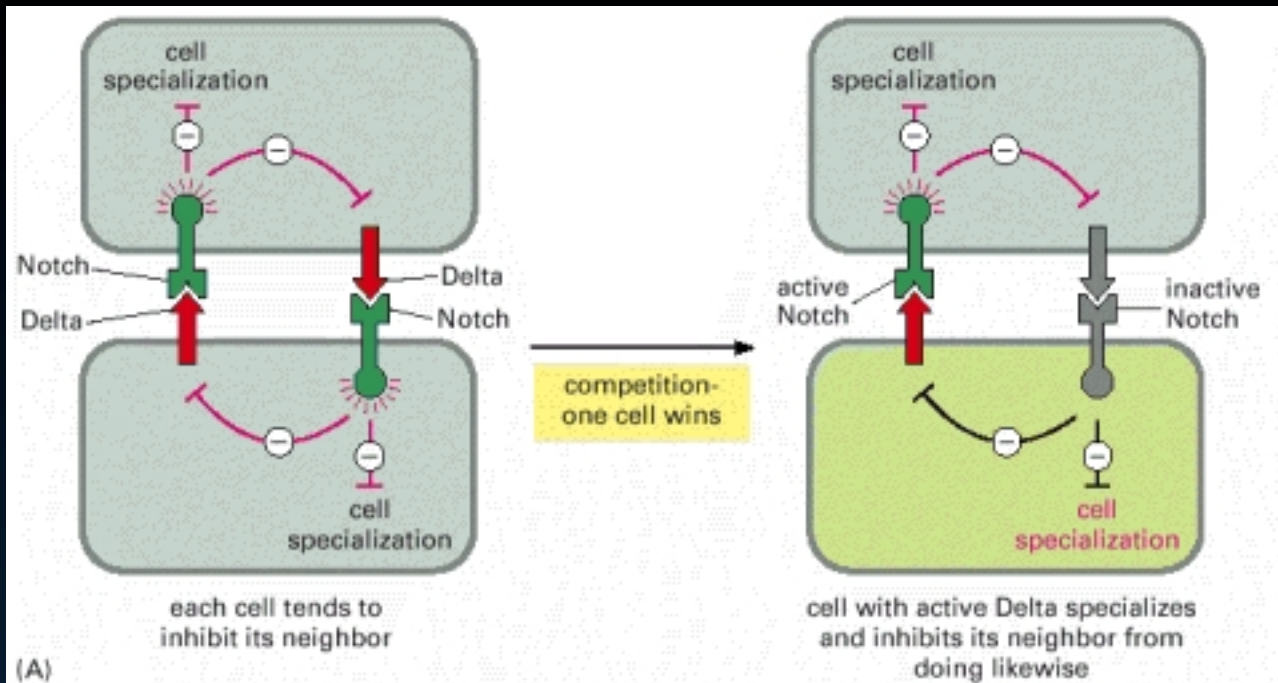


Dasyatis novemcinctus

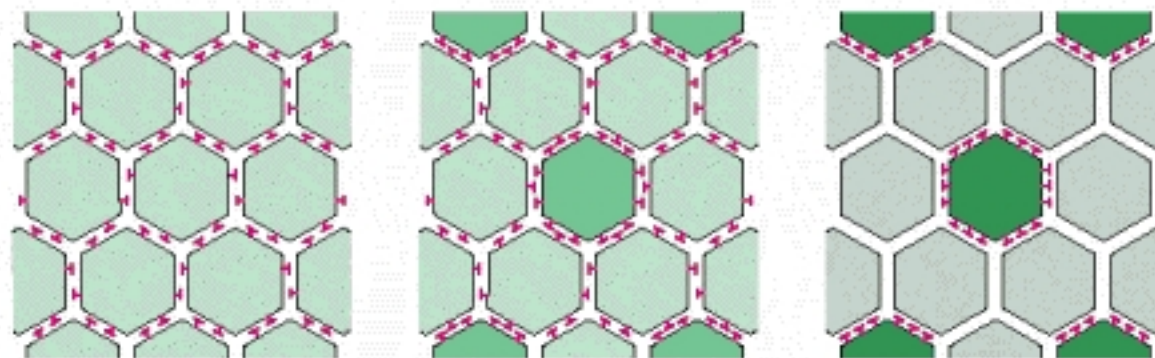


DORSAL view. Hrs at 20°C. Based on Sharma-Kishore et al., 1999



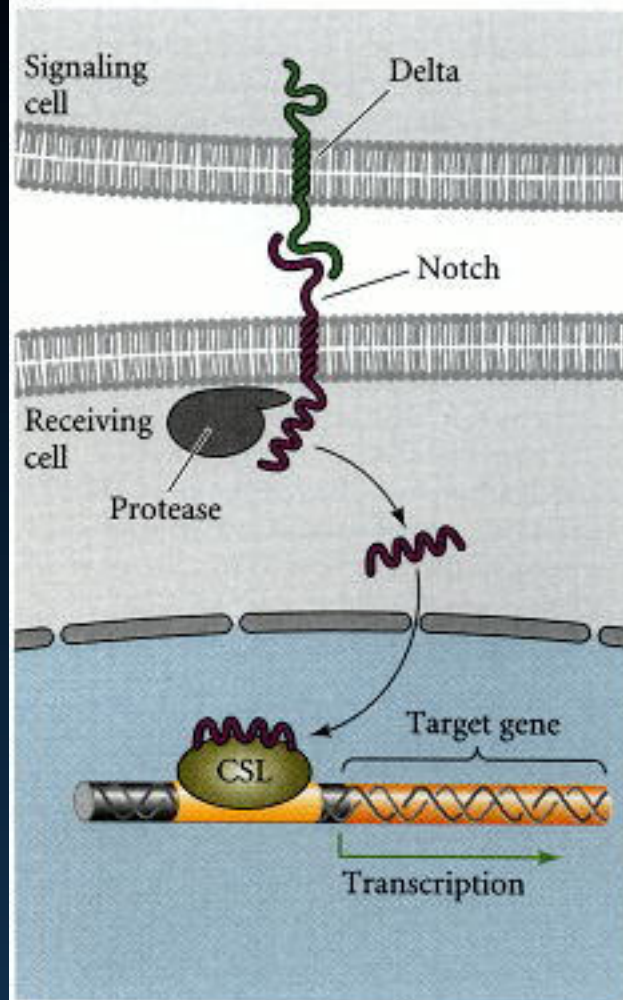


(A)

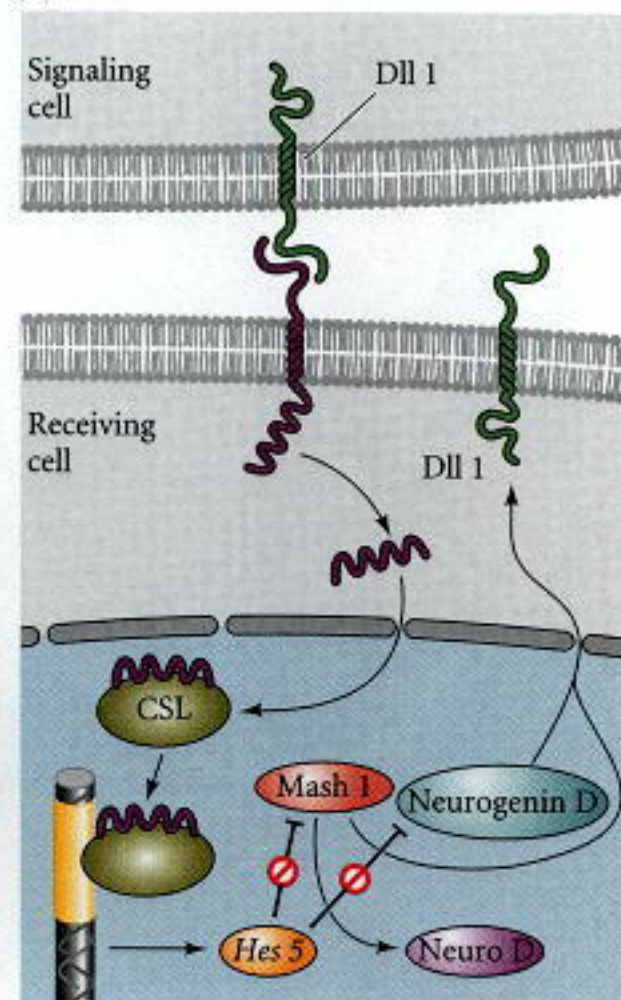


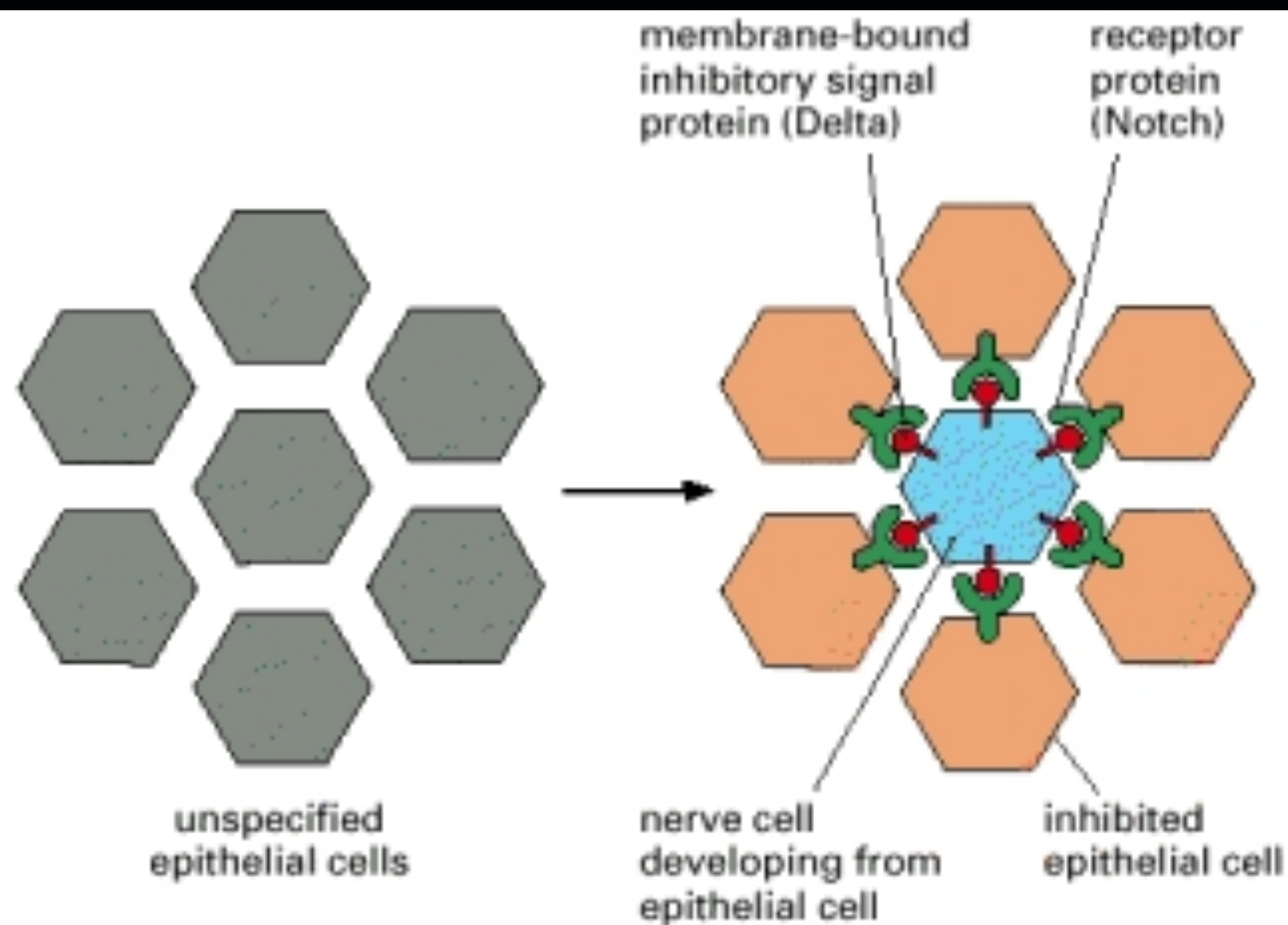
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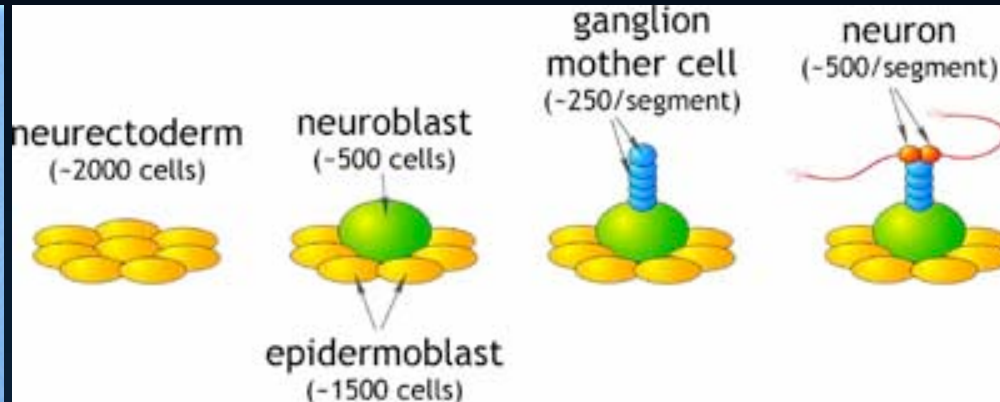
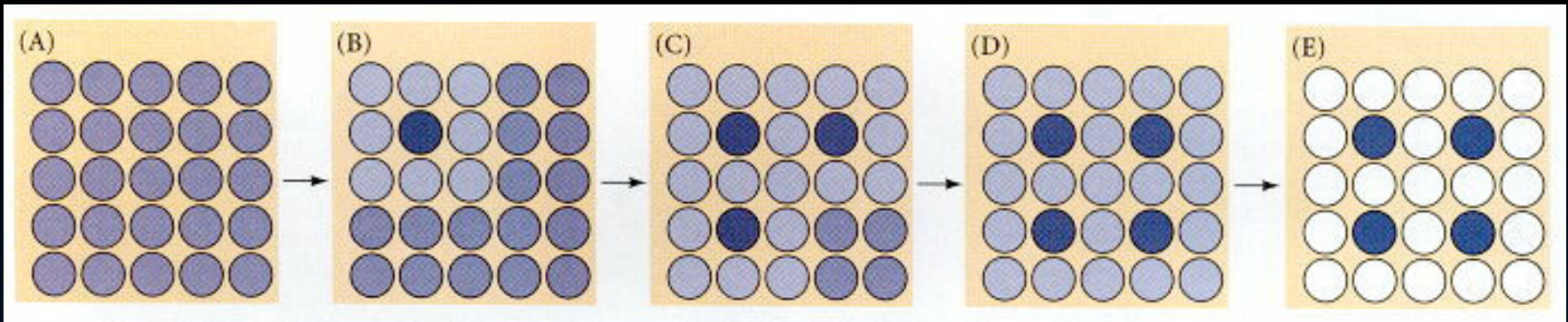
(A)



(B)



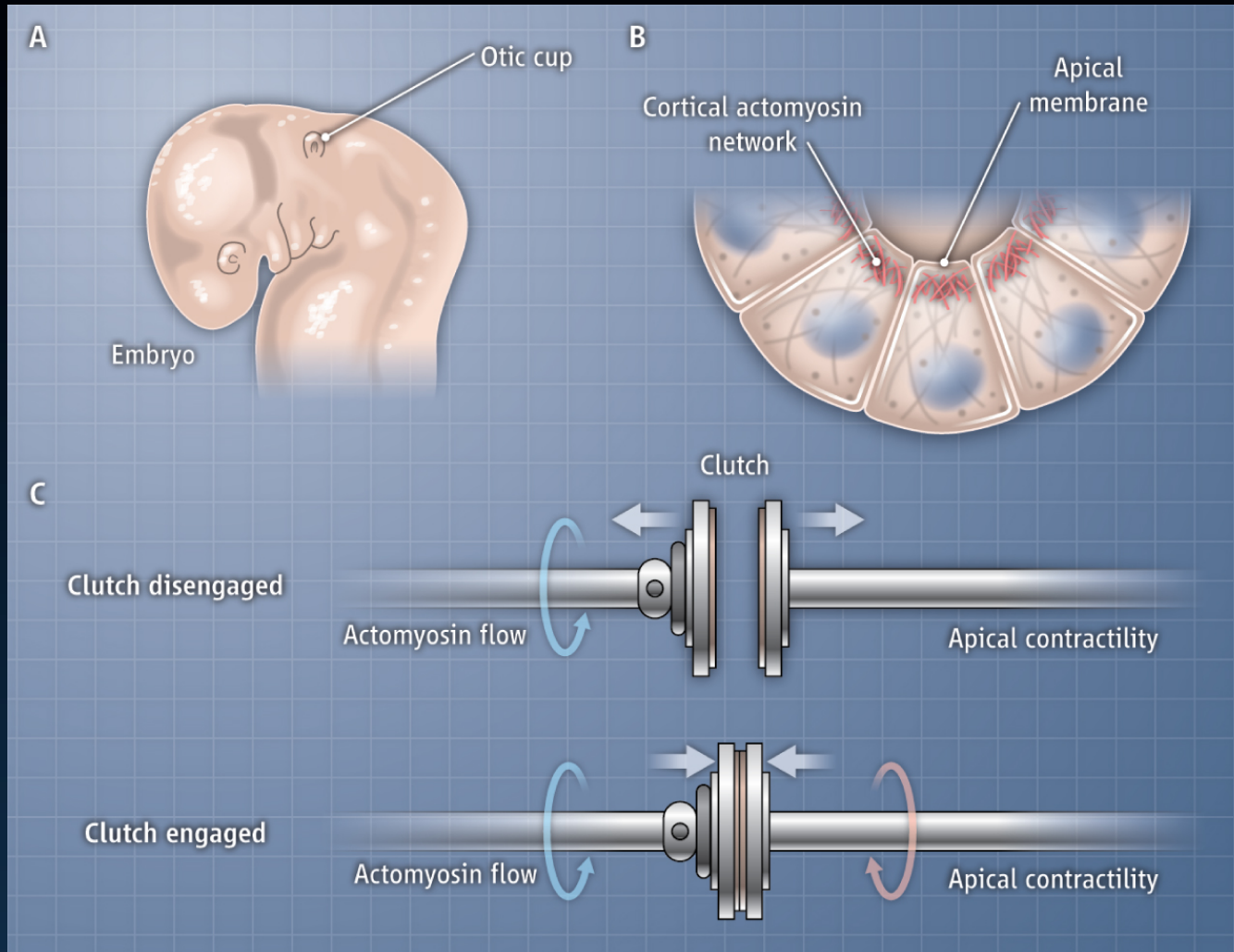




Interneurons

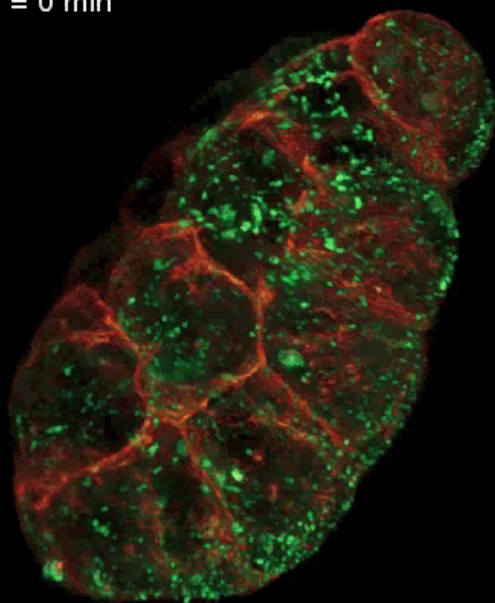
Glial cells

Cell apical constrictions during embryonic morphogenesis.

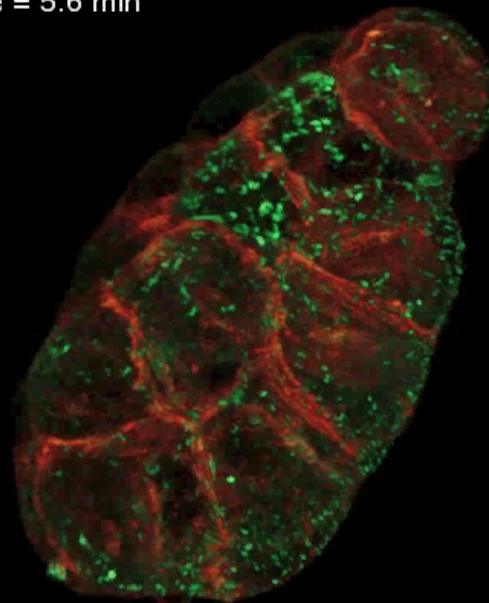


W Razzell, P Martin Science 2012;335:1181-1182

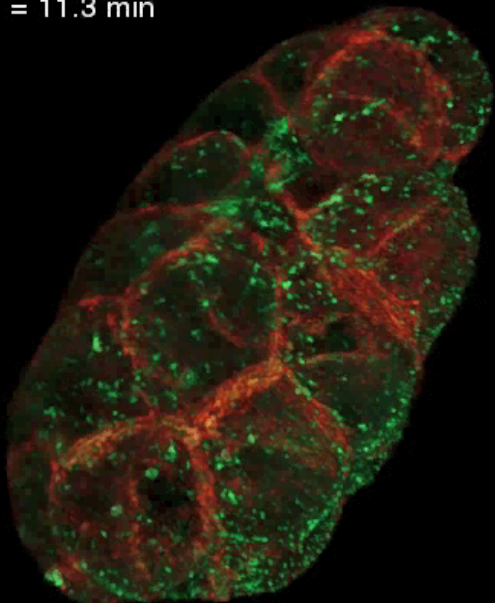
Time = 0 min



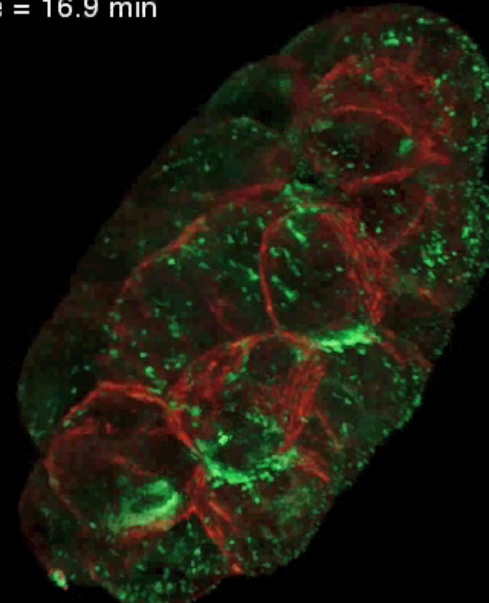
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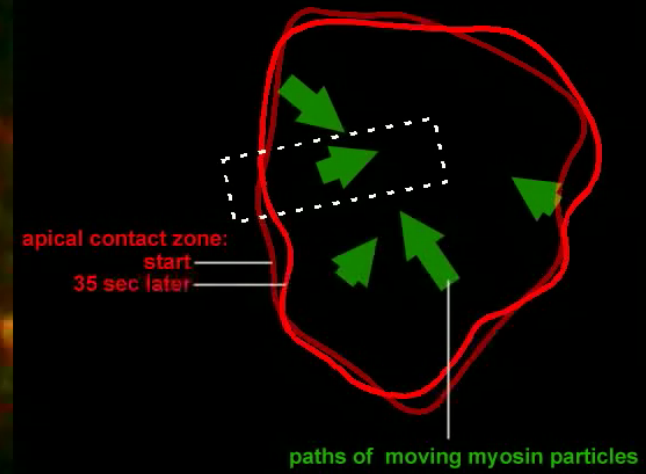
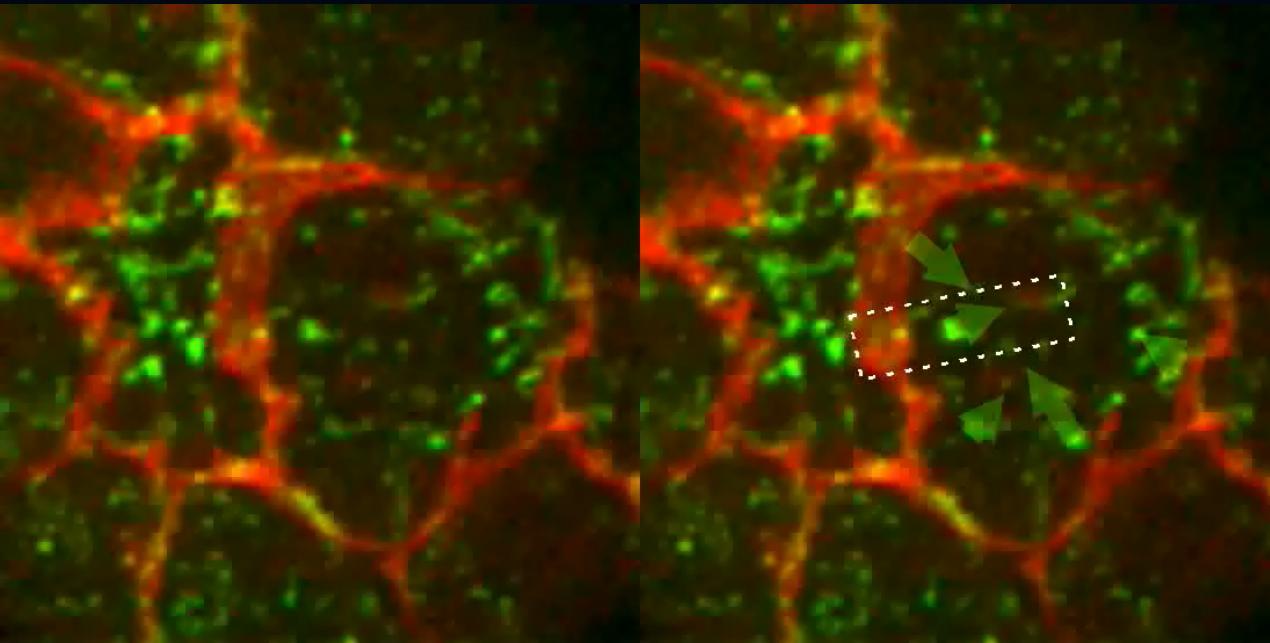
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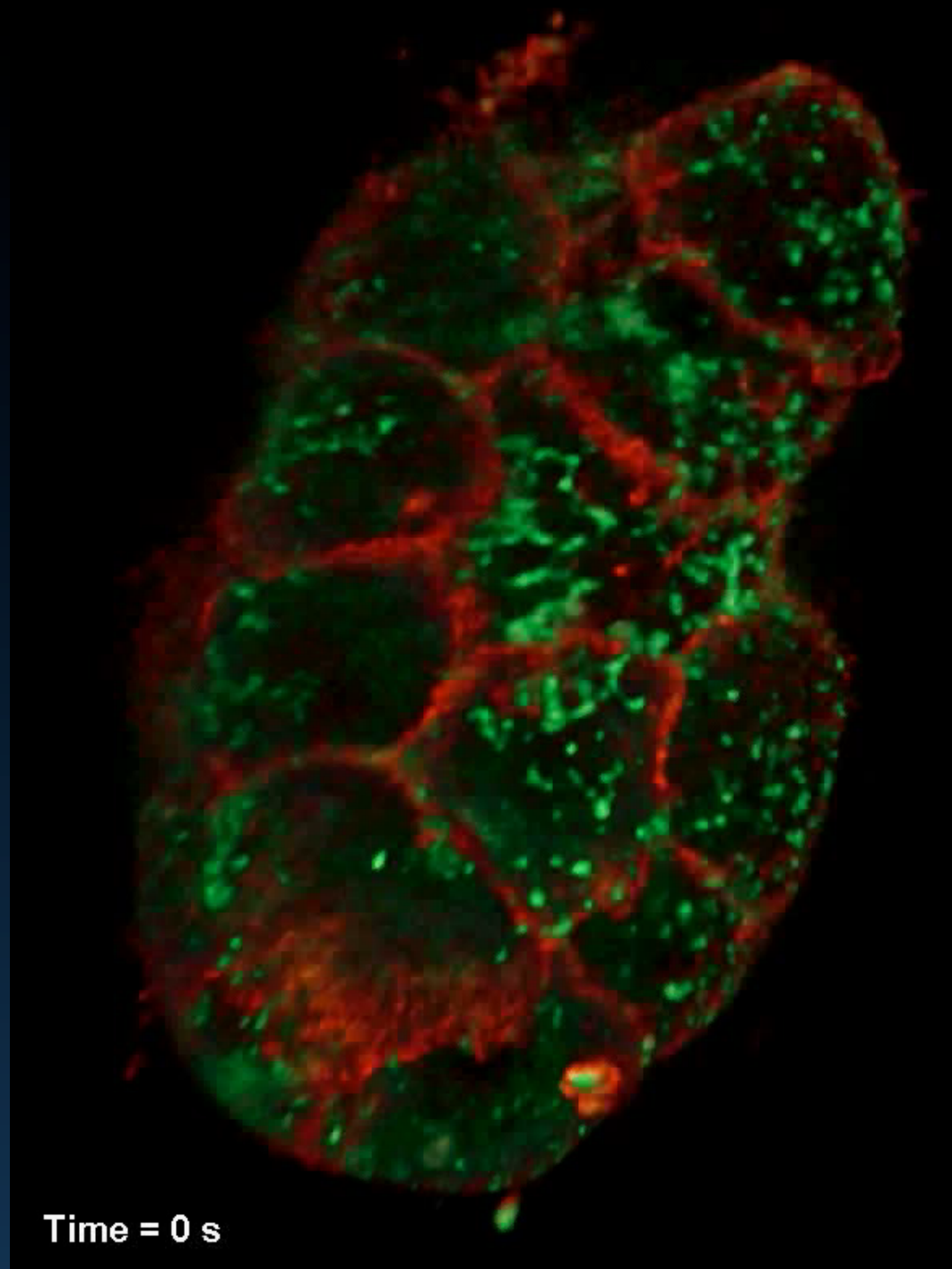
Time = 16.9 min



myosin







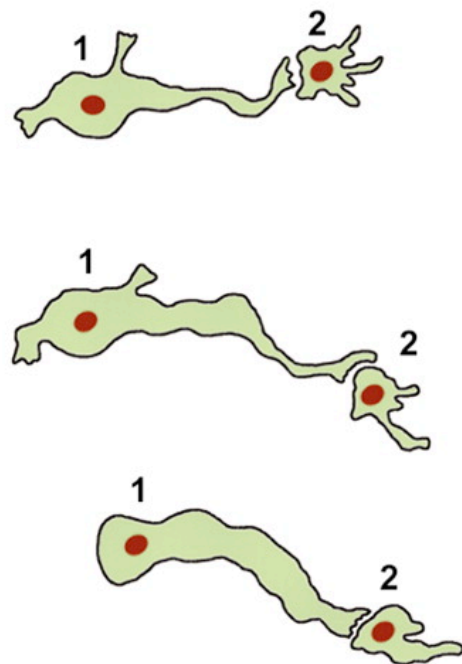
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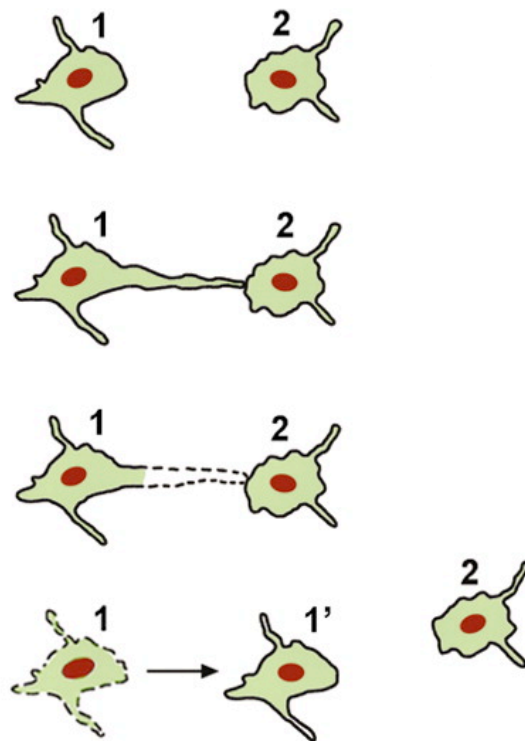
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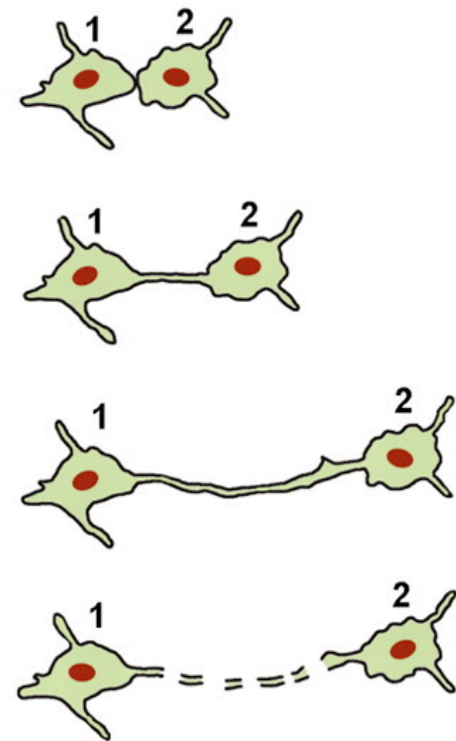
A



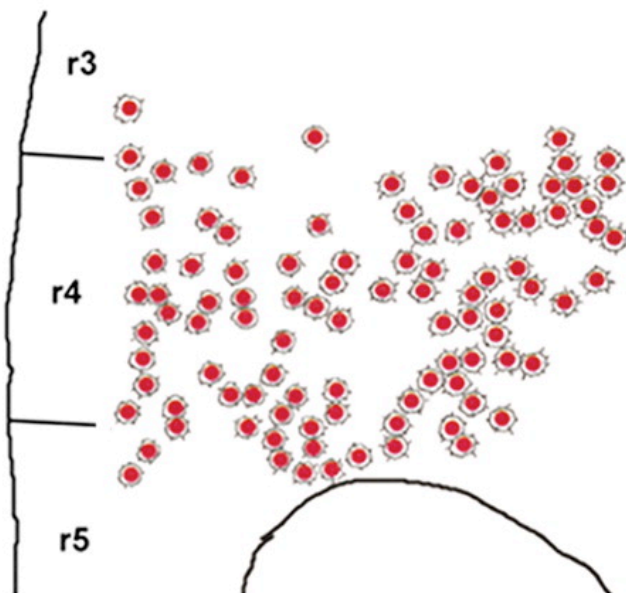
B



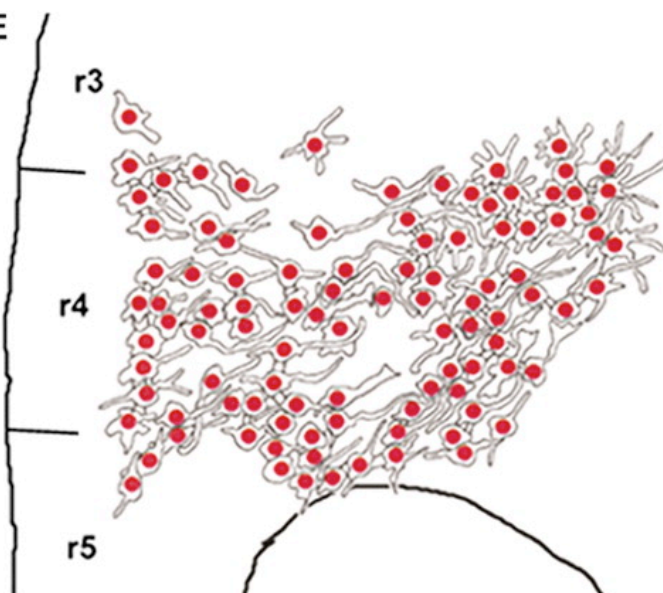
C



D



E



Problem solving 1.

- a. Deletion of Gene A gives a phenotype
- b. The phenotype involves many cells
- c. Too many cells

Is the phenotype cell-autonomous?

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