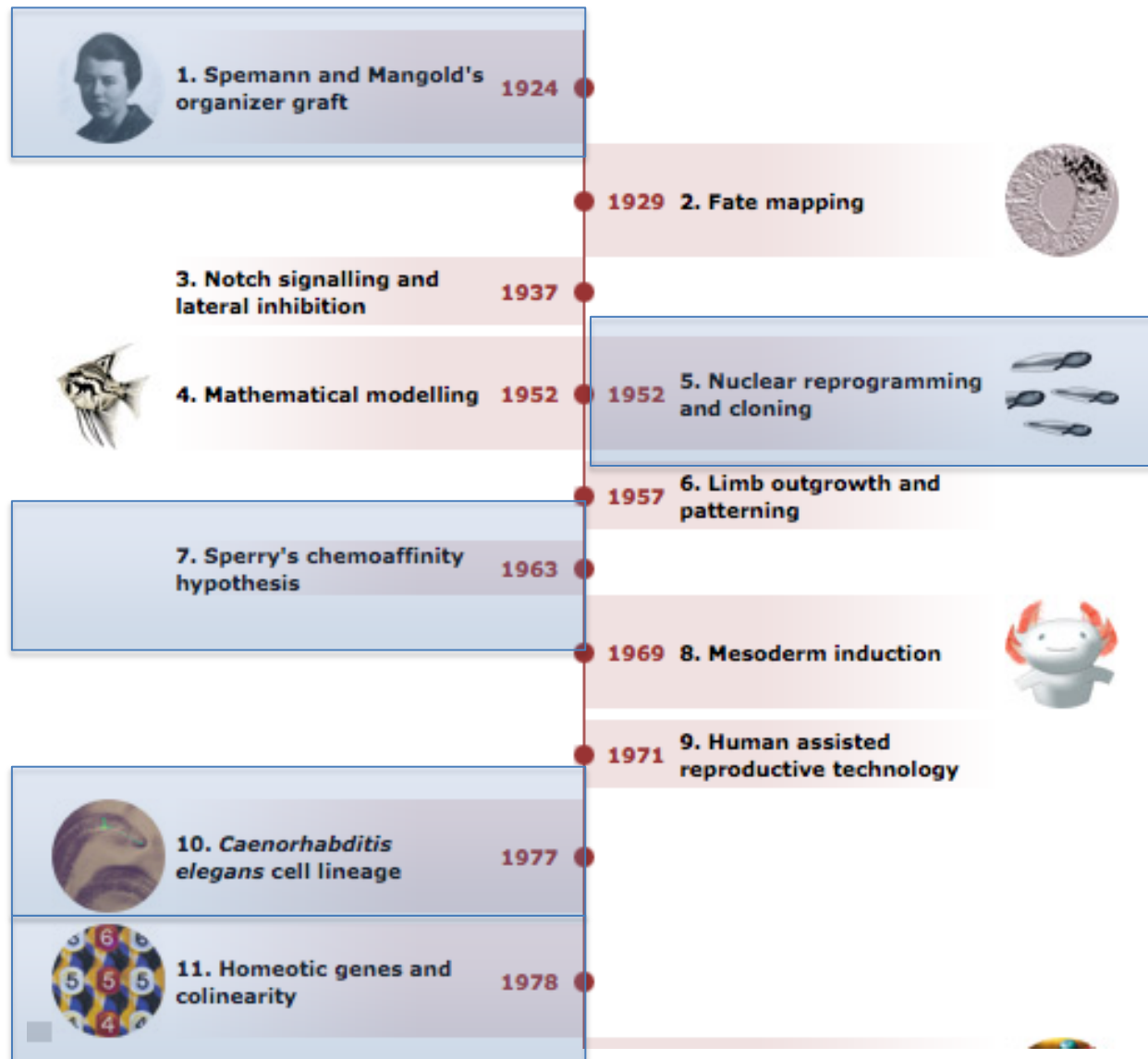


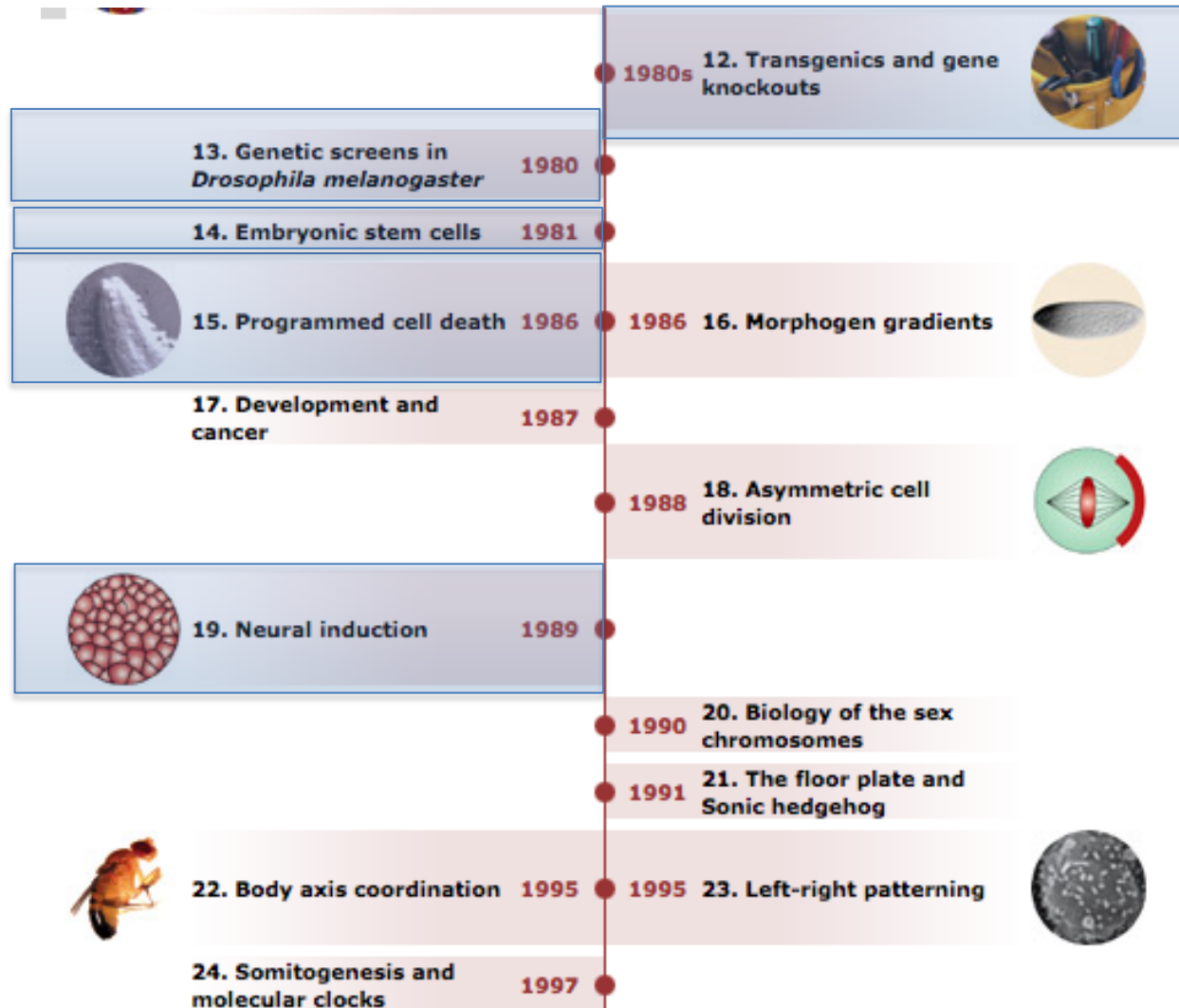
Programa aula de hoje

1. Massinha e origami (20 min)
2. Discussão leitura (40 min)
3. Palestra células tronco e regeneração (40 min)
4. Atividade prática: regeneração planárias (80 min)

Impacto da biologia do desenvolvimento na ciência do século XX



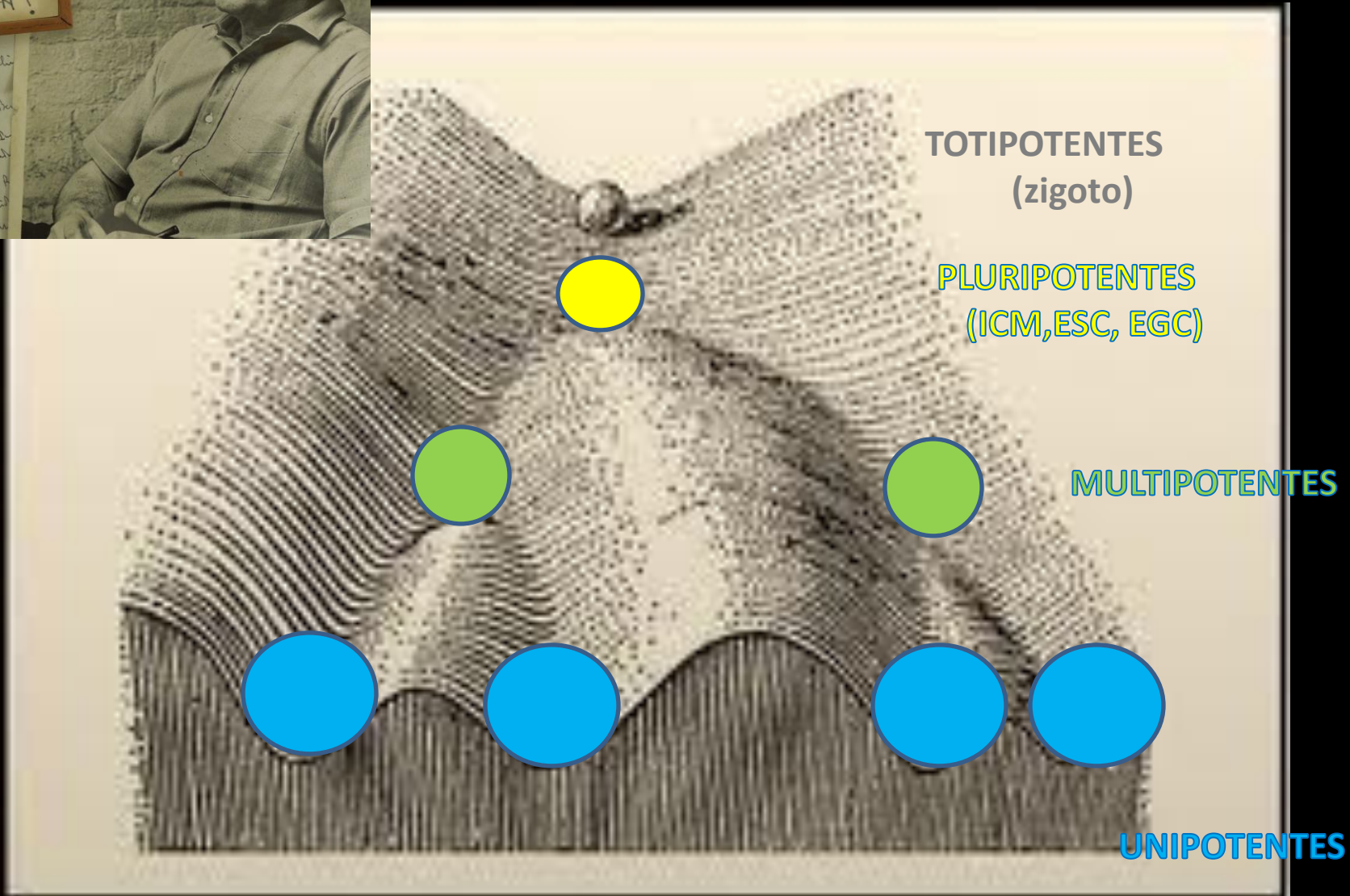
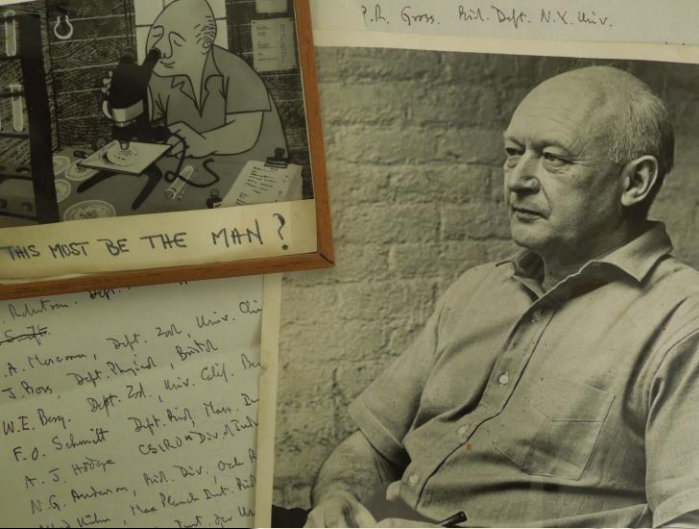
Impacto da biologia do desenvolvimento na ciência do século XX





CÉLULAS TRONCO REGENERAÇÃO EM ANIMAIS

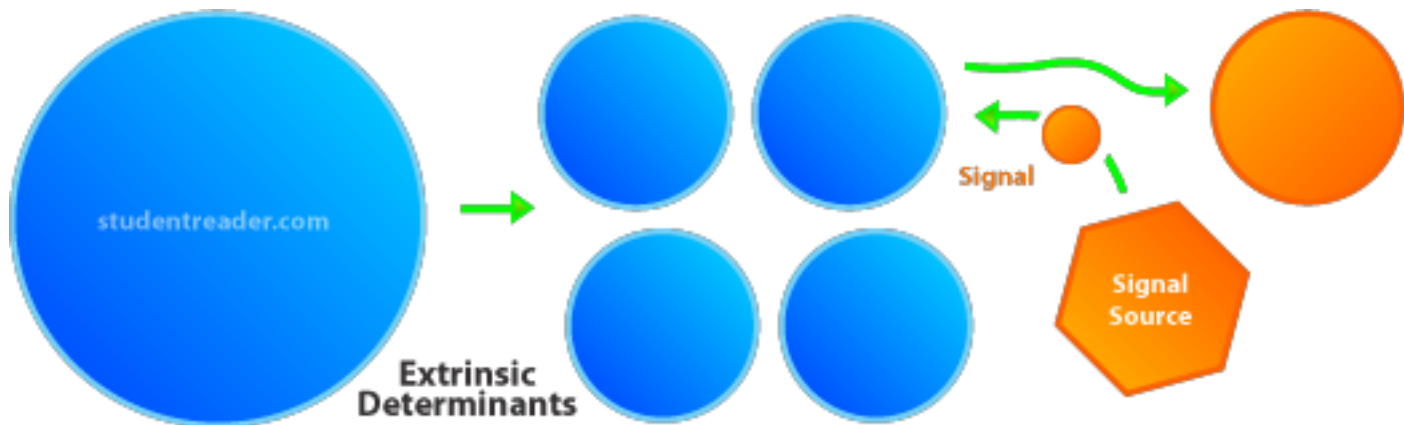
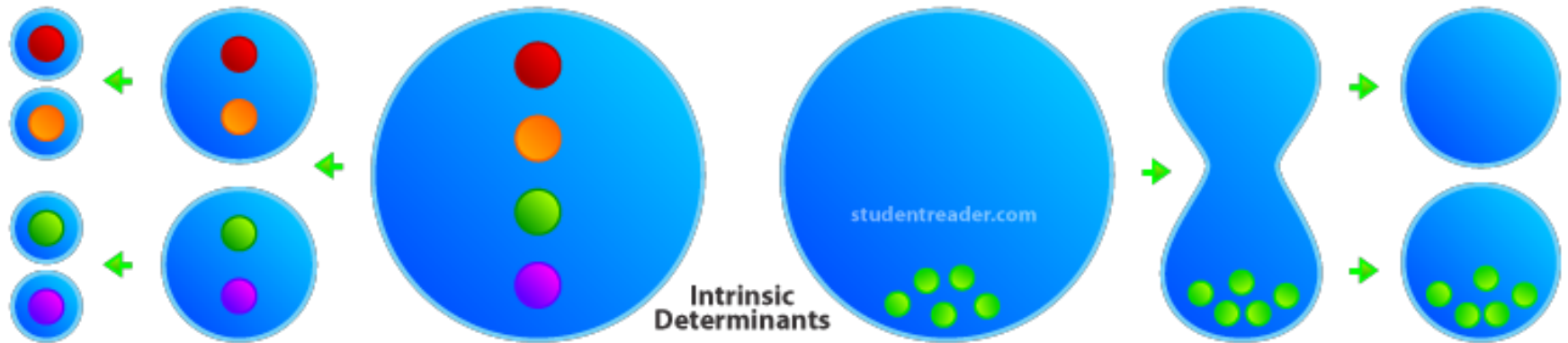




Waddington's Epigenetic Landscape

XX-XI Ideias Contemporâneas do desenvolvimento

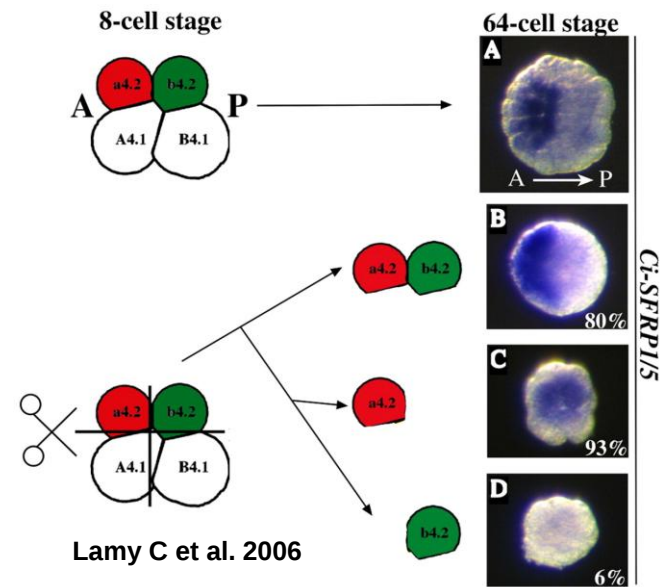
Indução e determinantes:



Revisão conceitos:

1. Especificação autônoma

- Especificação determinativa



1. Especificação condicional

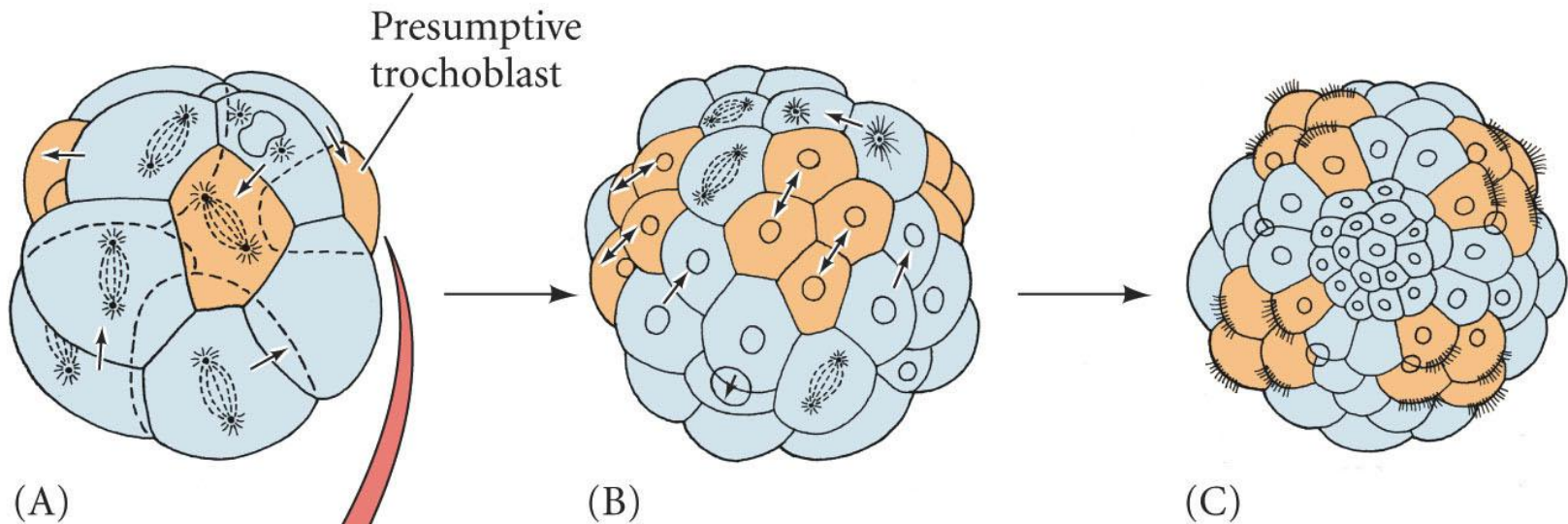
- Especificação regulativa (!!!!)

Especificação condicional: gemelos
(armadilo de nove bandas)

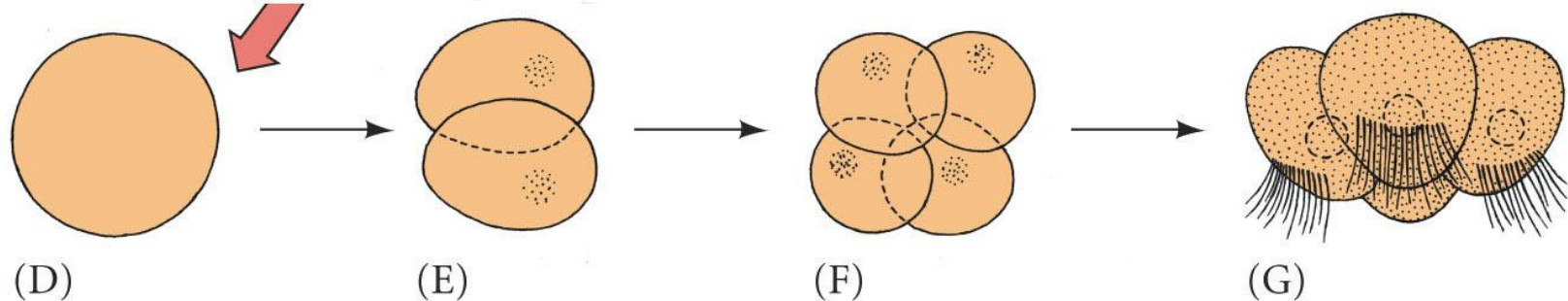


Especificação autônoma

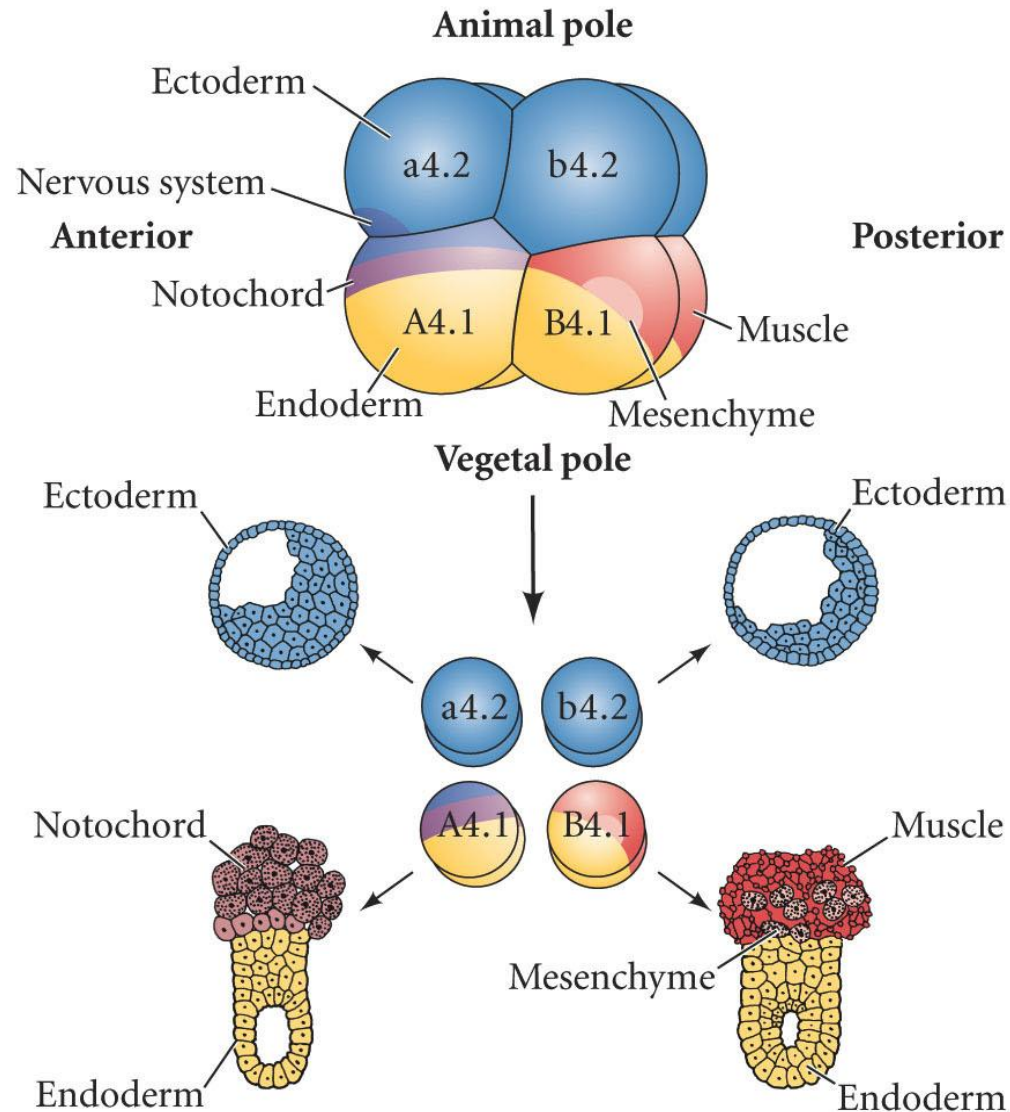
Normal development of *Patella*



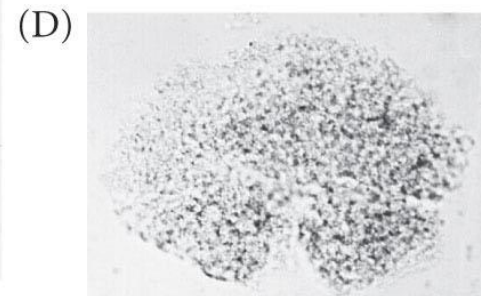
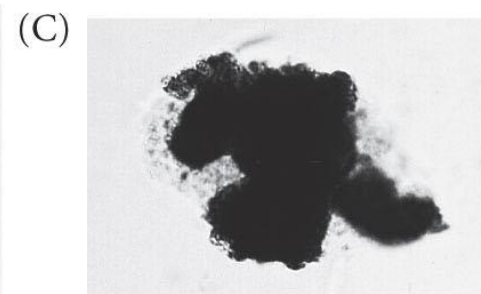
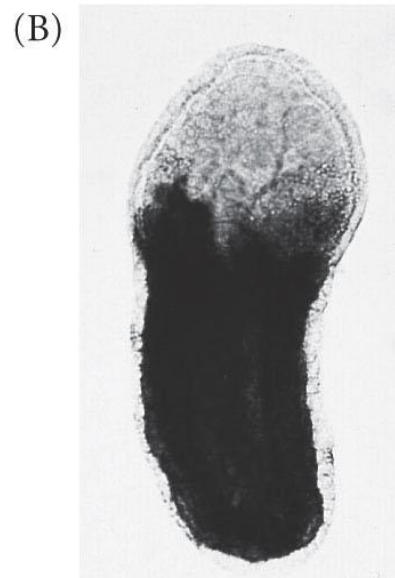
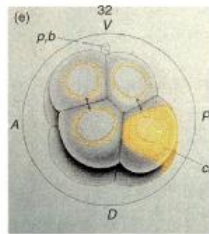
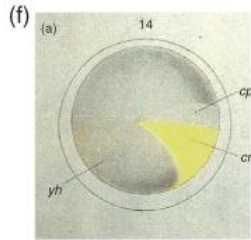
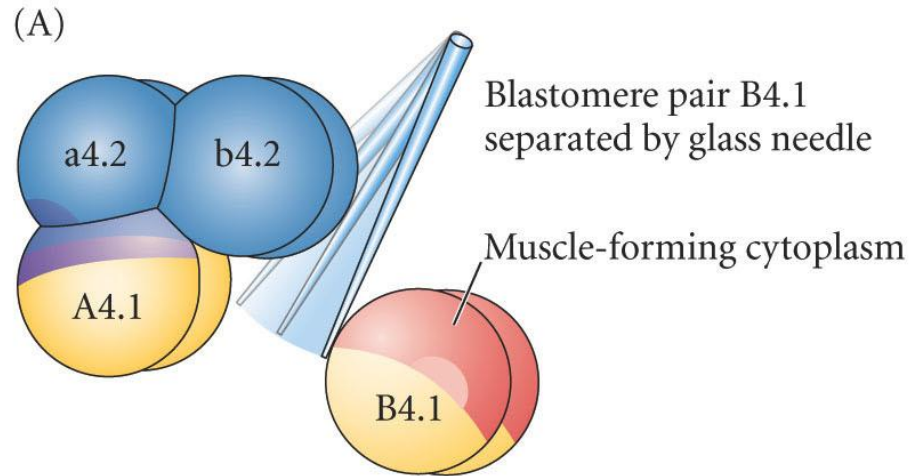
Isolated trochoblast development



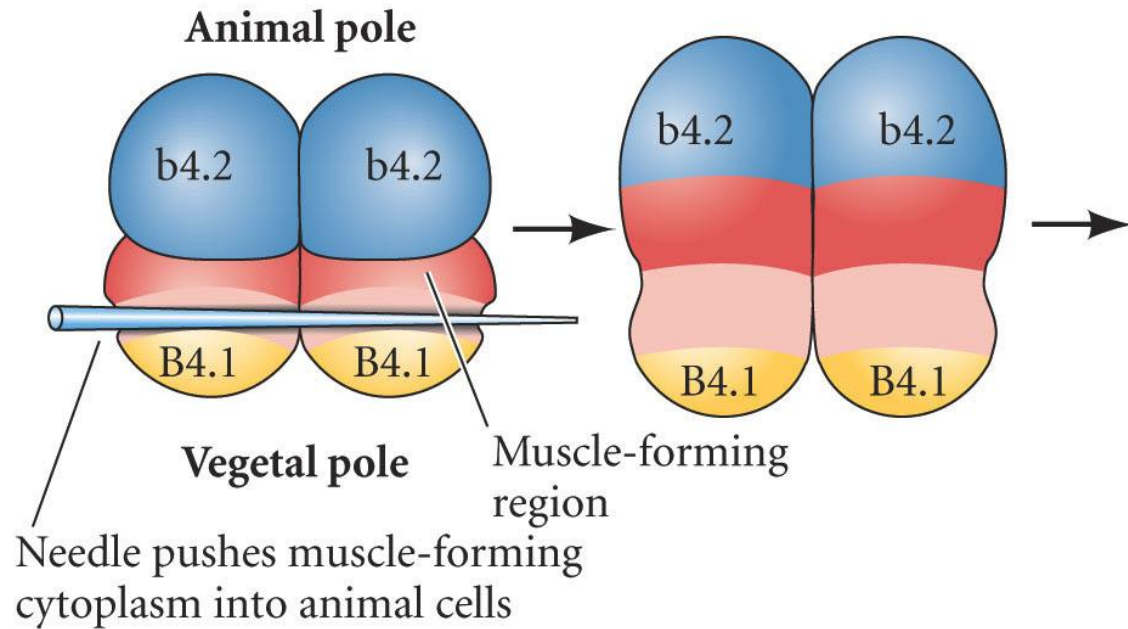
Especificação autónoma nos tunicados



Desenvolvimento do músculo em tunicados

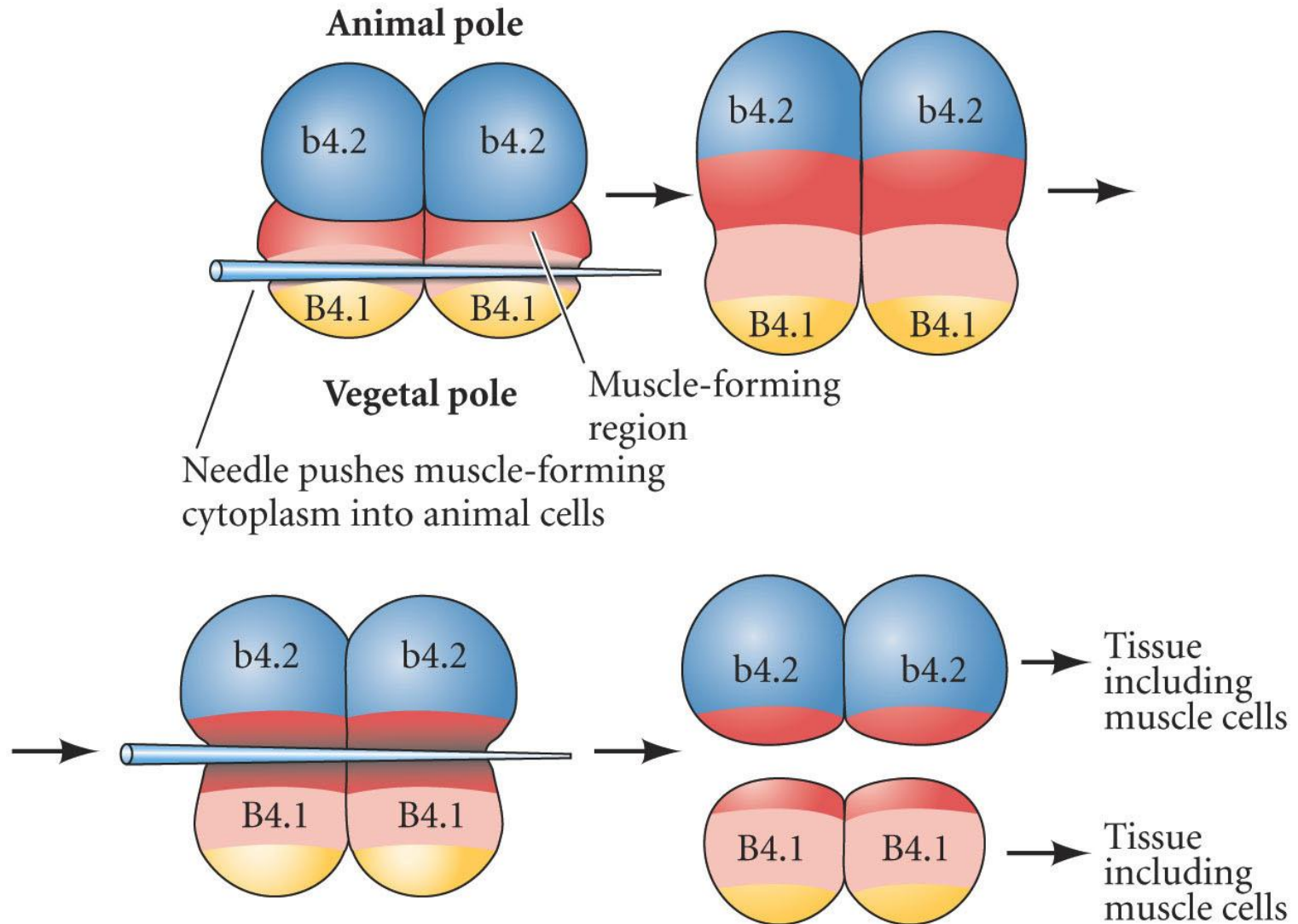


Citoplasma da crecente amarelhenta determina o destino das células musculares



?

Citoplasma da crecente amarelhenta determina o destino das células musculares



Especificação autônoma

Divisões assimétricas: Kemphues
(1988) identifica PARs em nemátodos

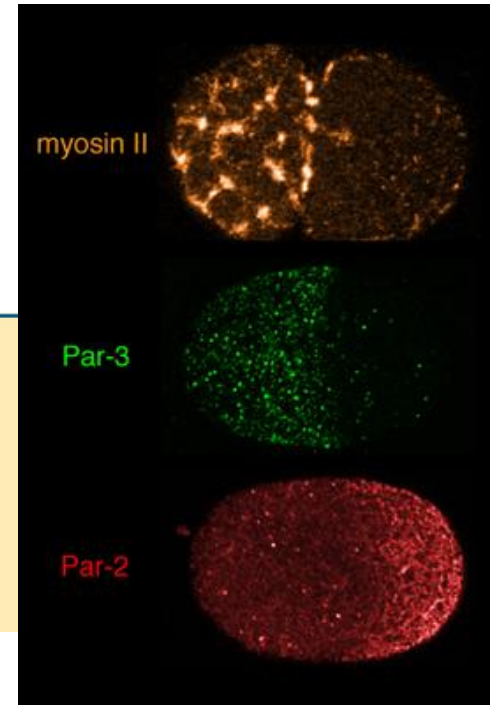


TABLE 3.2 Modes of cell type specification and their characteristics

I. Autonomous specification

Characteristic of most invertebrates.

Specification by differential acquisition of certain cytoplasmic molecules present in the egg.

Invariant cleavages produce the same lineages in each embryo of the species. Blastomere fates are generally invariant.

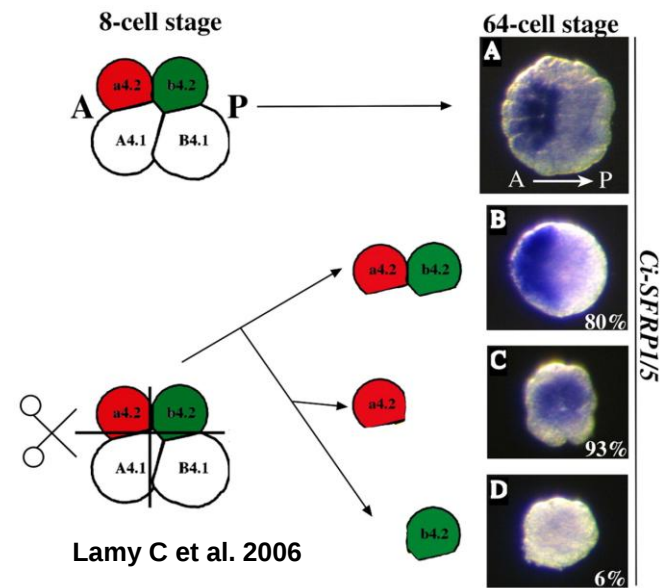
Cell type specification precedes any large-scale embryonic cell migration.

Produces “mosaic” development: cells cannot change fate if a blastomere is lost.

Revisão conceitos:

1. Especificação autônoma

- Especificação determinativa



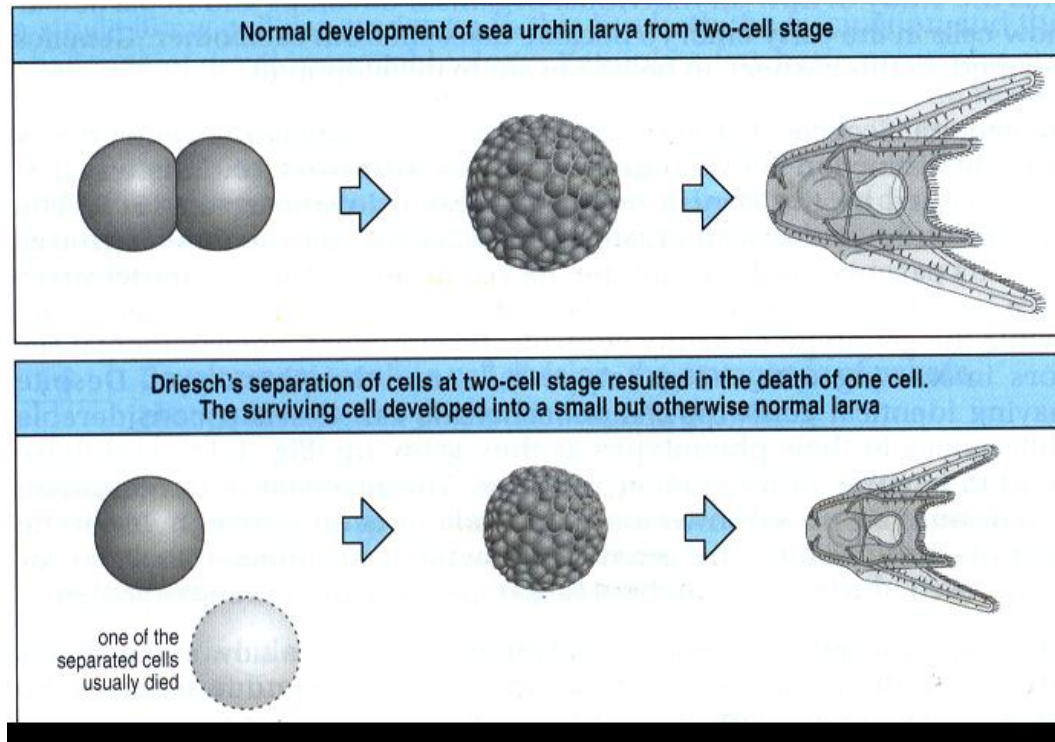
1. Especificação condicional

- Especificação regulativa

Especificação condicional: gemelos
(armadilo de nove bandas)

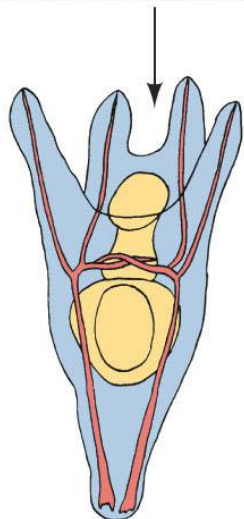
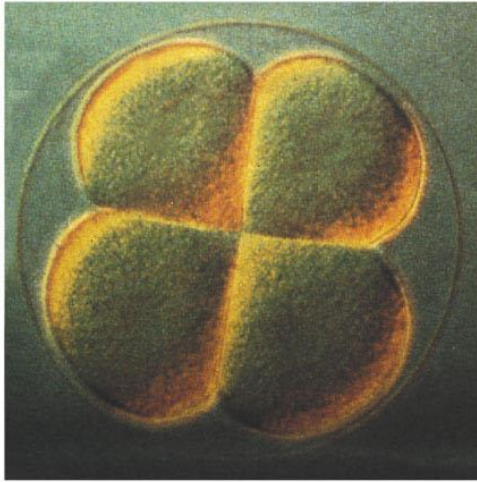


Especificação condicional: Desenvolvimento regulativo em Ouriço



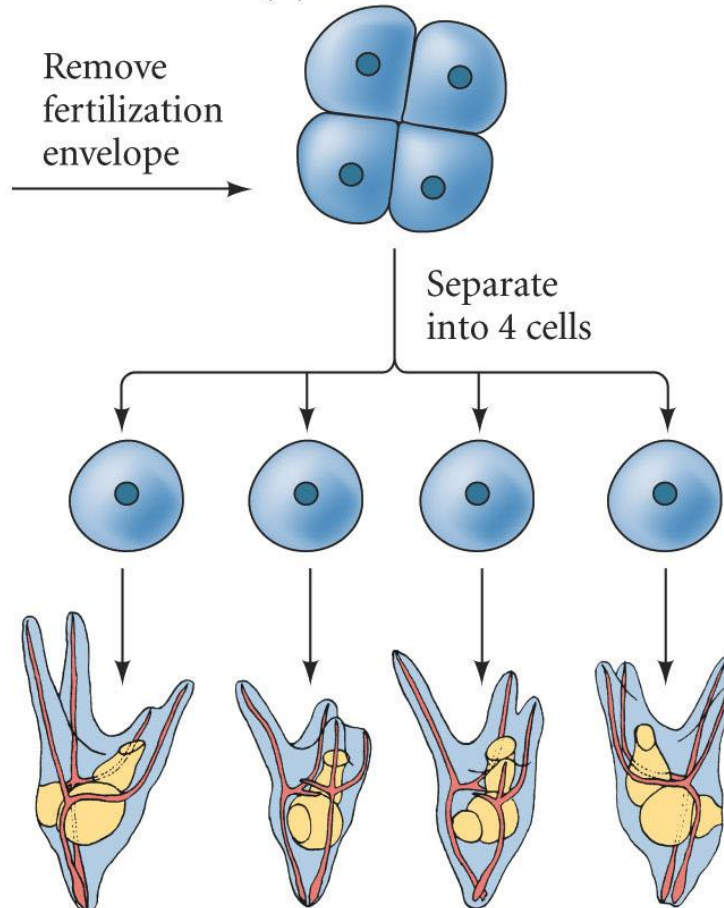
Especificação condicional: Desenvolvimento regulativo em Ouriço

(A) Fertilization envelope

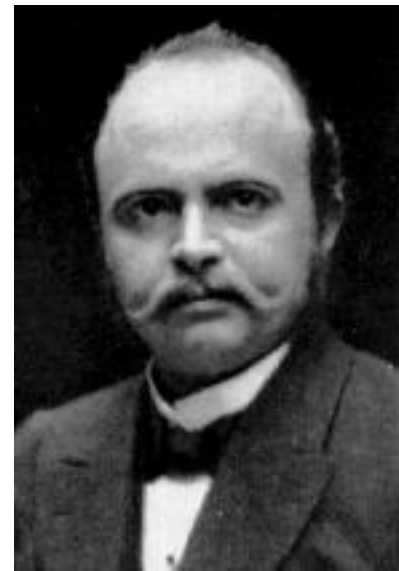


Normal pluteus larva

(B)



Plutei developed from single cells of 4-cell embryo



Especificação condicional

II. Conditional specification

Characteristic of all vertebrates and few invertebrates.

Specification by interactions between cells. Relative positions are important.

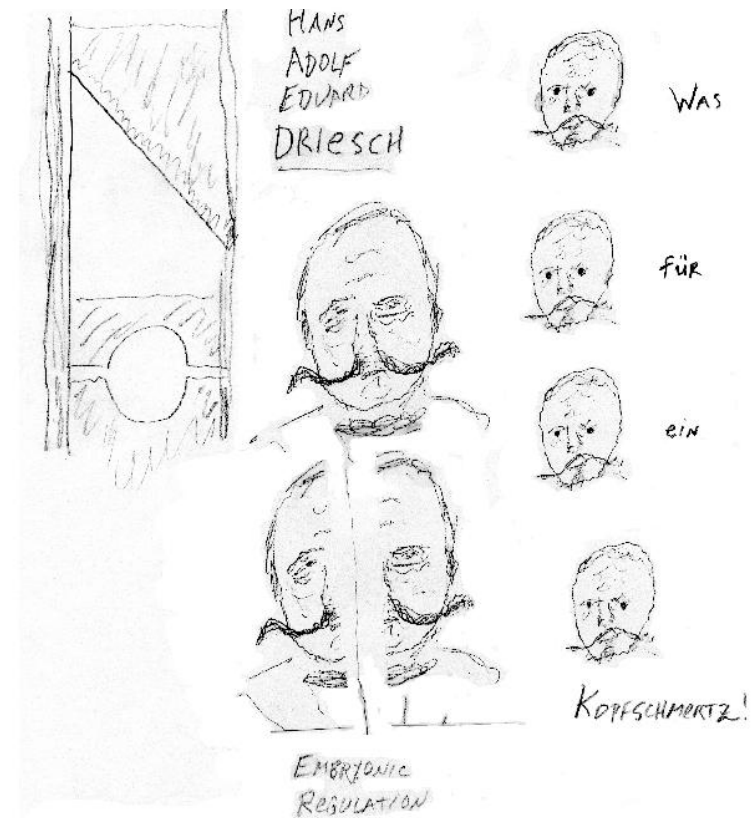
Variable cleavages produce no invariant fate assignments to cells.

Massive cell rearrangements and migrations precede or accompany specification.

Capacity for “regulative” development: allows cells to acquire different functions.

Source: After Davidson 1991.

DEVELOPMENTAL BIOLOGY, Eighth Edition, Table 3.2 © 2006 Sinauer Associates, Inc.



Especificação condicional

II. Conditional specification

Characteristic of all vertebrates and few invertebrates.

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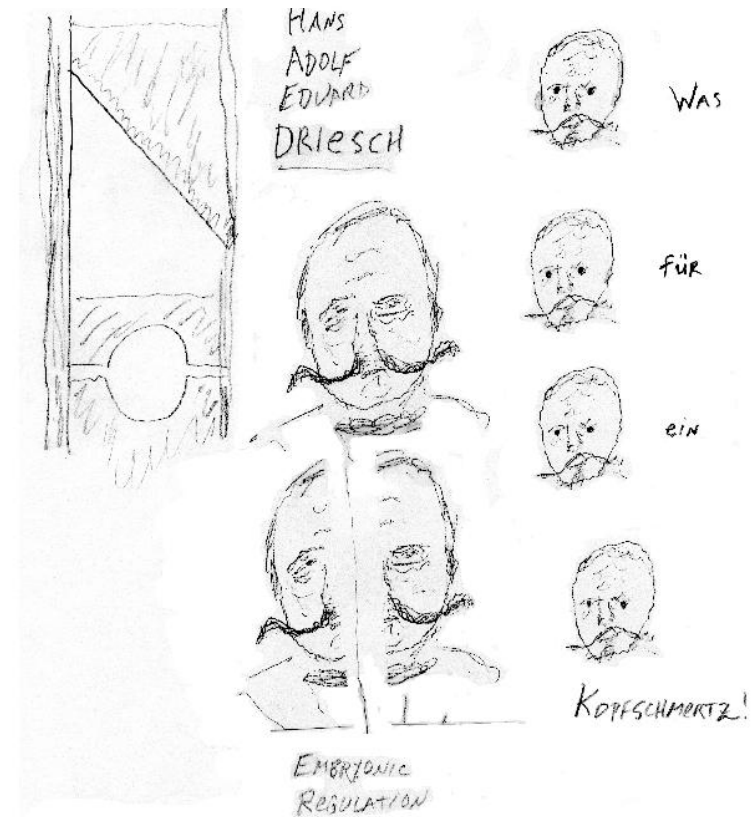
Variable cleavages produce no invariant fate assignments to cells.

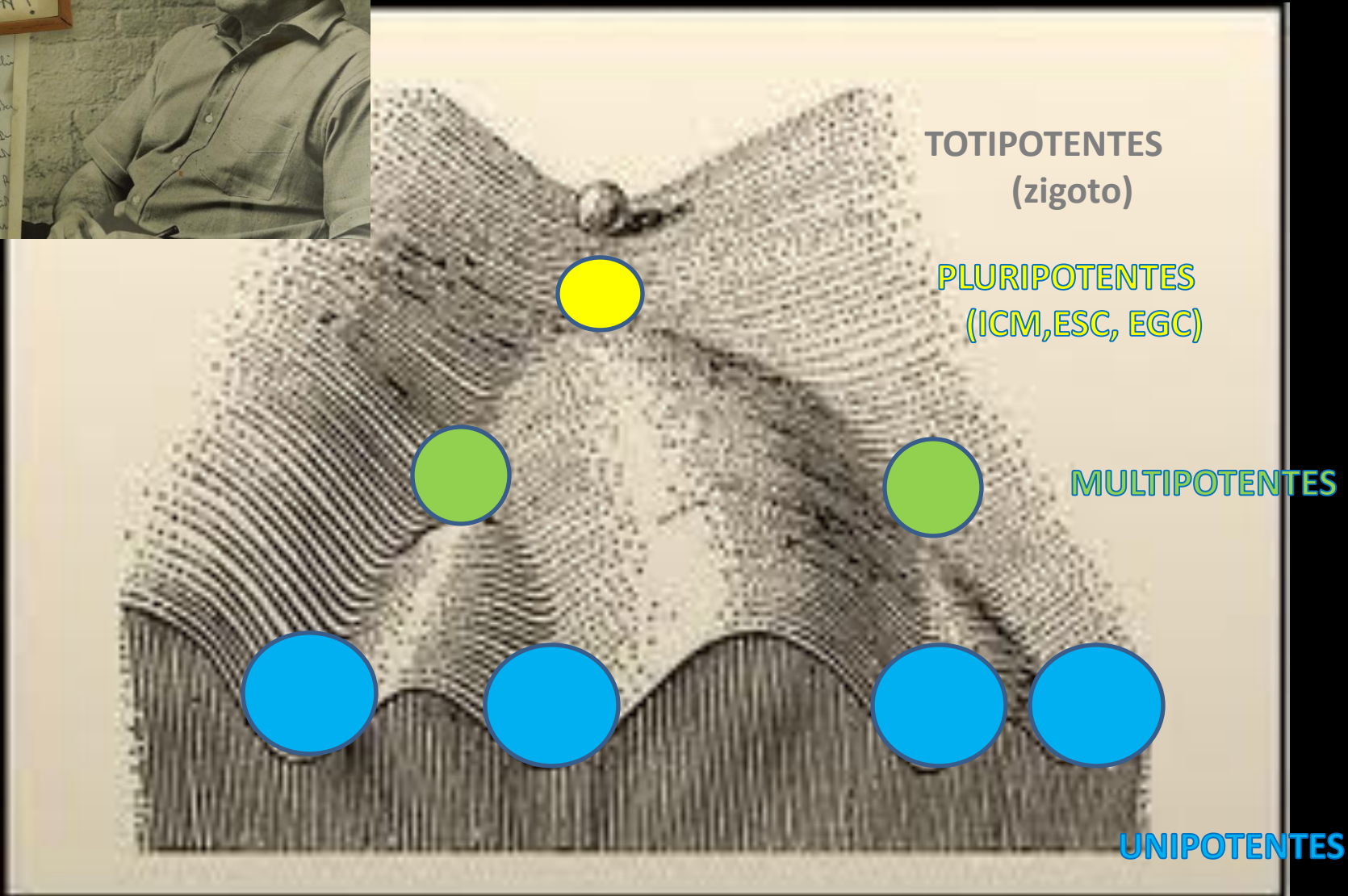
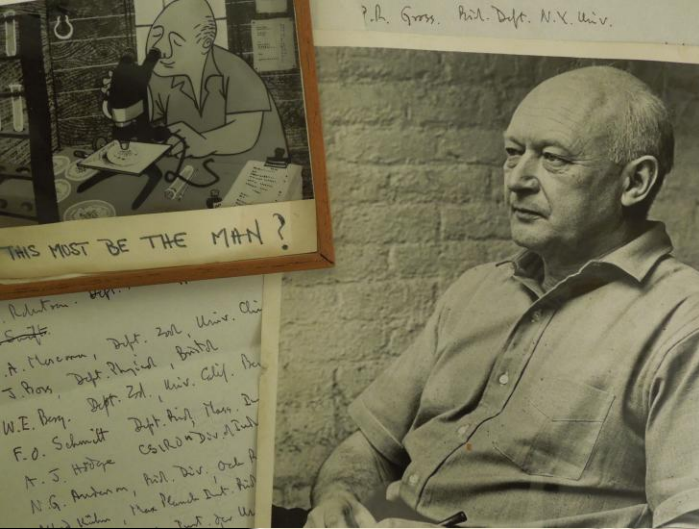
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Capacity for “regulative” development: allows cells to acquire different functions.

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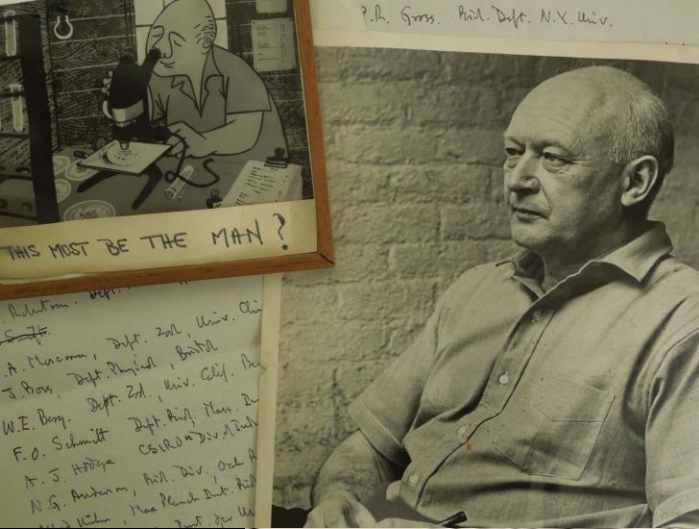
TOTIPOTENTES
(zigoto)

PLURIPOTENTES
(ICM, ESC, EGC)

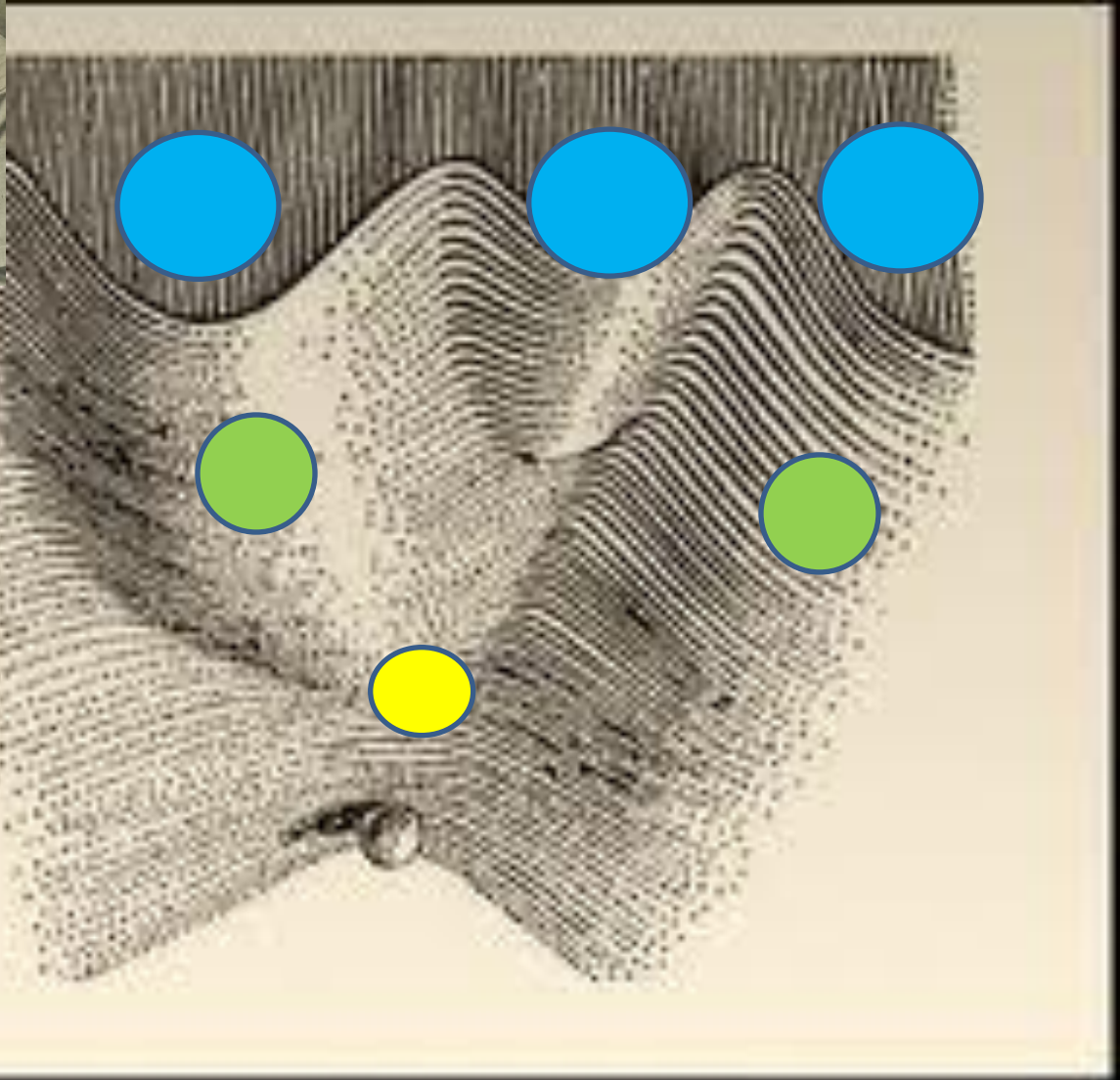
MULTIPOTENTES

UNIPOTENTES

Waddington's Epigenetic Landscape

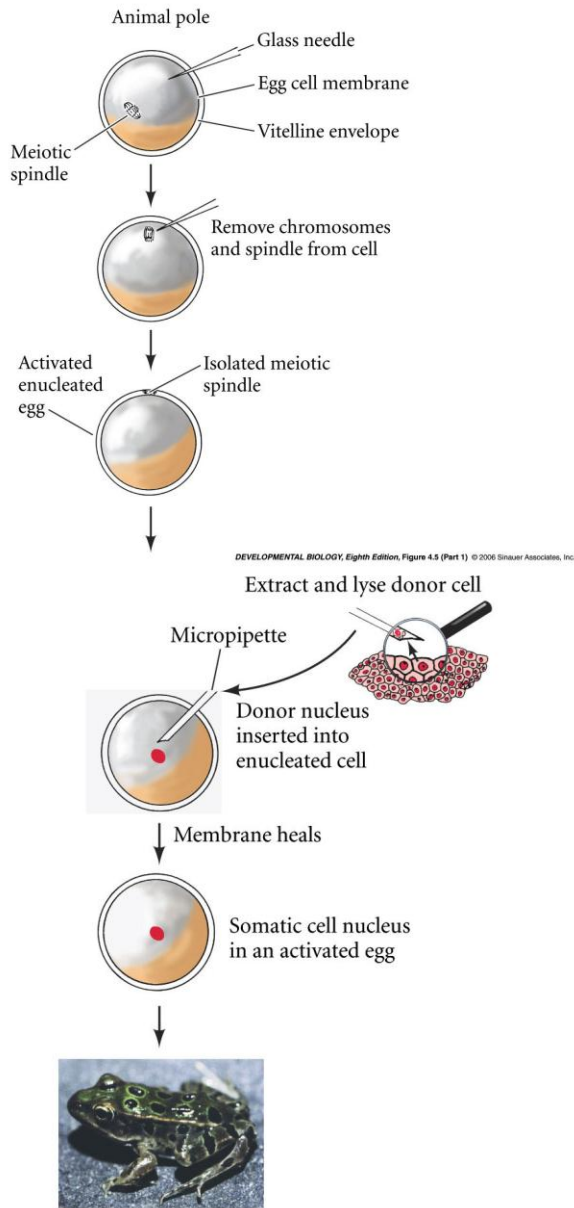


?



Waddington's Epigenetic Landscape

Reprogramação nuclear e clonagem

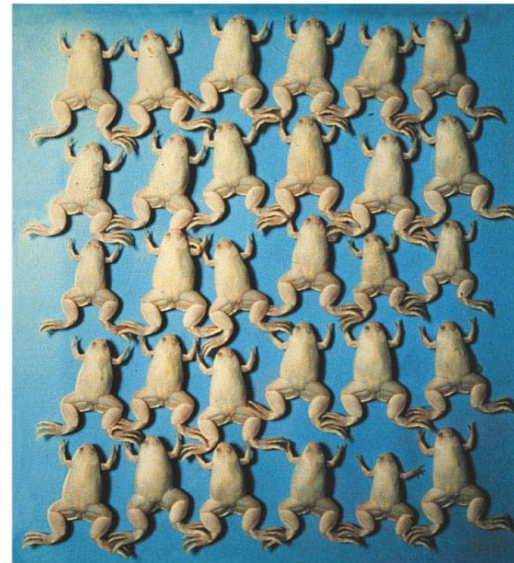


- Robert Briggs e Tomas King transplantam núcleos de **blastocistos** em ovos anucleados em *Rana pipiens* (1952)
- John Gurdon transplanta núcleo do epitélio intestinal de **girinos** em ovos de *Xenopus laevis* (1962)



Wild-type donor
of enucleated eggs

Albino parents
of nucleus donor



Cloned mammals, whose nuclei came from adult somatic cells (Part 1)

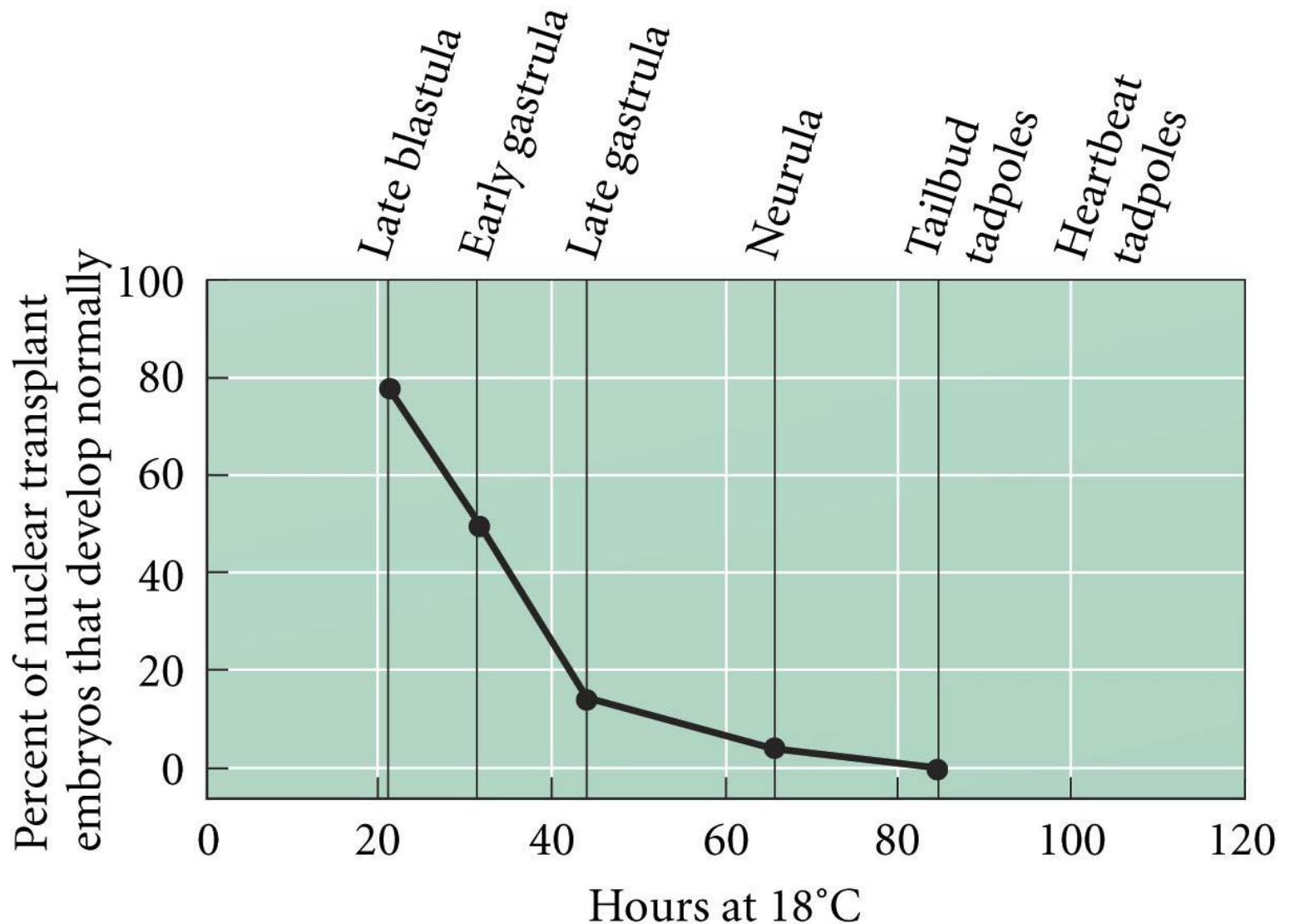
(A)

- Ian Wilmut clona Dolly a partir de células do **adulto** (g. mamárias) (1997)



Percentage of successful nuclear transplants as a function of the developmental age of the donor nucleus

Developmental stage from which nuclei were taken



Cell fate restriction: Is it all in the nucleus?

Developmental potential

Totipotent
Zygote

Pluripotent
ICM/ES cells, EG cells,
EC cells, mGS cells
iPS cells

Multipotent
Adult stem cells
(partially
reprogrammed cells?)

Unipotent
Differentiated cell
types

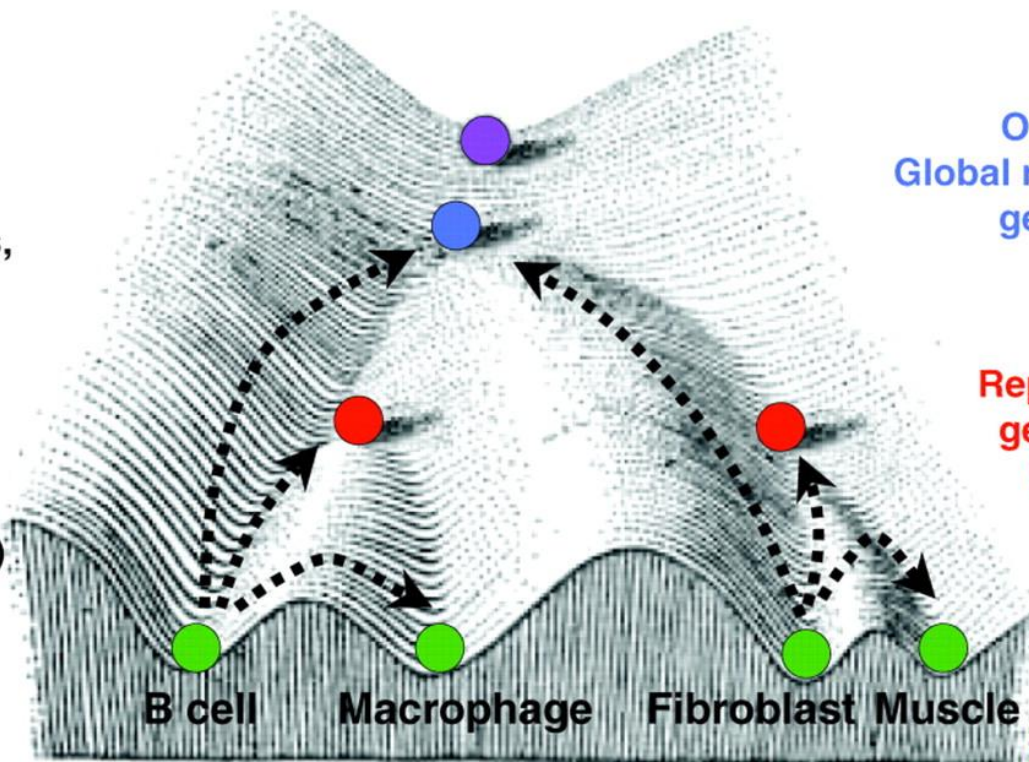
Epigenetic status

Global DNA demethylation

Only active X chromosomes;
Global repression of differentiation
genes by Polycomb proteins;
Promoter hypomethylation

X inactivation;
Repression of lineage-specific
genes by Polycomb proteins;
Promoter hypermethylation

X inactivation;
Derepression of
Polycomb silenced
lineage genes;
Promoter hypermethylation



Hochedlinger & Path, *Development* 2009

The kitten “CC” (A) is a clone produced using somatic nuclear transfer from “Rainbow” (B)

(A)



(B)



Developmental potential

Totipotent

Zygote

Pluripotent

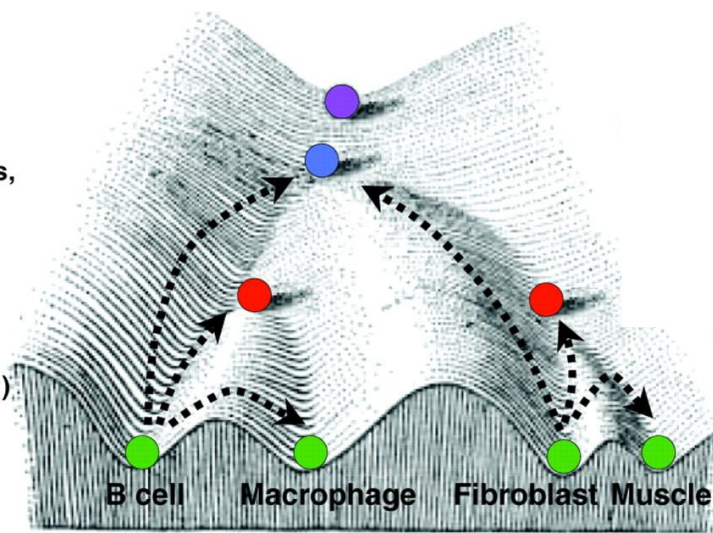
ICM/ES cells, EG cells,
EC cells, mGS cells
iPS cells

Multipotent

Adult stem cells
(partially
reprogrammed cells?)

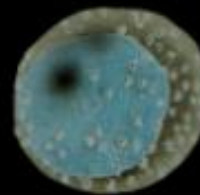
Unipotent

Differentiated cell
types



PROGENITOR CELL

(e.g., myeloid
progenitor cell)



SPECIALIZED CELL

(e.g., neutrophil)



SPECIALIZED CELL

(e.g., red blood cell)



STEM CELL

(e.g., hematopoietic
stem cell)

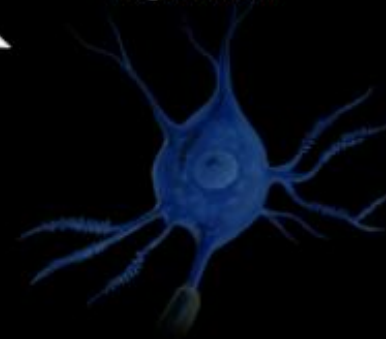


STEM CELL



SPECIALIZED CELL

(e.g., neuron)



CÉLULAS TRONCO

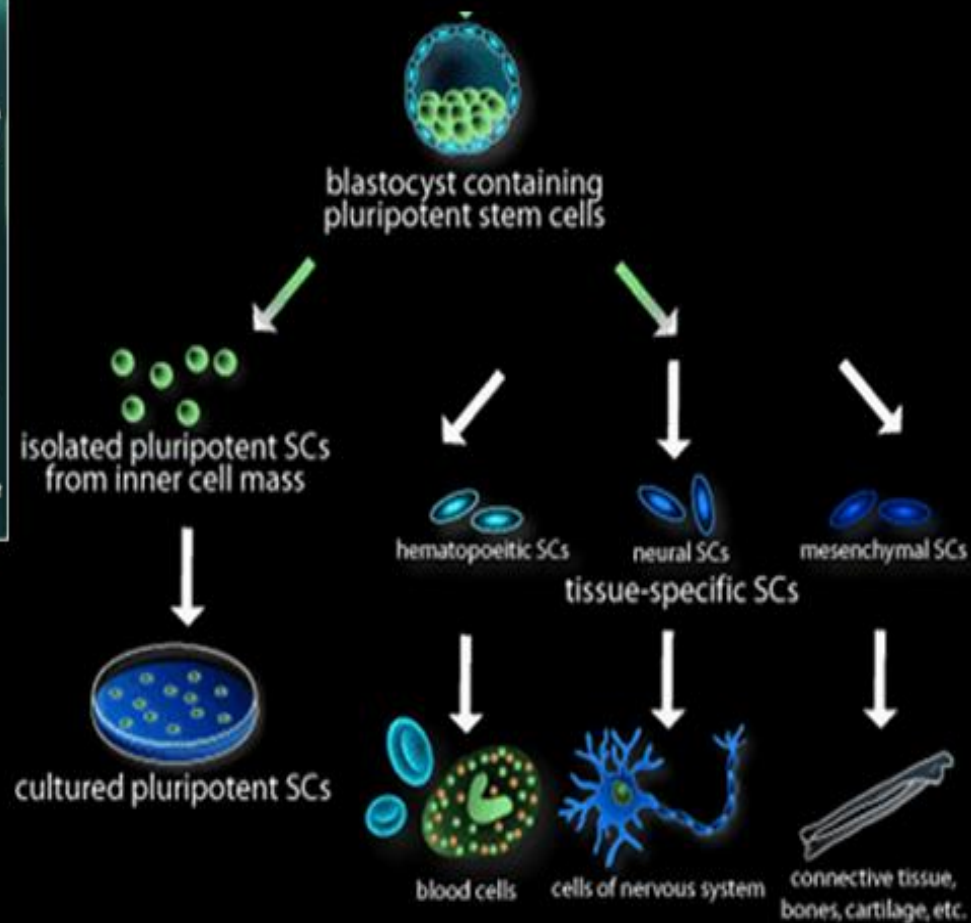
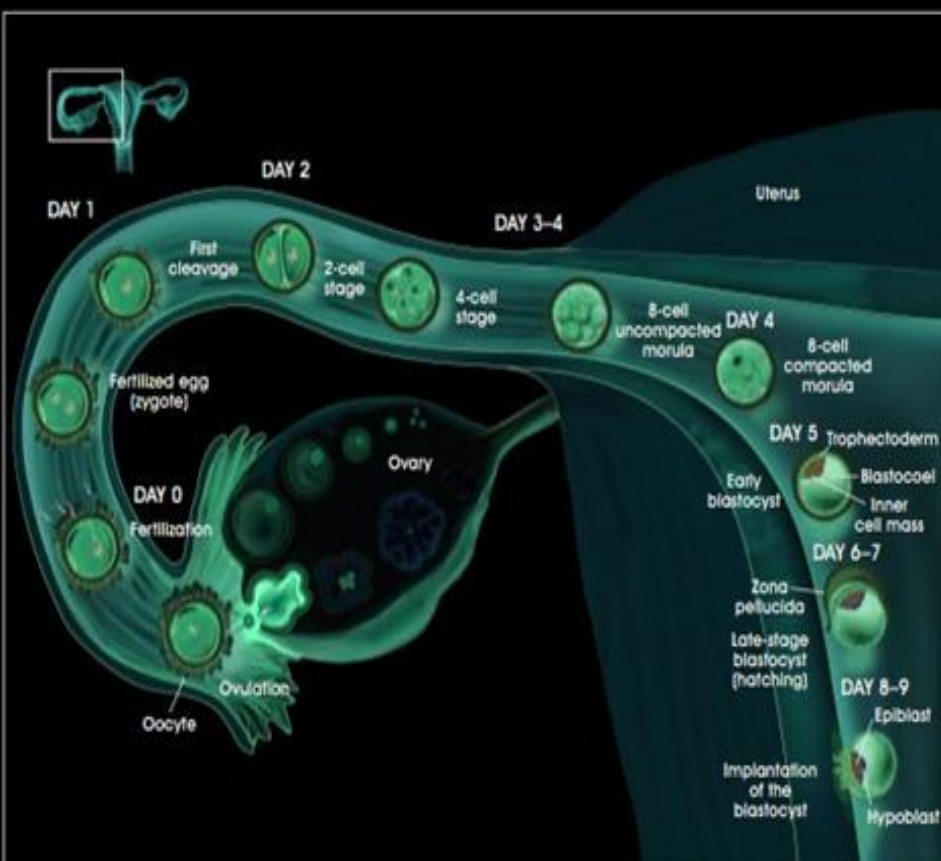
Definição:

Células indiferenciadas que tem a capacidade de se auto-renovar por divisão celular e podem se especializar em diferentes tipos de células

Dentro de certas condições experimentais ou fisiológicas, podem ser induzidas a se converterem em células de tecidos ou órgãos específicos com funções especiais .

TIPOS DE CÉLULAS TRONCO

- 1. Células tronco embrionárias (ESC)**—Células primitivas indiferenciadas, derivadas da massa celular interna do blastocisto (um embrião? de 5-6 dias).
 - São capazes de se renovar indefinidamente por um longo período de tempo sem se diferenciar.
 - Capacidade de se diferenciar em células e tecidos das 3 camadas germinativas do embrião (ectoderme, mesoderme e endoderme).

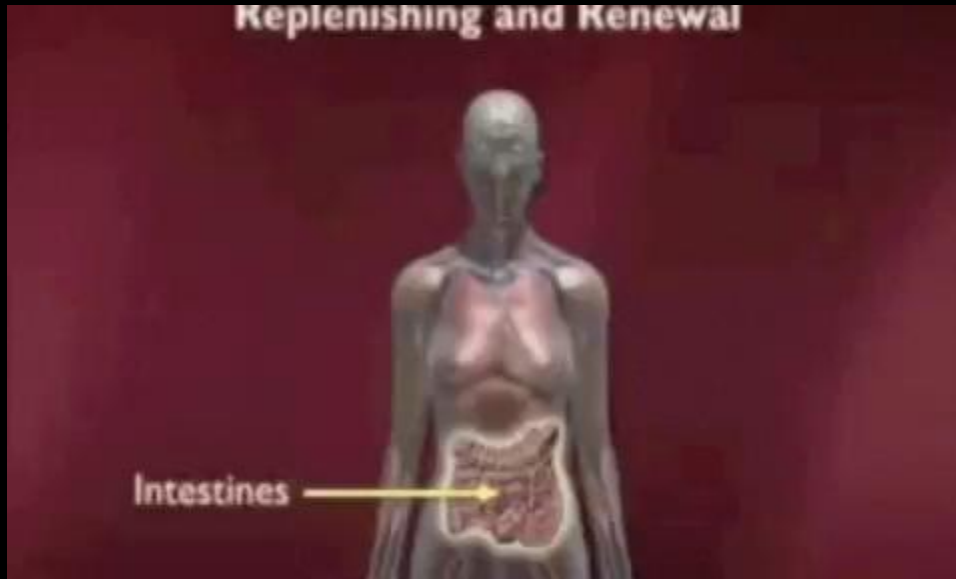


TIPOS DE CÉLULAS TRONCO

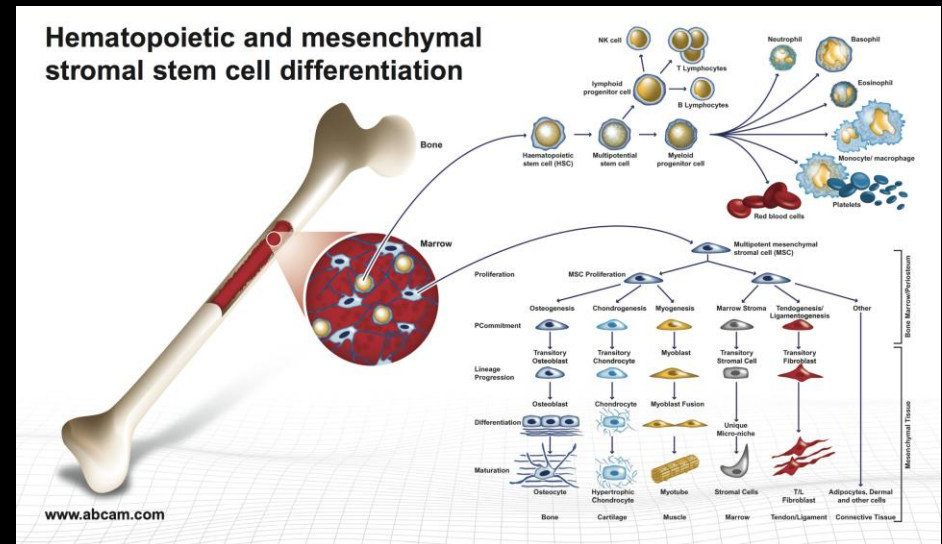
2. Células tronco adultas, somáticas ou não embrionárias (ASC)— Células indiferenciadas, relativamente raras, que se encontram em muitos órgãos e tecidos diferenciados.

- Tem capacidades limitadas de auto-renovação e diferenciação.
- Normalmente limitadas ao tipo de células do órgão de origem para manter e reparar qualquer dano.
- Não se conhece exatamente sua origem.

Células tronco em humanos: substituição de tecido



HHMI Stem Cell Series



Células tronco em humanos: regeneração de estruturas

Trapped Fingers and Amputated Finger Tips in Children

By Cynthia M. Illingworth

Journal of Pediatric Surgery, Vol. 9, No. 6 (December), 1974

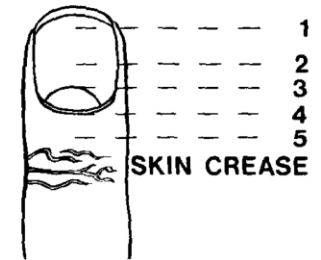


Fig. 5. Grading of level of tissue loss.

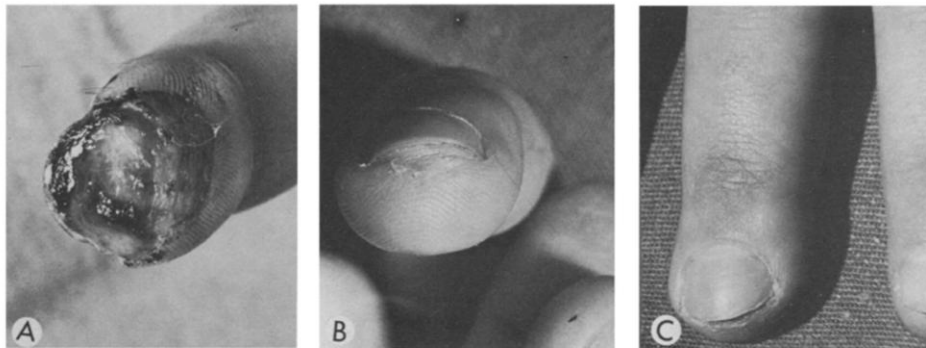


Fig. 2. (A) Amputation of finger tip in 5-yr-old girl. (B), (C) Twelve weeks after accident.

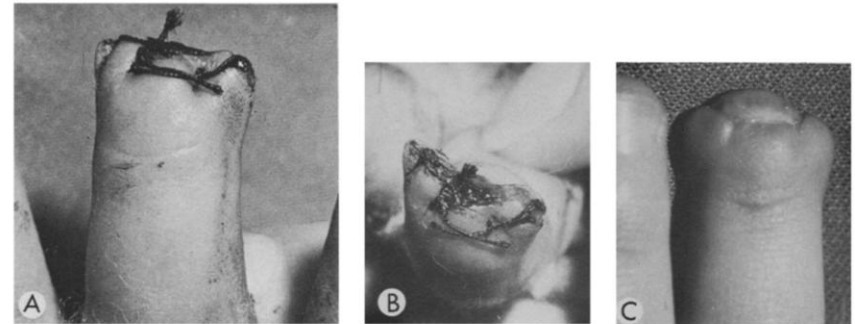


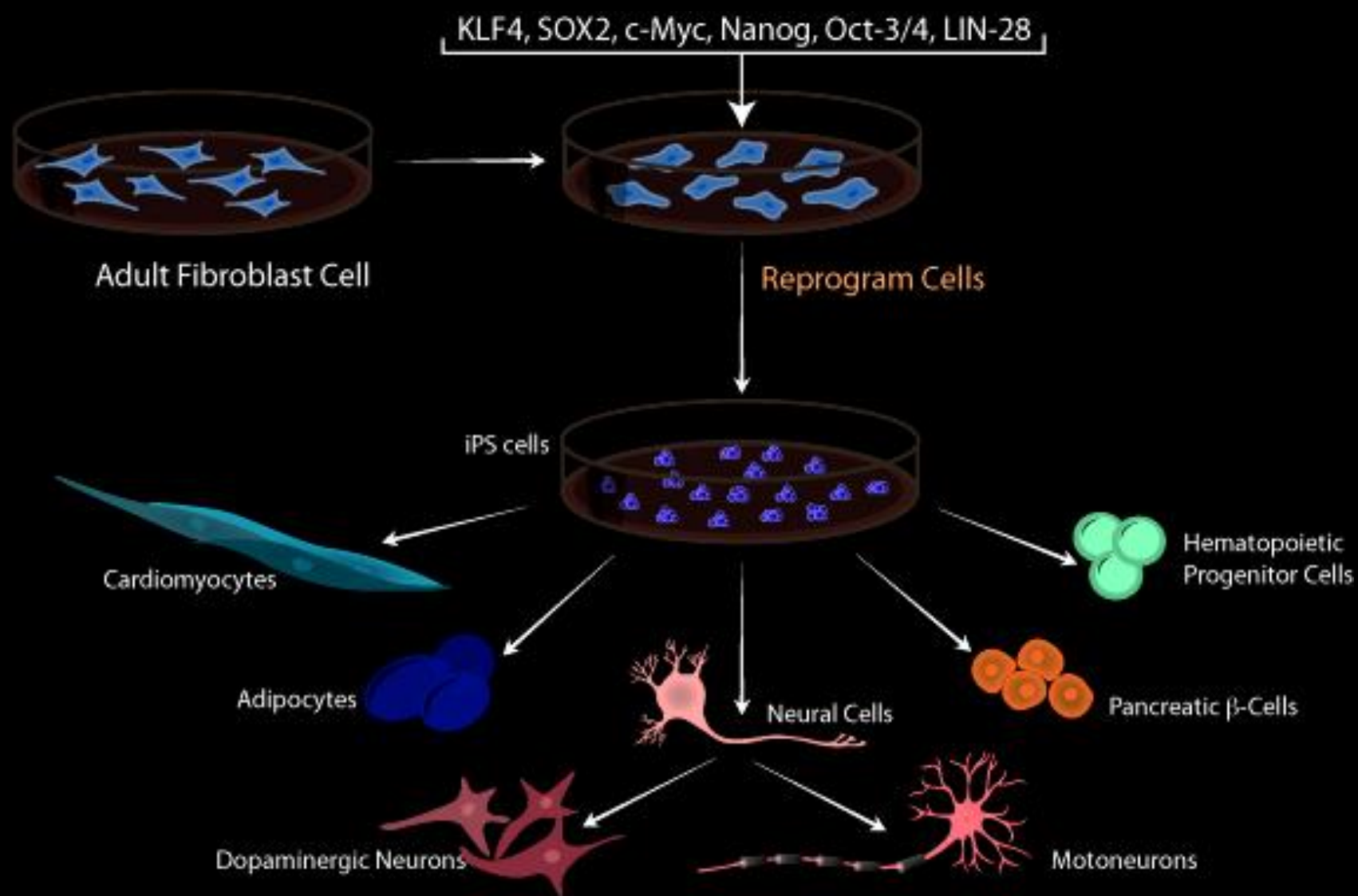
Fig. 4. (A and B) Guillotine amputation of finger tip treated surgically in girl of 3-yr. (C) Four months after accident.

TIPOS DE CÉLULAS TRONCO

3. Células tronco pluripotentes inducidas (iPSC) — células adultas especializadas, reprogramadas genéticamente (introducción de genes embrionarios) para asumir un estado indiferenciado de célula tronco

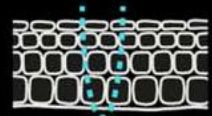
S. Yamanaka generan iPSCs en 2006 en ratón



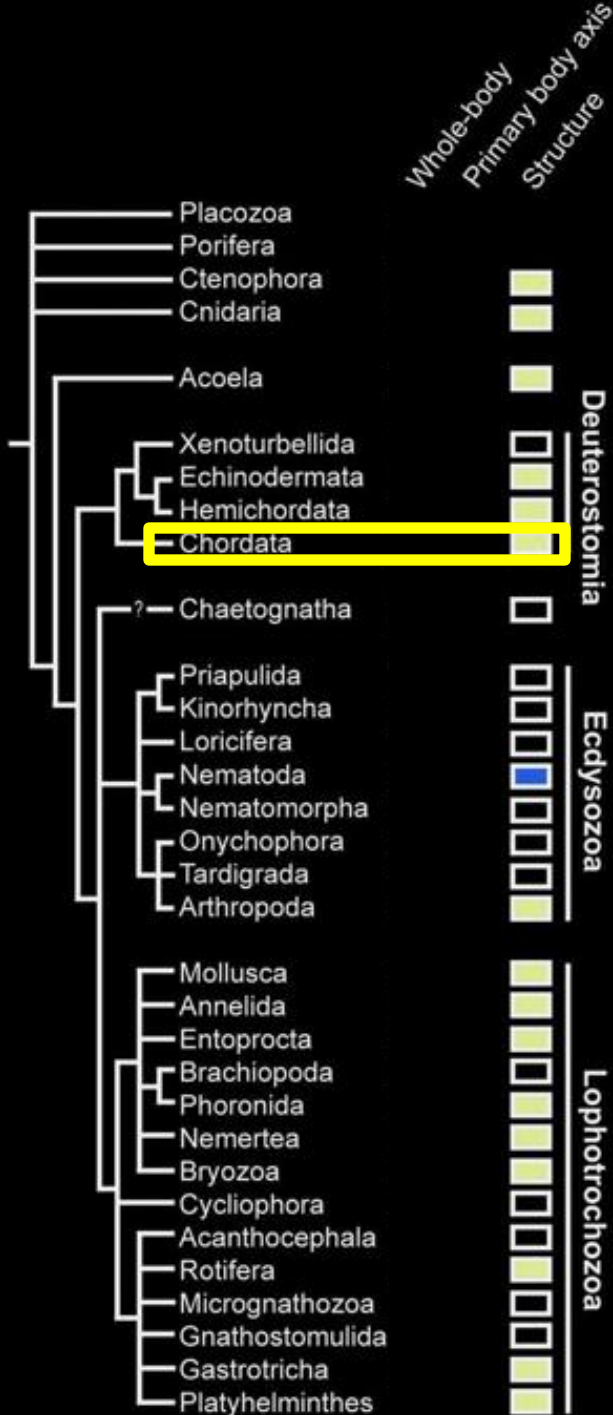


REGENERAÇÃO EM ANIMAIS

- Regeneração em diferentes níveis de organização biológica

Regeneration	Biological level	Examples	Pre-amputation	Post-amputation	Regenerate
	Whole body	Regeneration from a small body fragment			
	Structure	Limb, fin, tail, head, tentacle, siphon, arm, stalk			
	Internal organ	Heart, liver, lens			
	Tissue	Epidermis, gut lining			
	Cell	Axon, muscle fiber			

REGENERATION IN ANIMALS



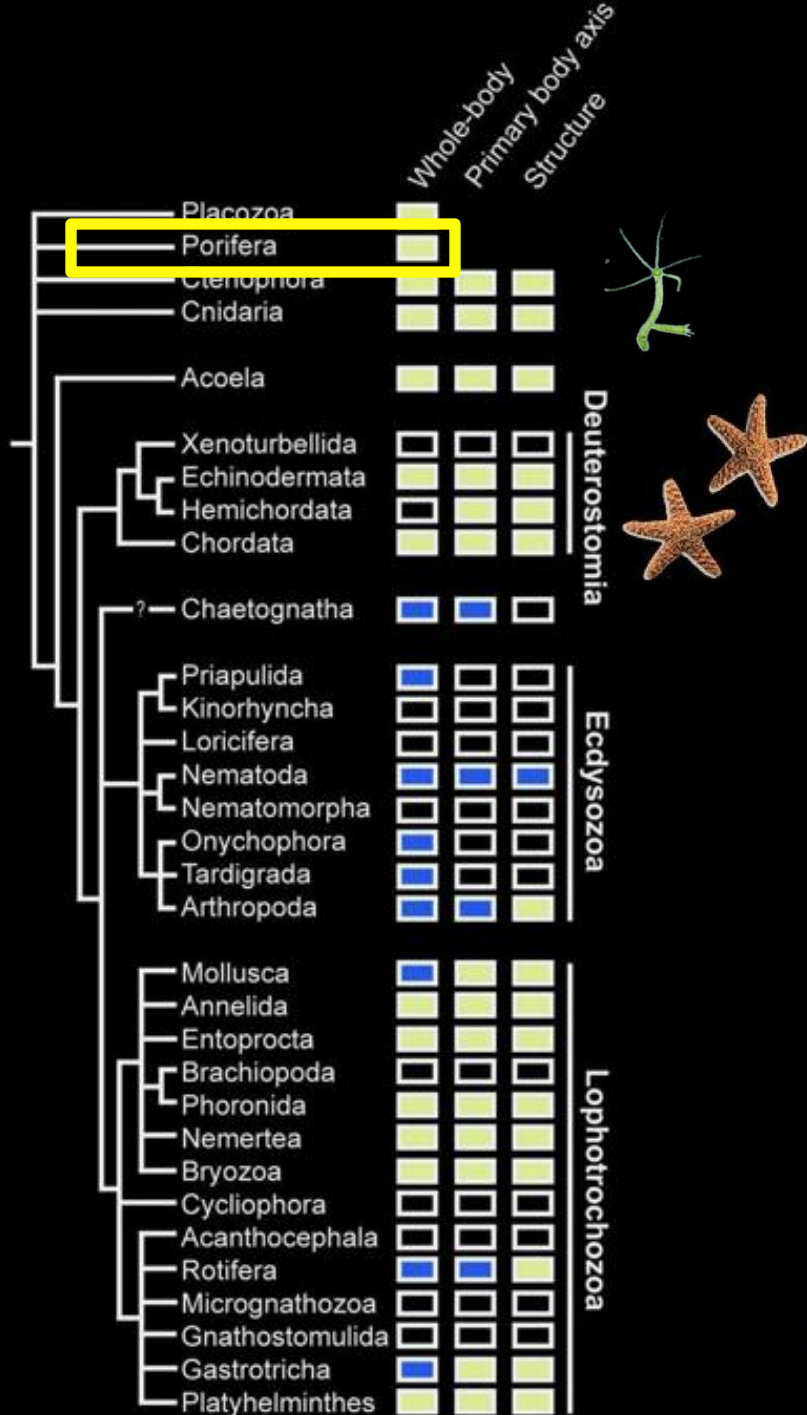
Structure regeneration on other vertebrates:

Salamander limbs

Zebrafish Heart

Yellow Presence of regeneration
 Blue Absence of regeneration
 White No documentation

REGENERATION IN ANIMALS



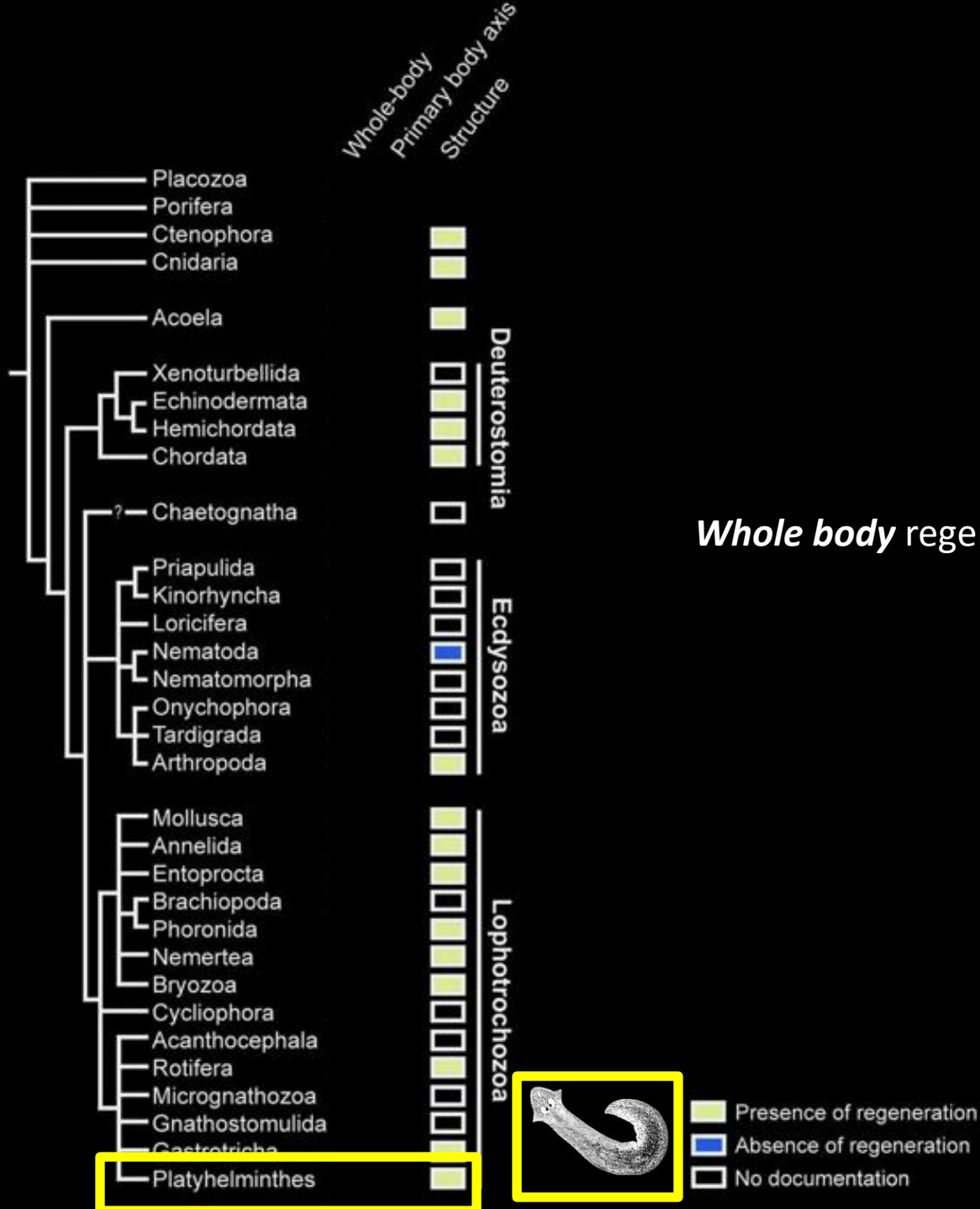
Whole-body regeneration in early animals:



Bernie Degnan (U. Queensland)
BBC's First Life Documentary

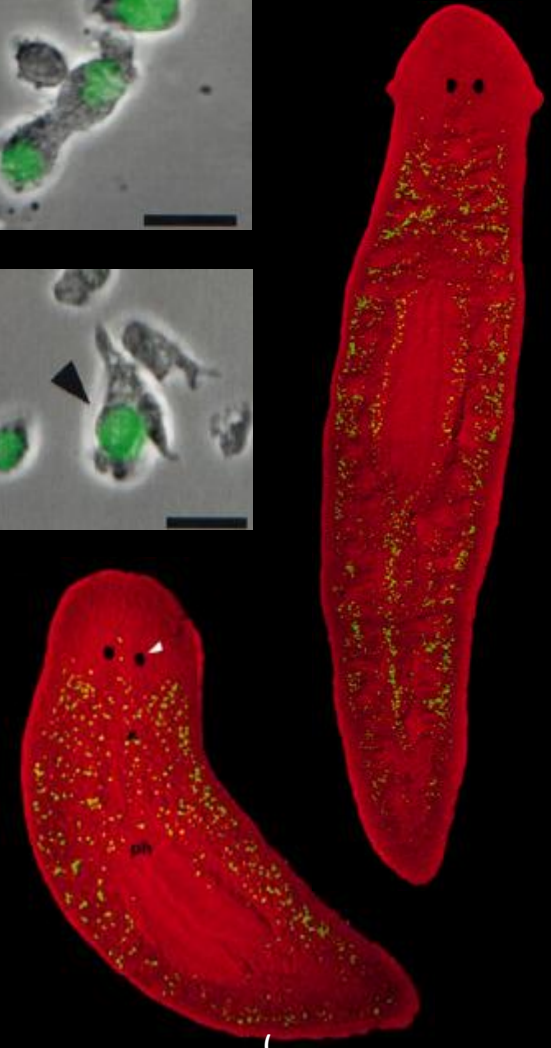
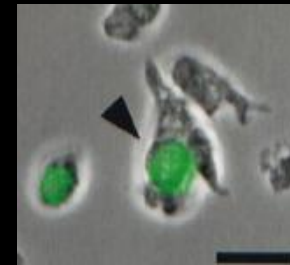
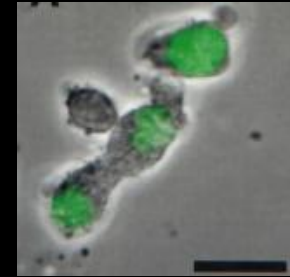
■ Presence of regeneration
■ Absence of regeneration
□ No documentation

REGENERATION IN ANIMALS



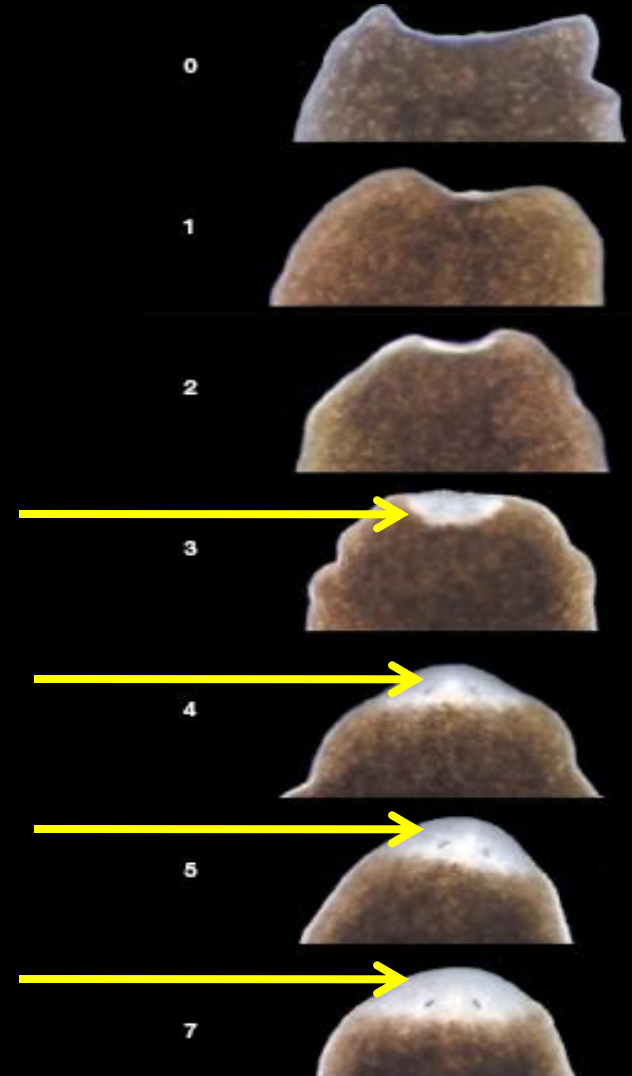
REGENERAÇÃO EM PLANÁRIAS

- Organismos morfológicamente simples
- Altos poderes de regeneração
- Fácil de manipular e cultivar em condições de laboratório
- Reprodução sexual e assexual
- Genoma pequeno (4.8×10^8 pb)
- Permitem manipulação molecular
- Presença de “Neoblastos”



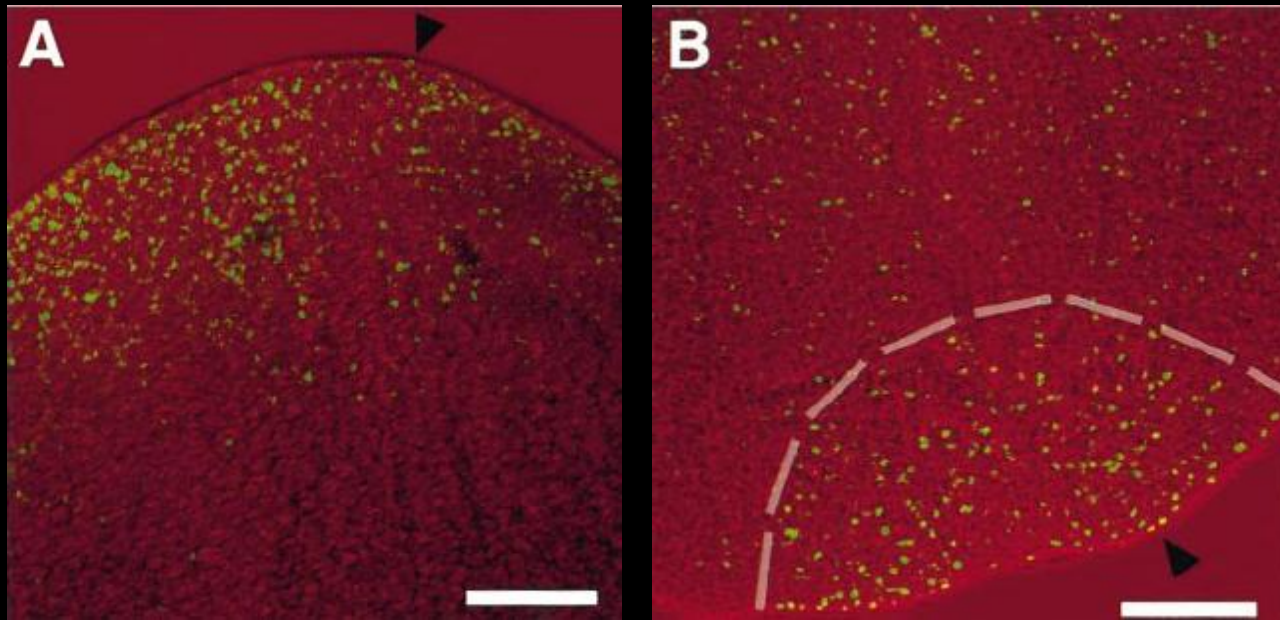
INTRODUCCIÓN

- **BLASTEMA:** Massa de células indiferenciadas e proliferantes que darão lugar a todos os tecidos da estrutura que vai se regenerar. Tecido não pigmentado formado debaixo do epitélio que cobre a ferida.

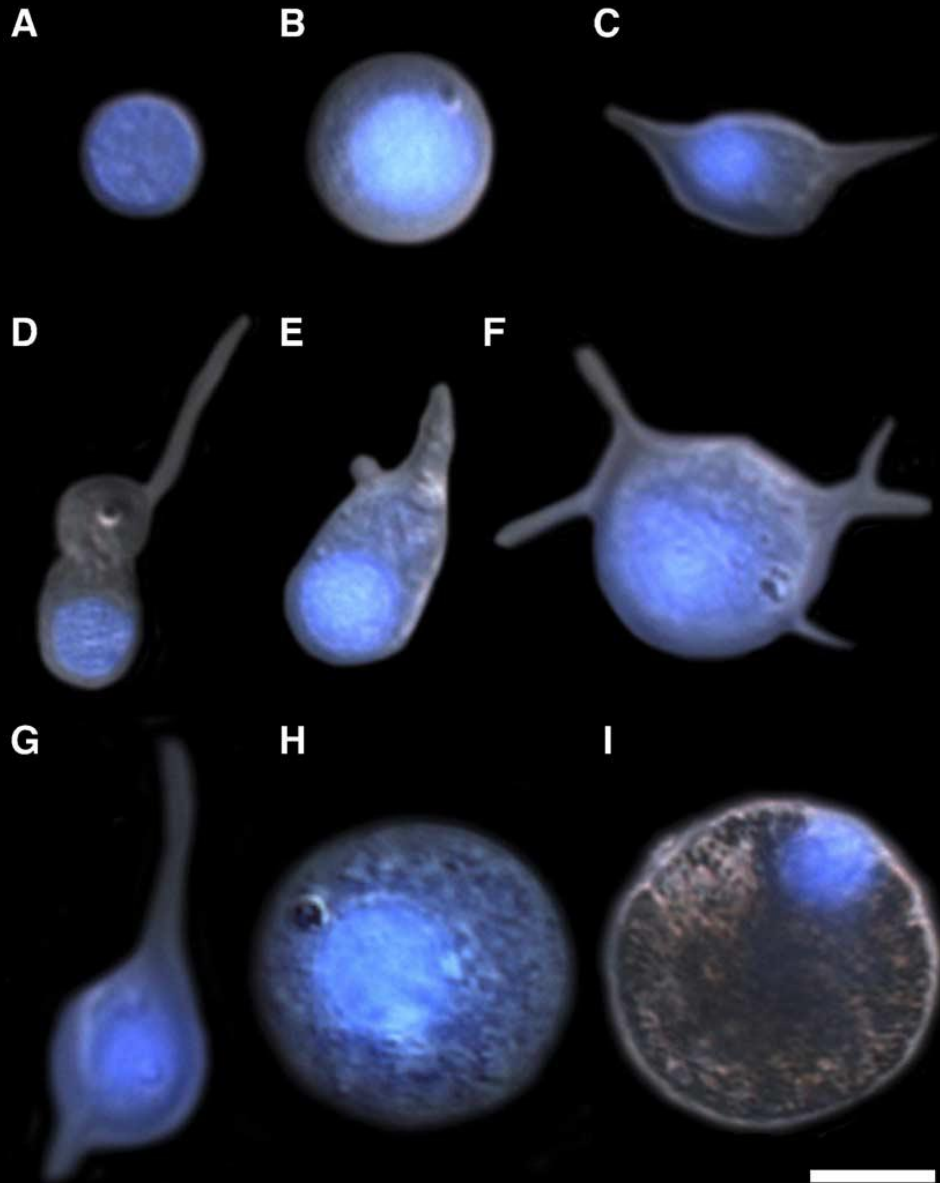


REGENERAÇÃO EM PLANÁRIAS

1. Localização dos neoblastos



REGENERAÇÃO EM PLANÁRIAS



**NEOBLASTOS =
CÉLULAS TRONCO**

Comparação de capacidades regenerativas dos platelmintos

		<u>Regeneração:</u>	<u>Vida:</u>
Turbellaria	"Archioophora"	Catenulida	excelente t (terrestre)
	1.2	Macrostomorpha	excelente m (marinha)>t
	3	Polycladida	bom m
	4	Lecithoepitheliata	bom t>m
	5.6	Proseriata	bom t & m
	9	Bothrioplanida	bom m
	8	Rhabdocoela	ruim t>>p (parasitario)
	7	Fecampiida	desconhecido p
		Prolecithophora	bom t=m
	8.9	Tricladida	excelente t>m
Neophora		Neodermata	bom p

*Collins et al.
nature 2013

Mari

Egger 2012

COMUNICADOS

Próxima semana: ESPERMOGRAMA

- Doadores anônimos
- Trazer máscara, jaleco, luvas
- Trazer questão/pesquisa preenchidas

(WikiEdit do estudante do ano passado, ler até coleta)
(<https://pt.wikipedia.org/wiki/Espermograma>)