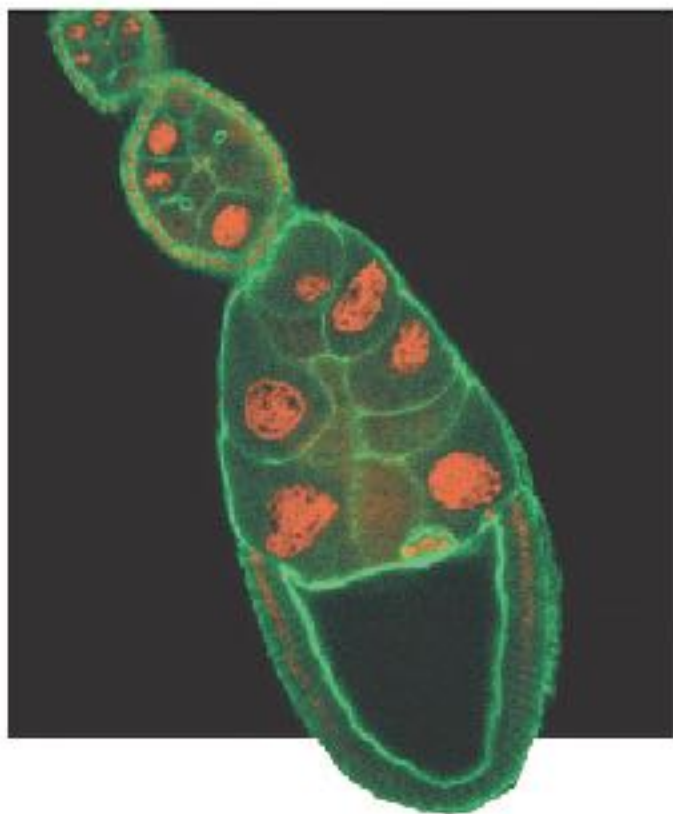


A linhagem germinativa é uma linhagem celular ainda enigmática e pouco estudada que contém células de grande importância para a herança genética. Ela apresenta caracteres morfológicos distintivos.



A linhagem germinativa (ovócito e células nodrizas do ovariolo) de *Drosophila*

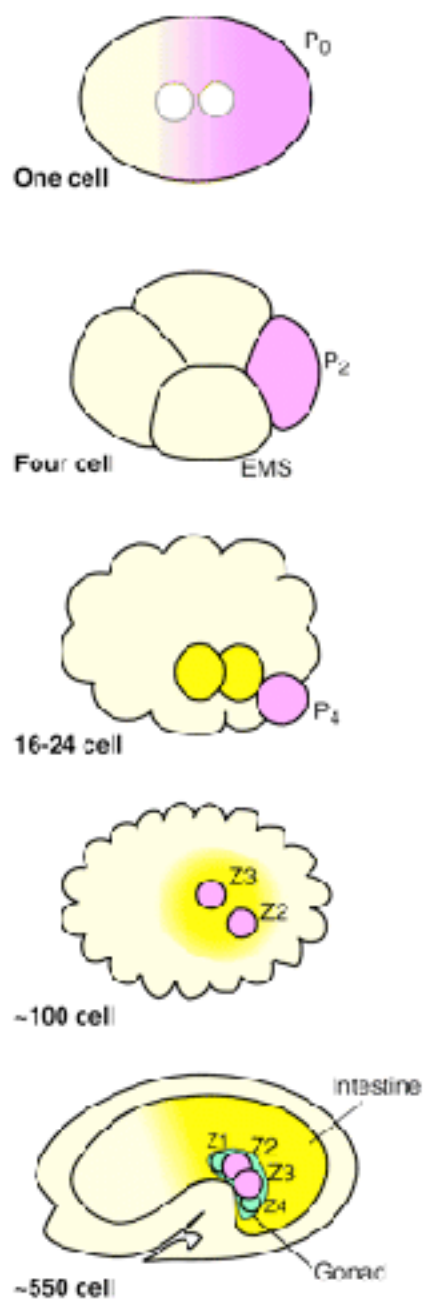


PGCs da crista gonadal da tartaruga *Sternoterus odoratus*

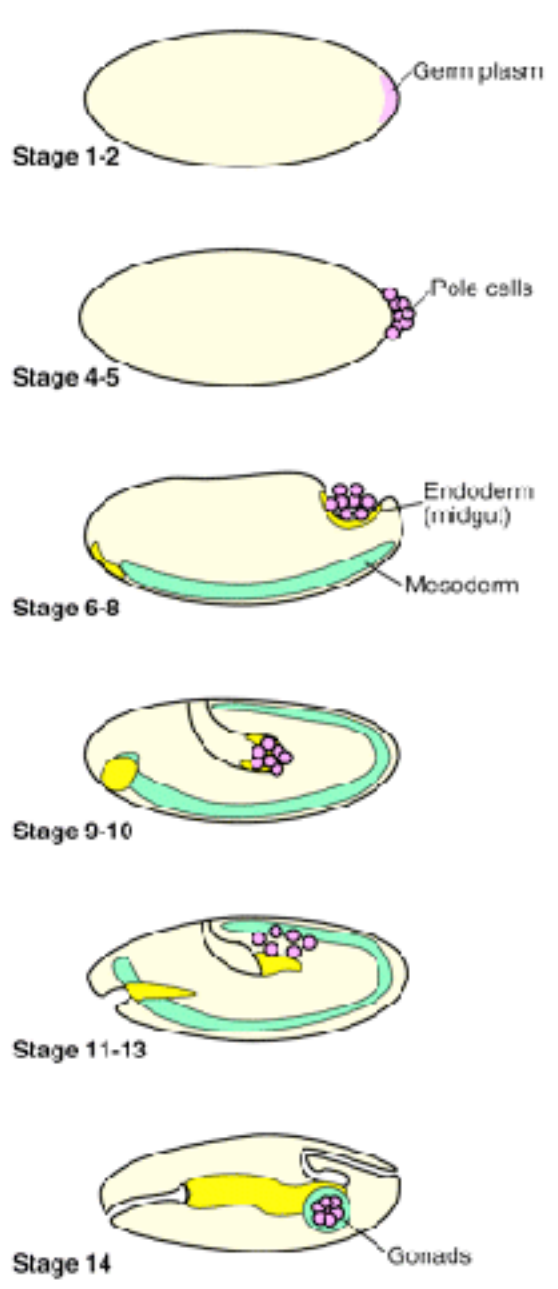
(Extavour, 2003)

Formas de determinação das células germinativas em modelos animais

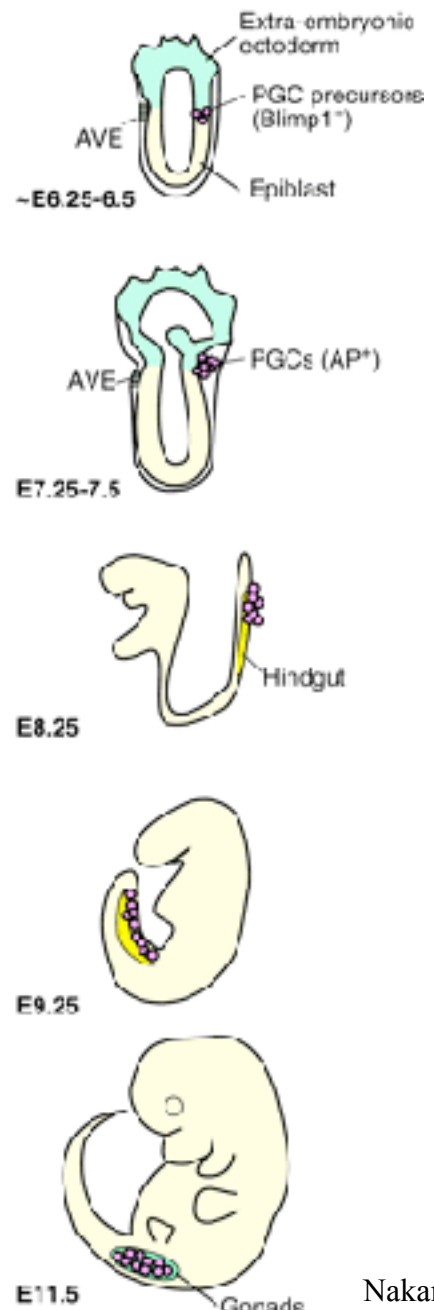
A *C. elegans*

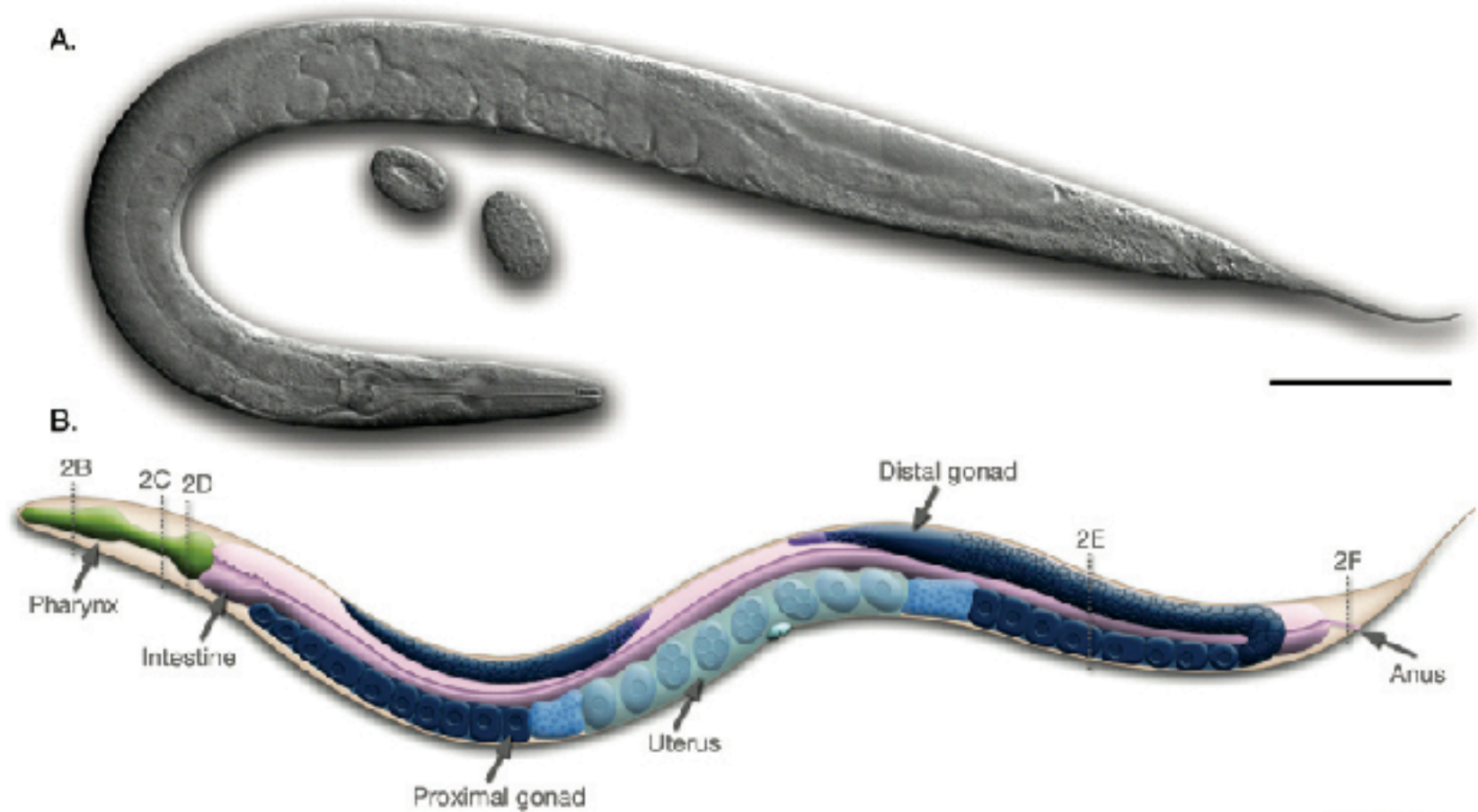


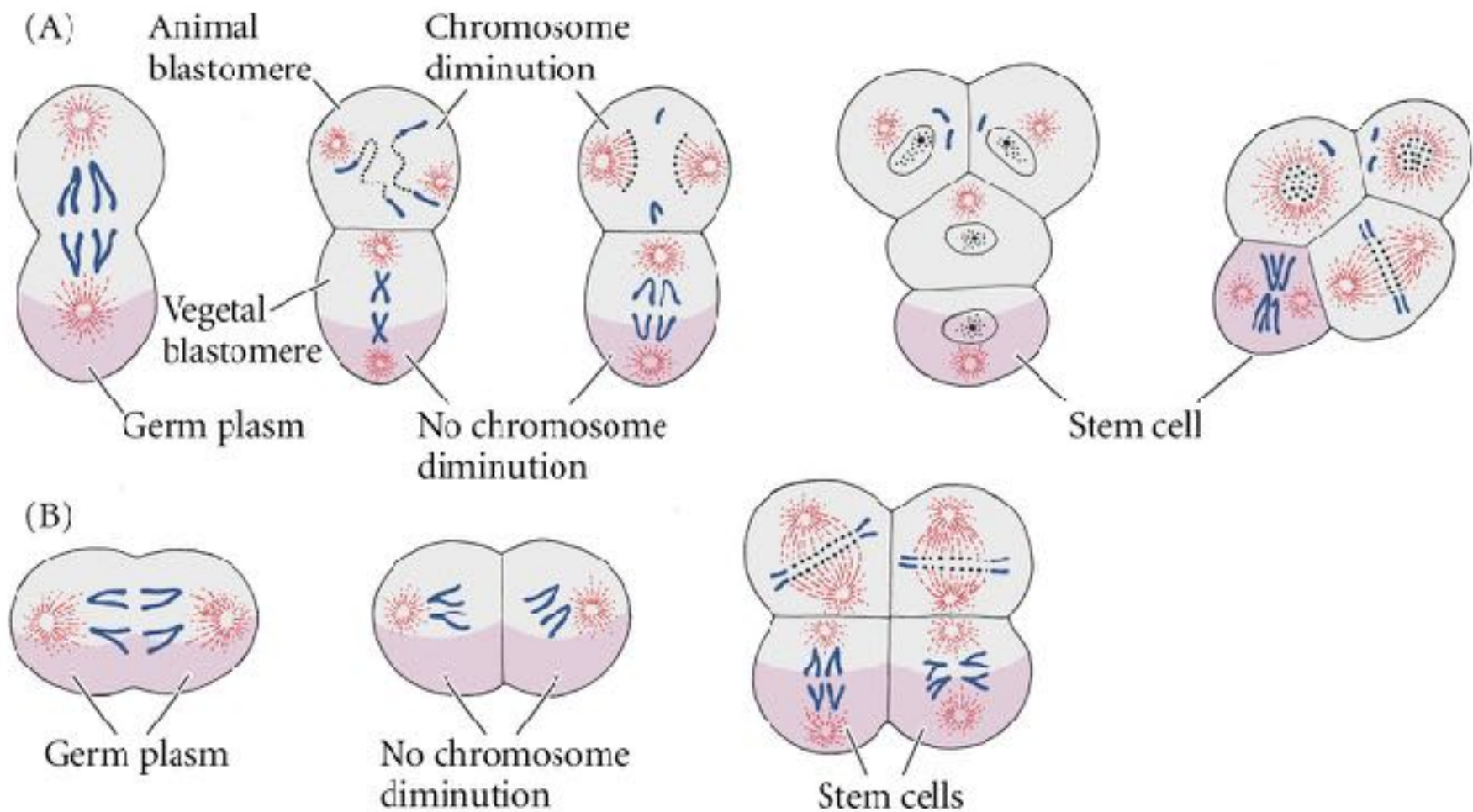
B *Drosophila*



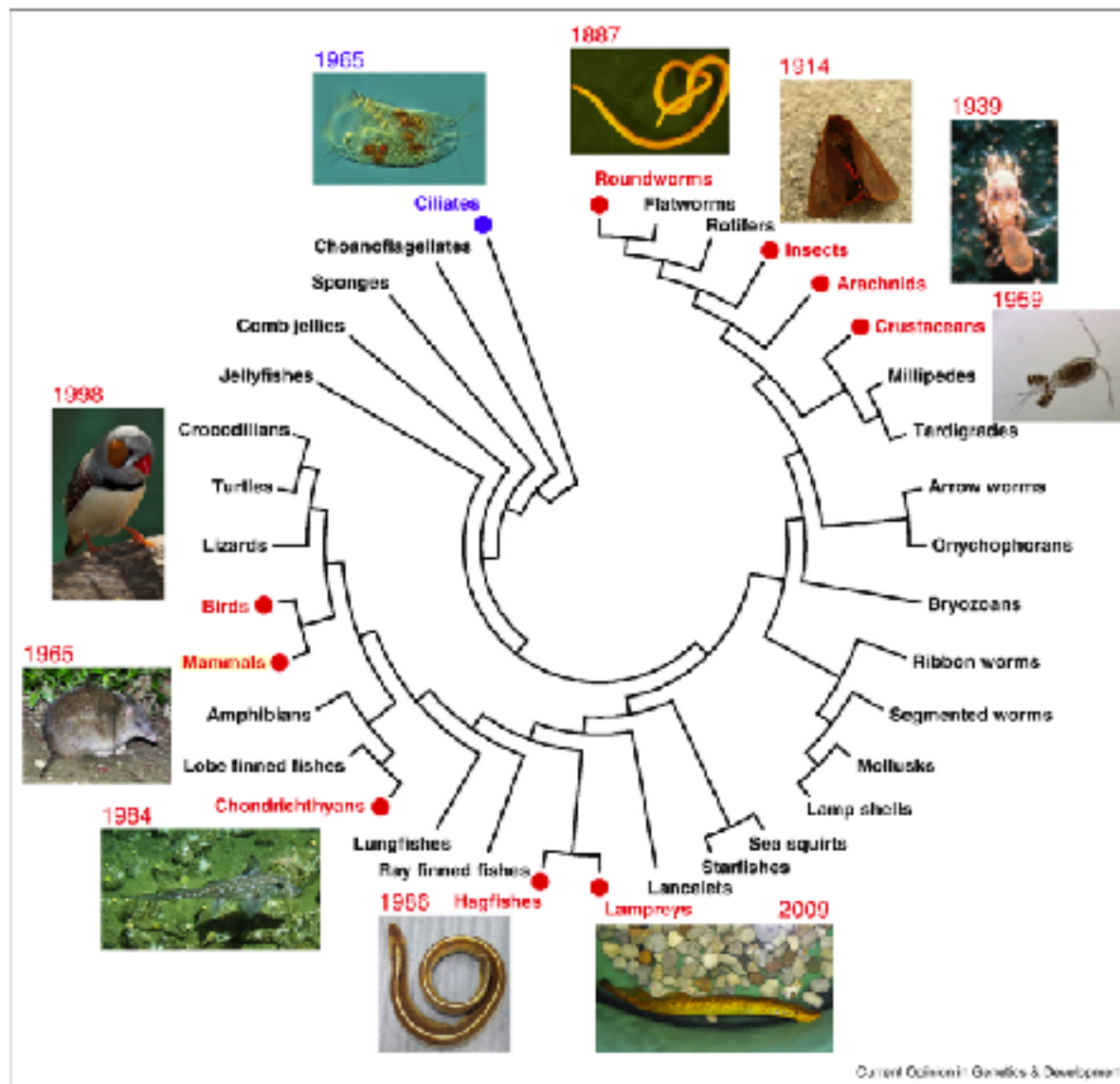
C Mouse



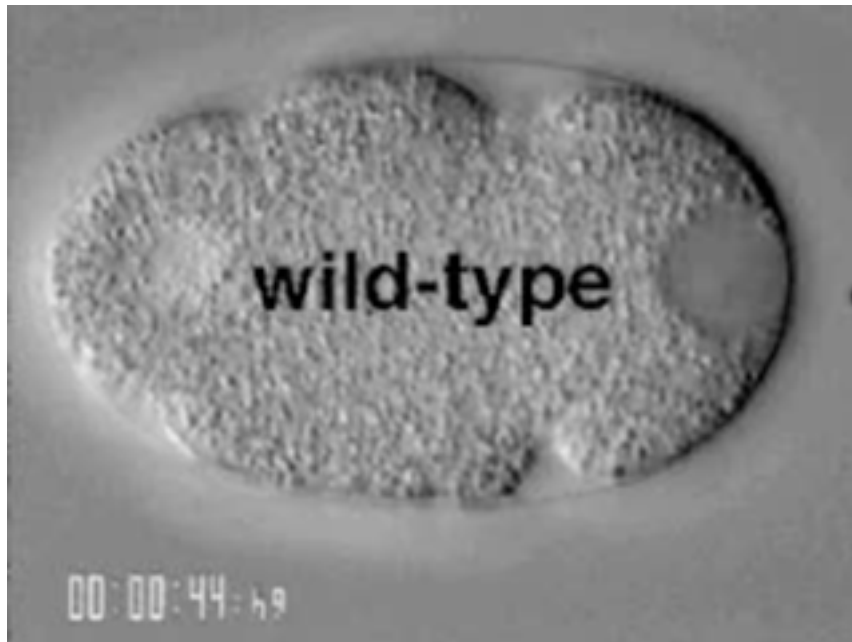




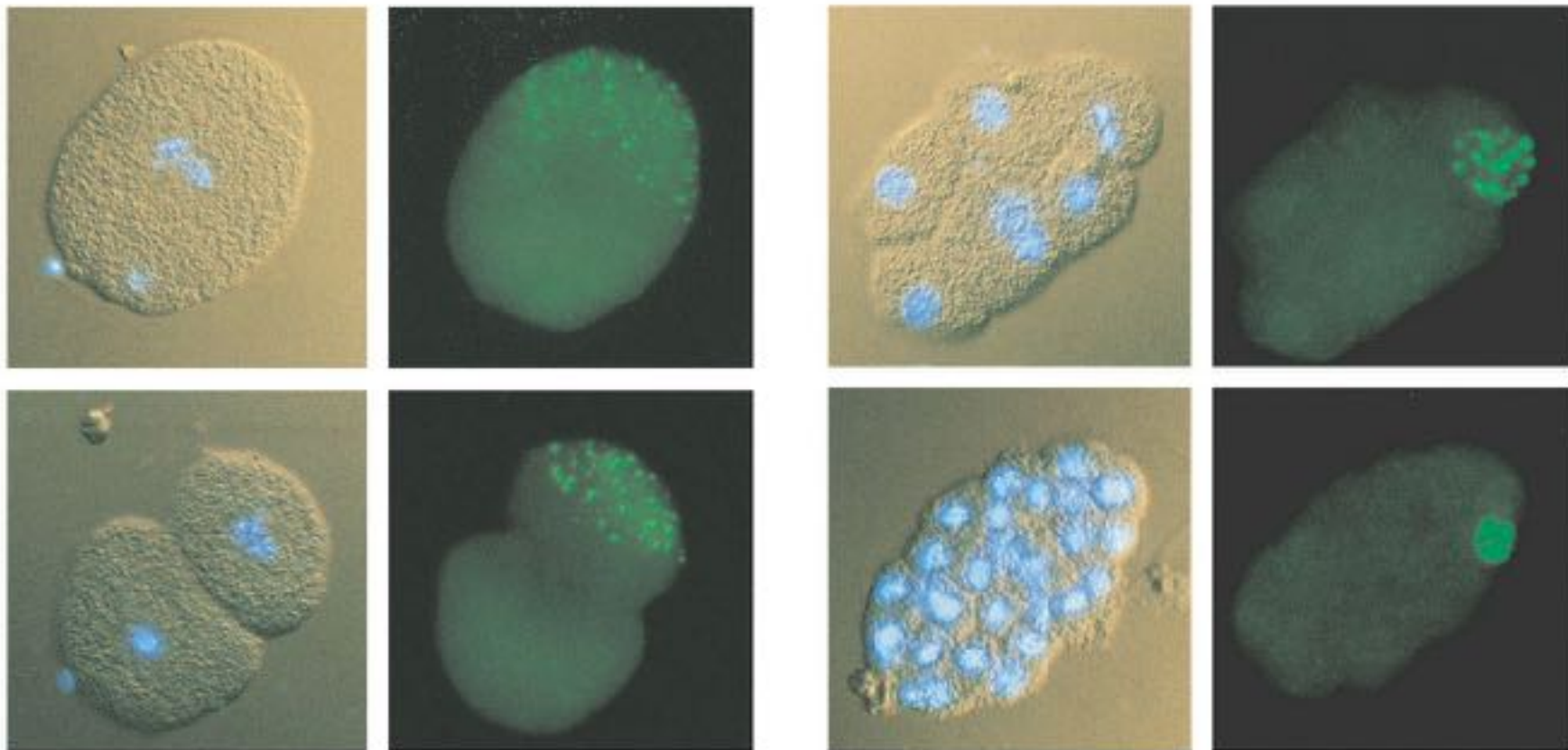
Nem todos os nematóides sofrem redução cromossômica!

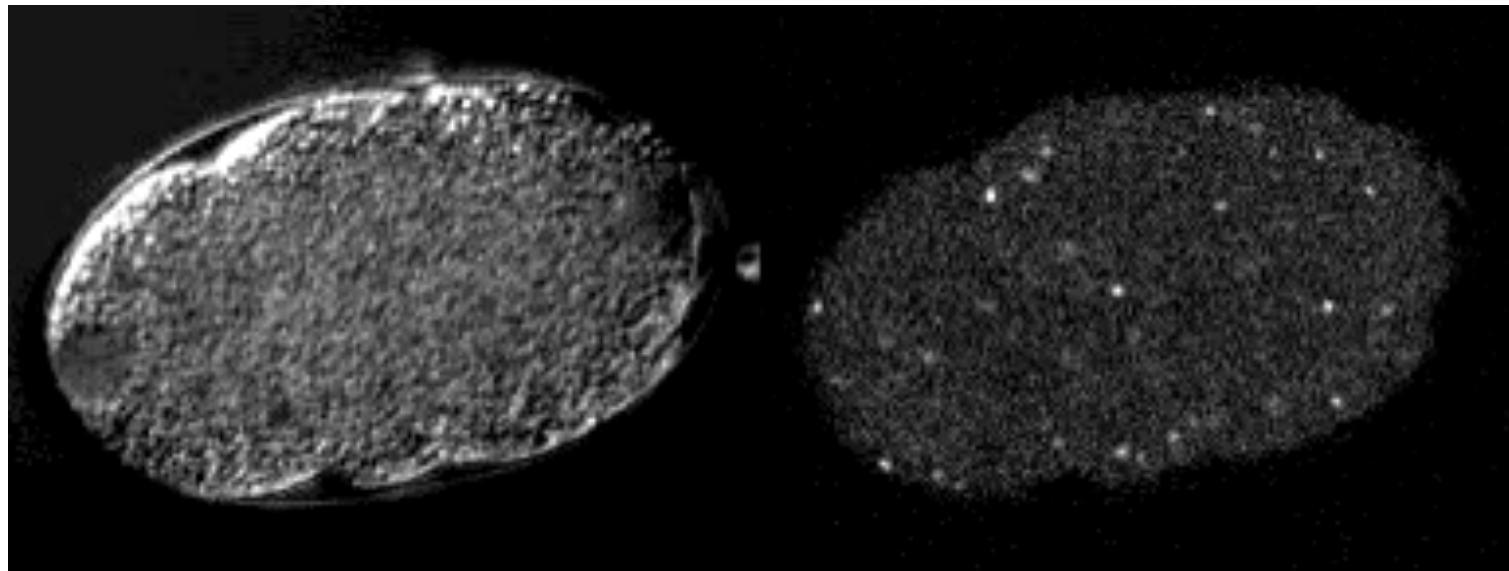


“A eliminação de ADN em alguns organismos parece ser uma forma novedosa de silenciamento gênico, compensação de dosagem, e determinação de sexo”

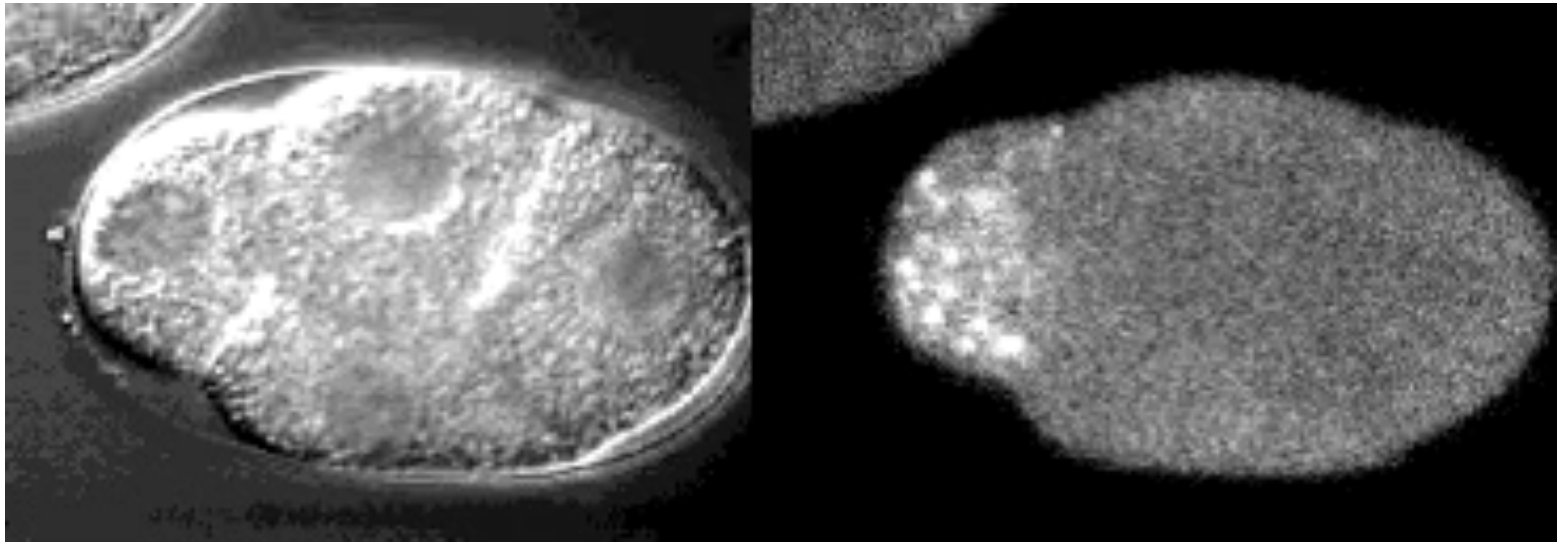


Segregação dos grânulos P na linhagem germinativa de *C. elegans*

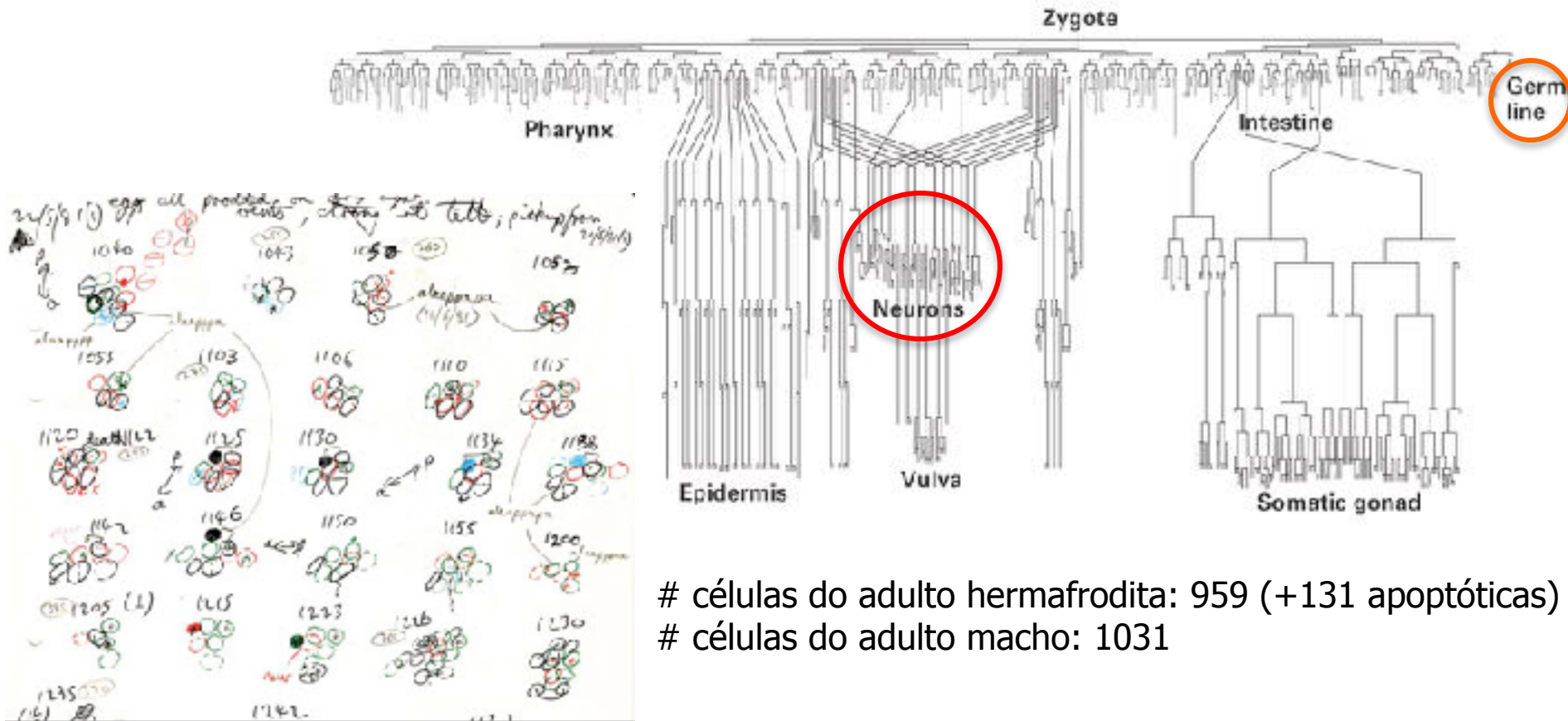




Milestone 18 (1988):
An unequal divide

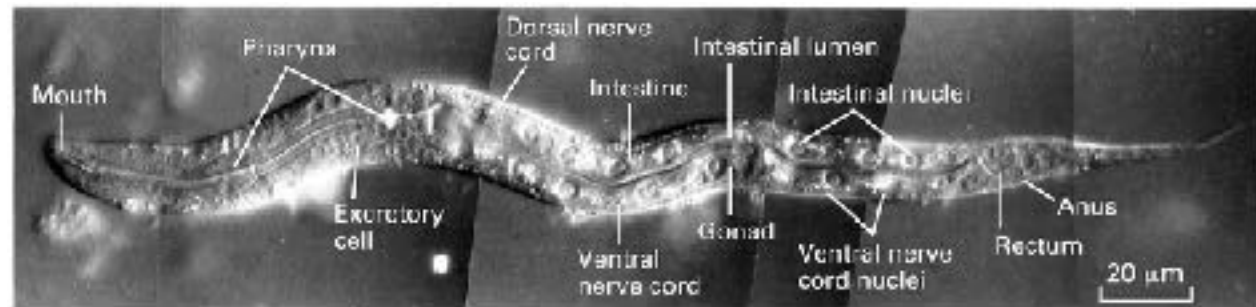


A linhagem germinativa é determinada muito cedo no desenvolvimento de *C. elegans*



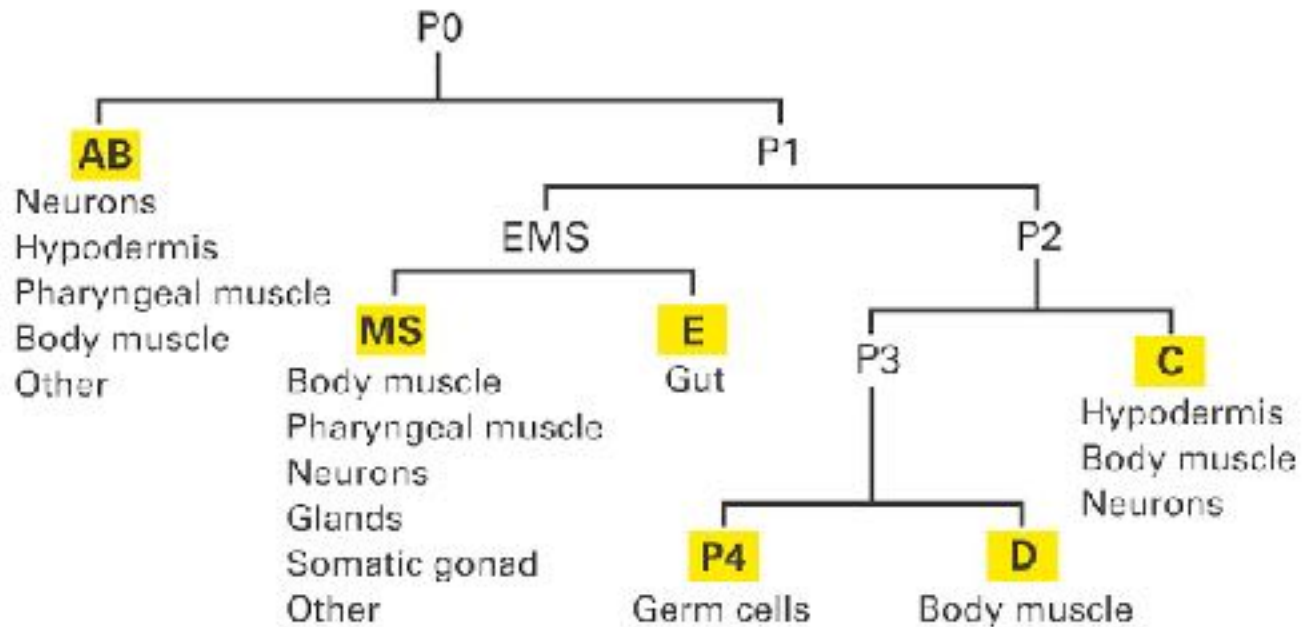
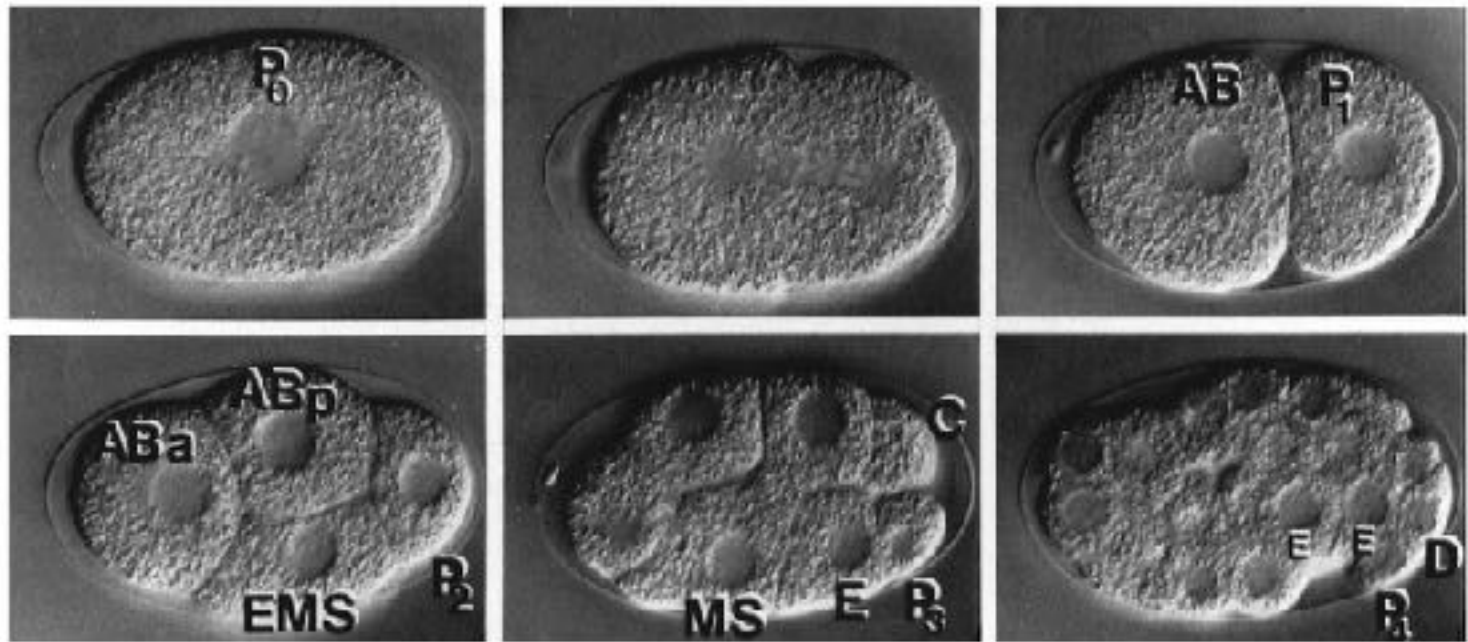
John Sulston

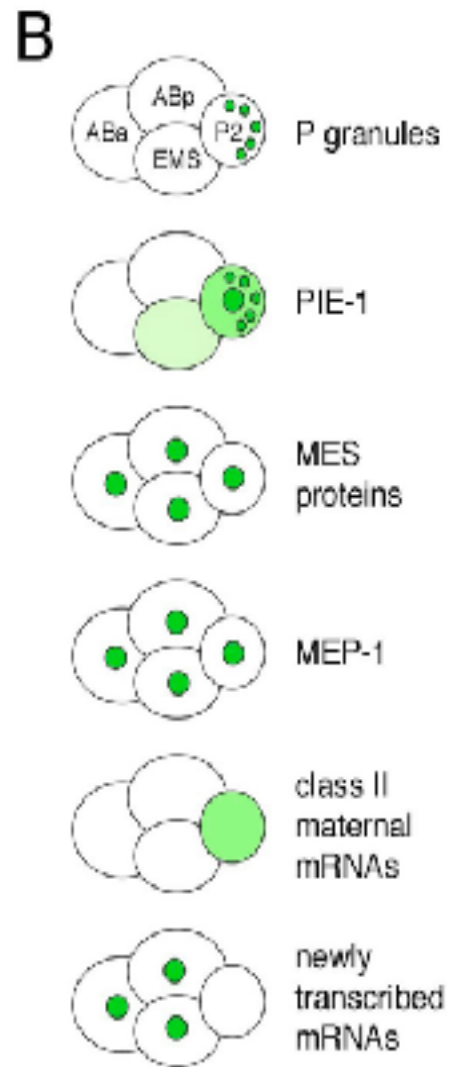
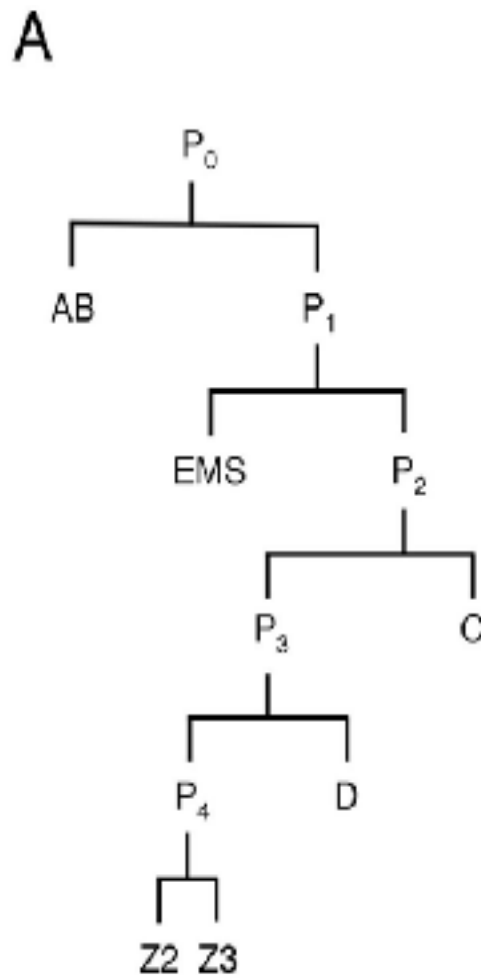
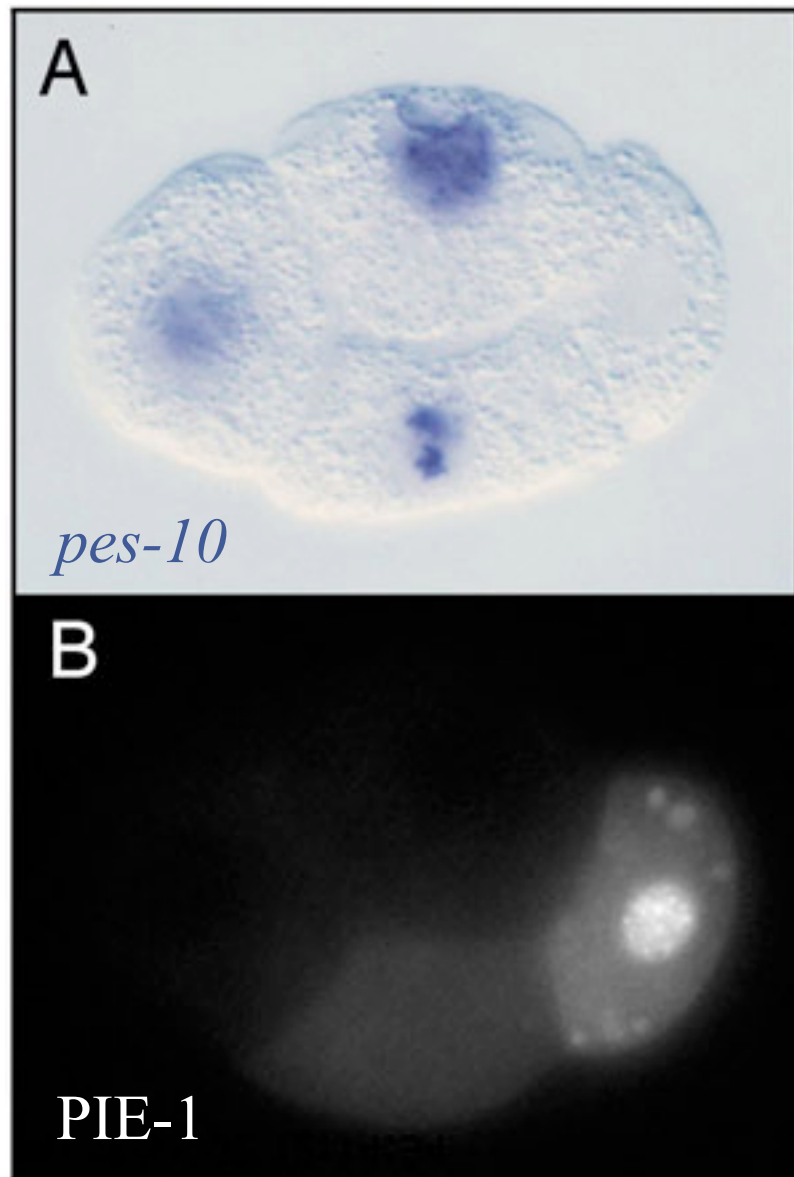
Milestone 15 (1986):
Programmed cell death



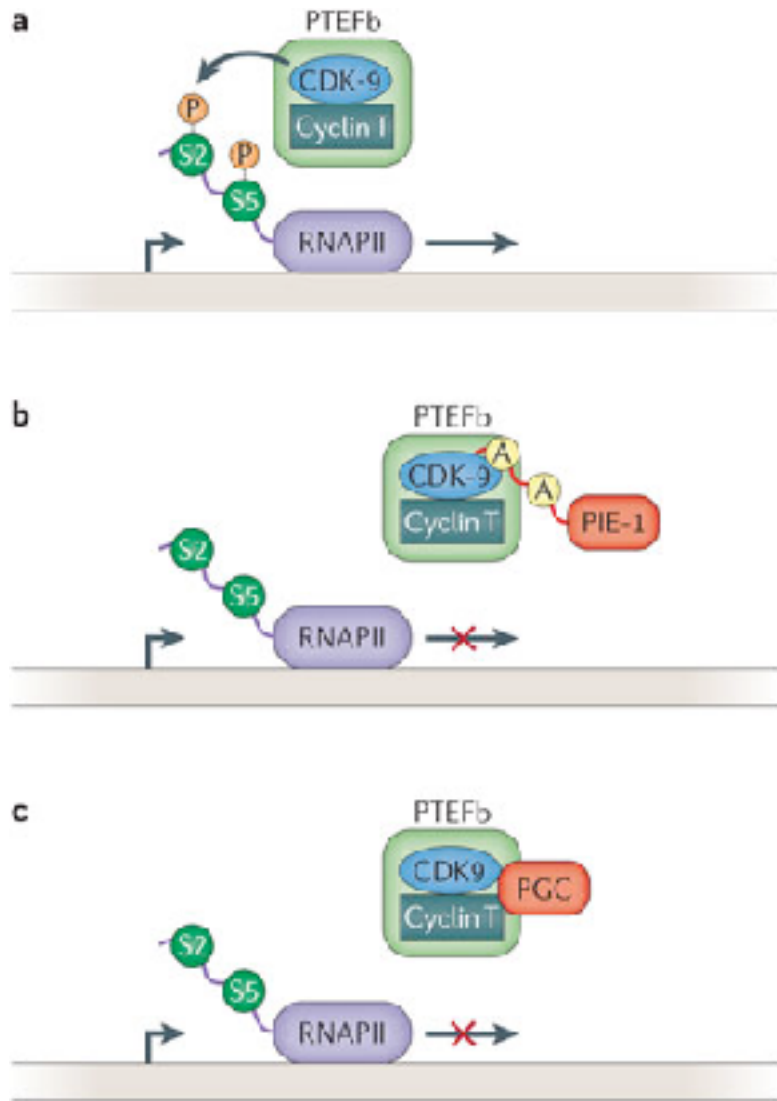
Molecular Cell Biology. 2004. Lodish et al. 5th Ed. WH Freeman and Co.

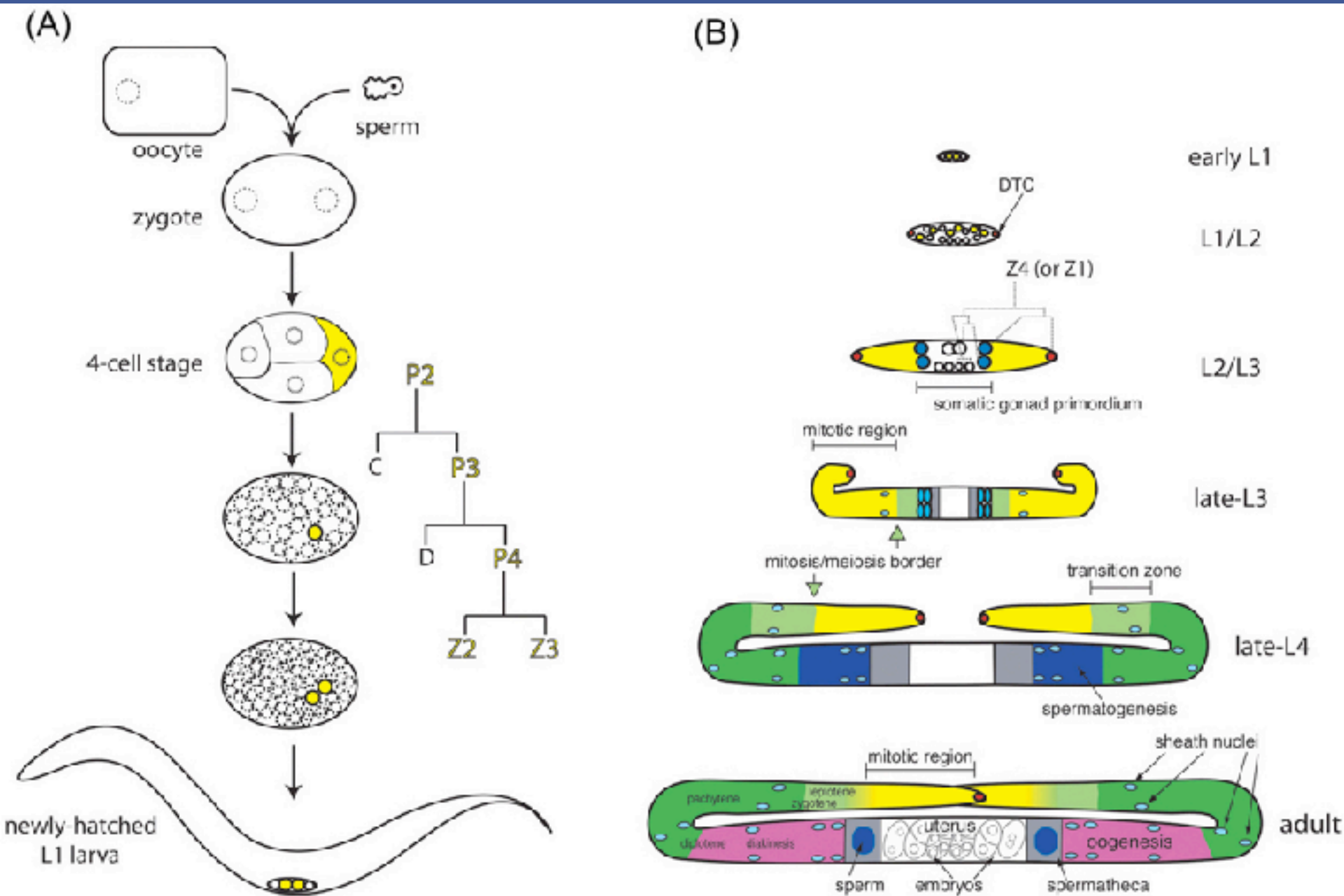
P4 dá origem as células germinativas primordiais (PGCs)



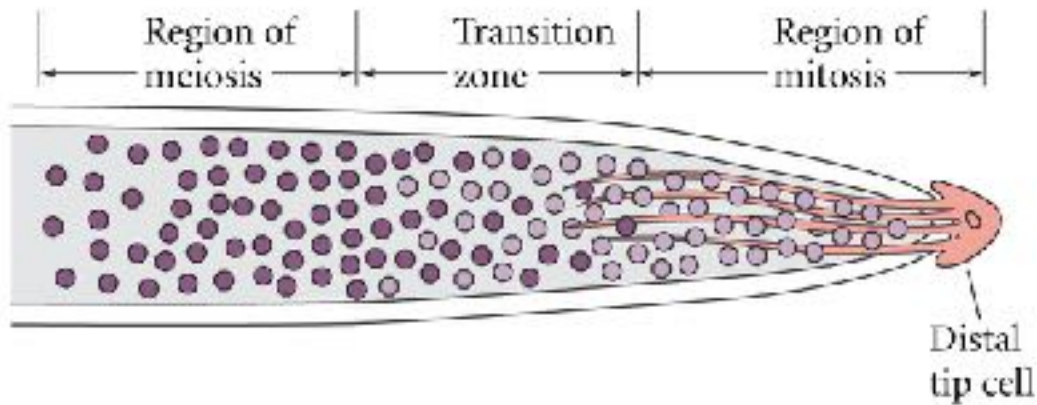


Inibição da transcrição por PIE-1 em *C. elegans* e PGC em *Drosophila*

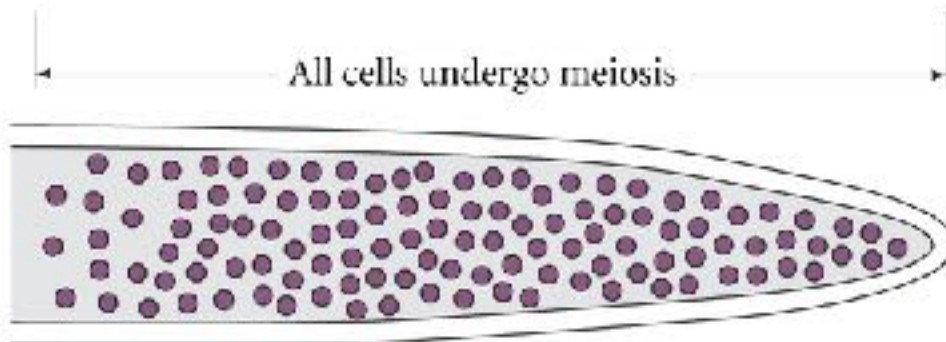




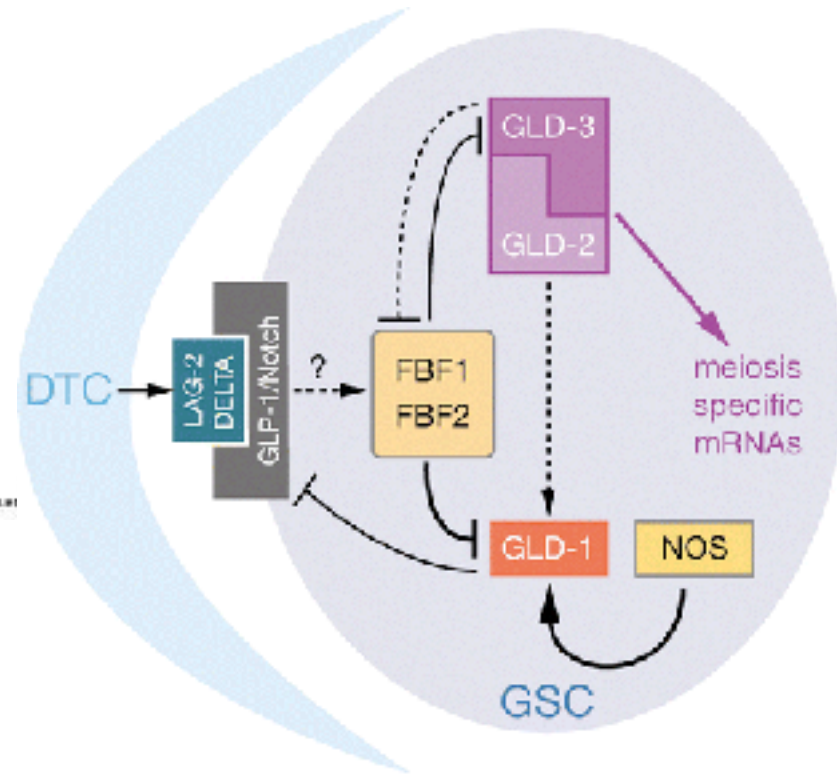
(A) Intact gonad



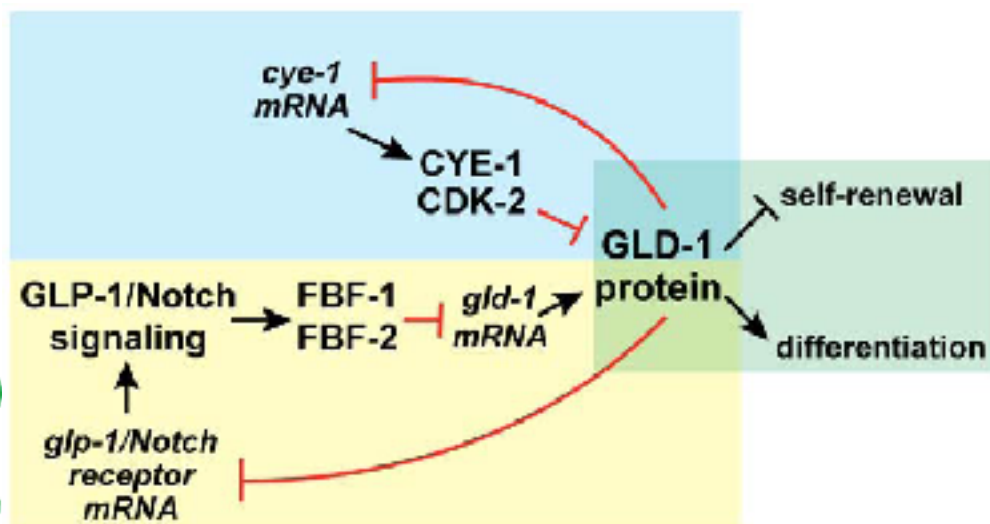
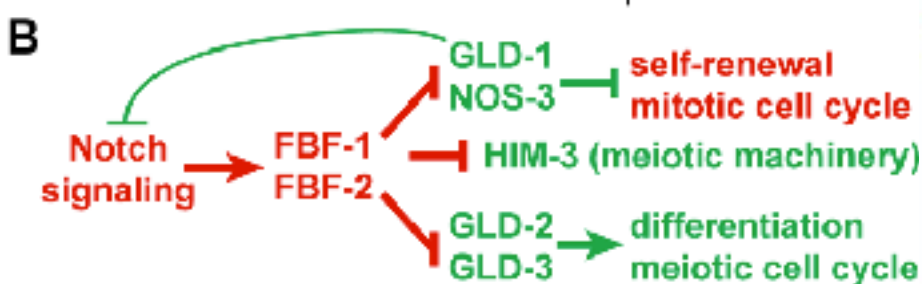
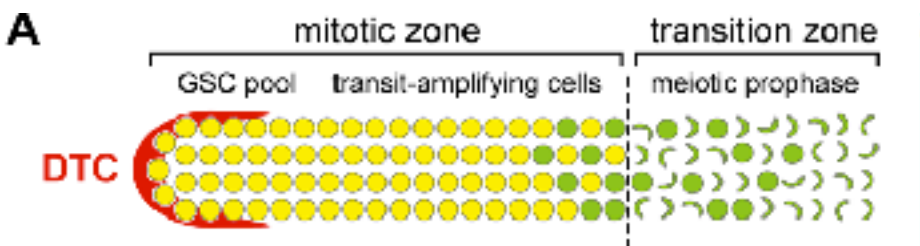
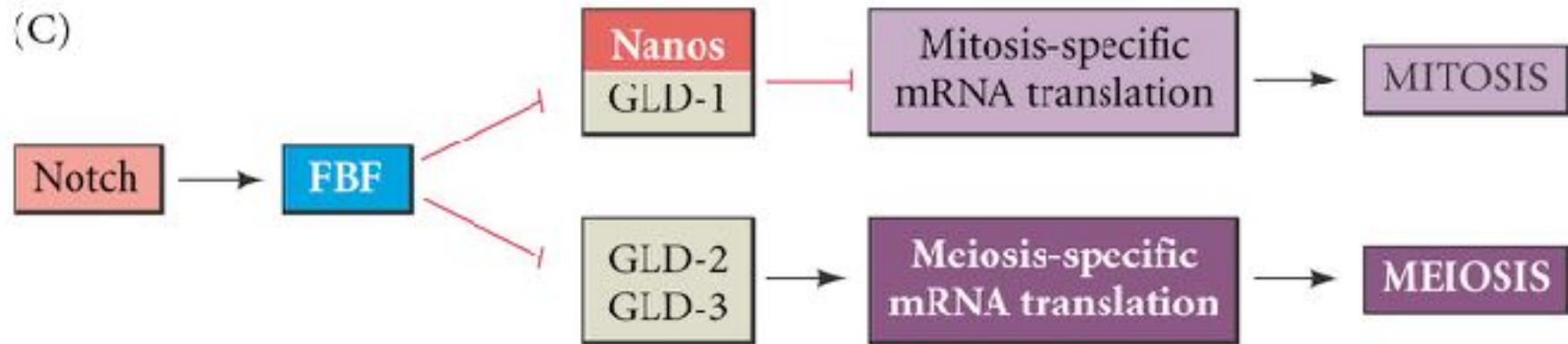
(B) Distal tip cell removed or *glp-1* mutation



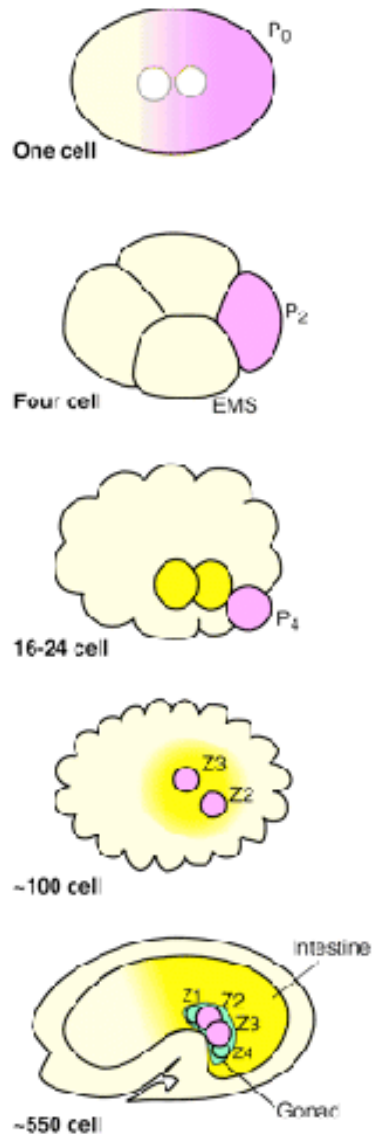
DEVELOPMENTAL BIOLOGY: Signaling Pathways Figure 19-13 (Part I) © 2005 Garland Science



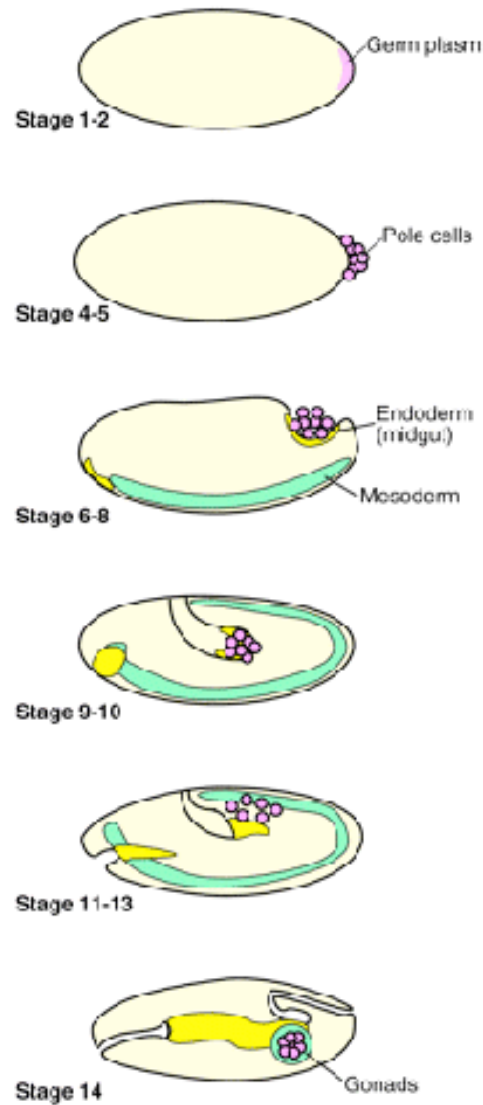
Milestone 3 (1937): Notch signaling and lateral inhibition



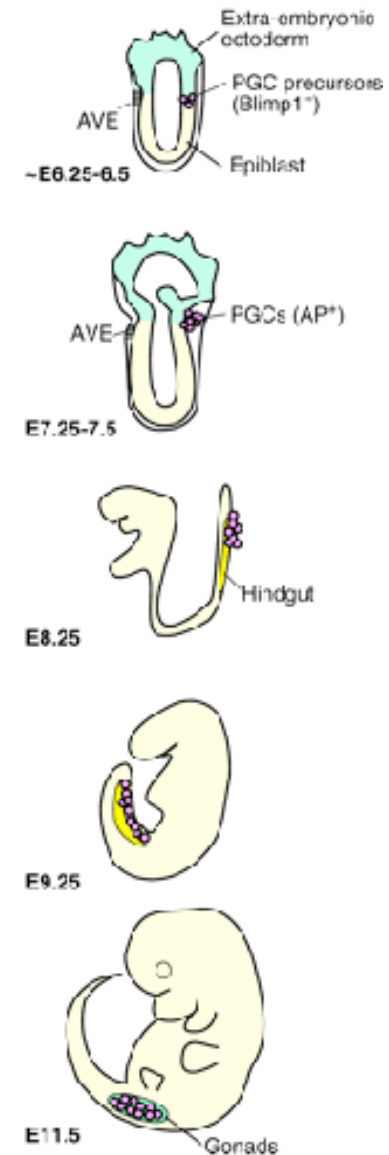
A *C. elegans*



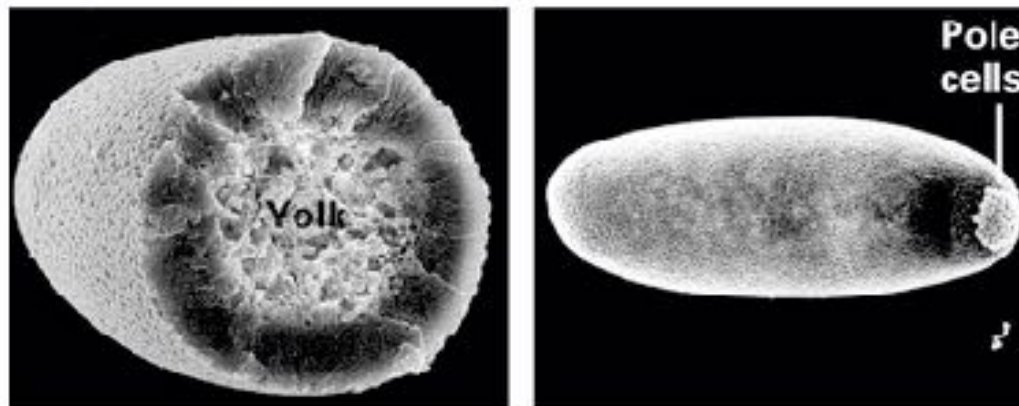
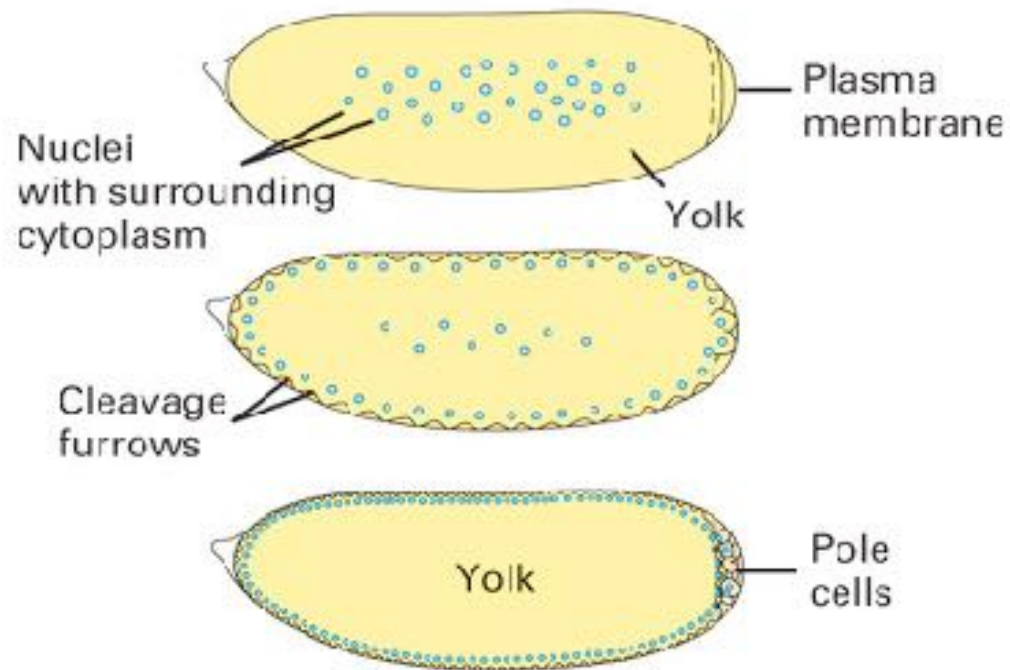
B *Drosophila*



C Mouse

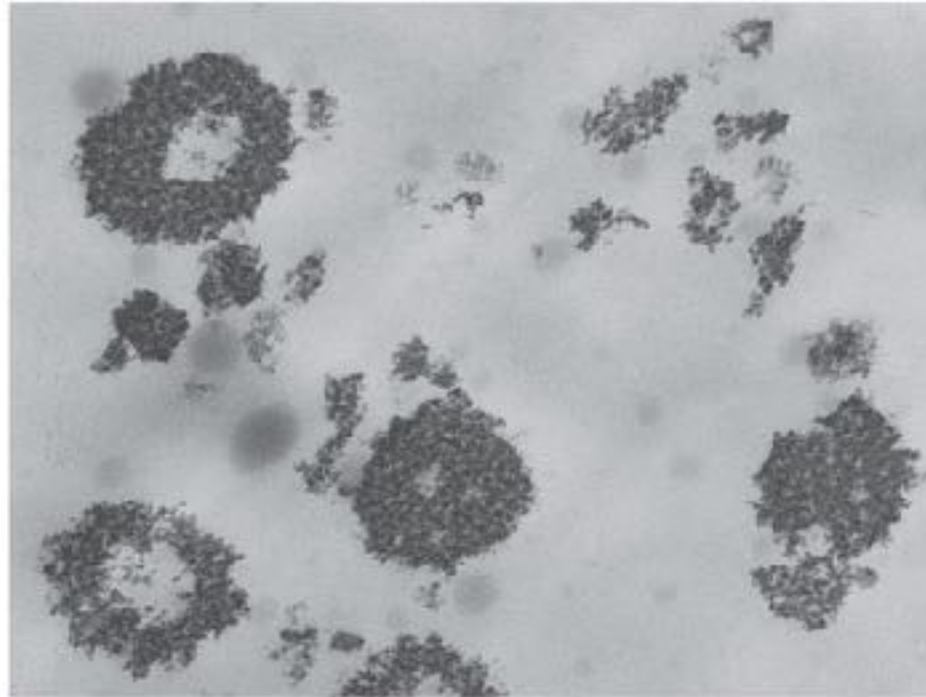


(a) NUCLEAR DIVISION AND MIGRATION

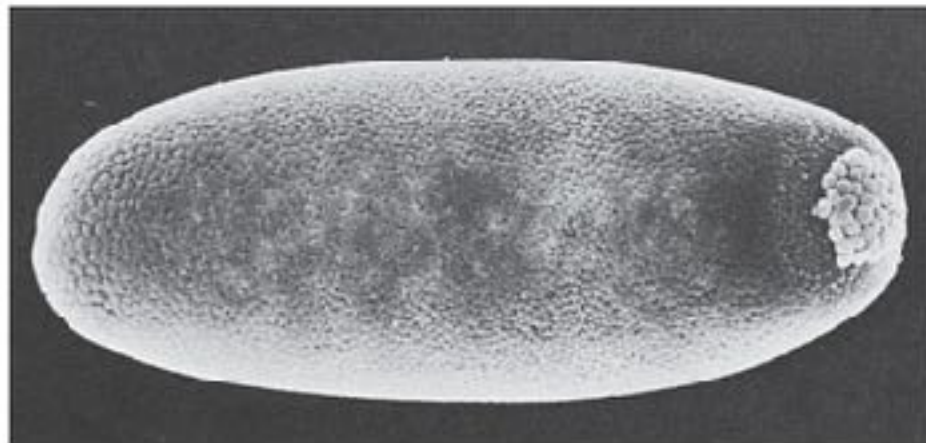


Syncytial blastoderm

(A)

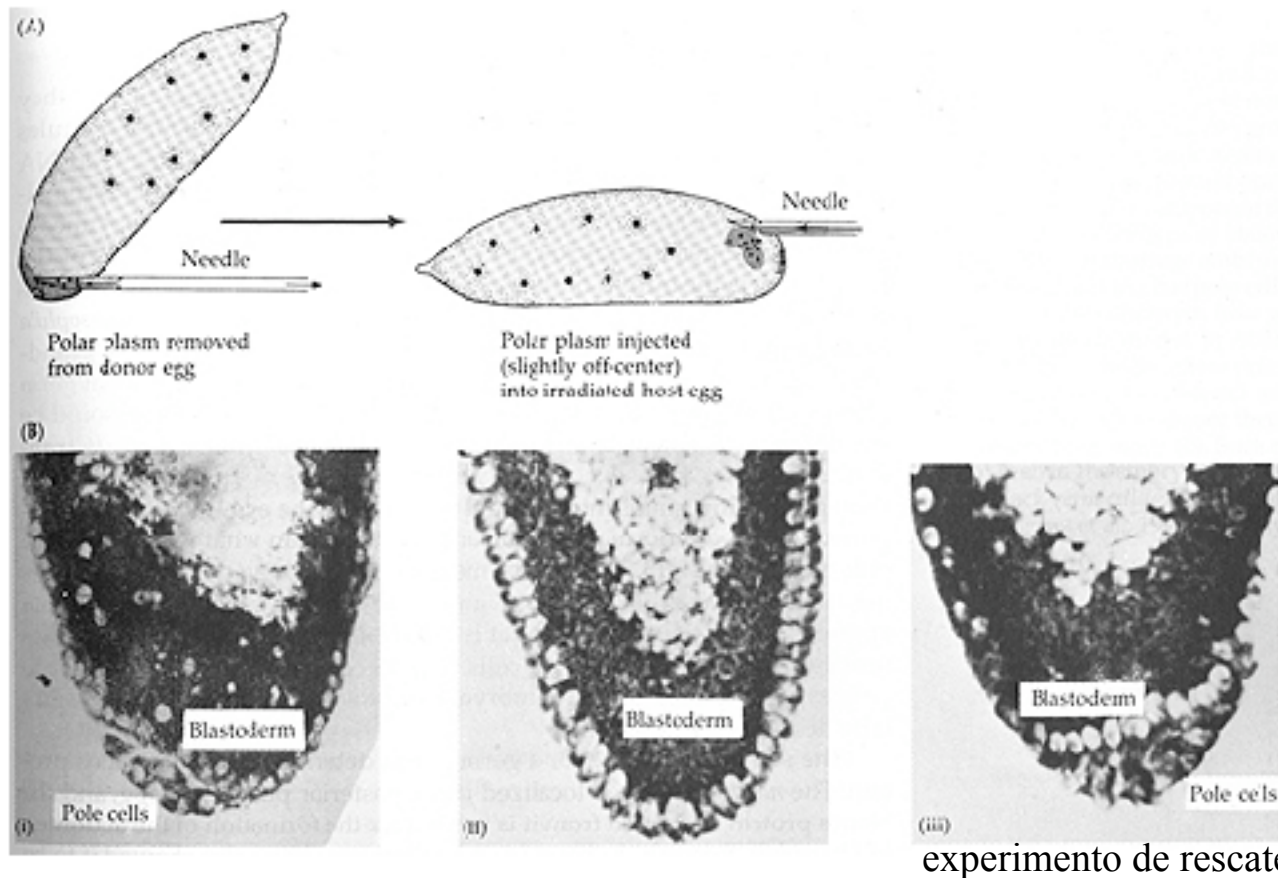


(B)

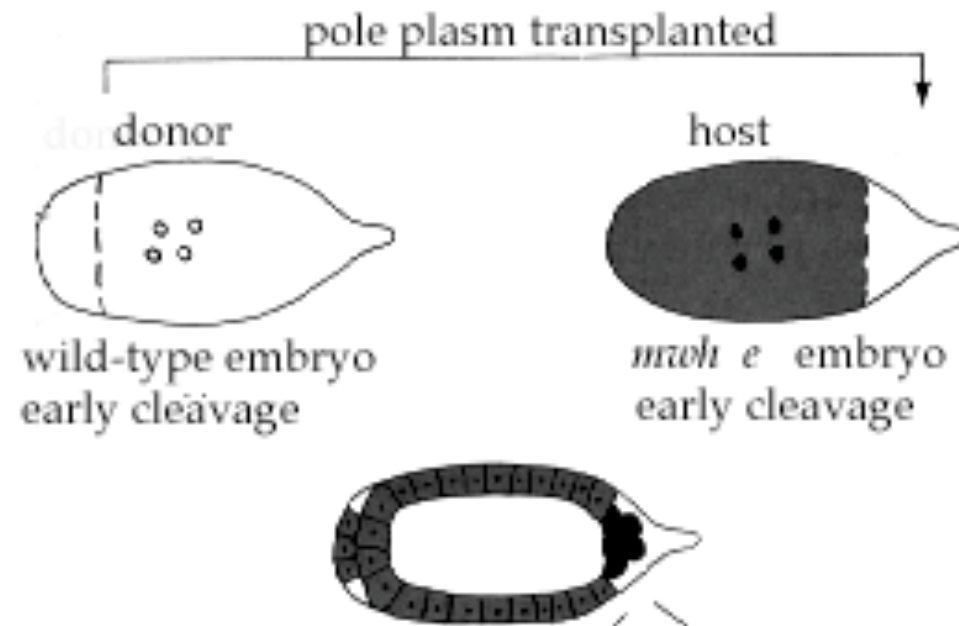


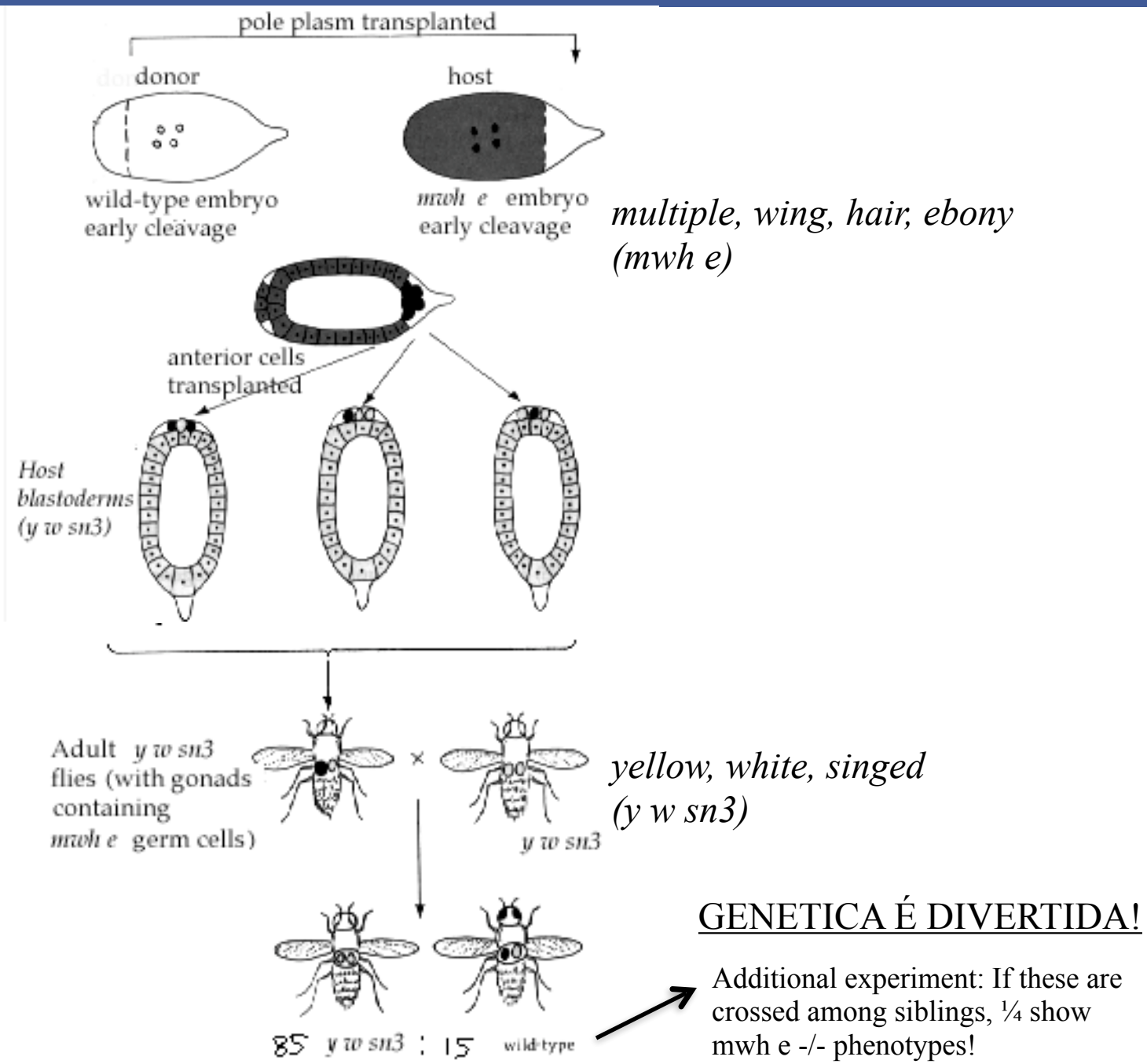
Como você poderia testar a importância do germoplasma (plasma polar) para a formação de células germinativas?

Experimento de Okada (1974):



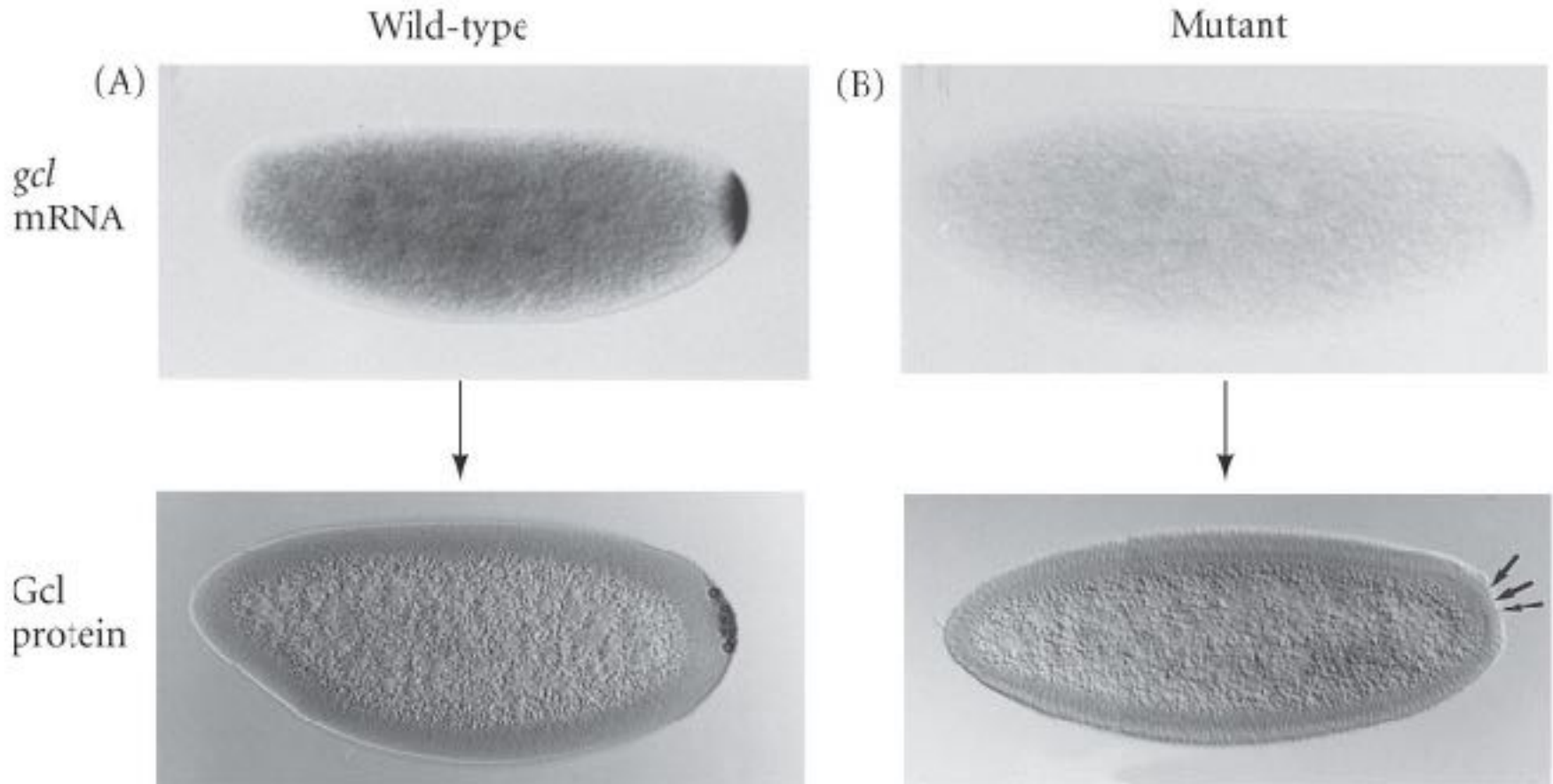
E cómo eu sé se o plasma germinativo é
SUFICIENTE para induzir células germinativas?





GENETICA É DIVERTIDA!

Additional experiment: If these are crossed among siblings, 1/4 show *mwh e* -/- phenotypes!



Outros genes que se expressam nas células polares e plasma germinativo:

- Gcl (RNA -> proteína)
- Oskar (proteína) -> **Vasa** (proteína)
- mtrRNA (RNA)
- PGC (RNA -> proteína)



(A) *Vasa* probe labeling the pole plasm

Cell movements of germ cells

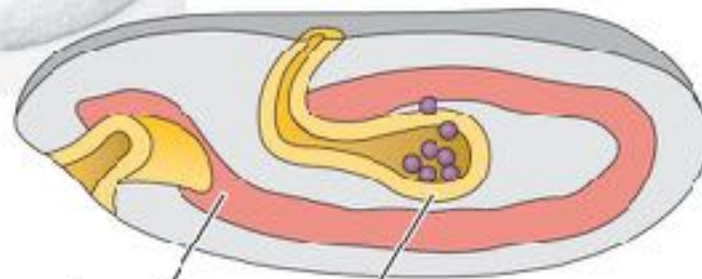


Pole cells



(B)

Attachment to endoderm and migration through midgut



Mesoderm

Posterior midgut

30 ou 40 PGCs

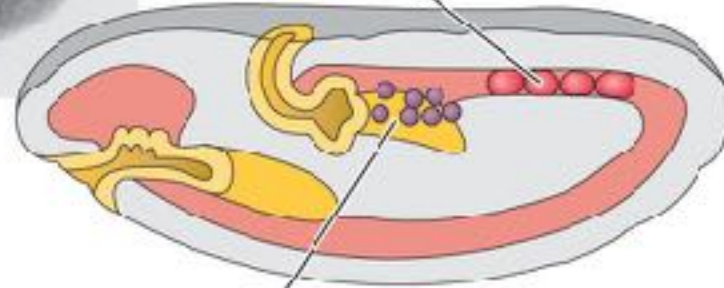
Attachment to mesoderm

wunen expressado na endoderme posterior repele PGCs da endoderme

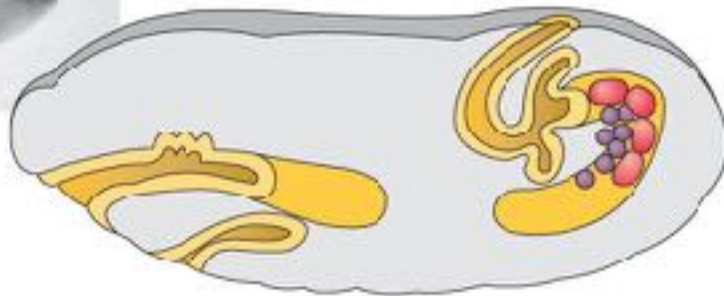


Gonad precursor cells

(C)



(D)

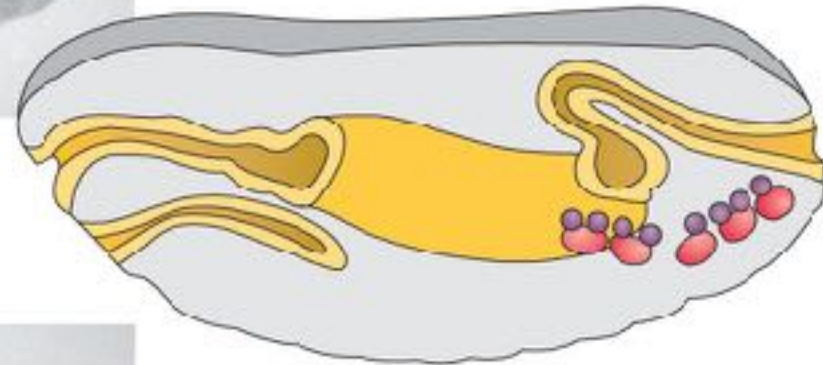


Hedgehog e *columbus* (expressados nas gônadas) atraem as PGC até as gônadas



(E)

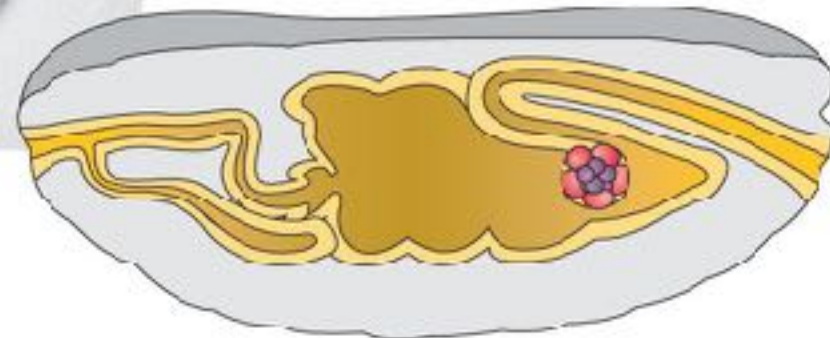
tin



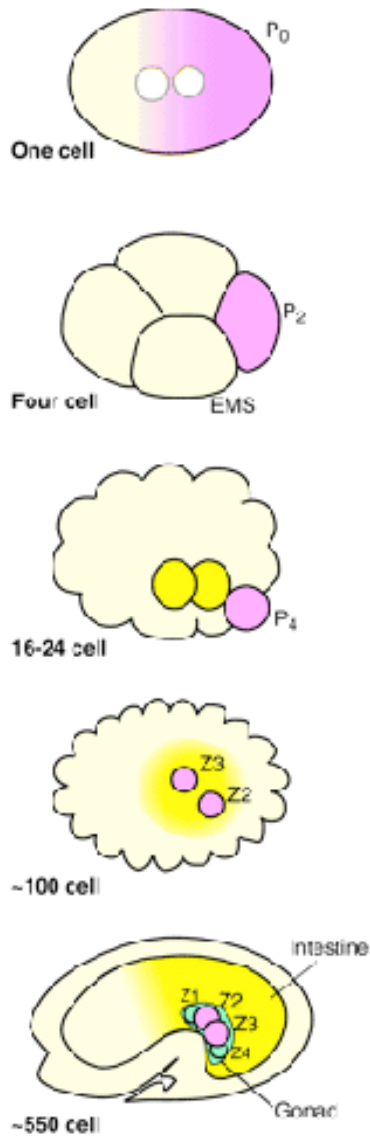
Gonad
coalescence



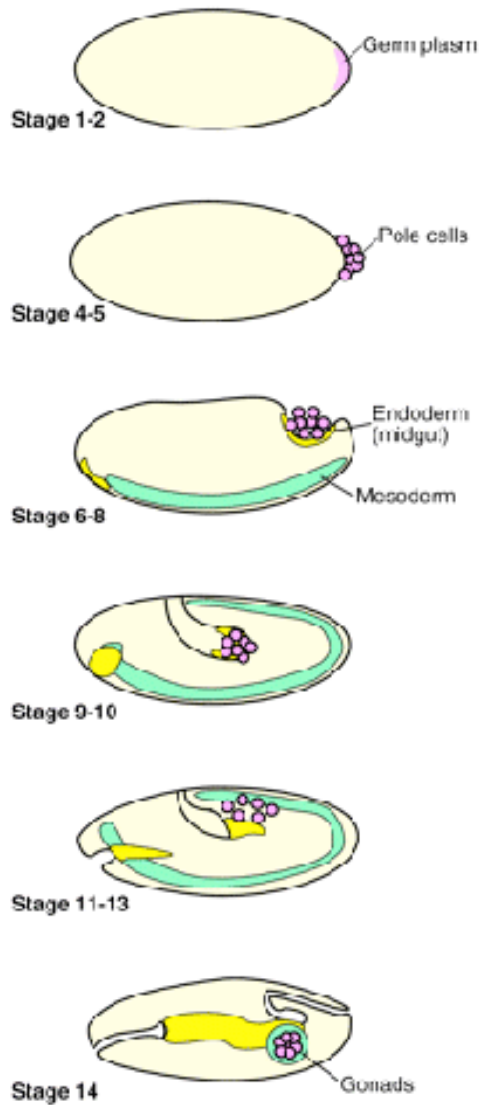
(F)



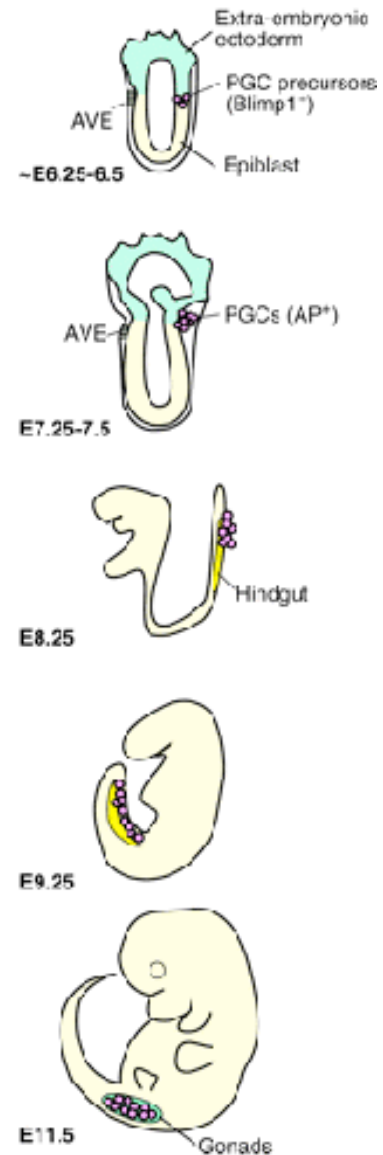
A *C. elegans*

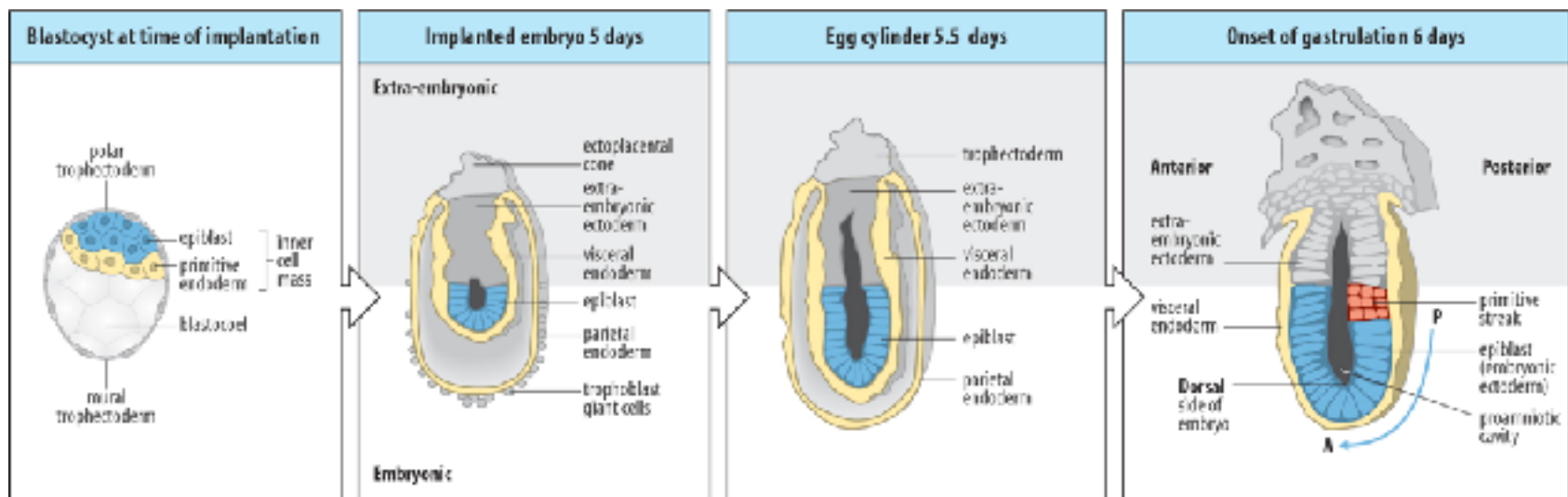


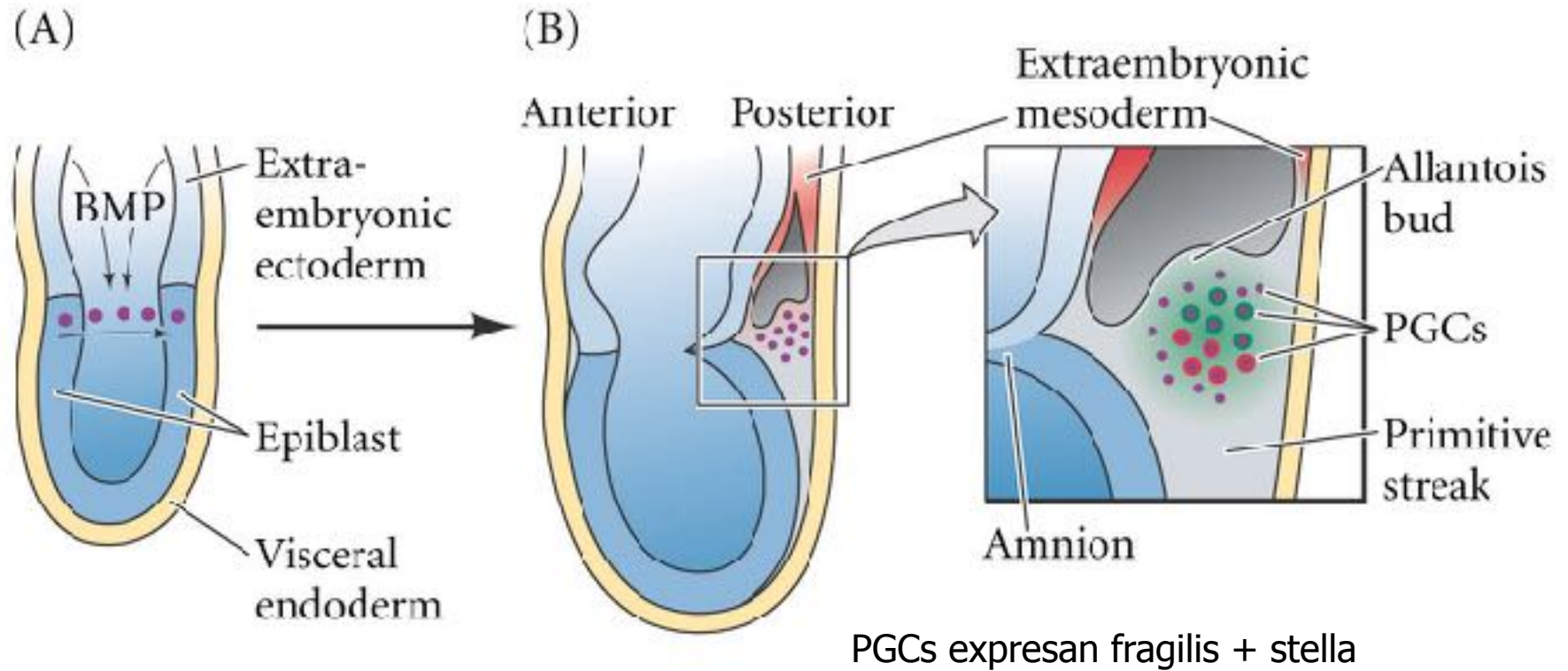
B *Drosophila*



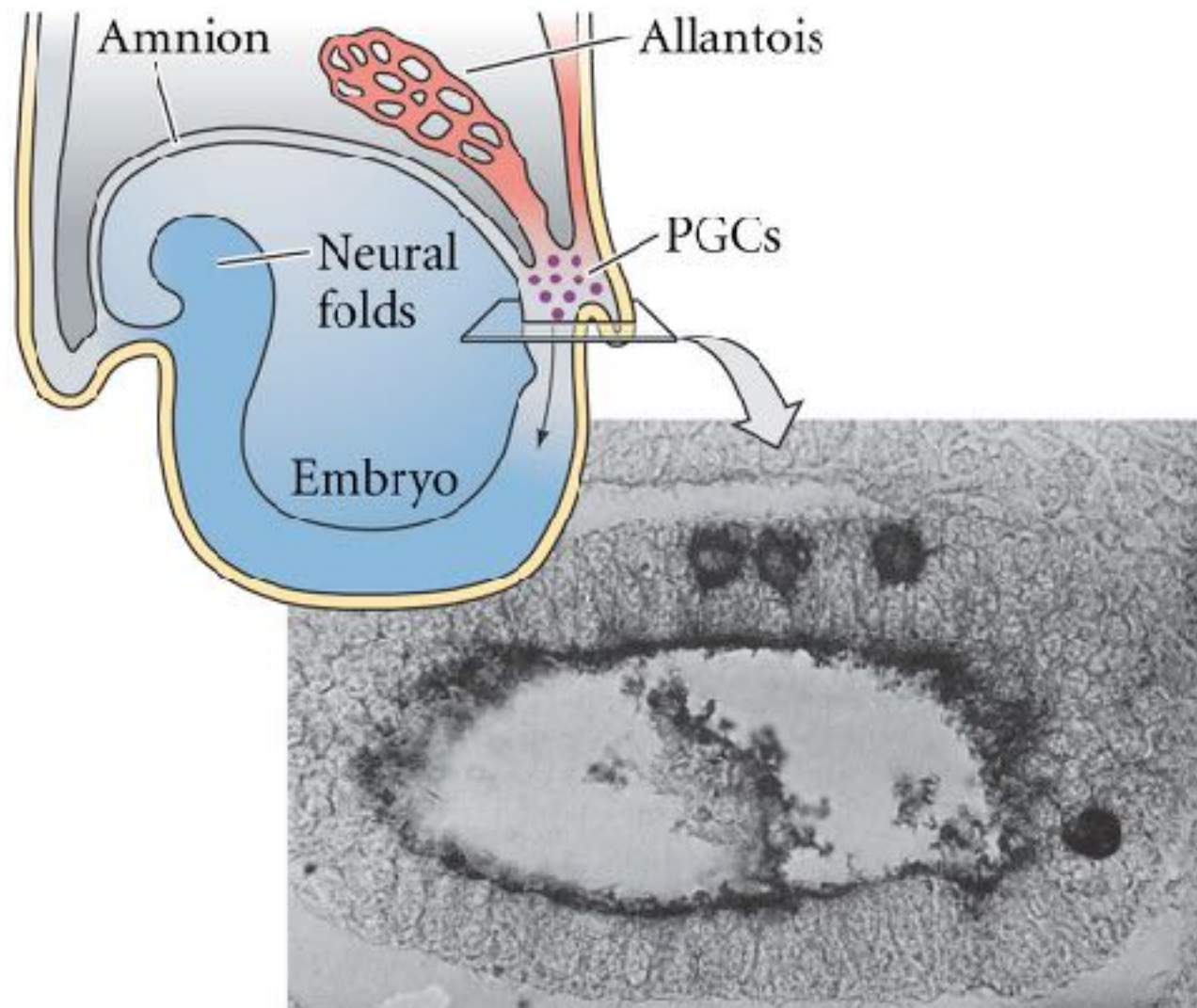
C Mouse



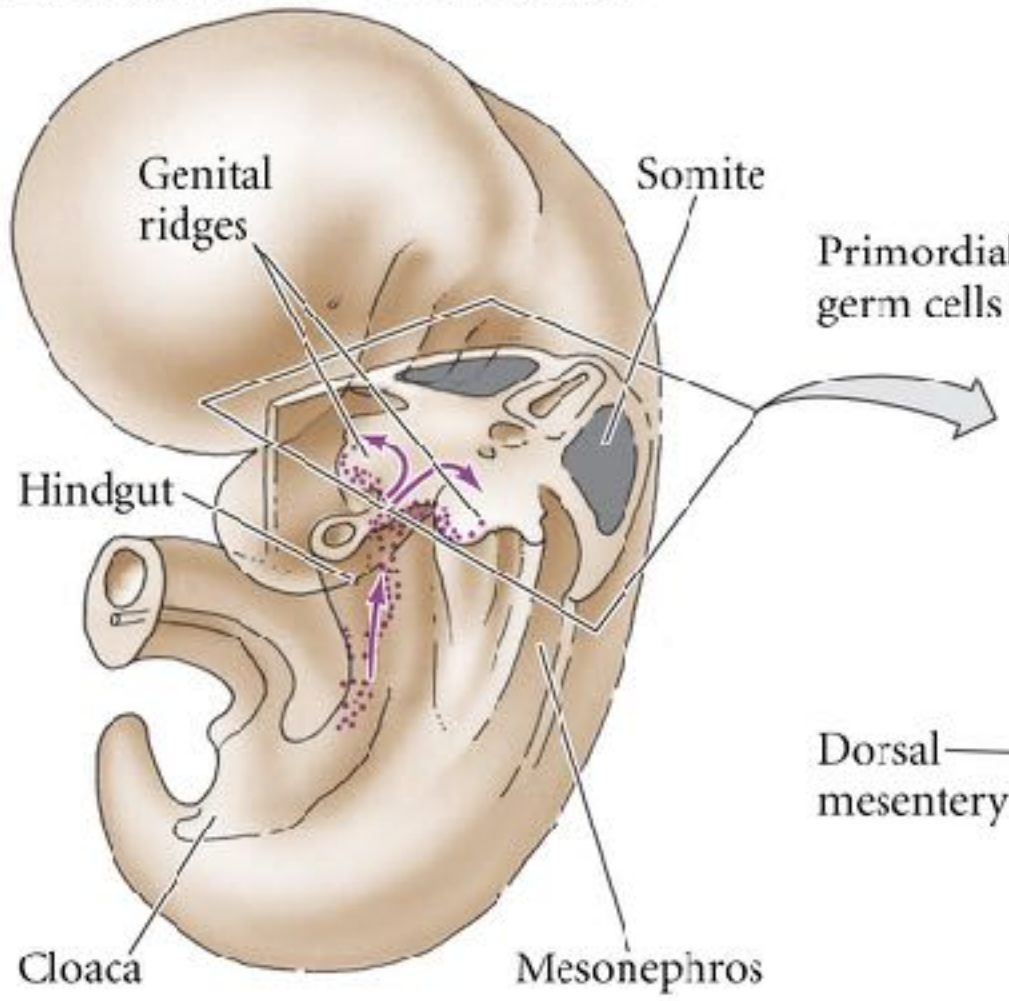




(A) Migration of PGCs to endoderm

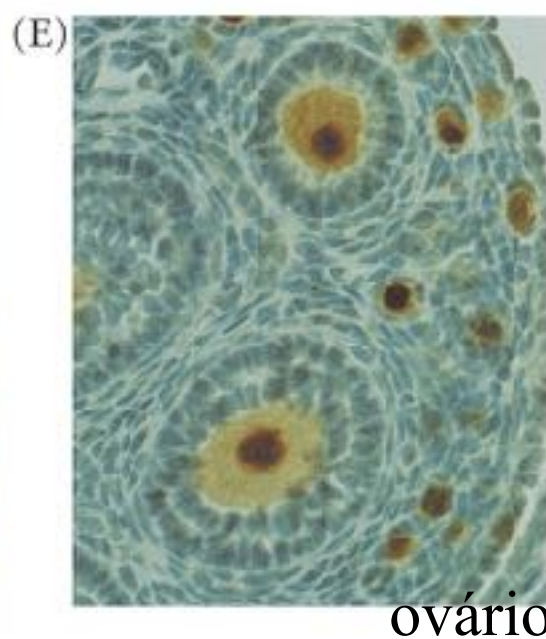
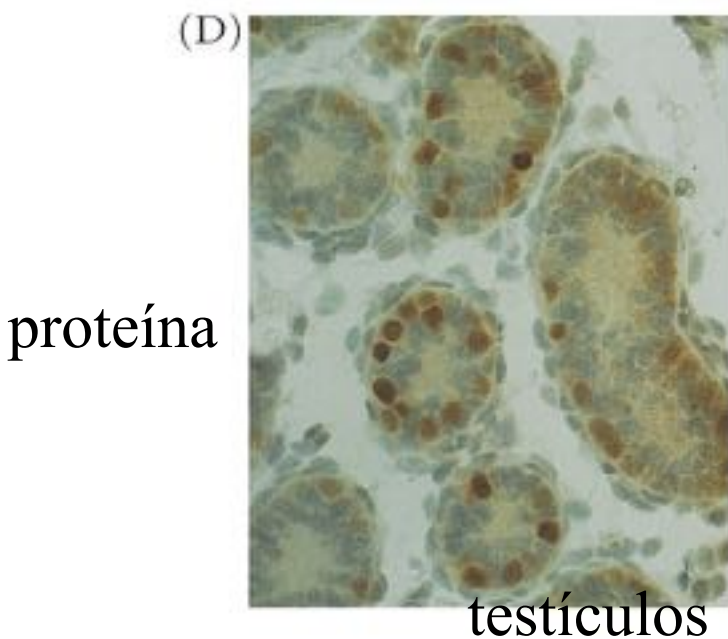
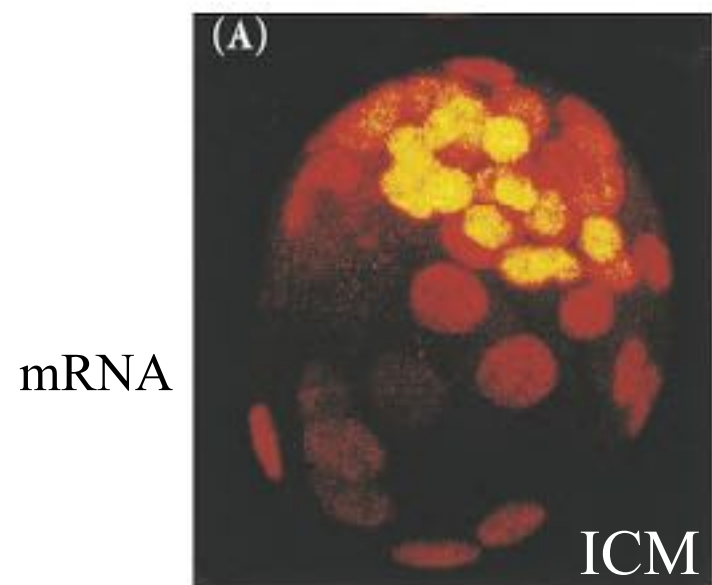


(B) Migration of PGCs into gonad

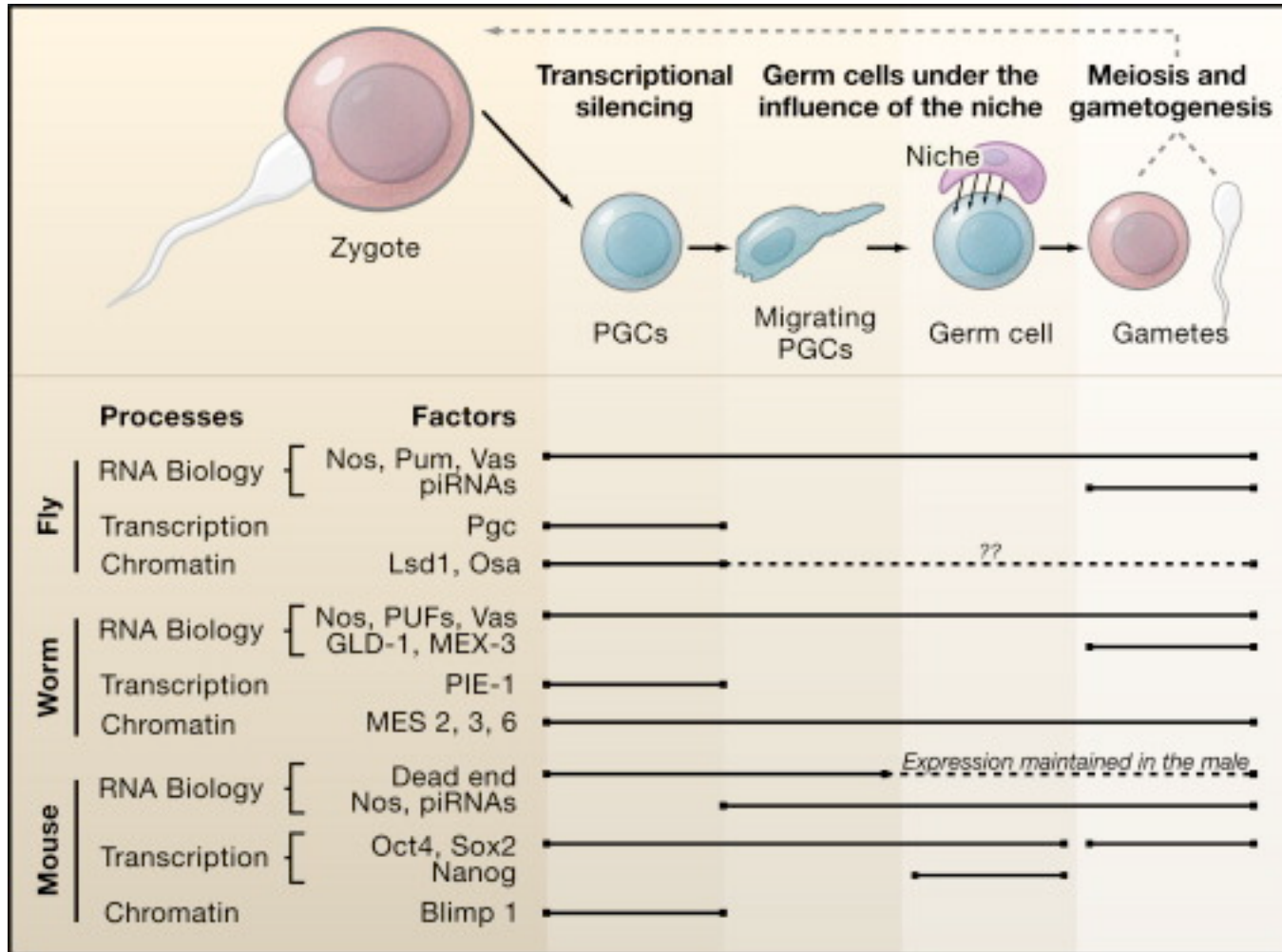


(C)

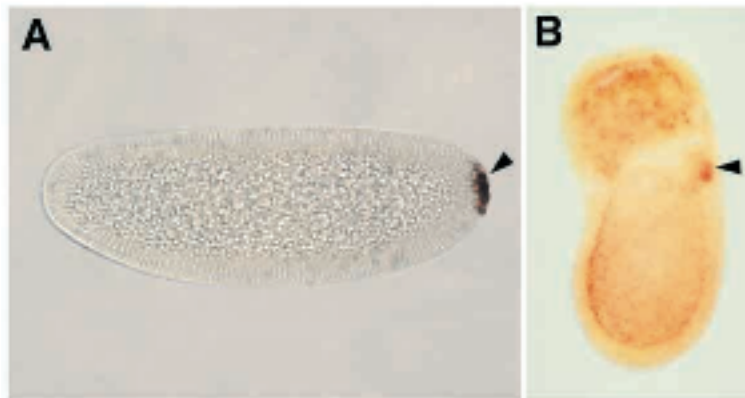
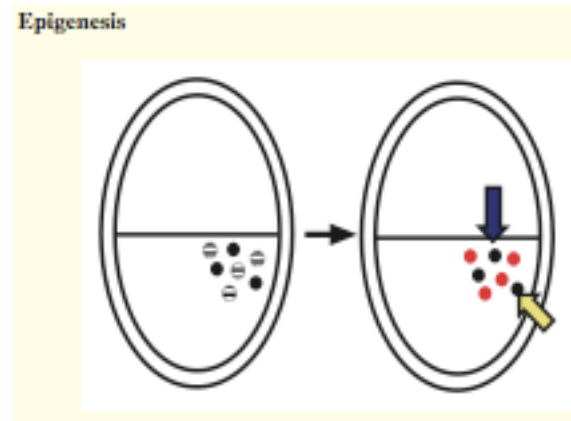
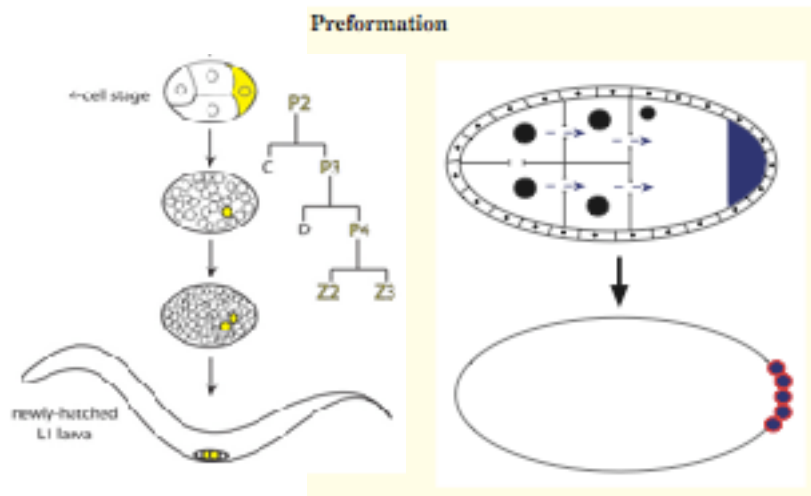




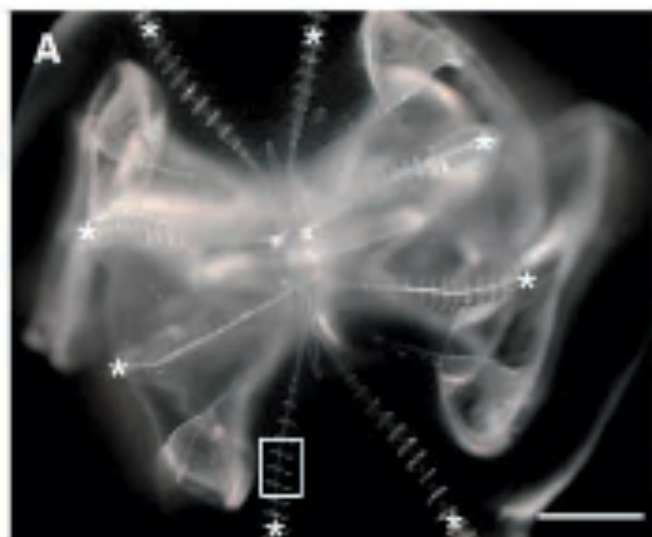
Totipotência mantida por Oct4; mais tarde no desenvolvimento, migração ativa através de gradientes de atração produzidos pelas cristas genitais (migração e proliferação de PGCs reguladas por Stem Cell Factor SCF e c-kit).



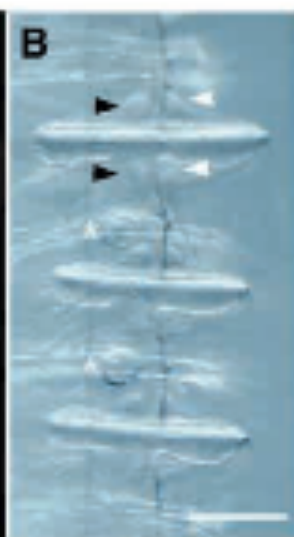
Duas formas extremas que formam as células germinativas em animais modelo



O que dizer das espécies que não são modelos animais?

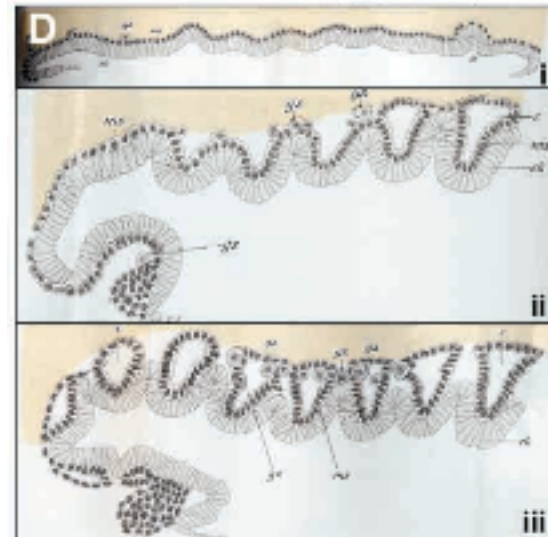


Ctenóforo *Mnemiopsis leidyi*

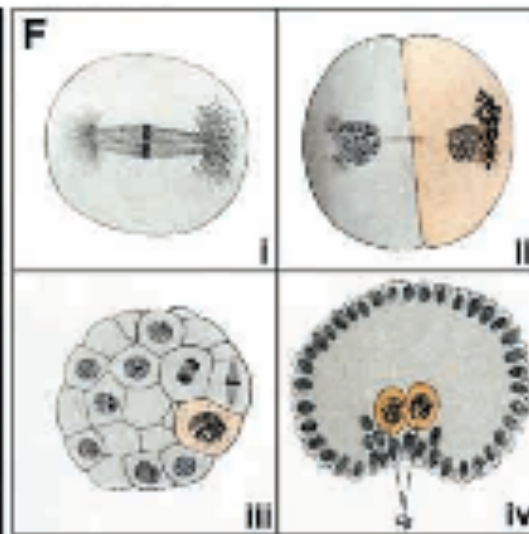


Extensión de la banda germinal:

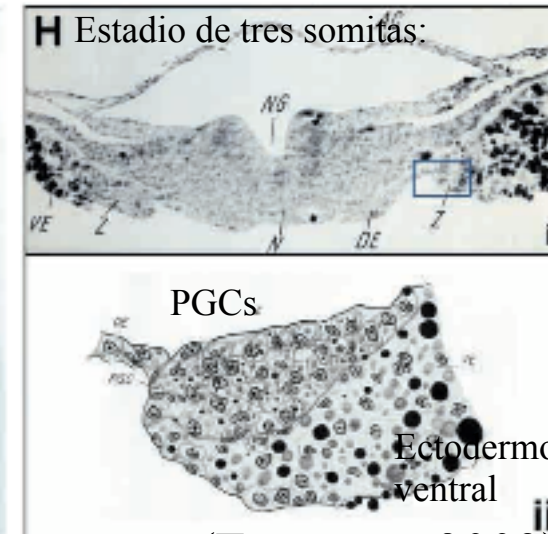
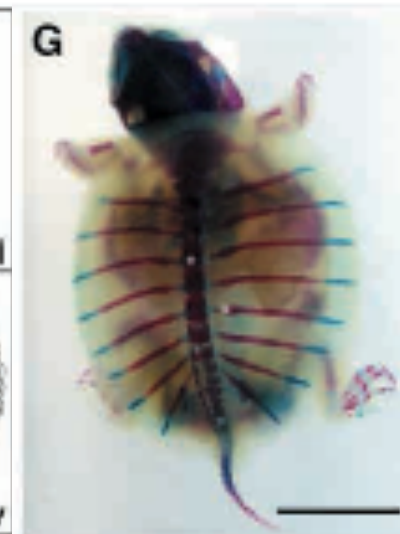
Barata *Blatta germanica*



Copépedo *Cyclops fuscusi*

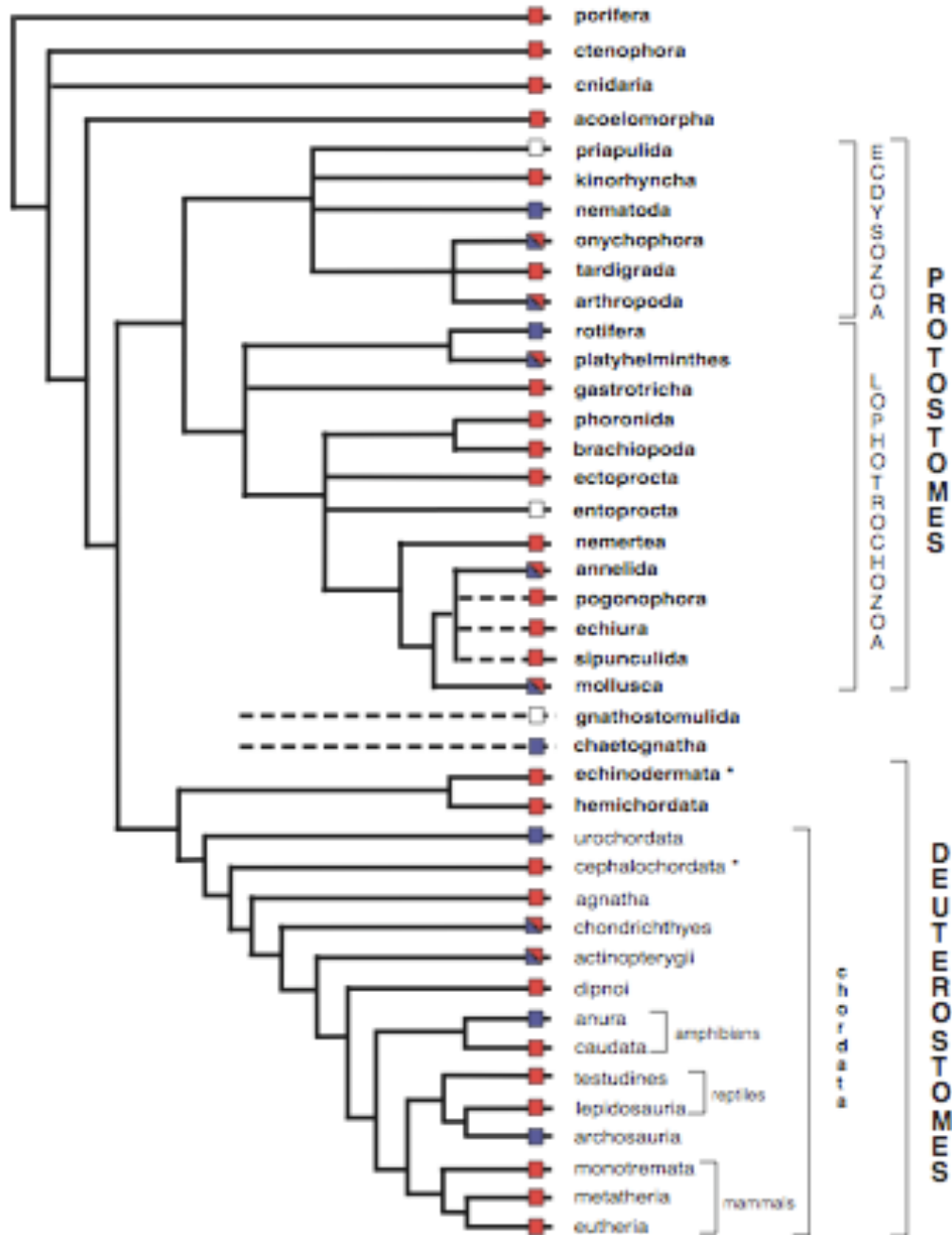


Tartaruga *Sternoterus odoratus*



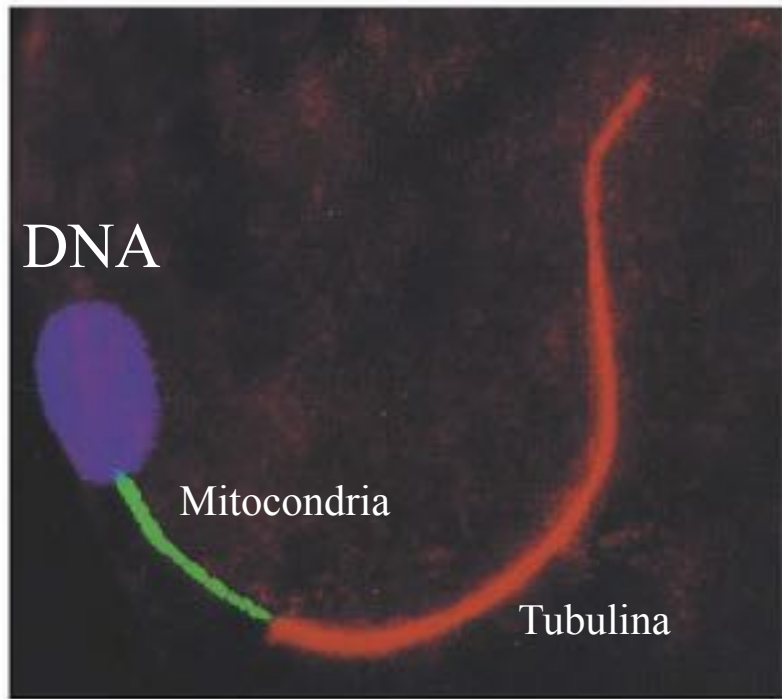
(Extavour, 2003)

O que dizer das espécies que não são modelos animais?

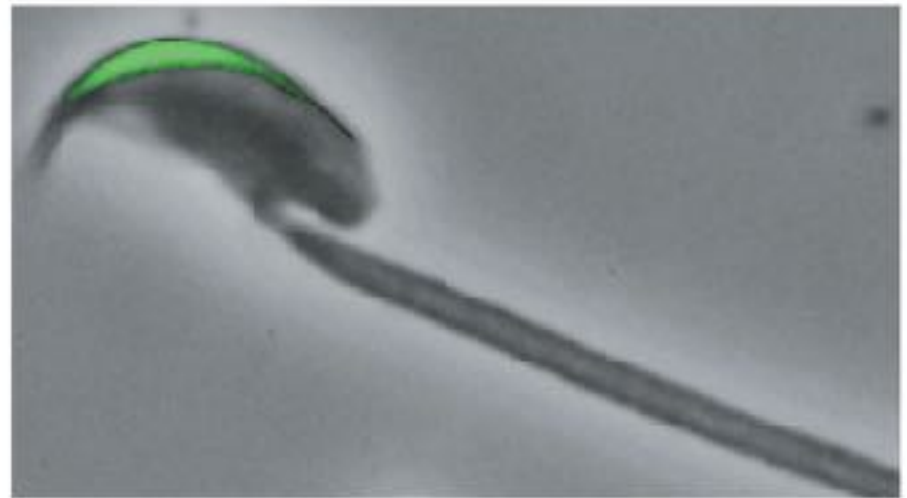


■ epigênese
■ pre-formação

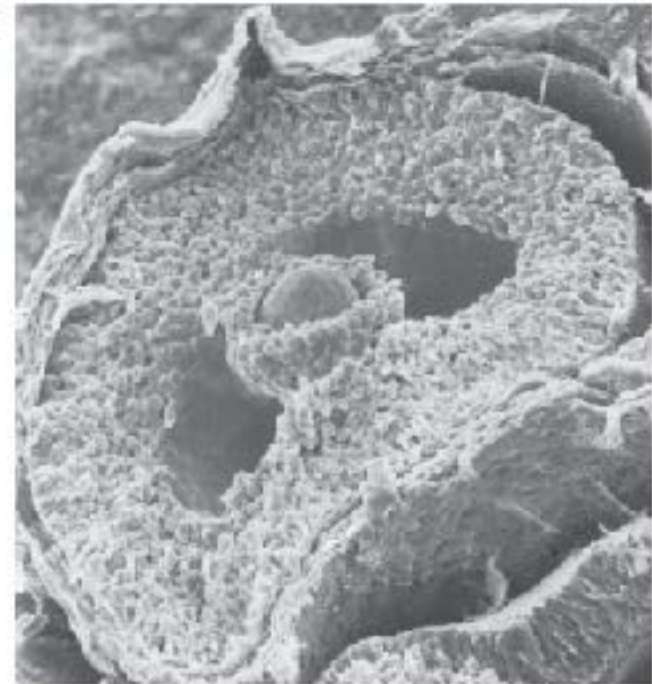




Touro

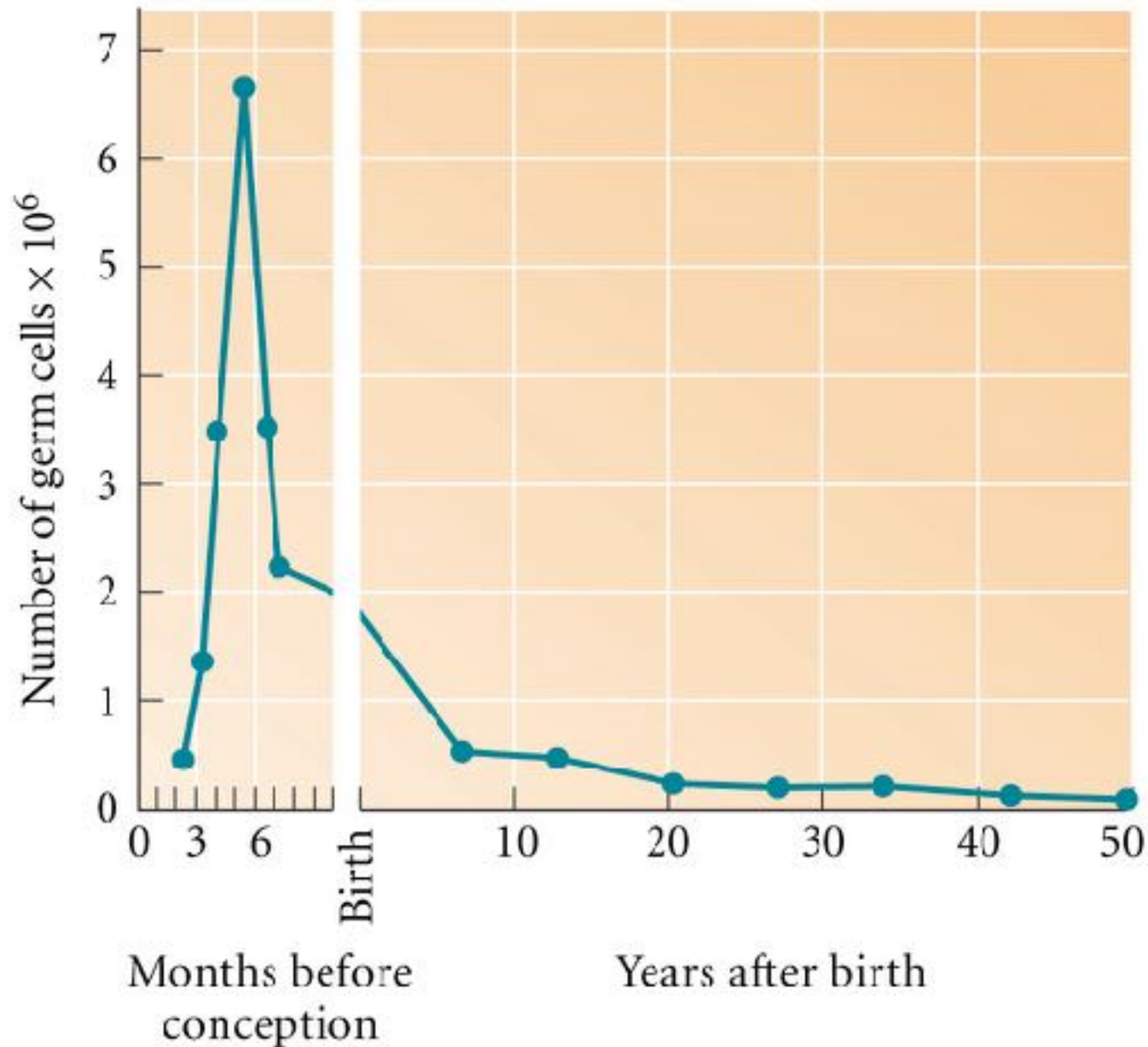


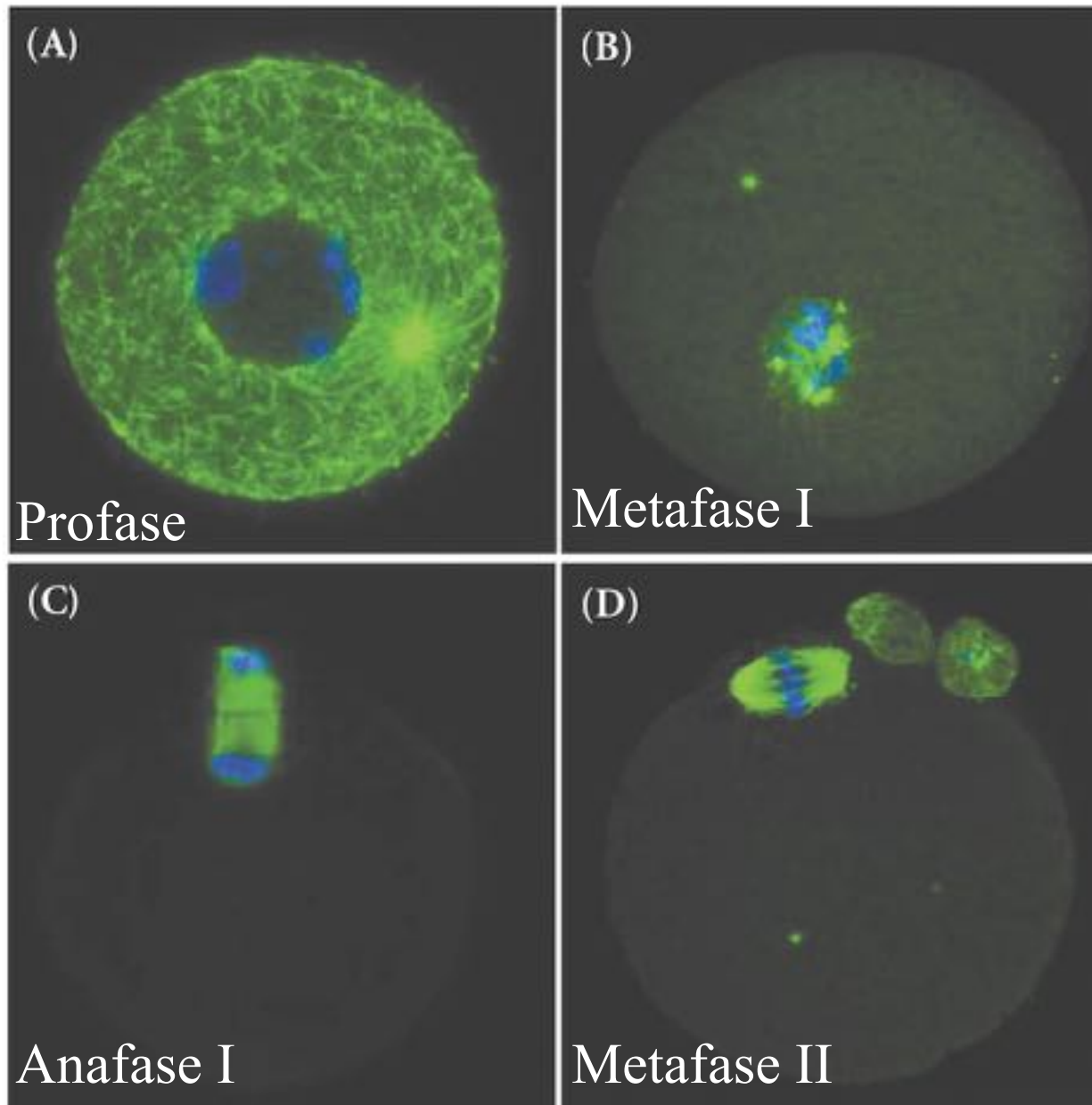
Acrossoma de rato



Folículo do ovário
de mamífero

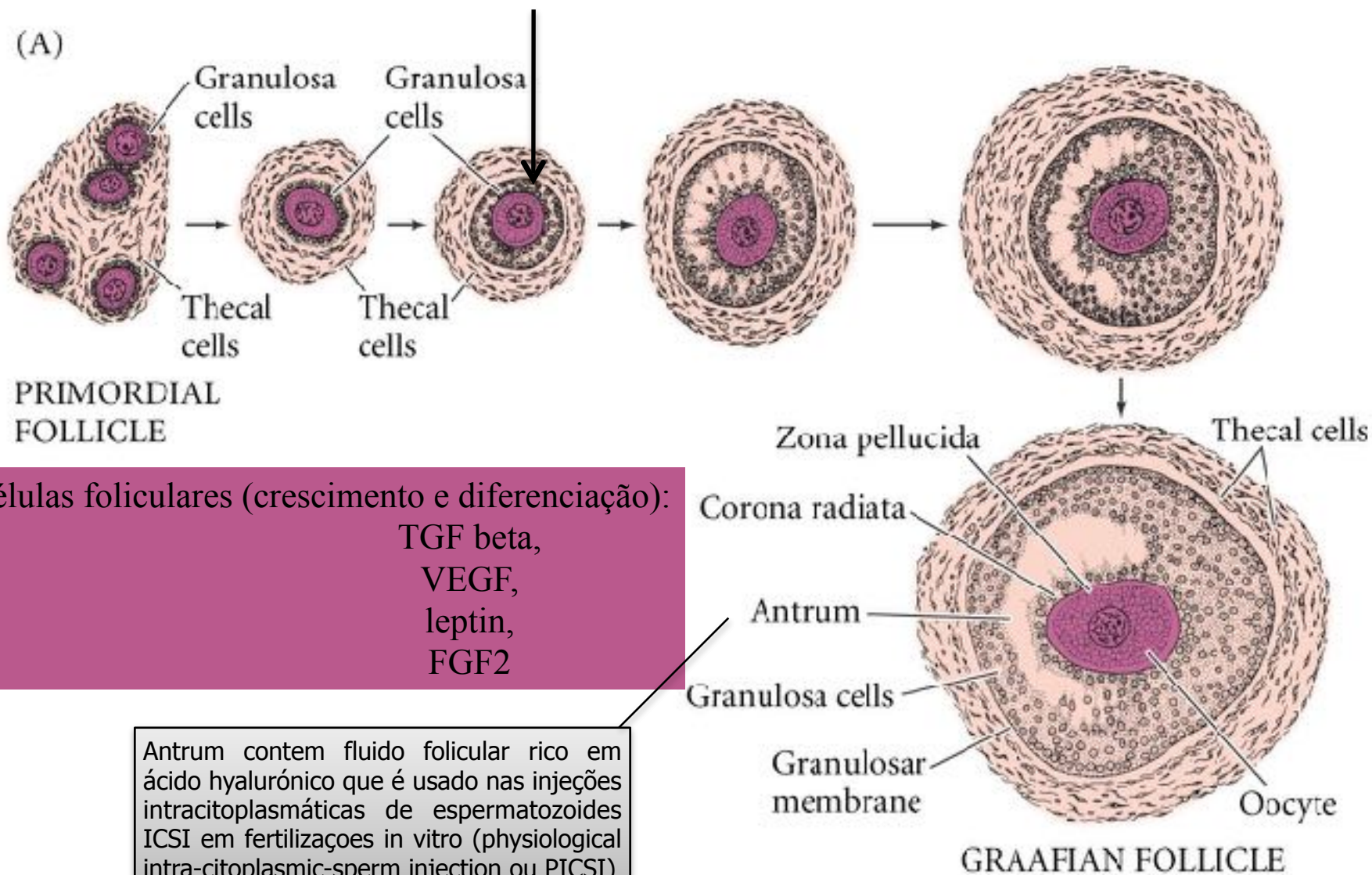
As alterações no número de células germinativas do ovário humano ao longo do período da vida





O folículo ovariano de mamíferos (crescimento e maturação do oócito)

Oócitos expressam GDF9 (TGF beta) que induz proliferação de células foliculares



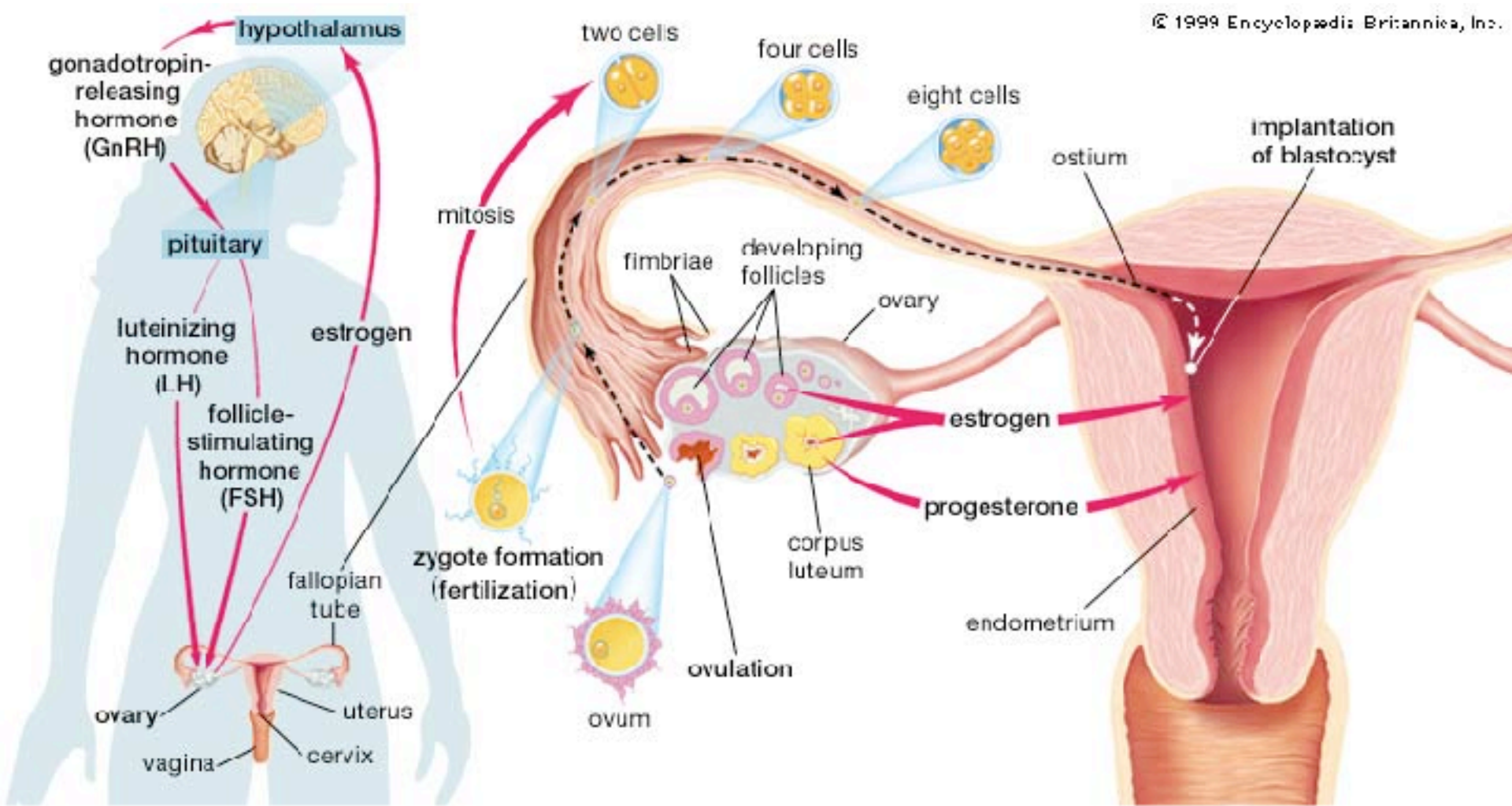
Células foliculares (crescimento e diferenciação):

TGF beta,
VEGF,
leptin,
FGF2

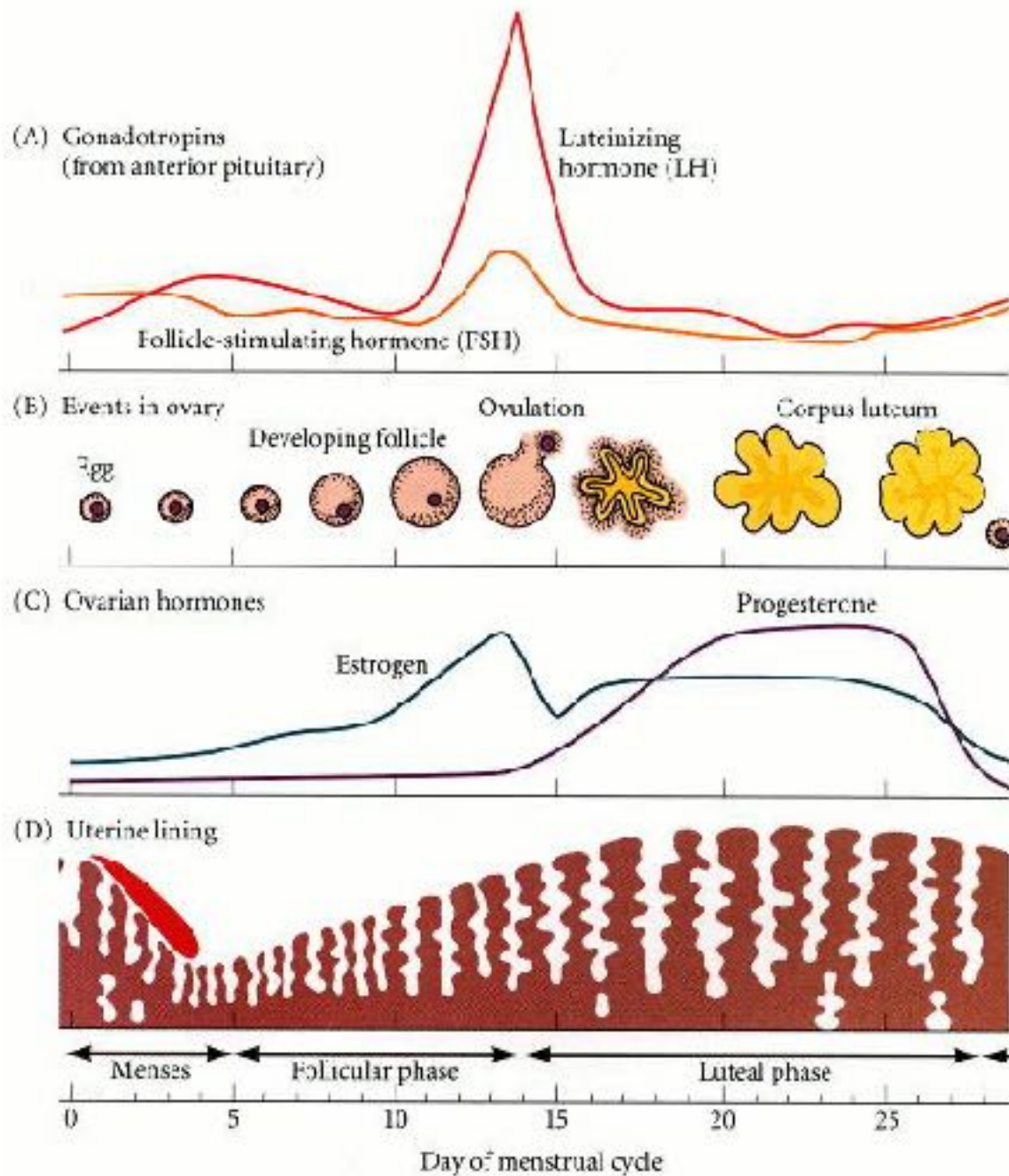
Antrum contém fluido folicular rico em ácido hialurônico que é usado nas injeções intracitoplasmáticas de espermatozoides ICSI em fertilizações in vitro (physiological intra-citoplasmic-sperm injection ou PICSI)

Milestone 9 (1971):
Reinventing reproduction

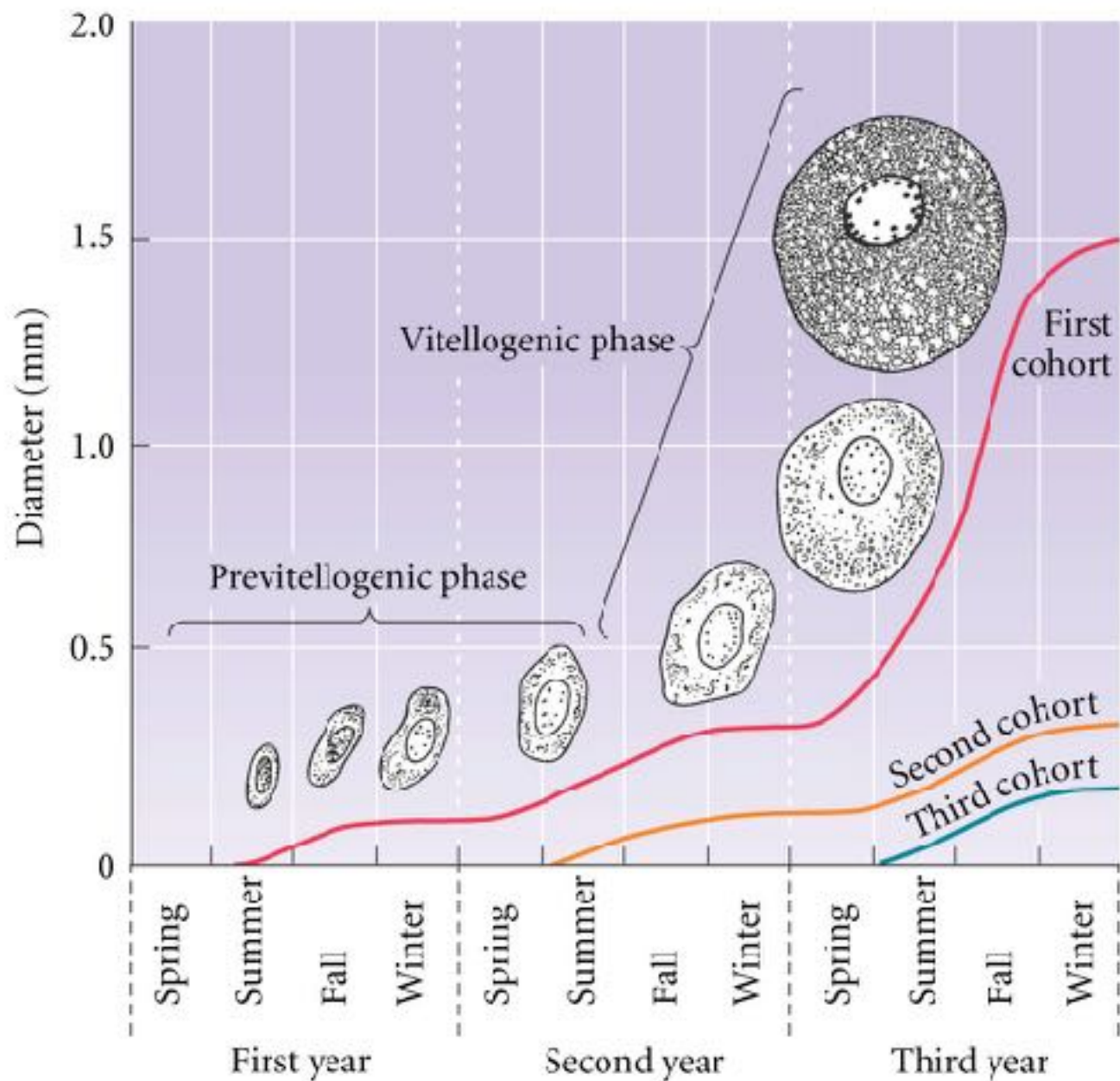
O ciclo menstrual humano

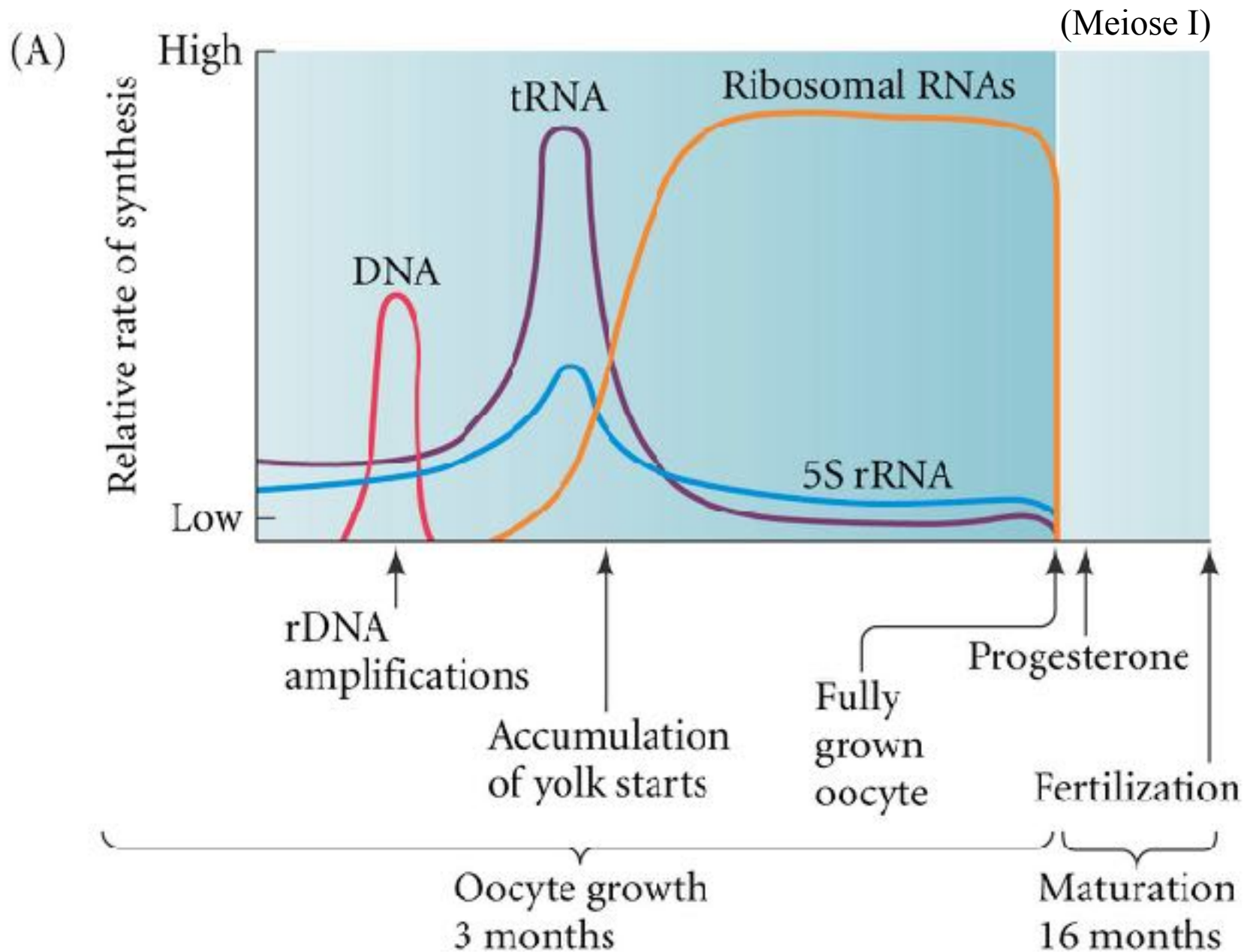


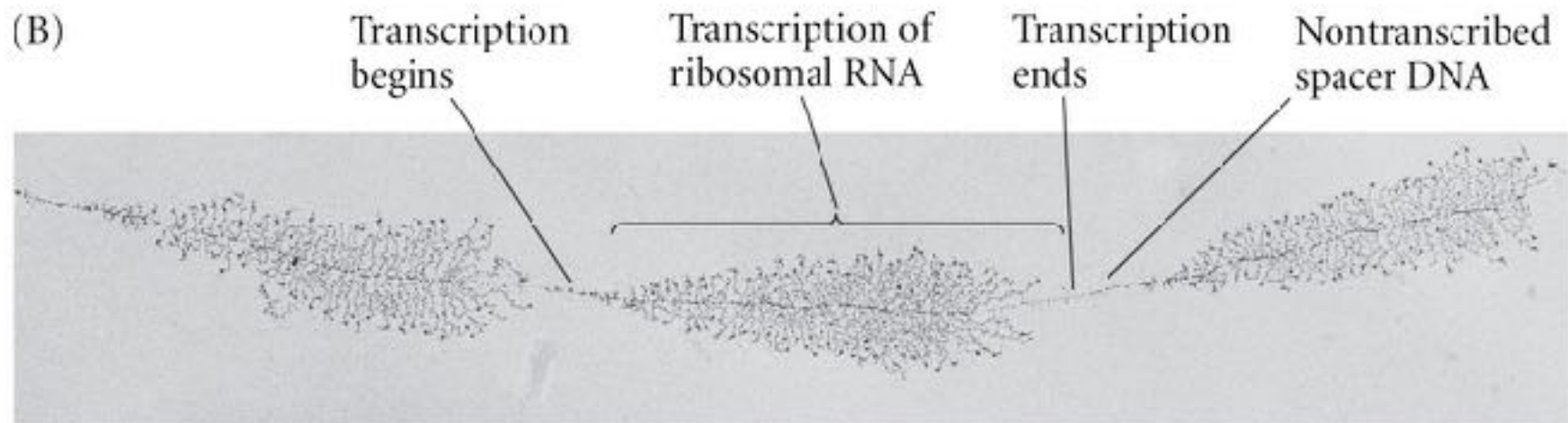
O ciclo menstrual humano



Crescimento de oócitos na rã



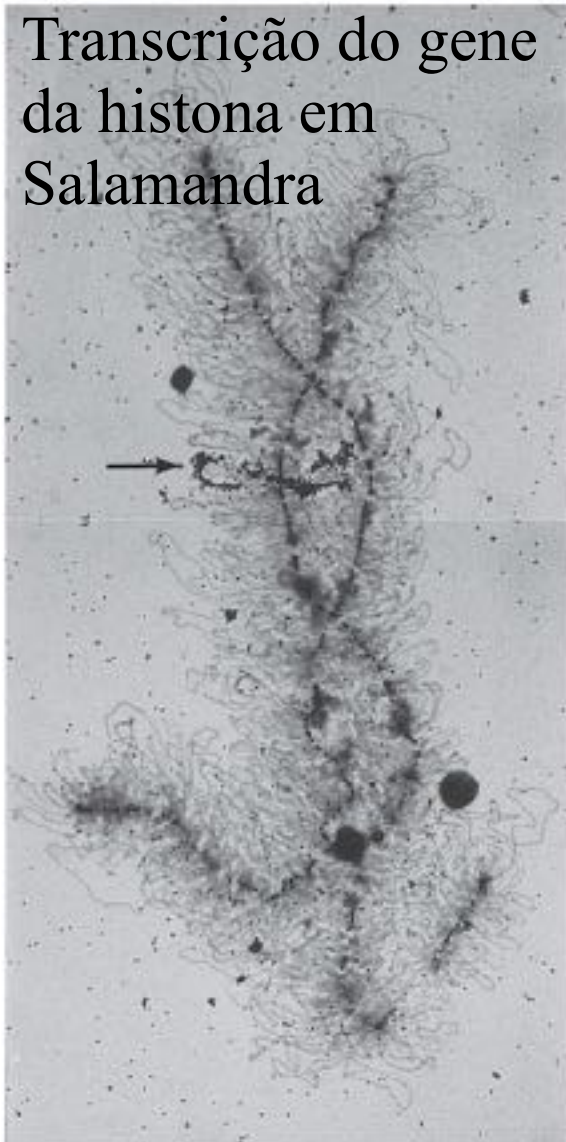




Em oócitos de anfíbios, cromossomos lampbrush são ativos no diplóteno da vesícula germinativa durante a primeira prófase meiótica

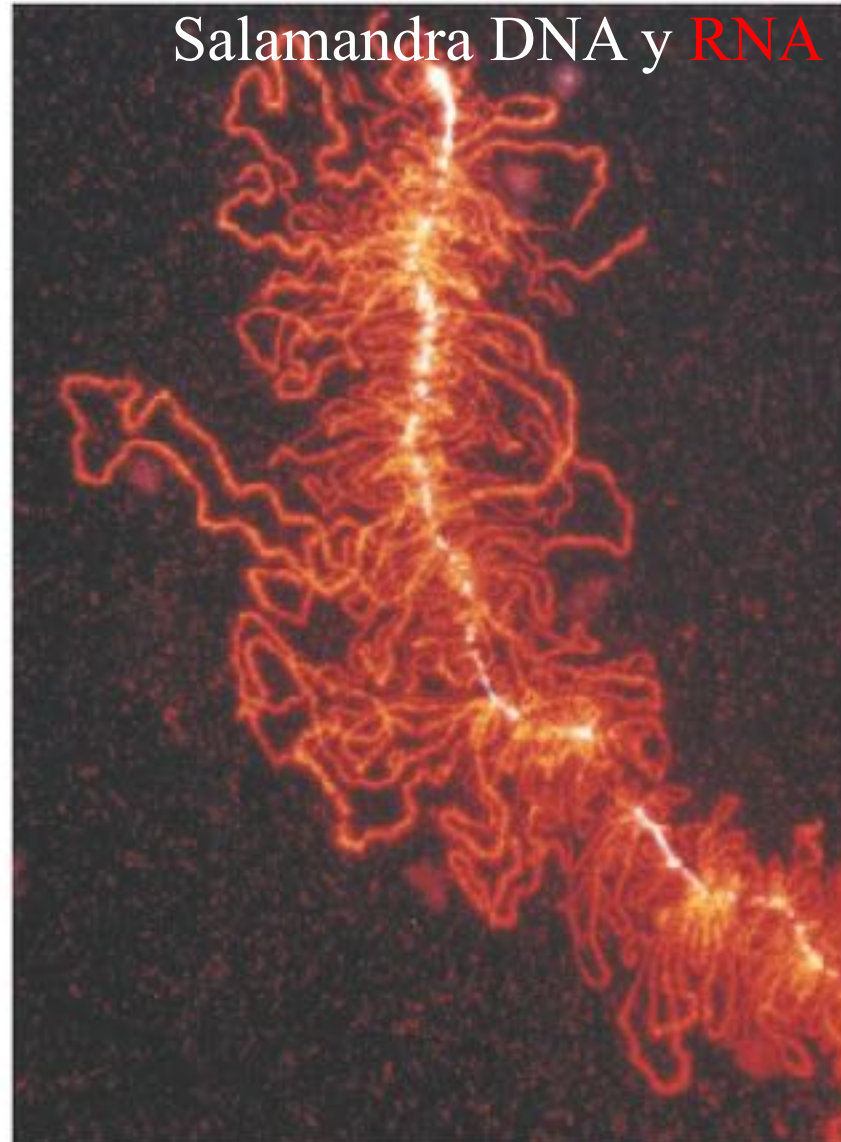
(A)

Transcrição do gene da histona em Salamandra



(B)

Salamandra DNA y RNA

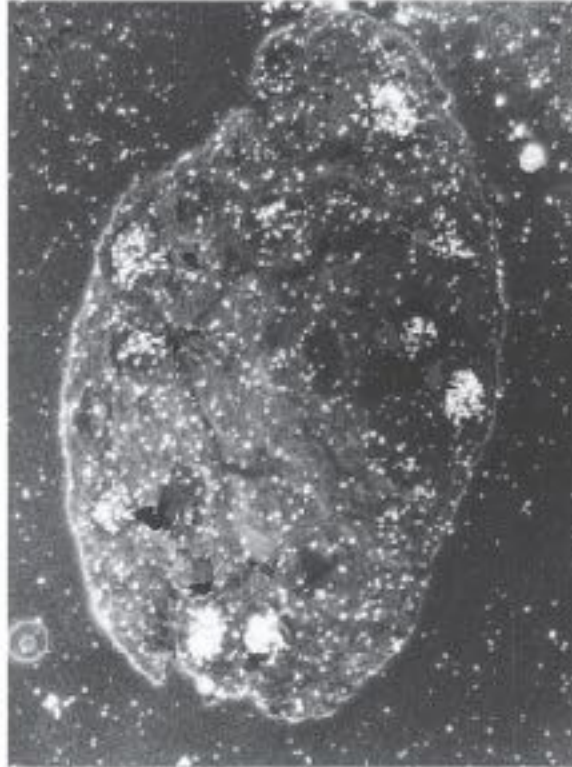


(A)



Oocyte
Ovary
Brain
Heart
Intestine
Kidney
Liver
Muscle
Testis
Uterus

(B)



(C)

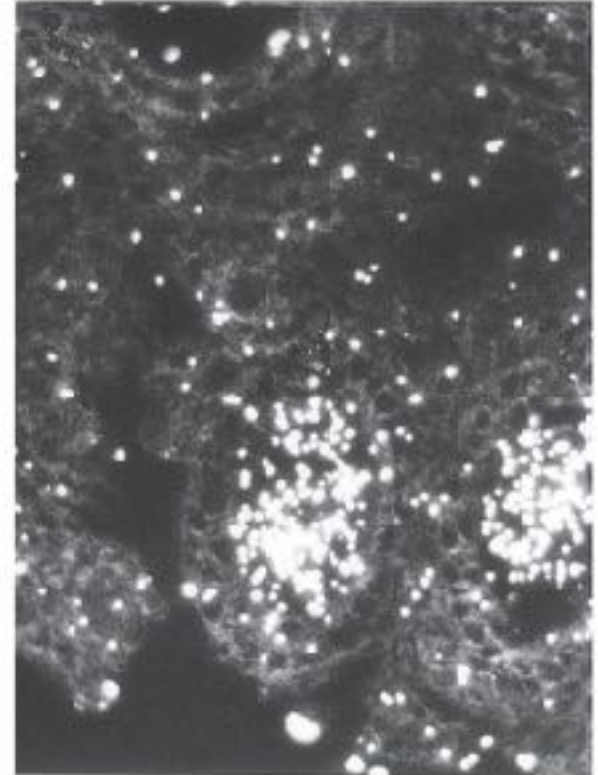


TABLE 19.2 Cellular components stored in the mature oocyte of *Xenopus laevis*

Component	Approximate excess over amount in larval cells
Mitochondria	100,000
RNA polymerases	60,000–100,000
DNA polymerases	100,000
Ribosomes	200,000
tRNA	10,000
Histones	15,000
Deoxyribonucleoside triphosphates	2,500

Source: After Laskey 1979.

Representação esquemática da maturação de oócitos de *Xenopus*, mostrando a regulação da divisão celular da meiose pela progesterona e a fertilização

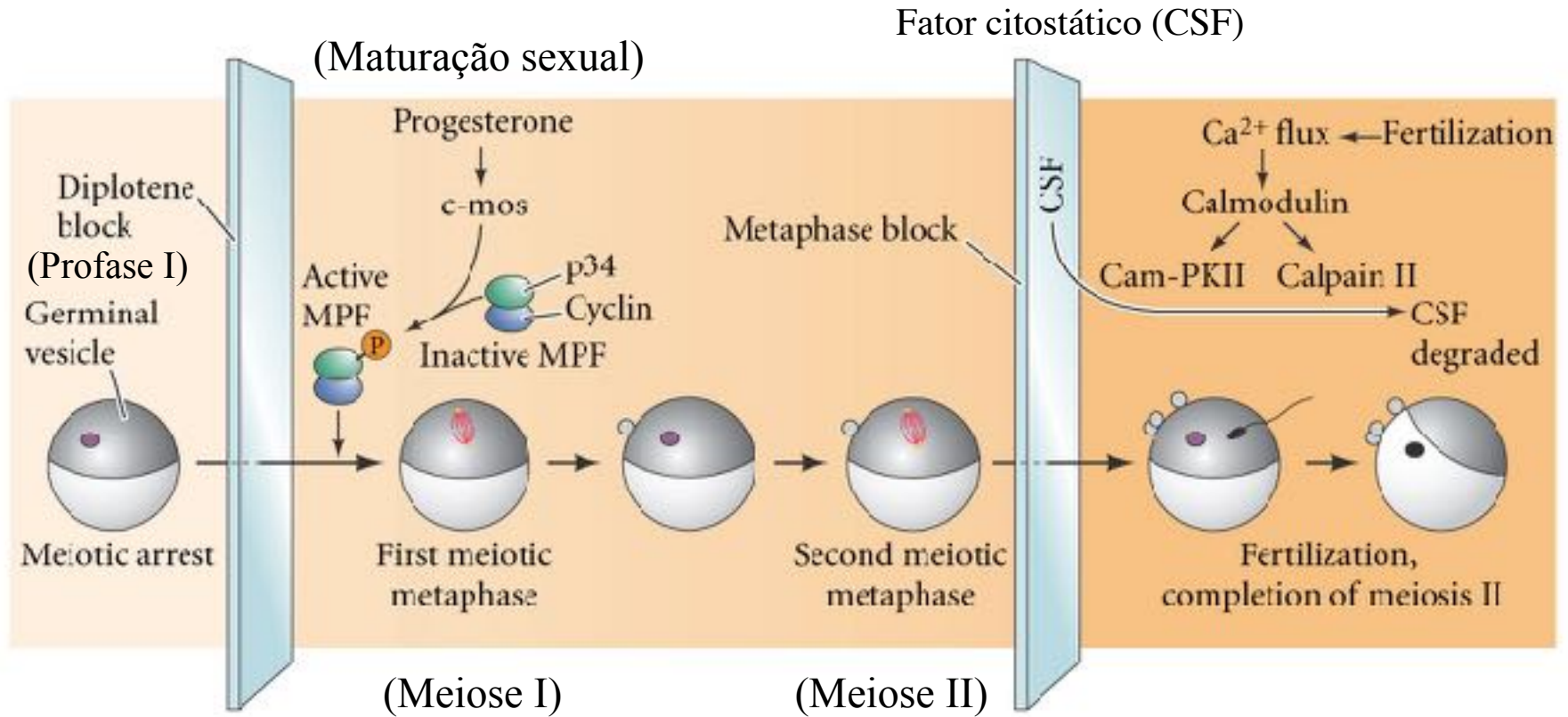


TABLE 19.1 Sexual dimorphism in mammalian meioses

Female oogenesis

Meiosis initiated once in a finite population of cells

One gamete produced per meiosis

Completion of meiosis delayed for months or years

Meiosis arrested at first meiotic prophase and reinitiated in a smaller population of cells

Differentiation of gamete occurs while diploid, in first meiotic prophase

All chromosomes exhibit equivalent transcription and recombination during meiotic prophase

Source: Handel and Eppig 1998.

a) *Drosophila mangabeirai* – um dos Corpos Polares atua como espermatozóide e induz a fertilização do ovo. PARTENOGENESE

Só fêmeas

b) Inseto *Moraba virgo* (gafanhoto) e lagarto *Cnemidophorus uniparens* – oogônia duplica seu número cromossômico antes da meiose e por isso termina com óocitos diplóides depois da meiose. PARTENOGENESE

Só fêmeas

c) Gafanhoto *Pycnoscelus surinamensis* – não precisa de meiose, o zigoto fêmea se forma mediante a mitose. PARTENOGENESE

Só fêmeas

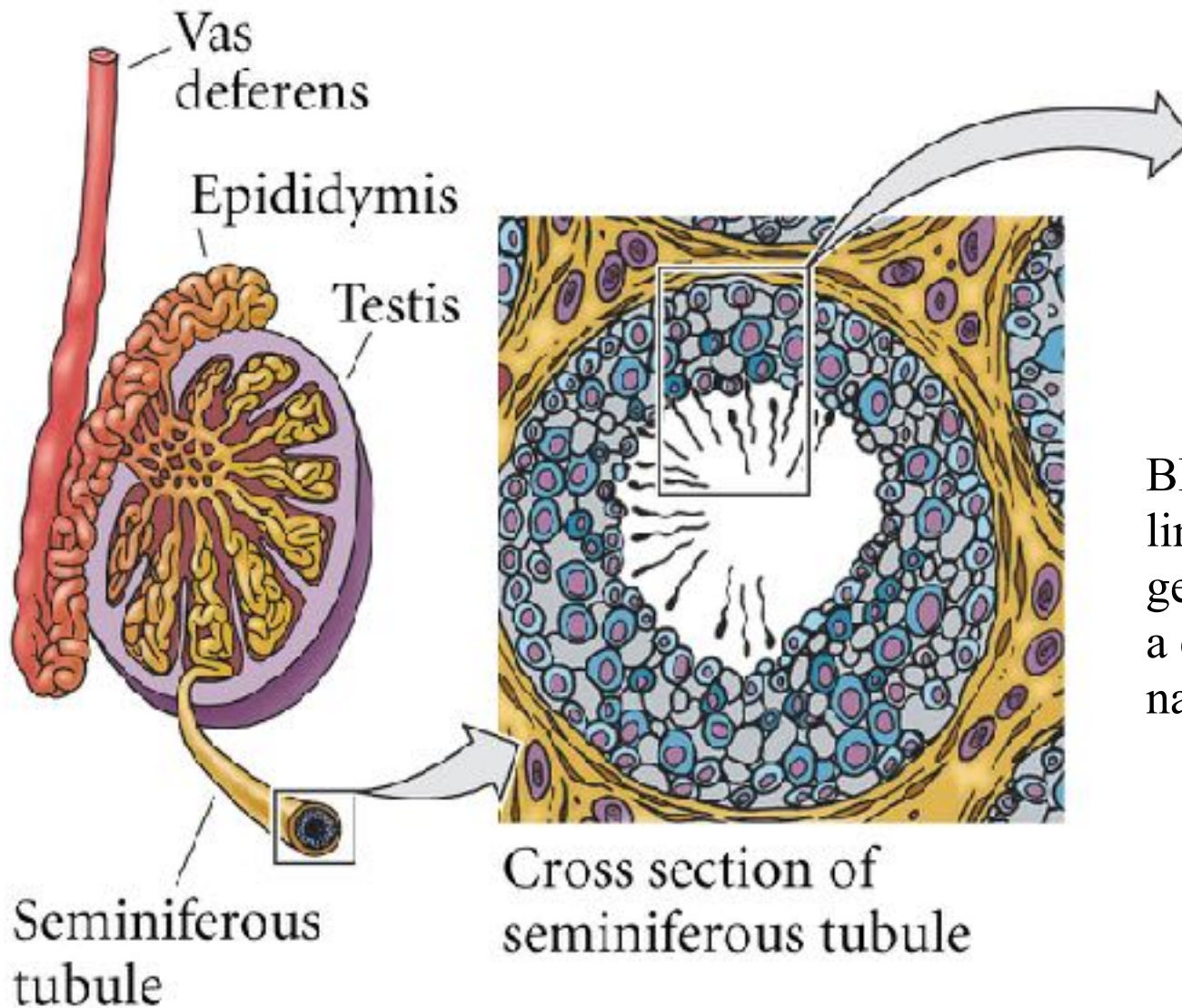
d) Himenoptera (abelhas, vespas e formigas) – ovos não fecundados (e portanto haplóides) se desenvolvem em machos; fecundação gera zigotos diplóides que produzirão fêmeas. PARTENOGENESE HAPLÓIDE

Machos podem formar esperma eliminando a meiose I
(espermatogênese só passa pela meiose II)

TABLE 19.1 Sexual dimorphism in mammalian meioses

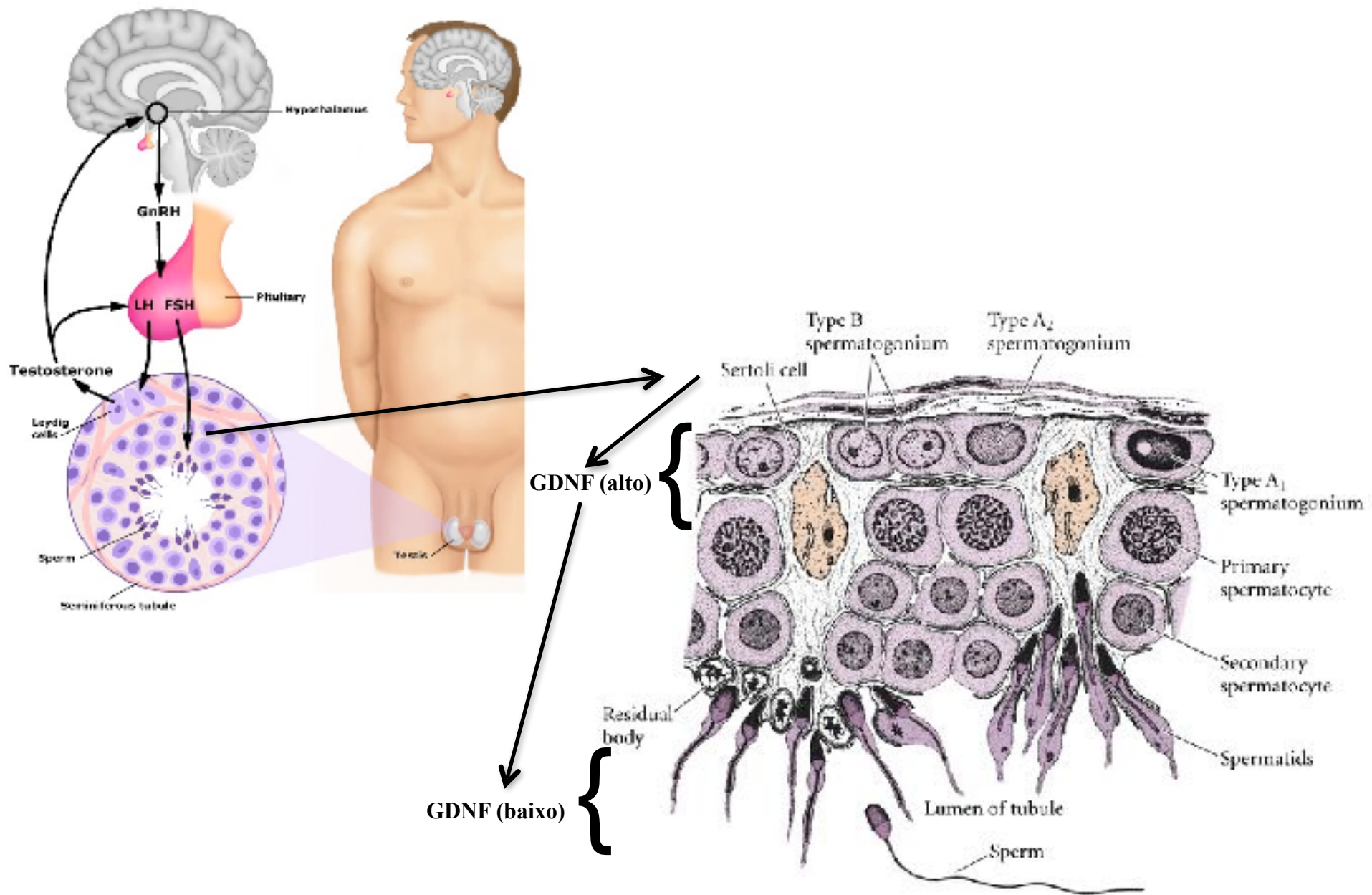
Female oogenesis	Male spermatogenesis
<p>Meiosis initiated once in a finite population of cells</p> <p>One gamete produced per meiosis</p> <p>Completion of meiosis delayed for months or years</p> <p>Meiosis arrested at first meiotic prophase and reinitiated in a smaller population of cells</p> <p>Differentiation of gamete occurs while diploid, in first meiotic prophase</p> <p>All chromosomes exhibit equivalent transcription and recombination during meiotic prophase</p>	

Source: Handel and Eppig 1998.

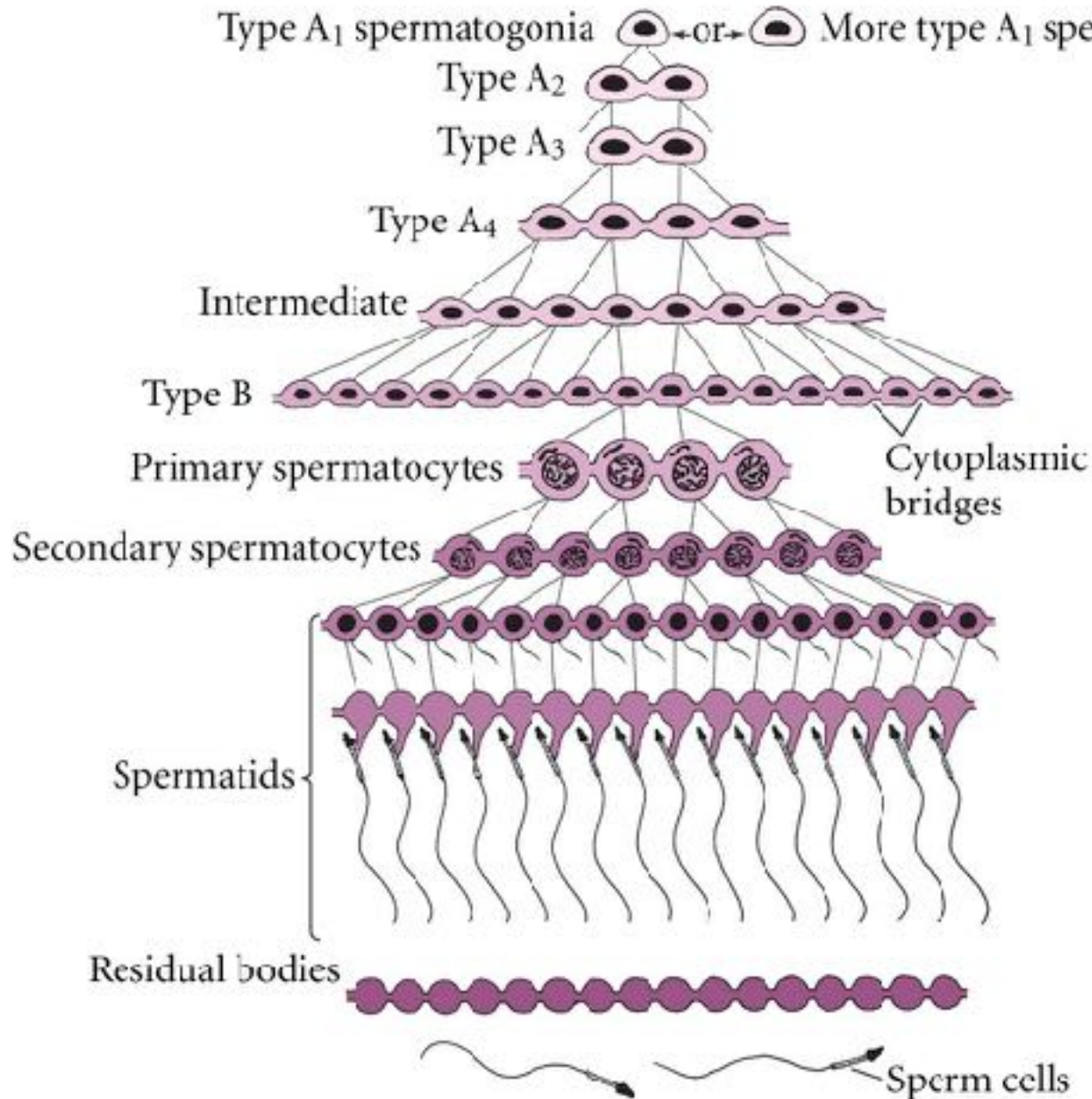


BMP8b da linhagem germinativa inicia a espermatogênese na puberdade

Seção do túbulo seminífero, mostrando a relação entre as células de Sertoli e o desenvolvimento do espermatozoário



A formação de clones sinciciais de células germinativas do macho de humanos

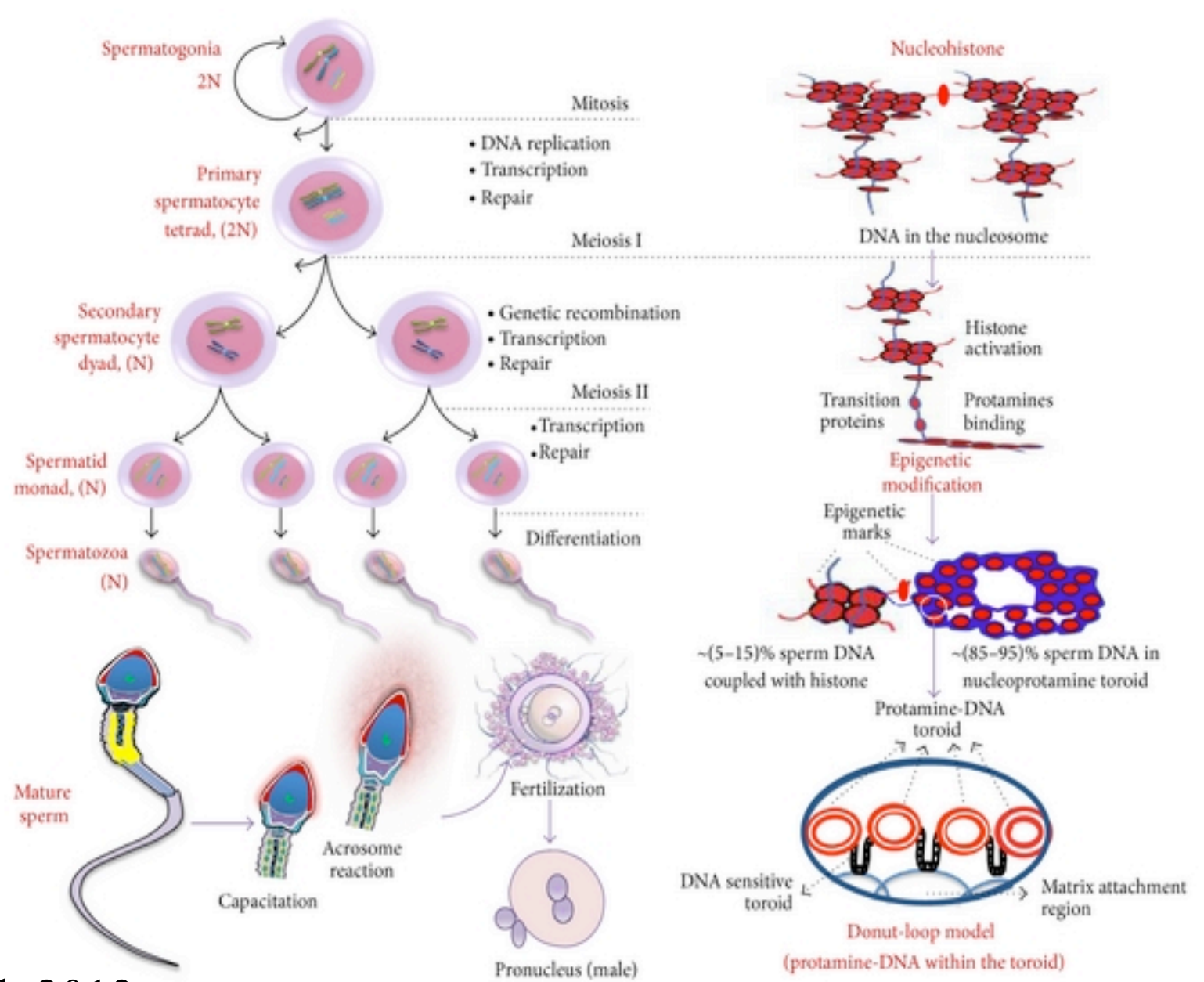


Dados interessantes:

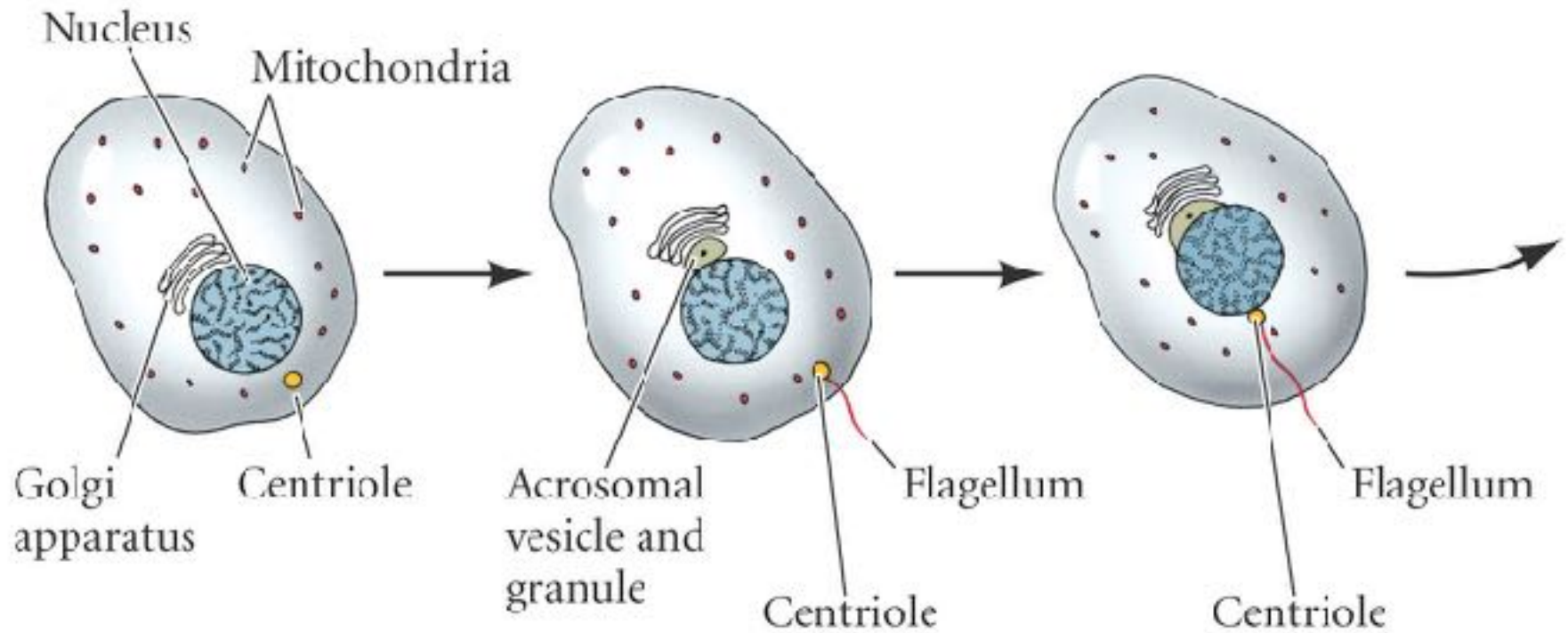
- 100 milhões de espermatozoides / dia
- 200 milhões de espermatozoides / ejaculação

Ultra compactação do DNA nos espermatozóides

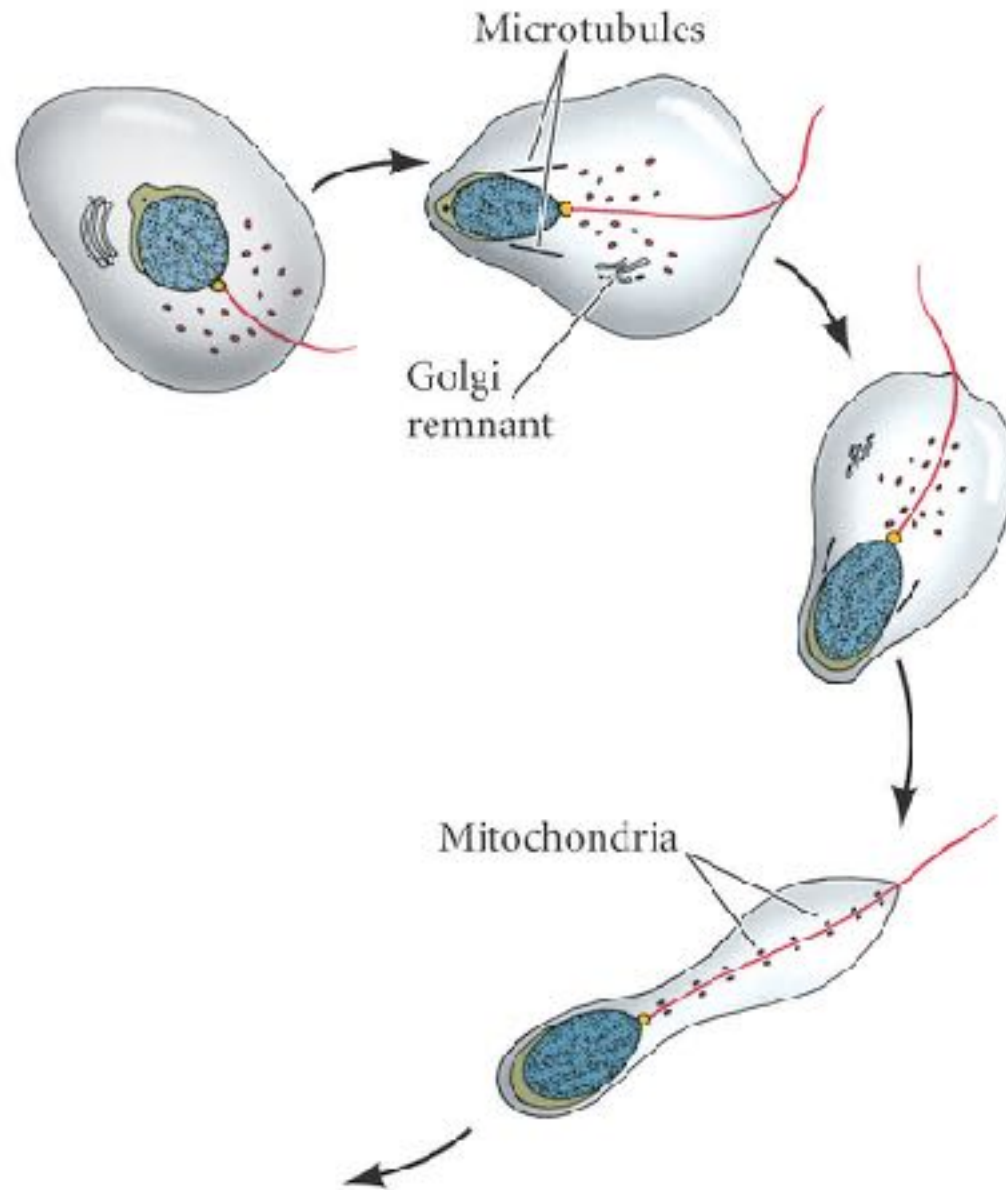
Protaminas:
possuem a
função de
compactar,
estabilizar e
proteger o
material
genético no
núcleo do
espermatozóide

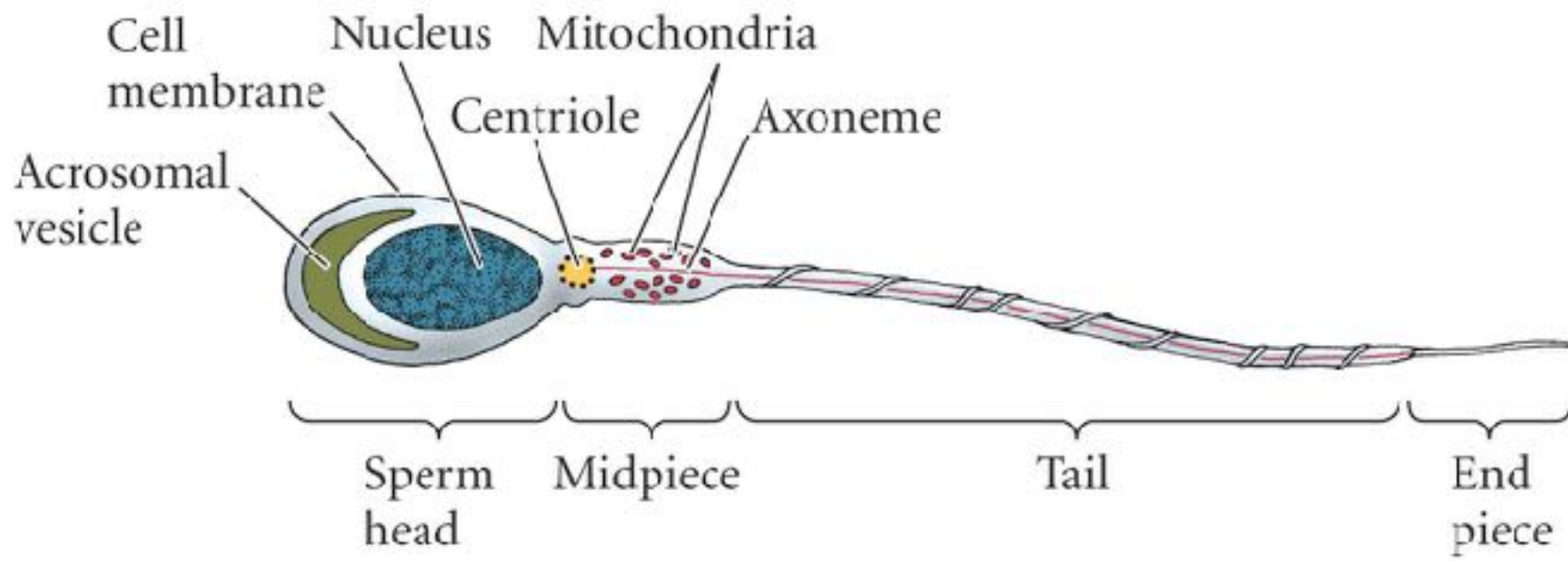


(A)



Espermiogênese ou maturação das espermátides (Parte II)

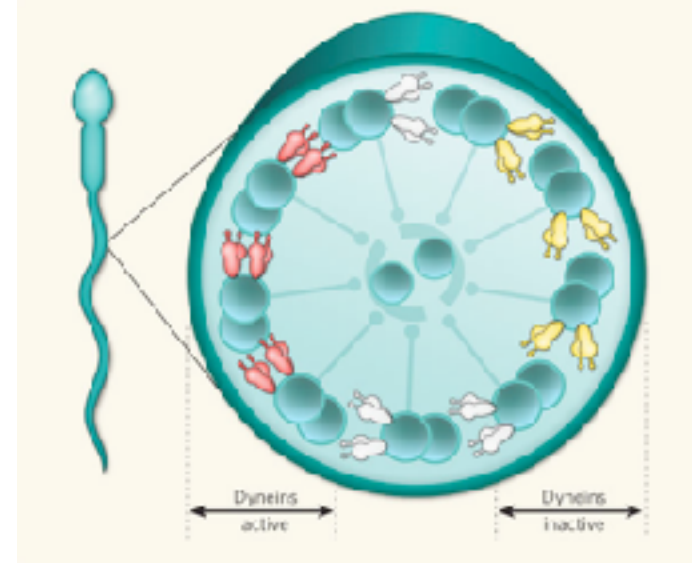
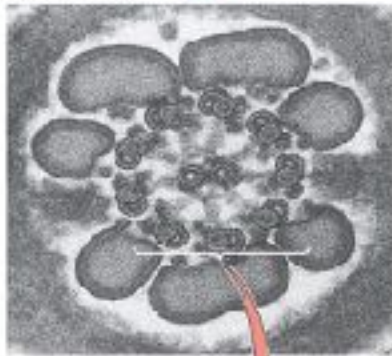




O aparelho móvel do esperma

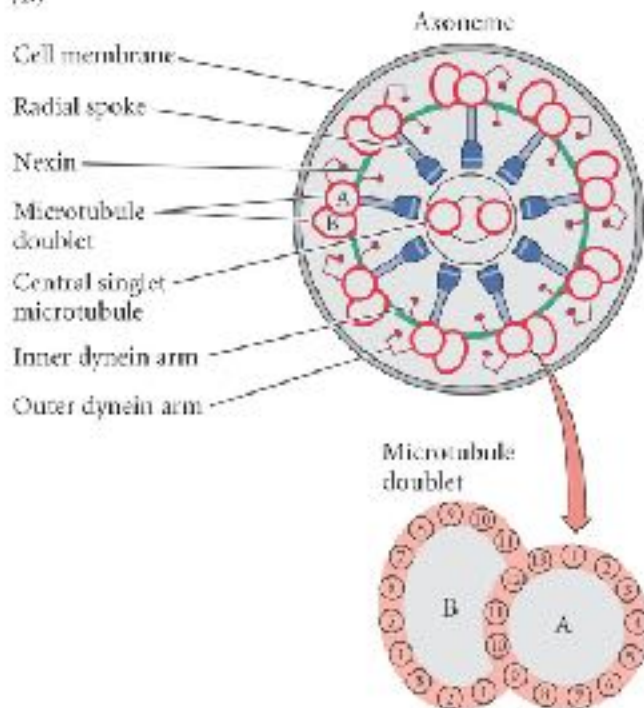
(A) Sperm

Crosssection of sperm tail

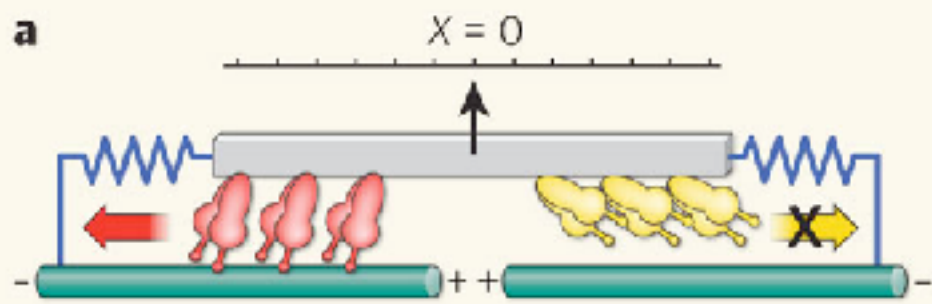


Mitchison & Mitchison 2010

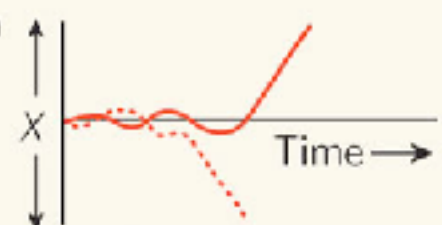
(B)



a

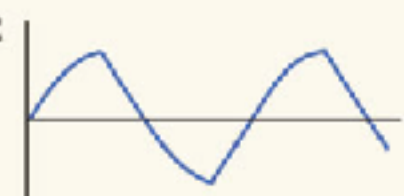


b



Without springs: one group of motors wins

c



With springs: stable oscillations

TABLE 19.1 Sexual dimorphism in mammalian meioses

Female oogenesis	Male spermatogenesis
Meiosis initiated once in a finite population of cells	Meiosis initiated continuously in a mitotically dividing stem cell population
One gamete produced per meiosis	Four gametes produced per meiosis
Completion of meiosis delayed for months or years	Meiosis completed in days or weeks
Meiosis arrested at first meiotic prophase and reinitiated in a smaller population of cells	Meiosis and differentiation proceed continuously without cell cycle arrest
Differentiation of gamete occurs while diploid, in first meiotic prophase	Differentiation of gamete occurs while haploid, after meiosis ends
All chromosomes exhibit equivalent transcription and recombination during meiotic prophase	Sex chromosomes excluded from recombination and transcription during first meiotic prophase

Source: Handel and Eppig 1998.