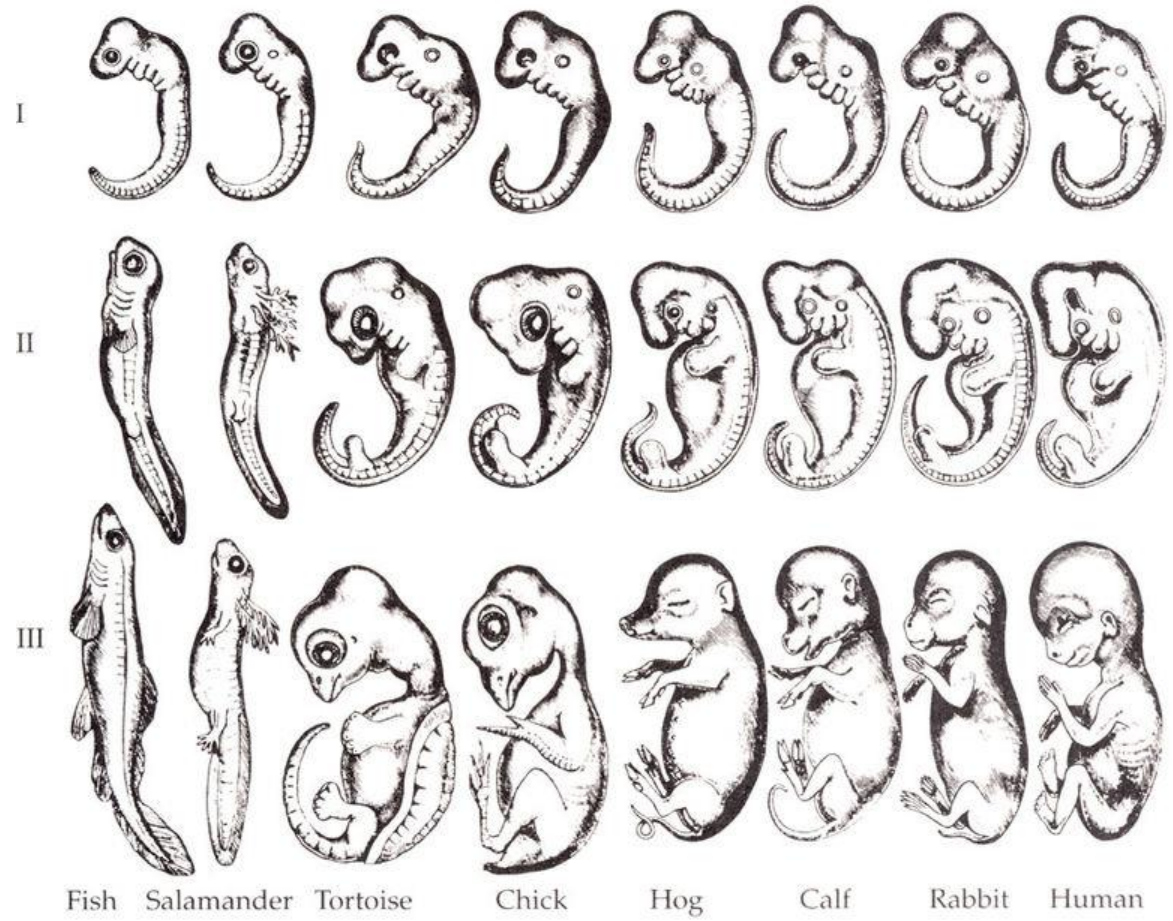
Mecanismos conservados del desarrollo (Evo-Devo)



Uriel Koziol
ukoziol@fcien.edu.uy

Bibliografía

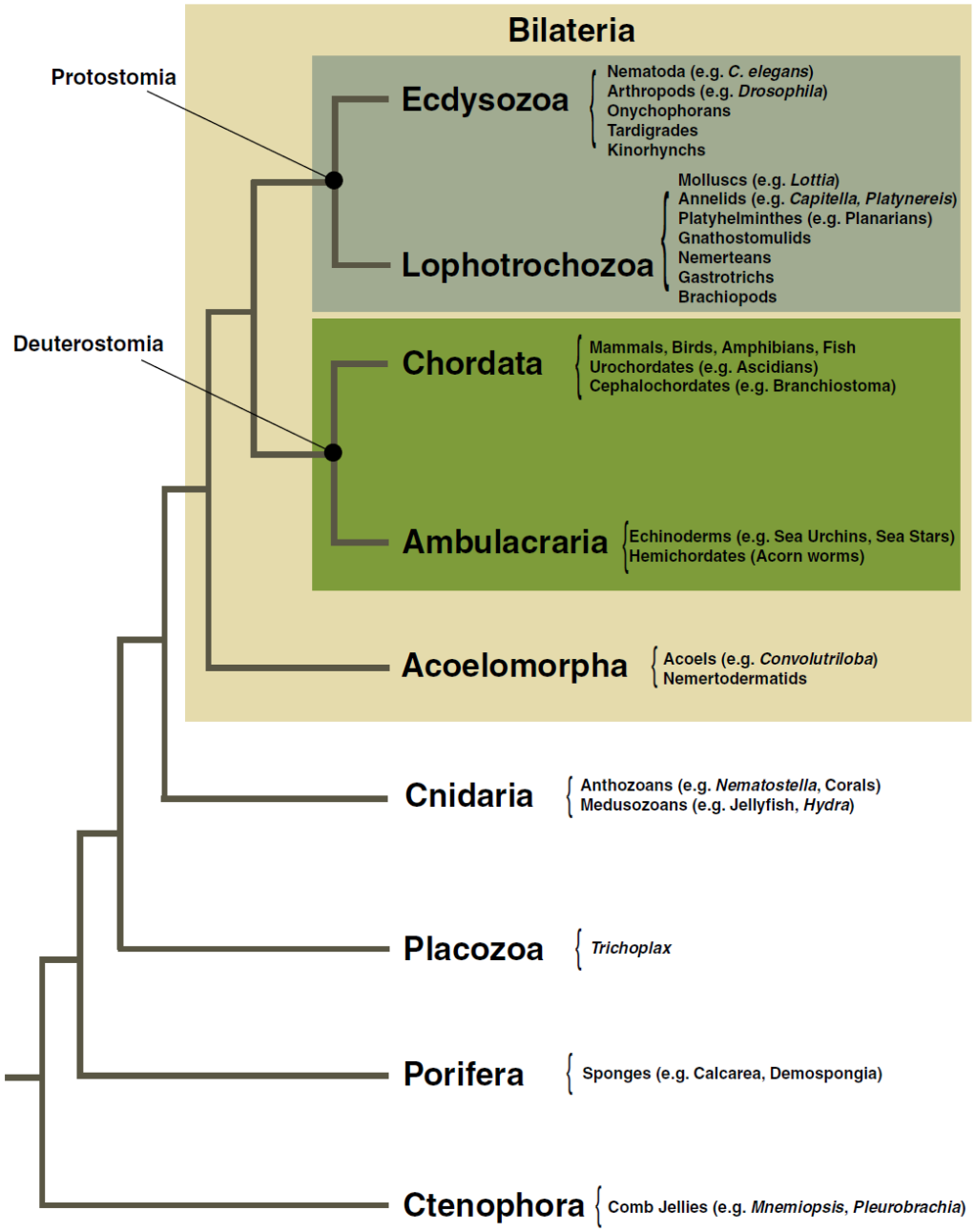
- S.F. Gilbert – **Developmental Biology** (10) – C. 4, 5, 8, 9, 10, 11, 12 (Hox), 22, 26
- S.F. Gilbert – **Developmental Biology** (11) – C. 1, 4, 5, 9, 10, 11, 22, 26
- B. Alberts et al. – **Molecular Biology of the Cell** (6) – C. **15**
- J. M. W. Slack – **Essential developmental Biology** – C. 11, 12, 13, 19, **20**
- Revisiones (Drive)

Prácticos / Seminarios

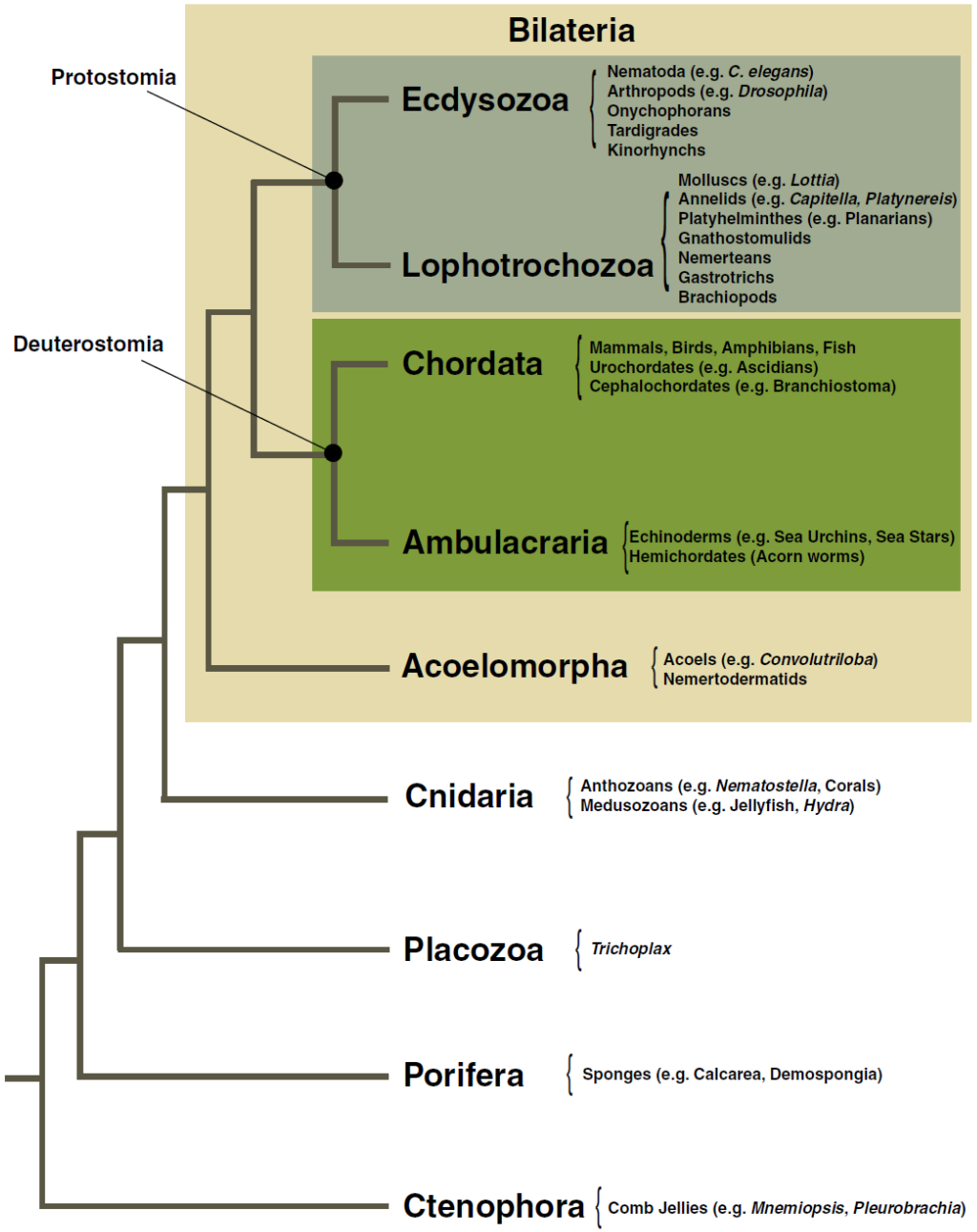
- Seminarios 25/10 – artículos sobre bases celulares de la regeneración

- Prácticos: 11/10-18/10; 24-25/10. 4 instancias + trabajo a distancia.

D1: ImageJ: análisis de embriones
D2: Image J: cuantificación de proliferación celular / Marcado EdU
D3: Detección EdU / Image J: pulso+caza EdU espermatogénesis
D4: Montaje, microscopía de resultados
Opcional: WMIHF



Un poco de Filogenia…



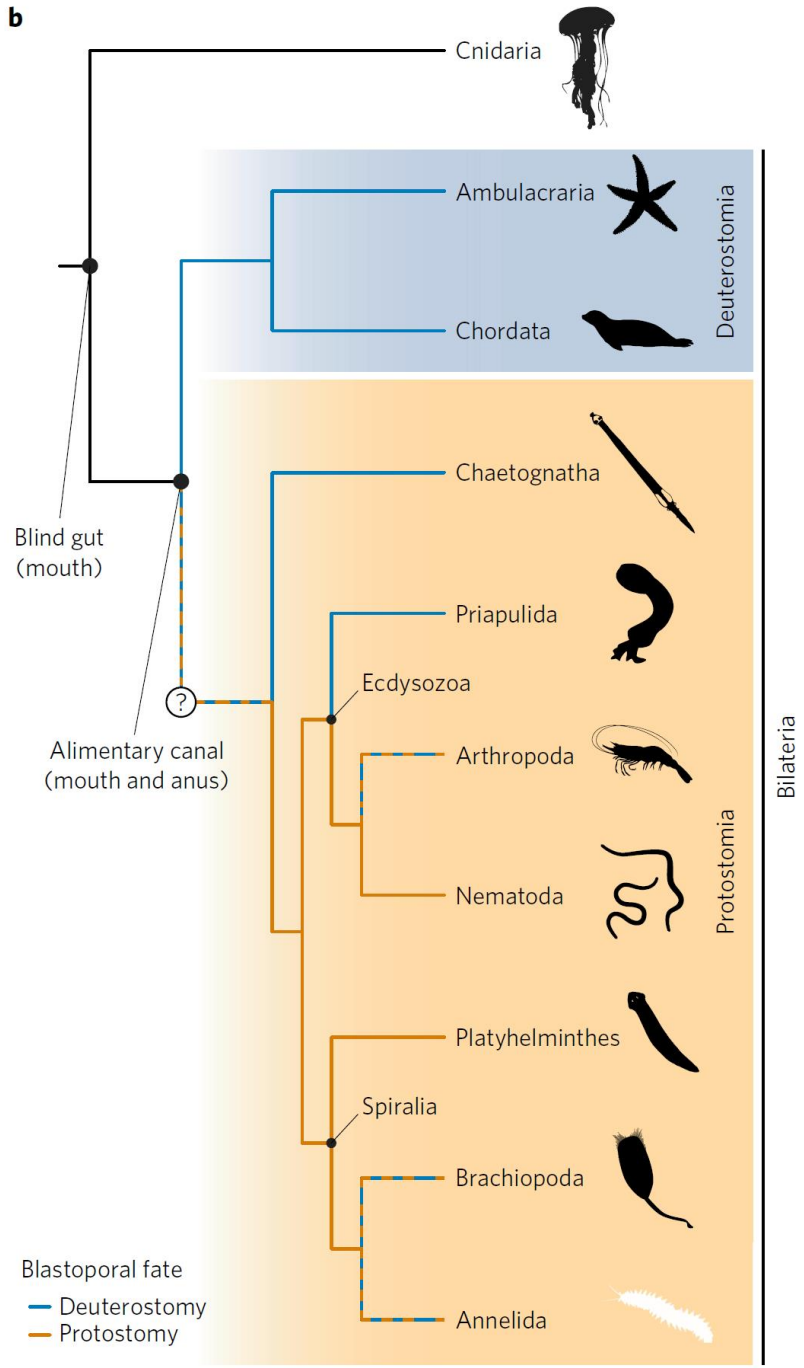
INVERTEBRADOS

"Vertebrados"

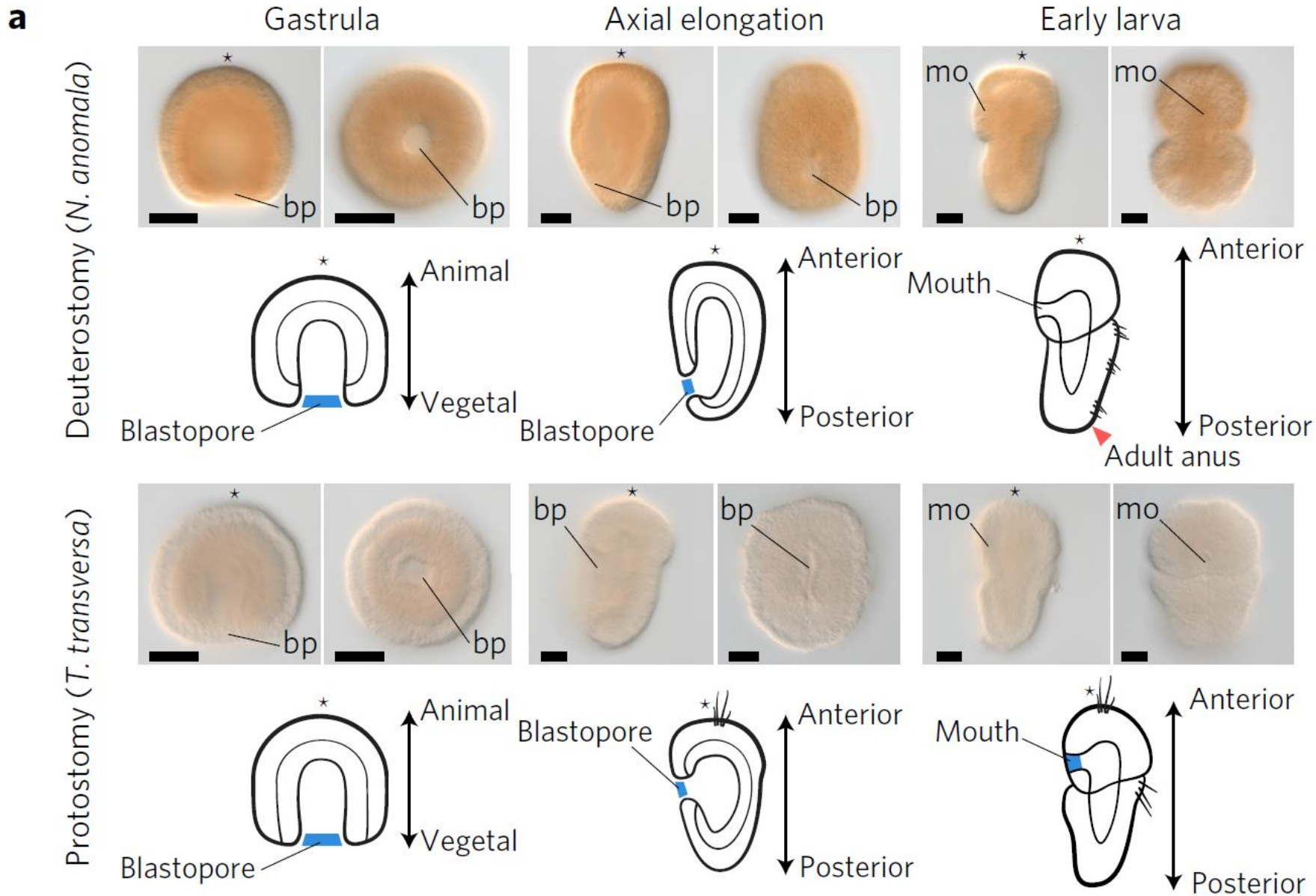
INVERTEBRADOS

Carácteres clásicos del desarrollo y evolución

- Tipos de clivaje, polo Animal y Vegetal
- Blastoporo y su destino (protostomados / deuterostomados)
- Capas germinales: diblásticos vs. triblásticos
- Formación del mesodermo, celomas
- Desarrollo “Regulatorio vs. Mosaico” (Condicional vs. Autónomo)



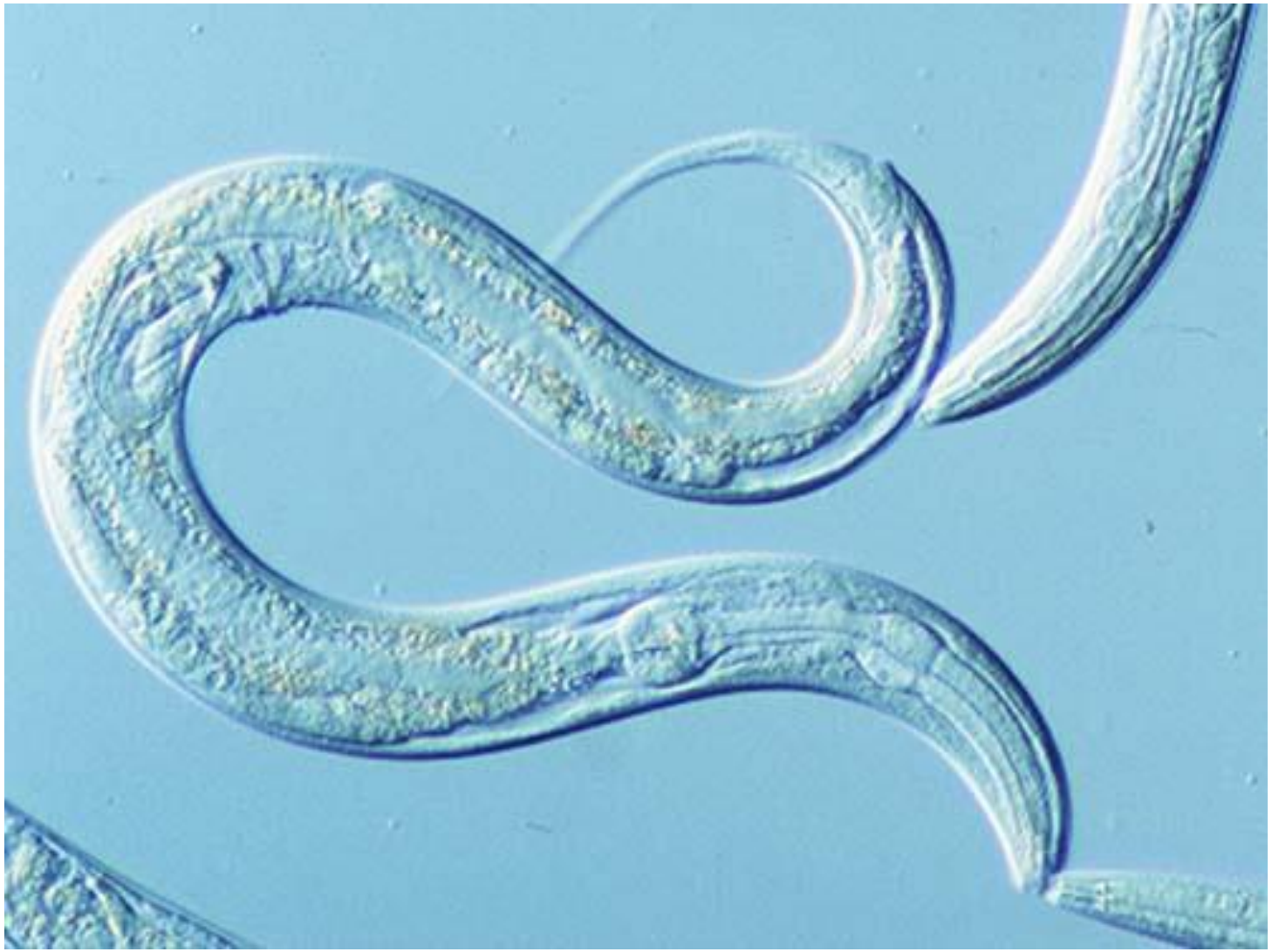
Martín-Durán et al 2016

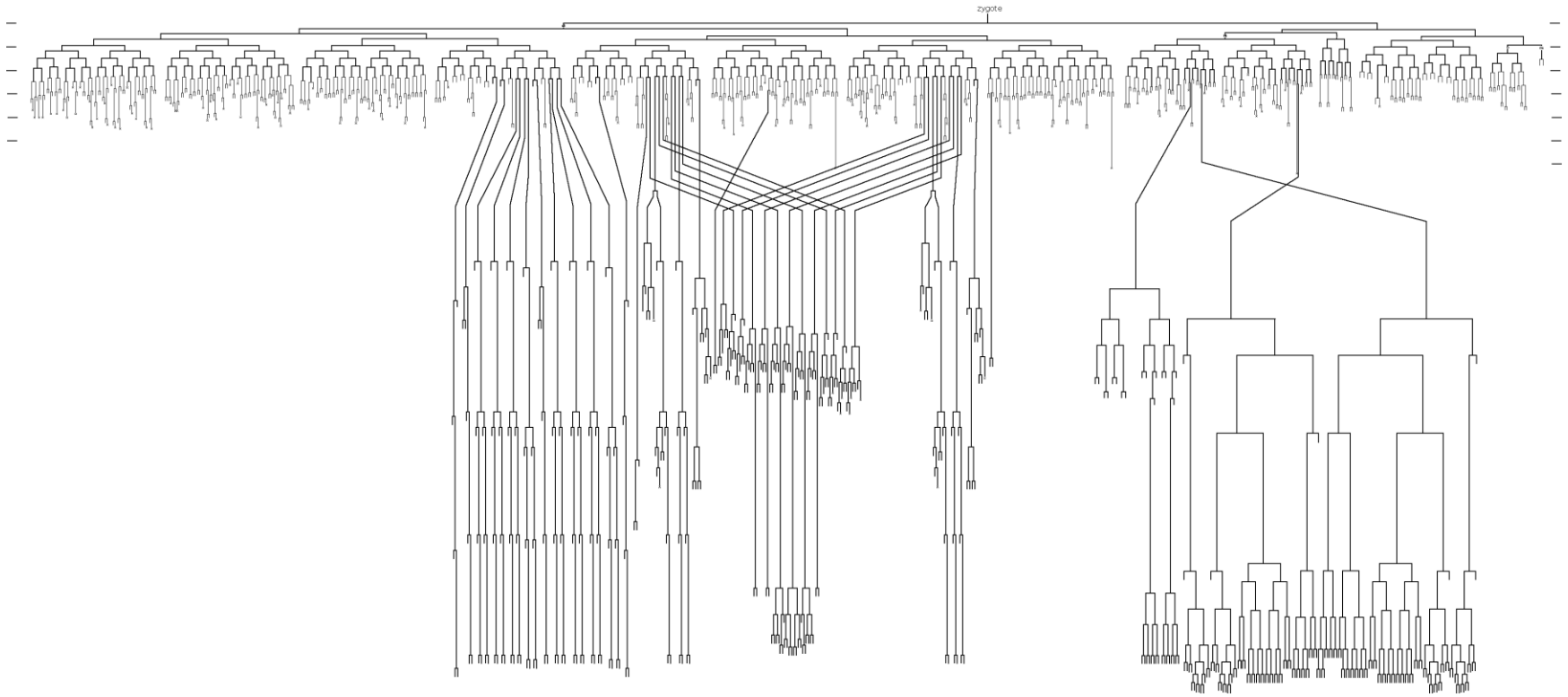


Martín-Durán et al 2016

Modelos clásicos de desarrollo invertebrados

Caenorhabditis elegans





Linaje invariable durante el desarrollo:

959 células somáticas
131 células mueren por apoptosis

The Nobel Prize in Physiology or Medicine 2002

Sydney Brenner
Prize share: 1/3

H. Robert Horvitz
Prize share: 1/3

John E. Sulston
Prize share: 1/3

The Nobel Prize in Physiology or Medicine 2002 was awarded jointly to Sydney Brenner, H. Robert Horvitz and John E. Sulston *"for their discoveries concerning genetic regulation of organ development and programmed cell death"*.

Cell, Vol. 44, 817–829, March 28, 1986, Copyright © 1986 by Cell Press

Genetic Control of Programmed Cell Death in the Nematode C. elegans

Hilary M. Ellis,* and H. Robert Horvitz
Department of Biology
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

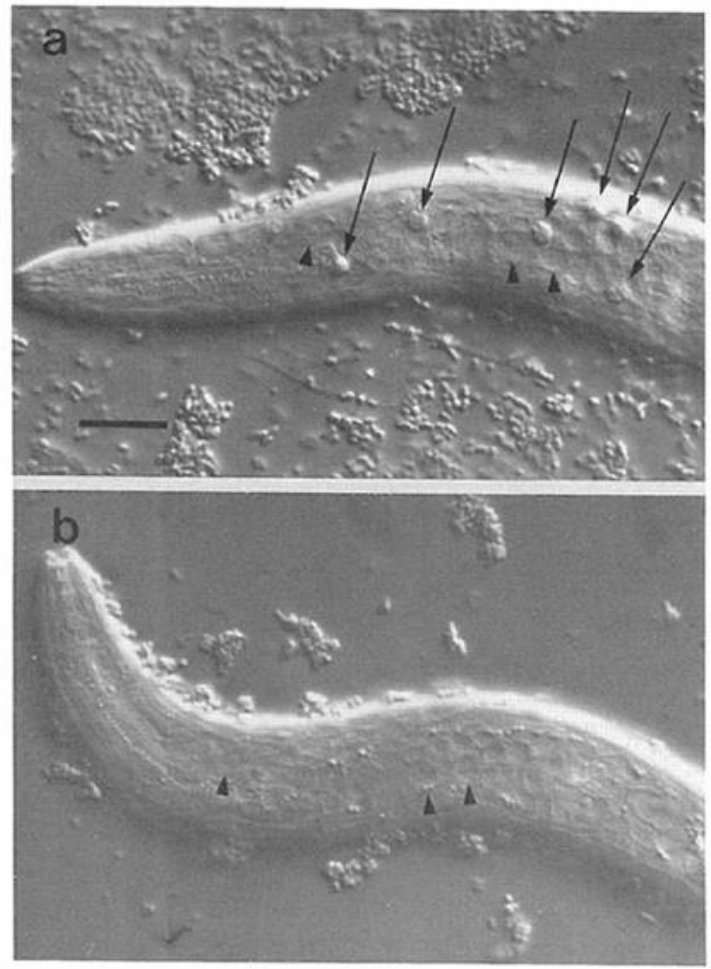


Figure 1. Absence of Cell Deaths in *ced-3* Animals

(a) Nomarski photomicrograph of a newly hatched *ced-1* larva. Arrows indicate dying cells. (b) Nomarski photomicrograph of a newly hatched *ced-1; ced-3* larva. Plane of focus is approximately that shown in (a). Arrowheads indicate several of the nuclei that can be seen in both (a) and (b). No cell deaths are seen in the *ced-1; ced-3* larva. Bar = 10 μ.

The Nobel Prize in Physiology or Medicine 2006

Photo: L. Cicero

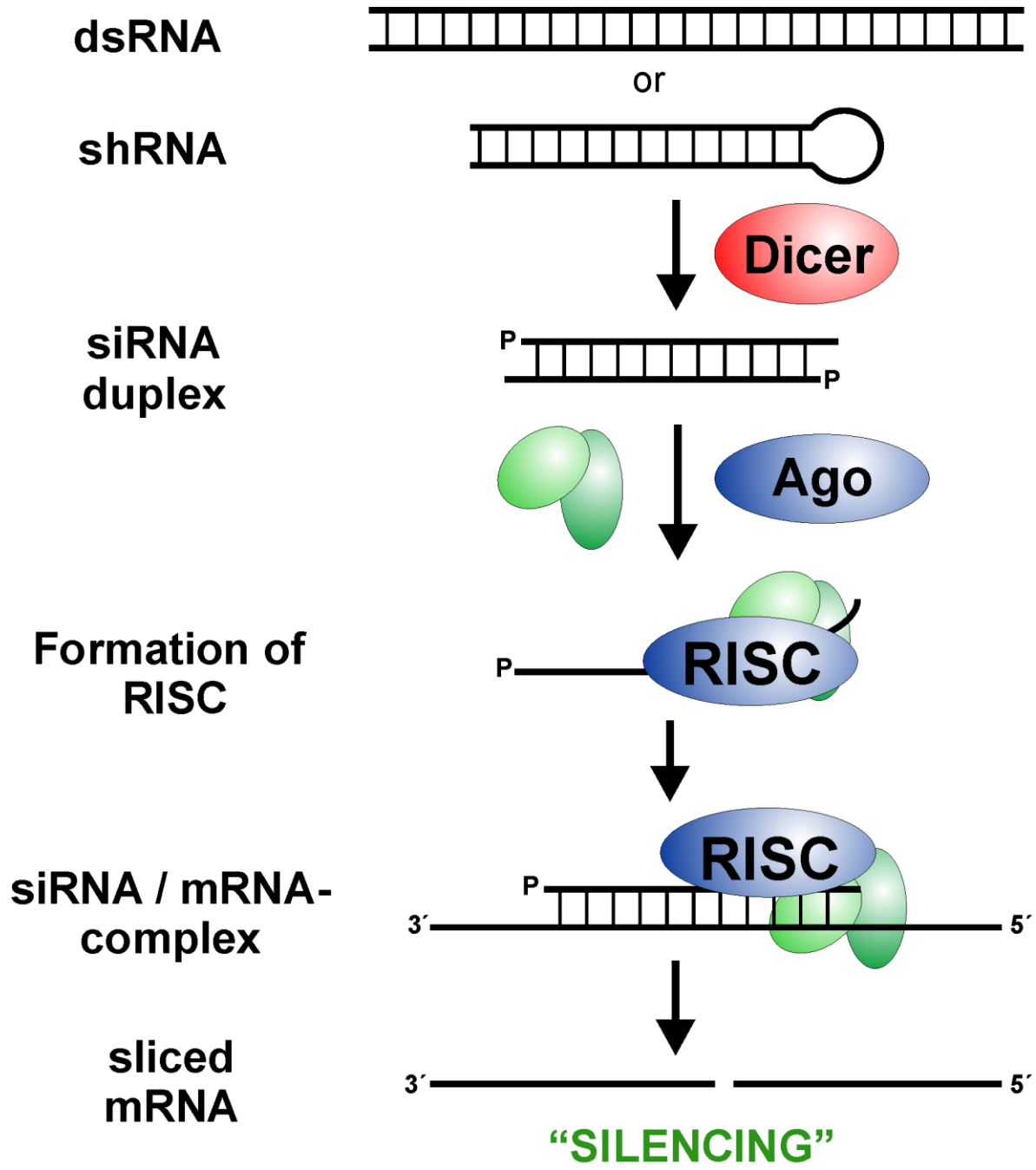
Andrew Z. Fire

Prize share: 1/2

Photo: J. Mottern

Craig C. Mello

Prize share: 1/2


dsRNA
or
shRNA
Dicer
siRNA
duplex
P
P
Ago
Formation of
RISC
P
RISC
RISC
siRNA / mRNA-
complex
P
3´
5´
sliced
mRNA
3´
5´
“SILENCING”

Drosophila melanogaster – Módulo 2019 Carmen Bolatto

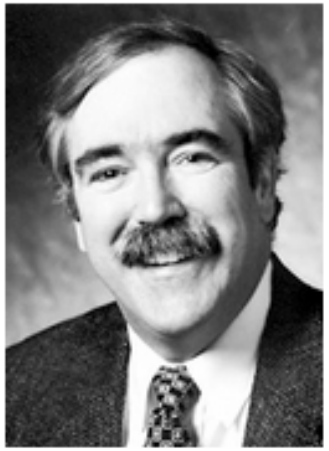
The Nobel Prize in Physiology or Medicine 1995

Edward B. Lewis

Prize share: 1/3

Christiane Nüsslein-Volhard

Prize share: 1/3



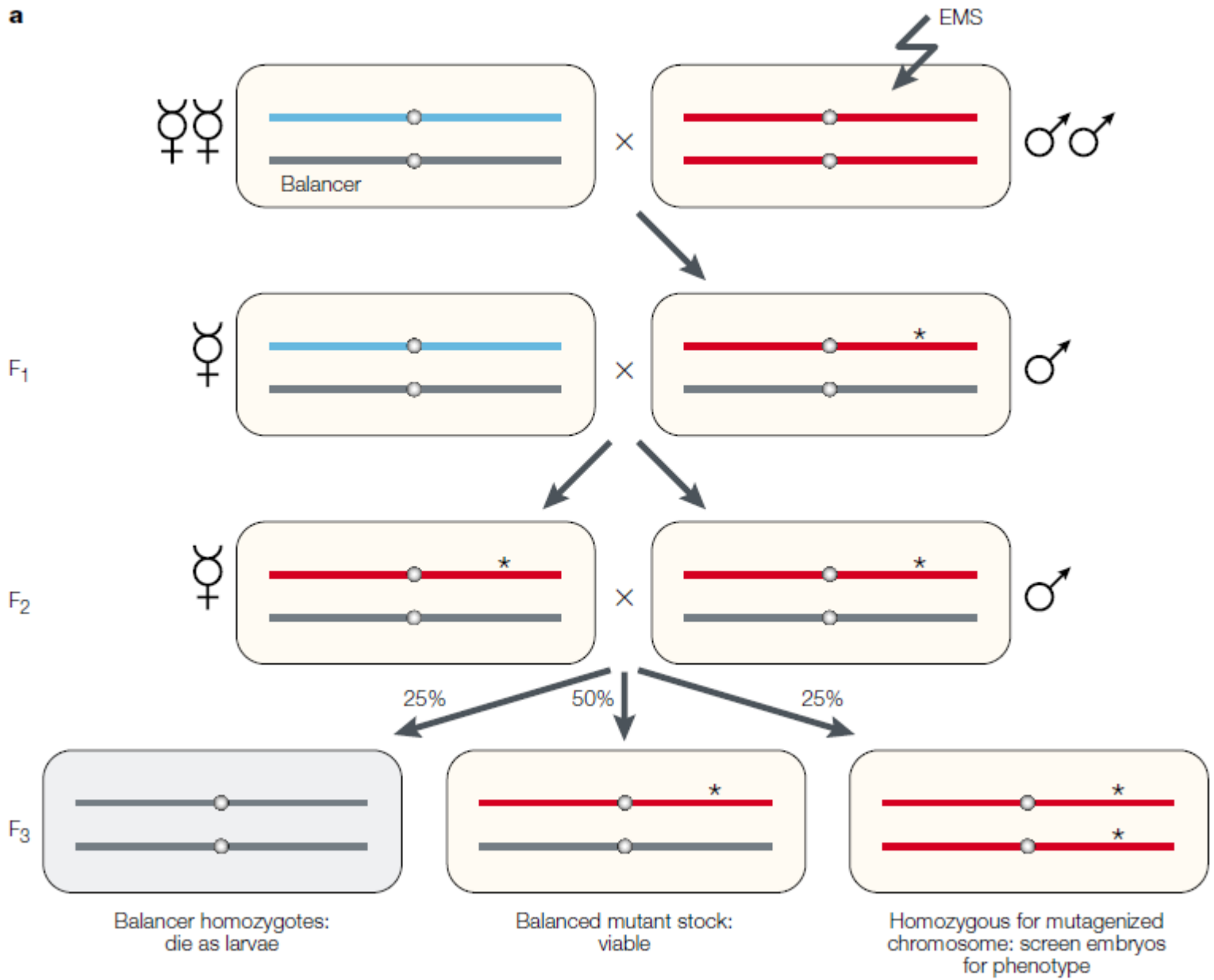
Eric F. Wieschaus

Prize share: 1/3

The Nobel Prize in Physiology or Medicine 1995 was awarded jointly to Edward B. Lewis, Christiane Nüsslein-Volhard and Eric F. Wieschaus *"for their discoveries concerning the genetic control of early embryonic development"*.

http://www.nobelprize.org

“El *screening* de Heidelberg”

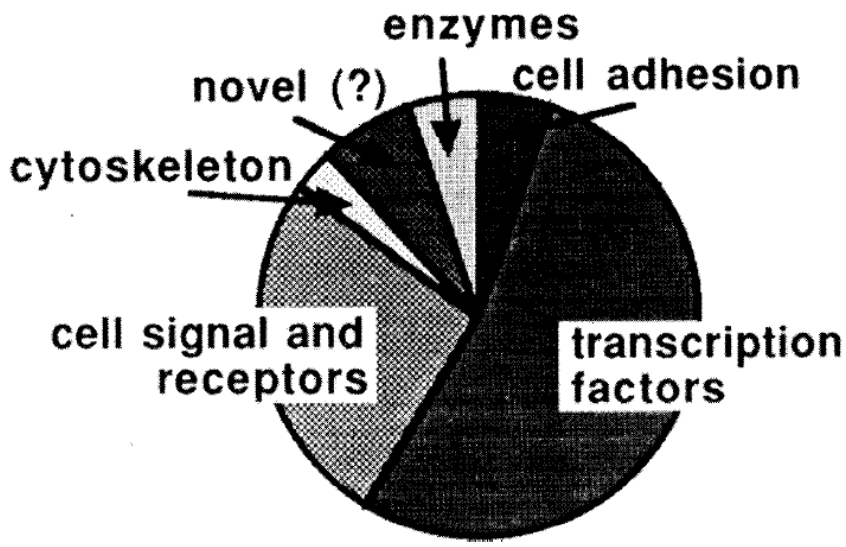


St Johnston 2002 Nature Review Genetics 3:176

Results of mutagenesis screens

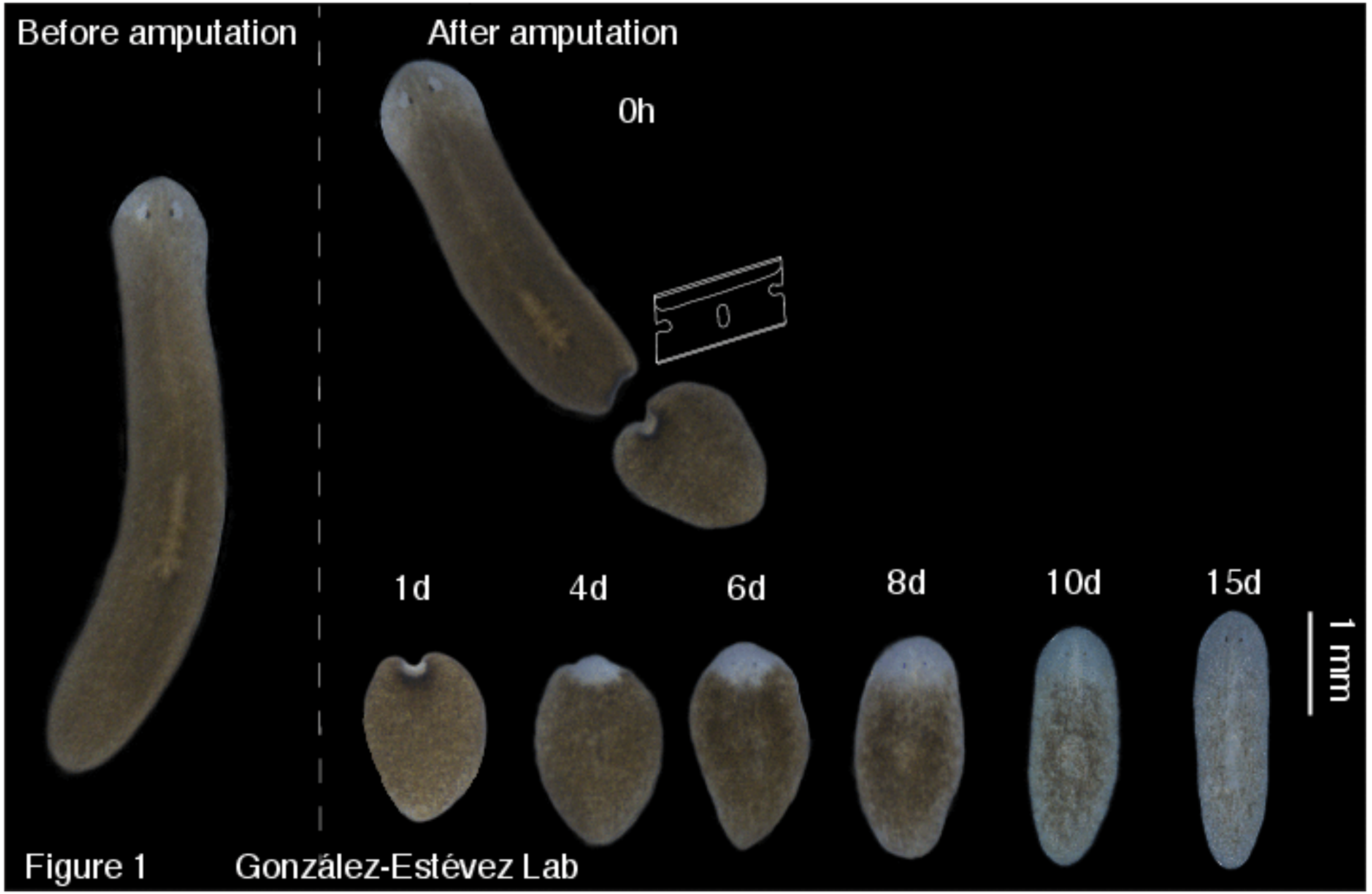
Total lines established and tested	26978
Lethal mutations	18136
Mutations causing embryonic lethality	4332
Mutations causing embryonic phenotypes	580
Complementation Groups (Genes)	139

Cellular Roles of Heidelberg Mutations

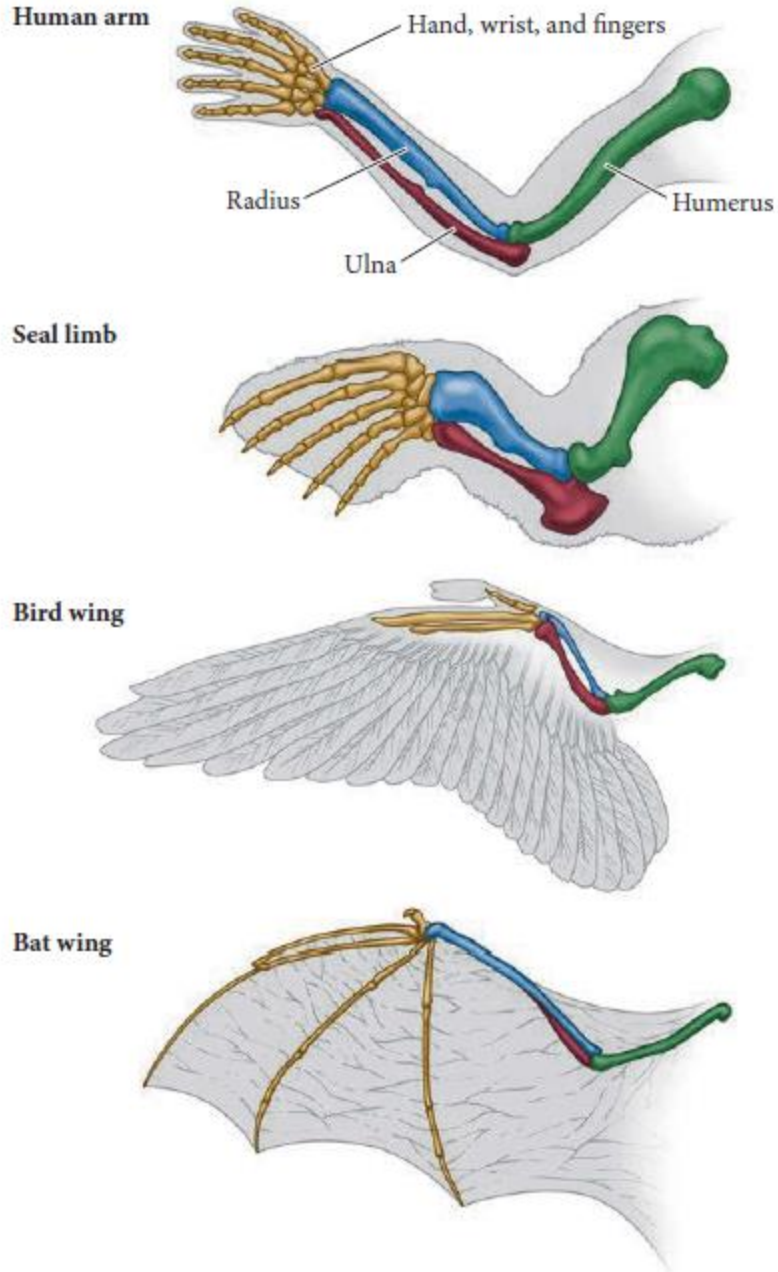


Wieschaus, 1995
http://www.nobelprize.org/nobel_prizes/medicine/laureates/1995/wieschaus-lecture.pdf

Planaria


Before amputation
After amputation
0h
1d
4d
6d
8d
10d
15d
1 mm
Figure 1
González-Estévez Lab

Homología a diferentes niveles


Human arm
Hand, wrist, and fingers
Radius
Humerus
Ulna
Seal limb
Bird wing
Bat wing

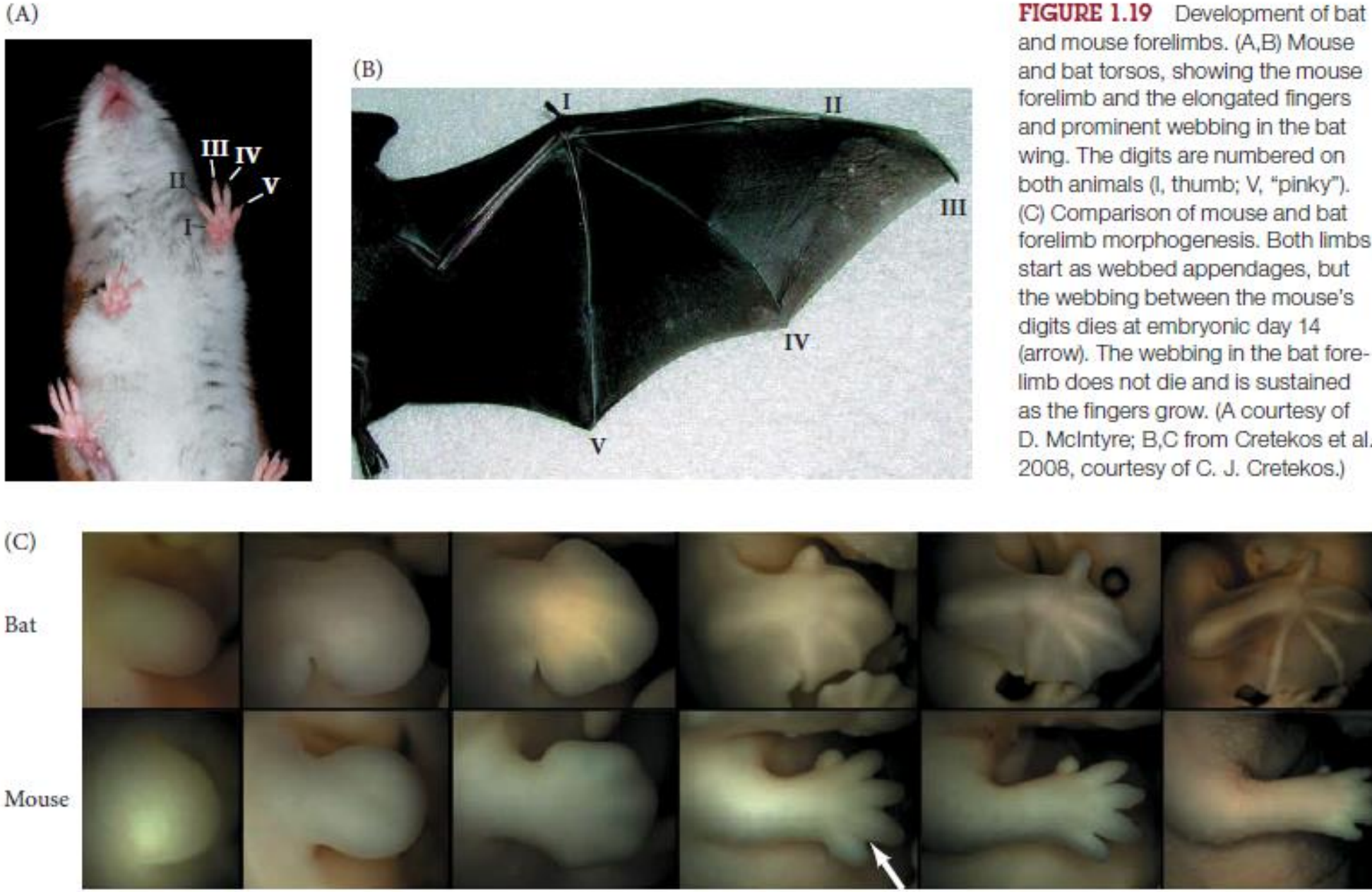


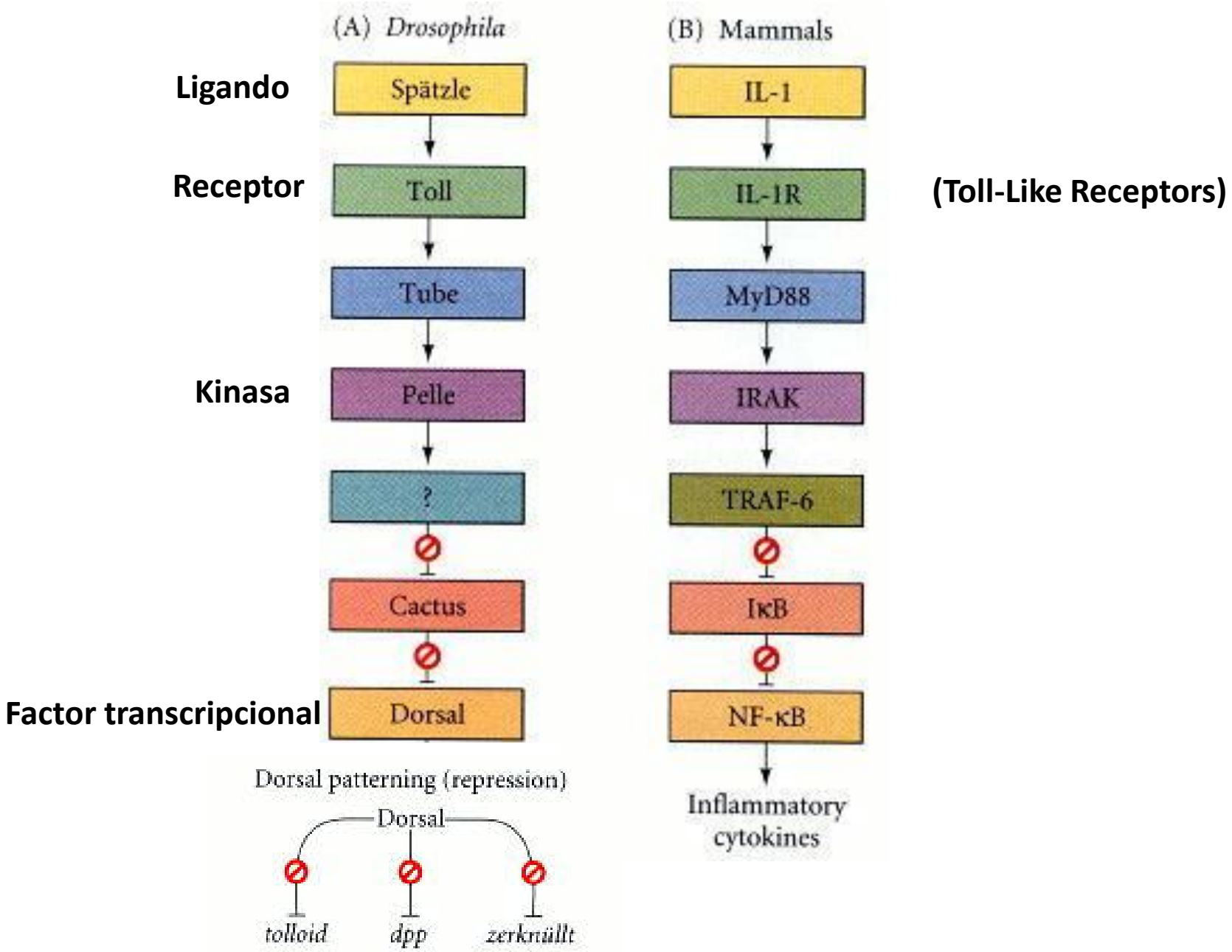
FIGURE 1.19 Development of bat and mouse forelimbs. (A,B) Mouse and bat torsos, showing the mouse forelimb and the elongated fingers and prominent webbing in the bat wing. The digits are numbered on both animals (I, thumb; V, "pinky"). (C) Comparison of mouse and bat forelimb morphogenesis. Both limbs start as webbed appendages, but the webbing between the mouse's digits dies at embryonic day 14 (arrow). The webbing in the bat forelimb does not die and is sustained as the fingers grow. (A courtesy of D. McIntyre; B,C from Cretekos et al. 2008, courtesy of C. J. Cretekos.)

Ligando

Receptor

Kinasa

Factor transcripcional

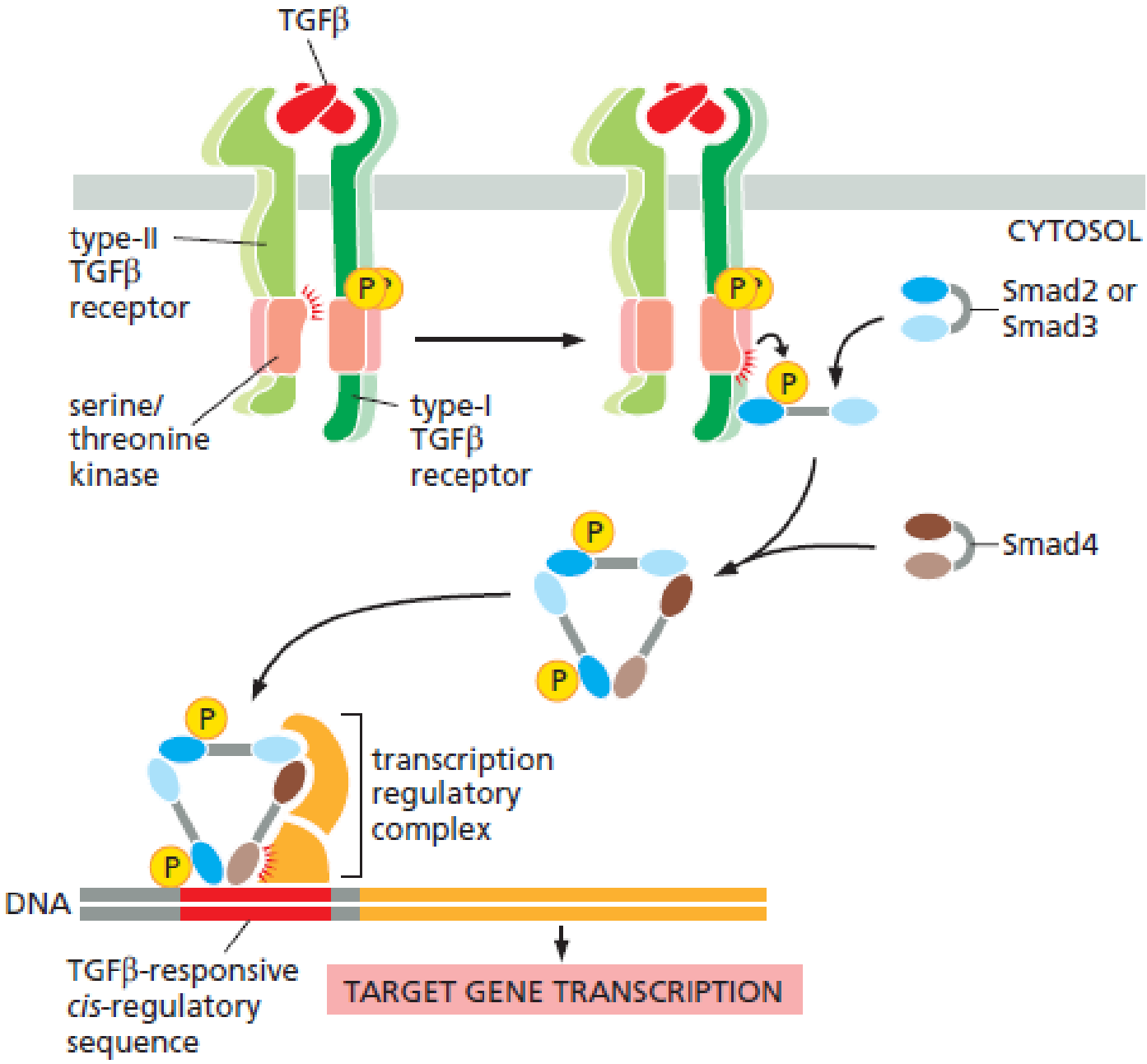


(Toll-Like Receptors)

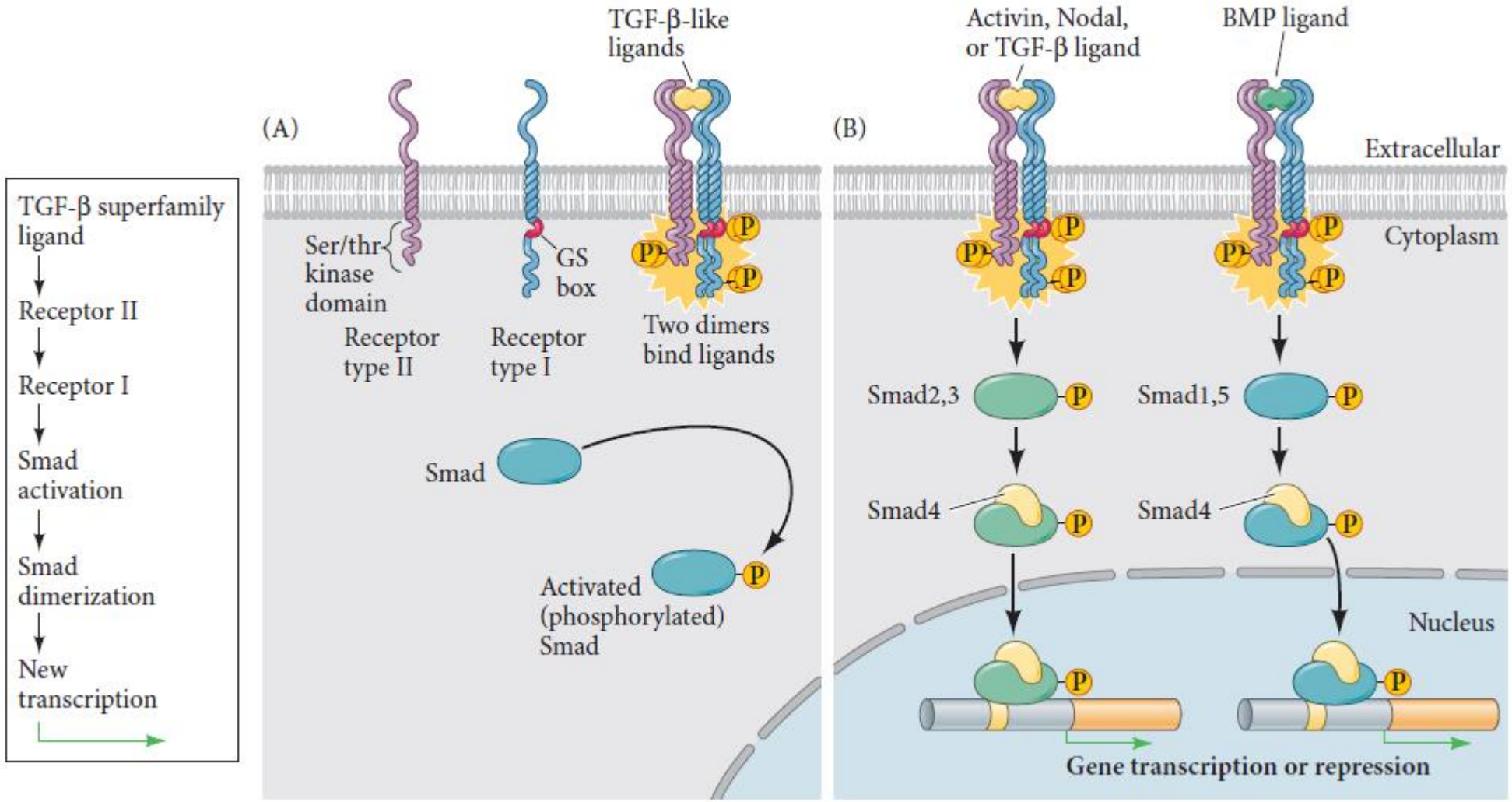
Mecanismos moleculares conservados: Señalización

- GPCRs
- RTK
- TGF-B
- JAK/STAT
- Delta/Notch
- Hedgehog
- Wnt/BCAT

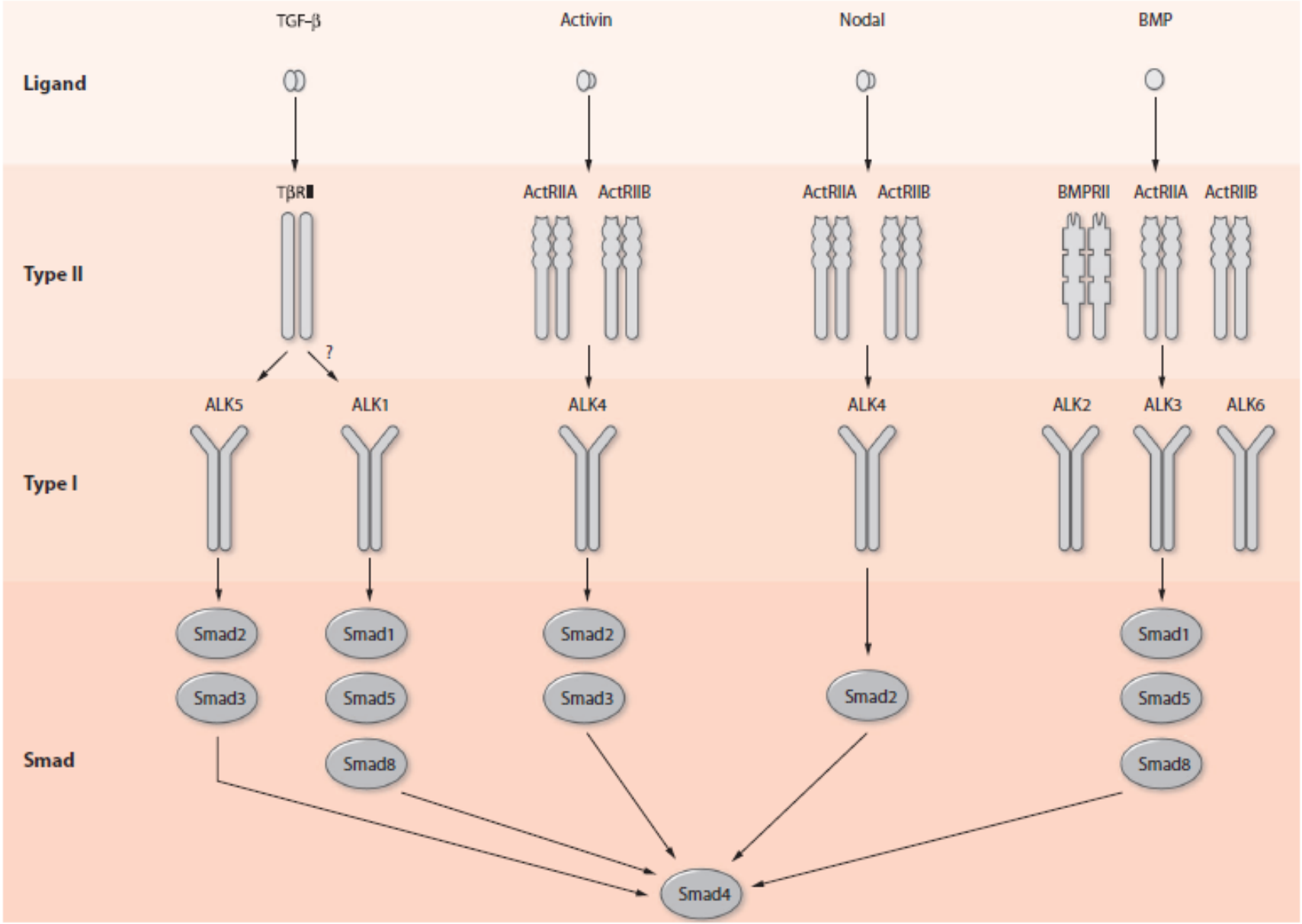
TGF-B y BMPs (RSTKs)



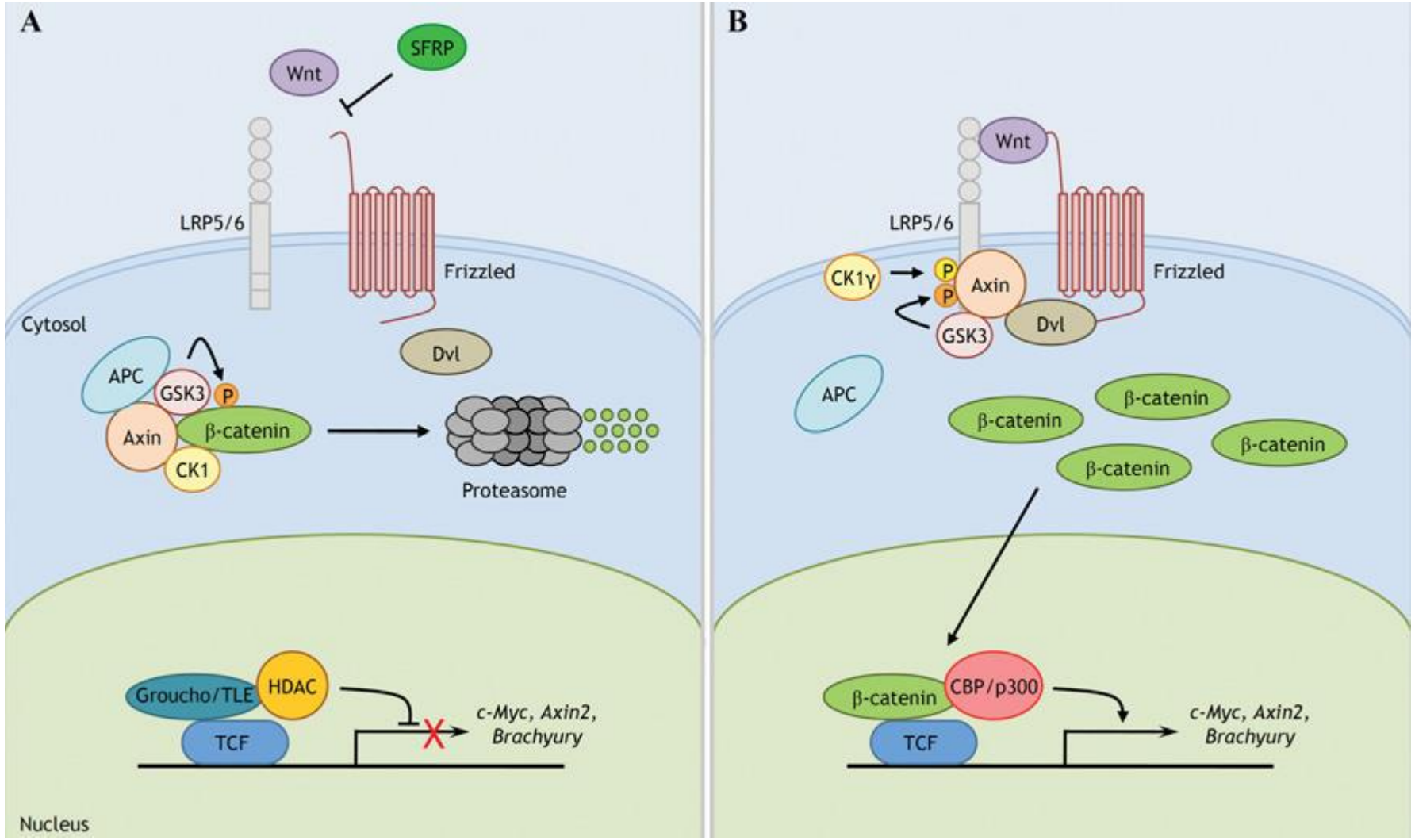
TGF-B y BMPs (RSTKs)



TGF-B y BMPs (RSTKs)

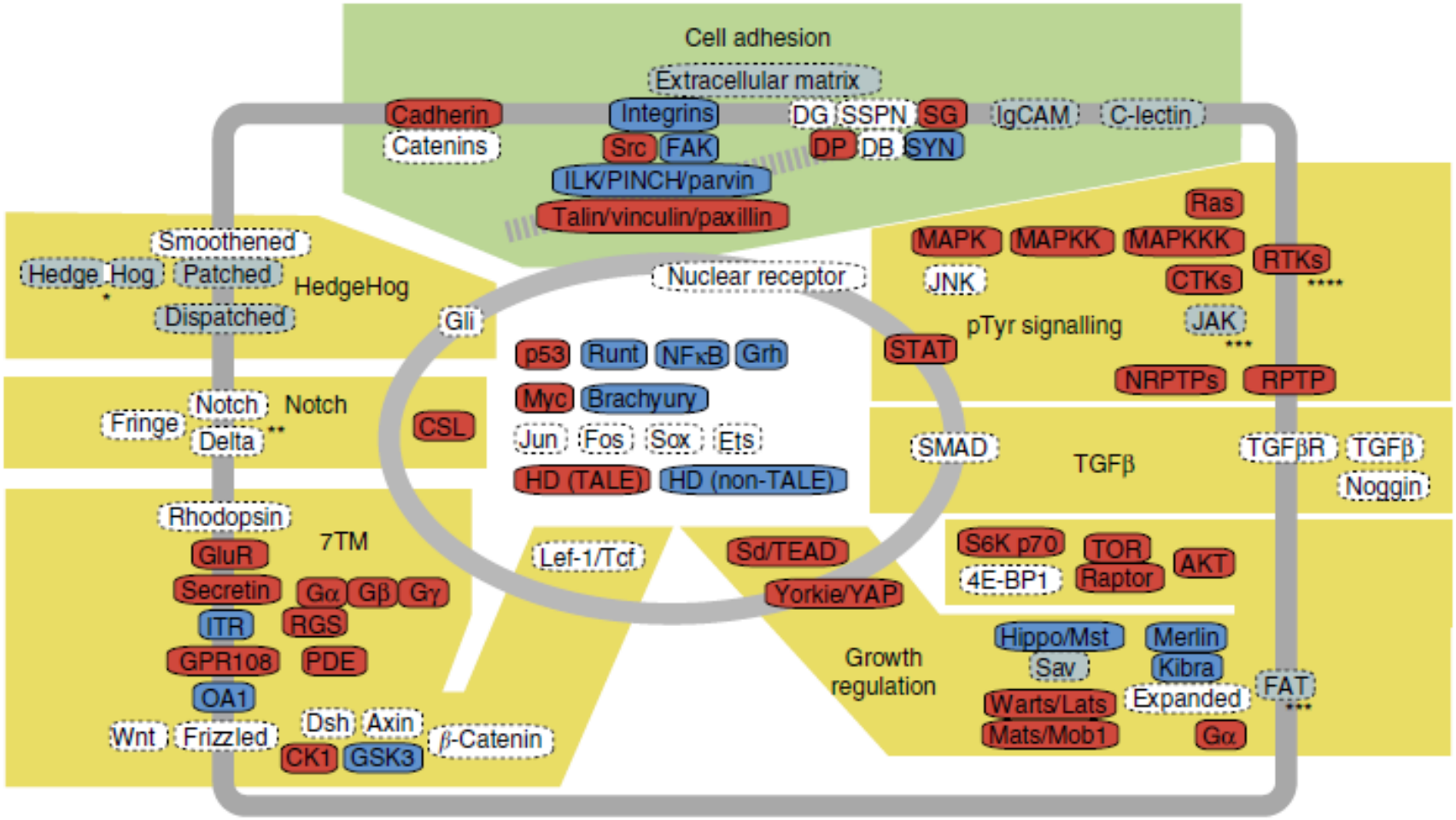


Wnt



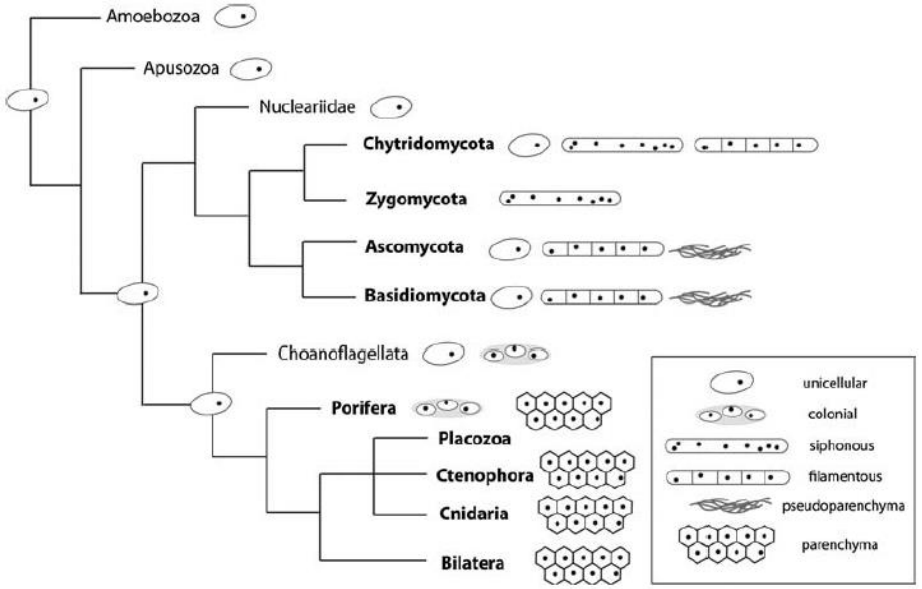
Kim & Jho 2013

Evolución de la señalización intercelular durante la transición a la multicelularidad

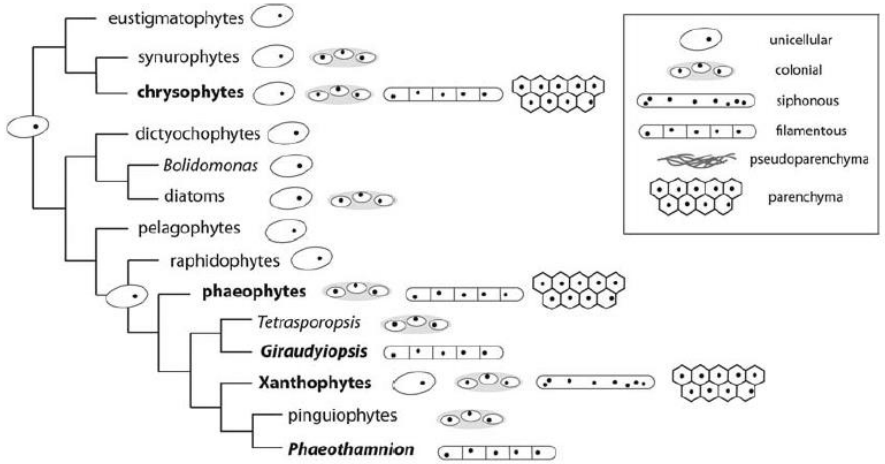


Suga et al 2013

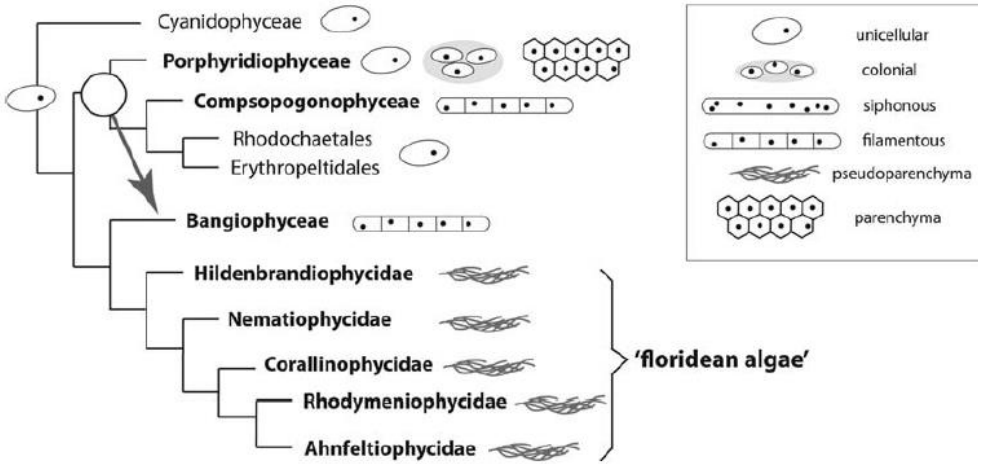
Opisthokonta



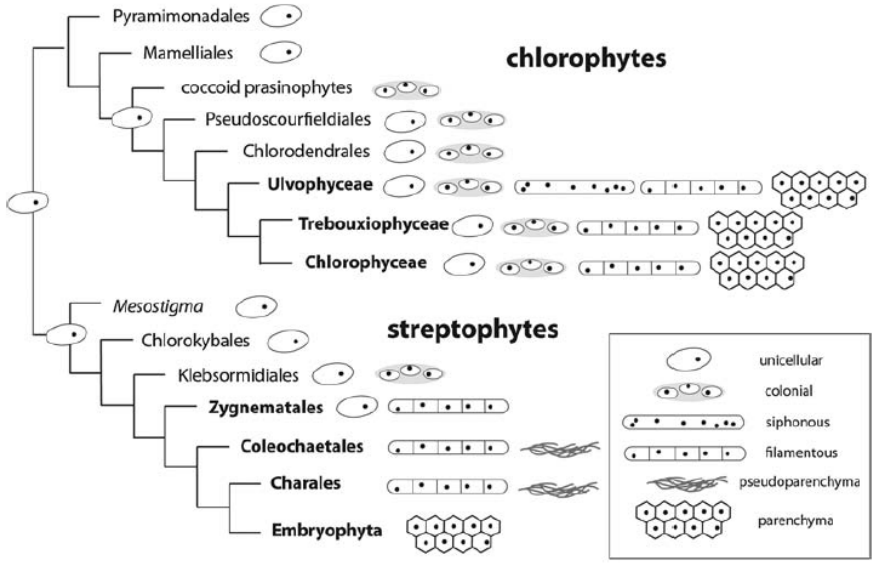
Stramenopiles (algas doradas y pardas)



Rhodophyta (algas rojas)

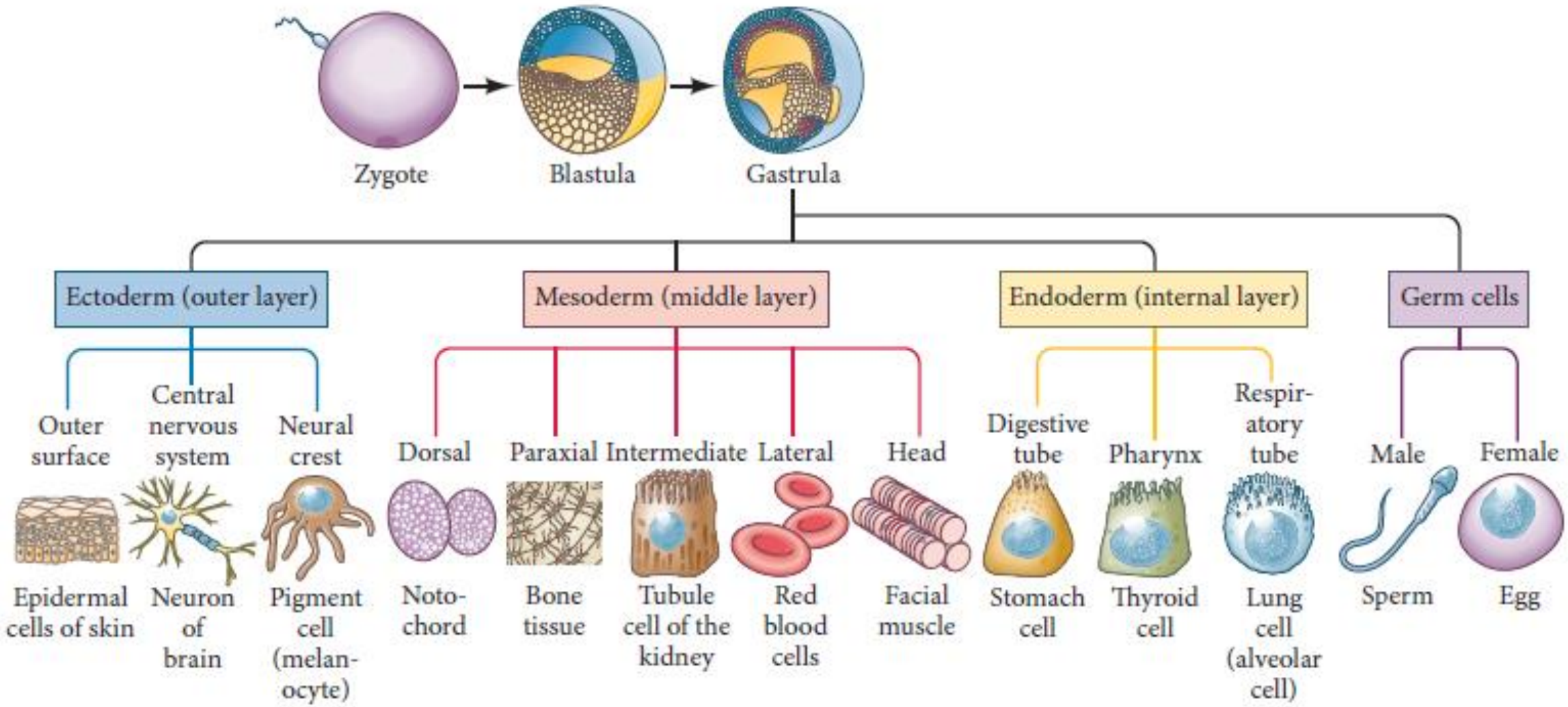


Viridiplantae (algas verdes, plantas)

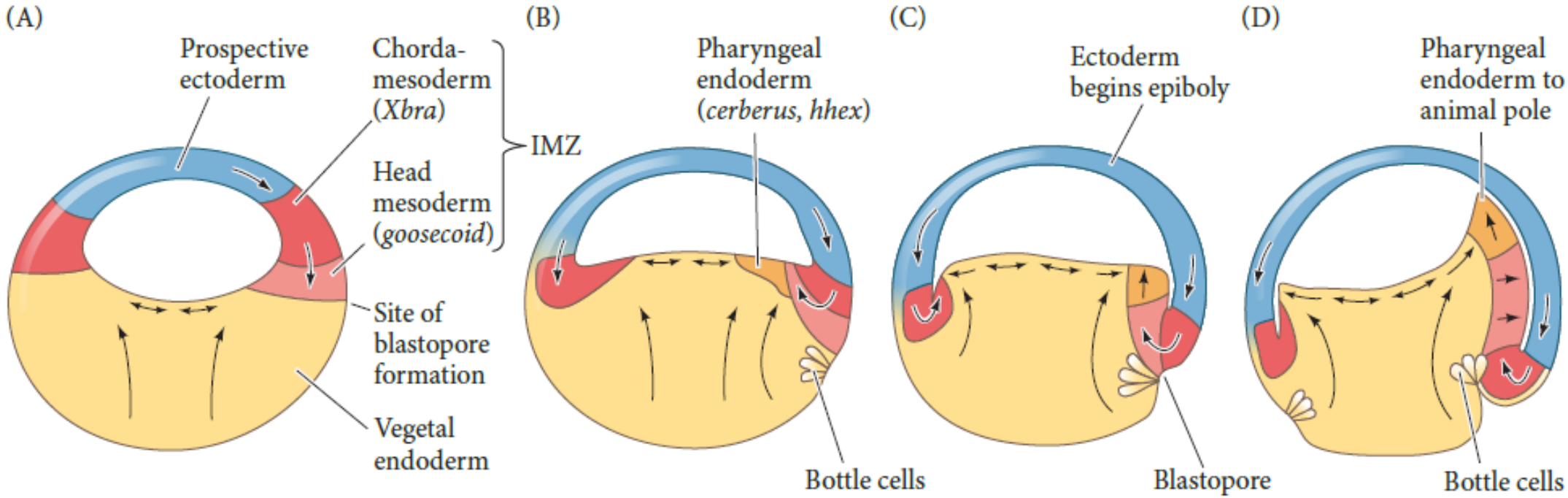


Niklas & Newman 2013

Gastrulación


Zygote
Blastula
Gastrula
Ectoderm (outer layer)
Mesoderm (middle layer)
Endoderm (internal layer)
Germ cells
Outer surface
Central nervous system
Neural crest
Dorsal
Paraxial
Intermediate
Lateral
Head
Digestive tube
Pharynx
Respir-atory tube
Male
Female
Epidermal cells of skin
Neuron of brain
Pigment cell (melan-ocyte)
Noto-chord
Bone tissue
Tubule cell of the kidney
Red blood cells
Facial muscle
Stomach cell
Thyroid cell
Lung cell (alveolar cell)
Sperm
Egg

Xenopus


(A)
Prospective ectoderm
Chorda-mesoderm (*Xbra*)
Head mesoderm (*goosecoid*)
IMZ
Site of blastopore formation
Vegetal endoderm
(B)
Pharyngeal endoderm (*cerberus, hhex*)
Bottle cells
(C)
Ectoderm begins epiboly
Blastopore
(D)
Pharyngeal endoderm to animal pole
Bottle cells

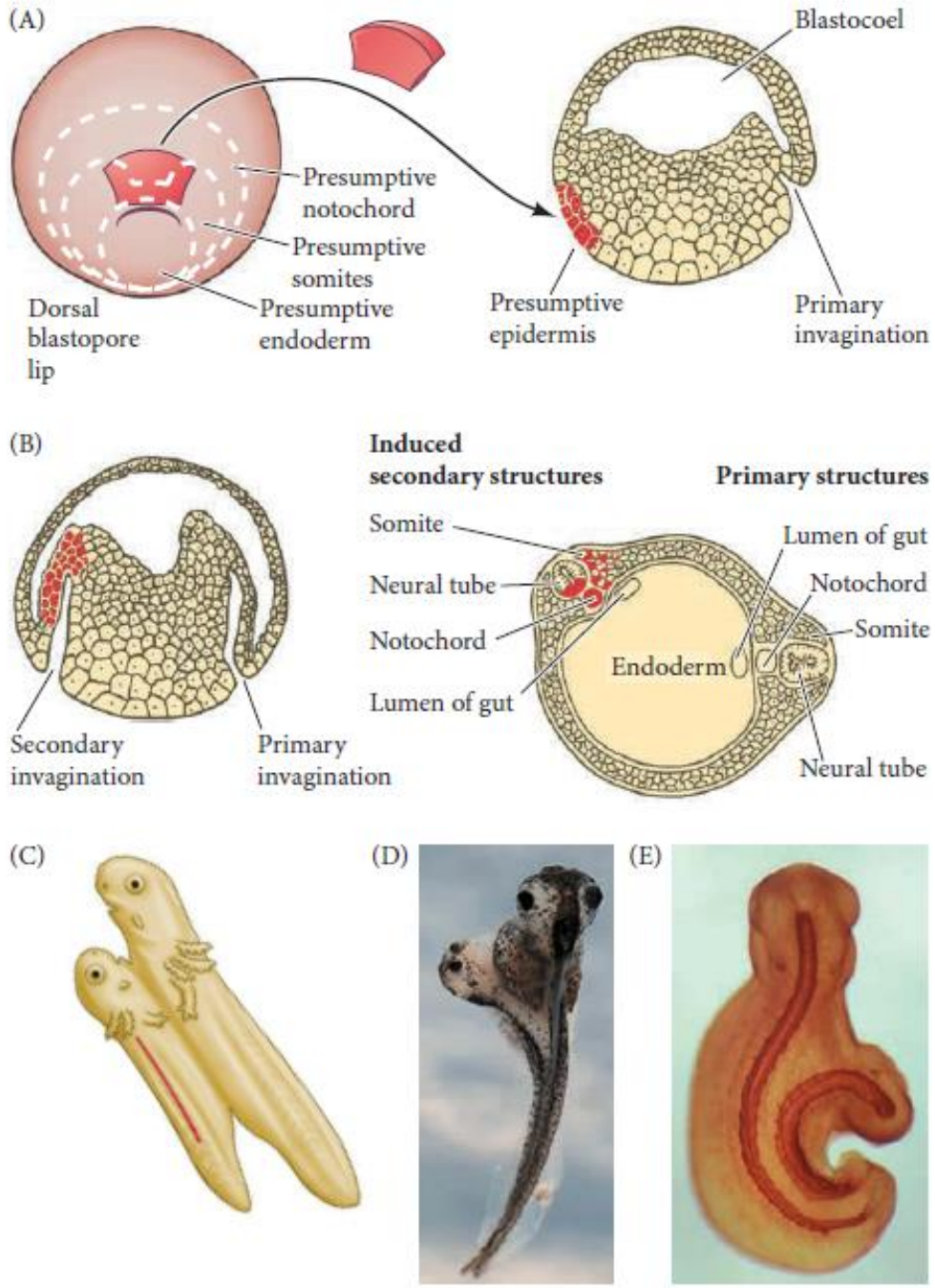
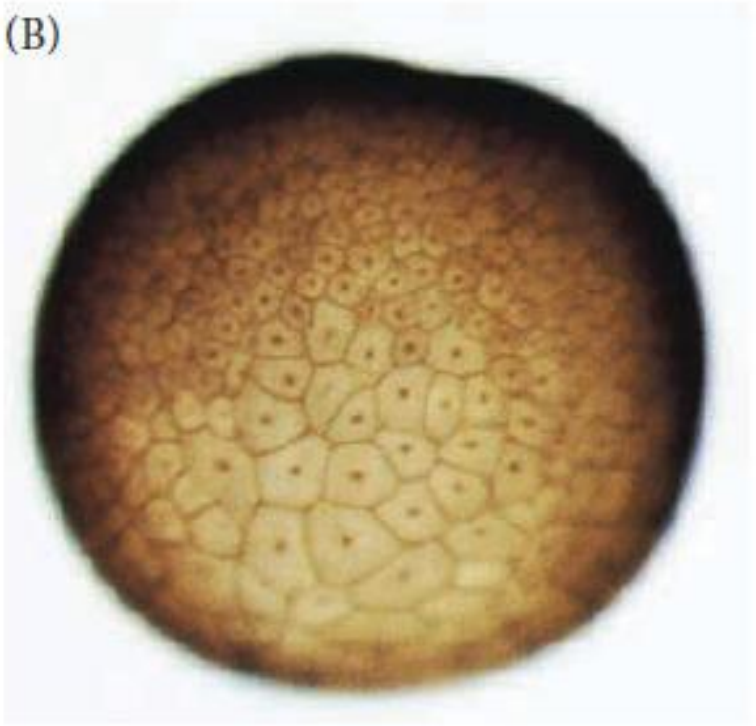
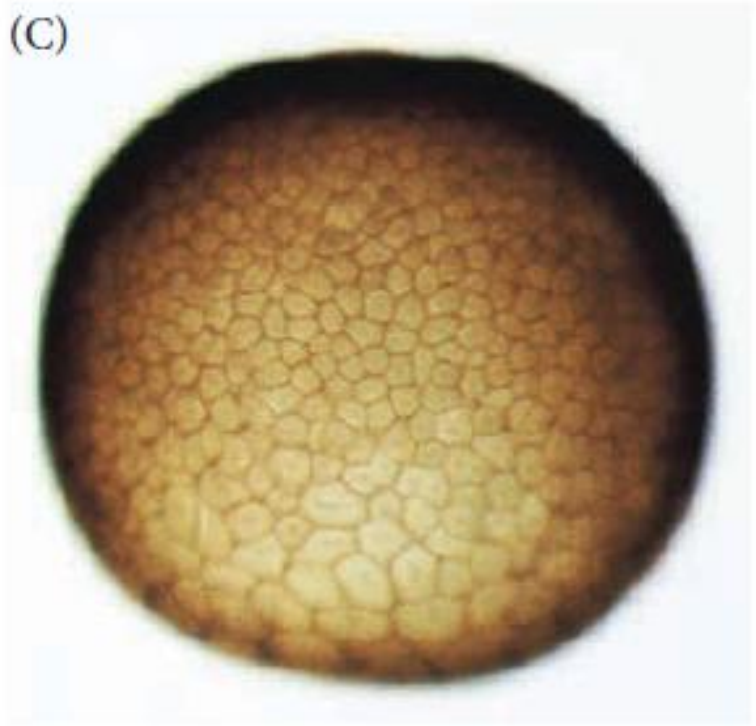


FIGURE 11.14 Organization of a secondary axis by dorsal blastopore lip tissue. (A–C) Spemann and Mangold's 1924 experiments visualized the process by using differently pigmented newt embryos. (A) Dorsal lip tissue from an early *T. taeniatus* gastrula is transplanted into a *T. cristatus* gastrula in the region that normally becomes ventral epidermis. (B) The donor tissue invaginates and forms a second archenteron, and then a second embryonic axis. Both donor and host tissues are seen in the new neural tube, notochord, and somites.(C) Eventually, a second embryo forms, joined to the host. (D) Live twinned *Xenopus* larvae generated by transplanting a dorsal blastopore lip into the ventral region of an early-gastrula host embryo. (E) Similar twinned larvae are seen from below and stained for notochord; the original and secondary notochords can be seen. (A–C after Hamburger 1988; D,E photographs by A. Wills, courtesy of R. Harland.)





β-catenin begins to accumulate in the dorsal region of the egg during the cytoplasmic movements of fertilization and continues to accumulate preferentially at the dorsal side throughout early cleavage

Experimental depletion of this molecule results in· the lack of dorsal structures. Moreover, injection of exogenous β-catenin into the ventral side of an embryo produces a secondary Axis.

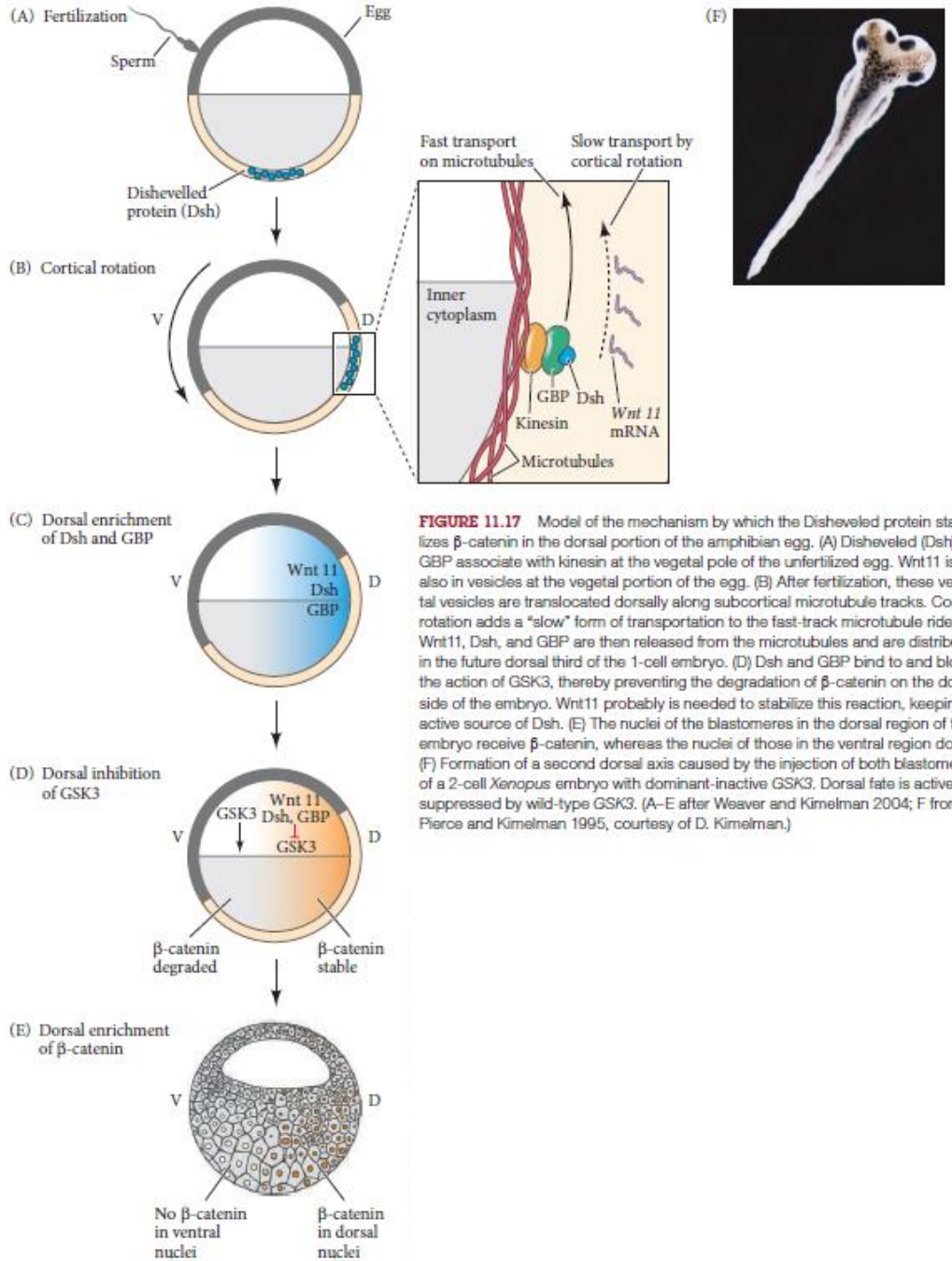
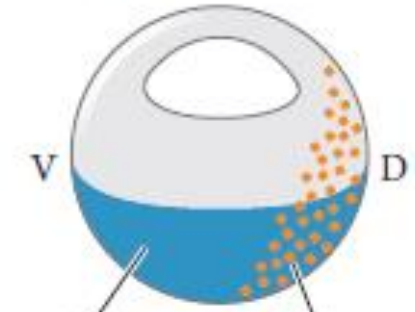


FIGURE 11.17 Model of the mechanism by which the Disheveled protein stabilizes β-catenin in the dorsal portion of the amphibian egg. (A) Disheveled (Dsh) and GBP associate with kinesin at the vegetal pole of the unfertilized egg. Wnt11 is also in vesicles at the vegetal portion of the egg. (B) After fertilization, these vegetal vesicles are translocated dorsally along subcortical microtubule tracks. Cortical rotation adds a "slow" form of transportation to the fast-track microtubule ride. (C) Wnt11, Dsh, and GBP are then released from the microtubules and are distributed in the future dorsal third of the 1-cell embryo. (D) Dsh and GBP bind to and block the action of GSK3, thereby preventing the degradation of β-catenin on the dorsal side of the embryo. Wnt11 probably is needed to stabilize this reaction, keeping an active source of Dsh. (E) The nuclei of the blastomeres in the dorsal region of the embryo receive β-catenin, whereas the nuclei of those in the ventral region do not. (F) Formation of a second dorsal axis caused by the injection of both blastomeres of a 2-cell *Xenopus* embryo with dominant-inactive *GSK3*. Dorsal fate is actively suppressed by wild-type *GSK3*. (A–E after Weaver and Kimelman 2004; F from Pierce and Kimelman 1995, courtesy of D. Kimelman.)

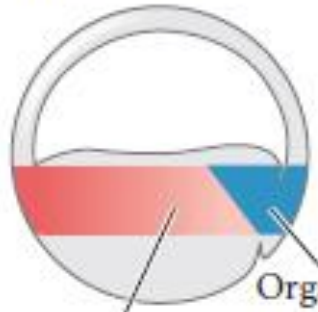
(A)

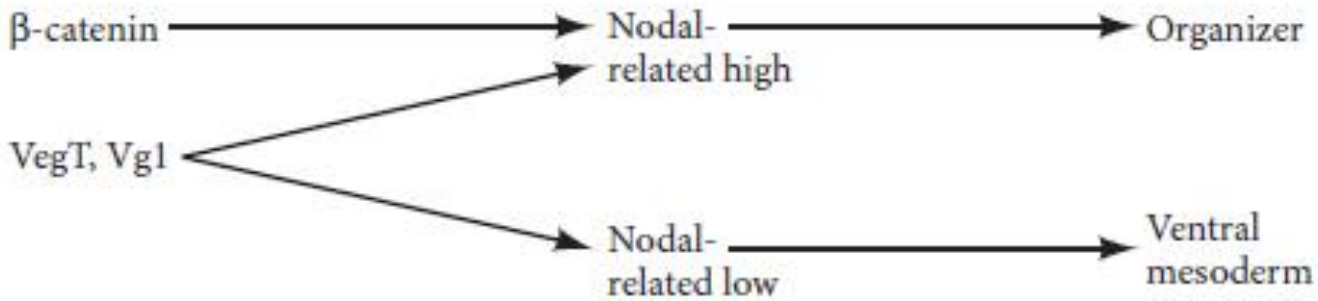
(B) Stage 8



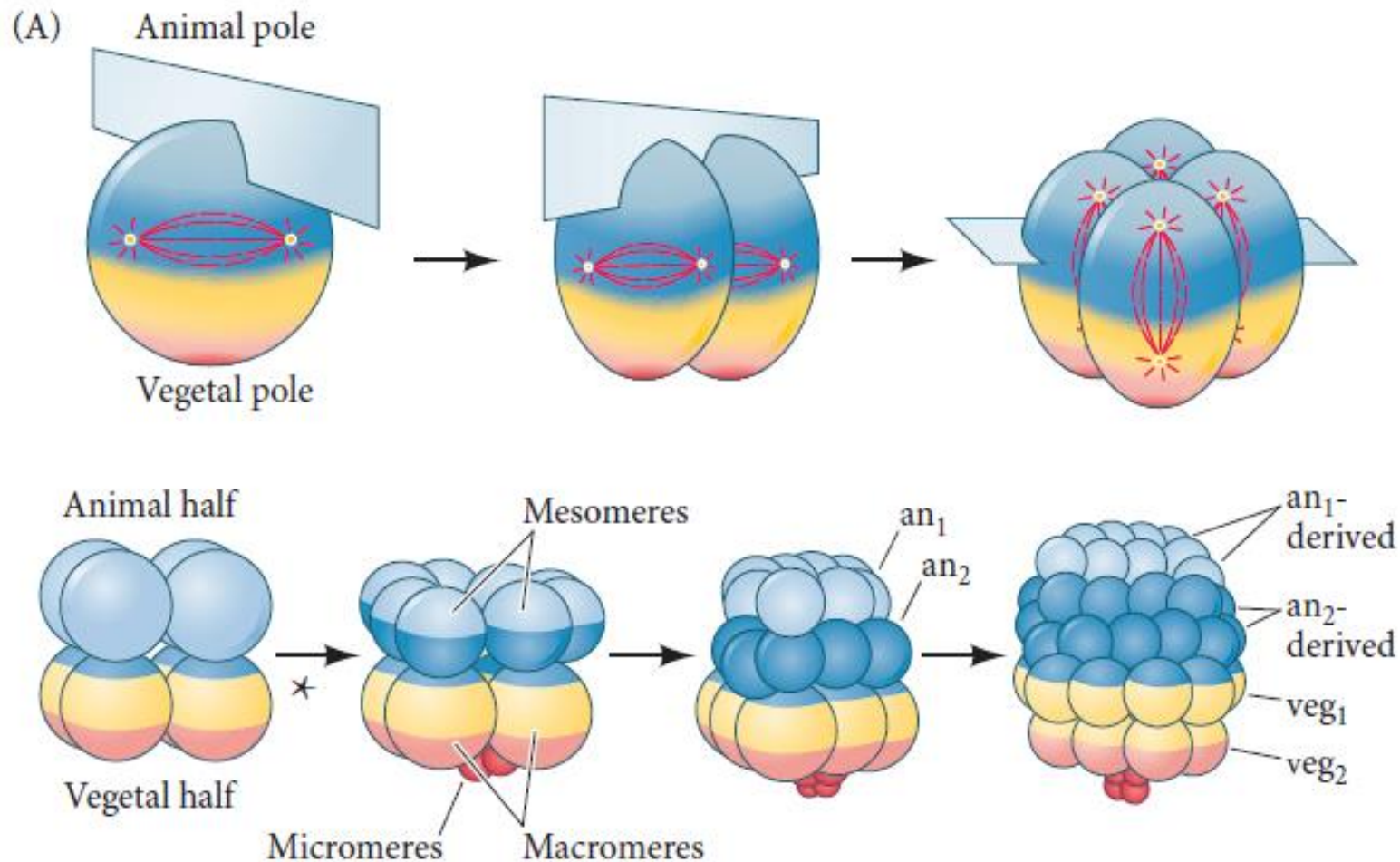
(C) Stage 9

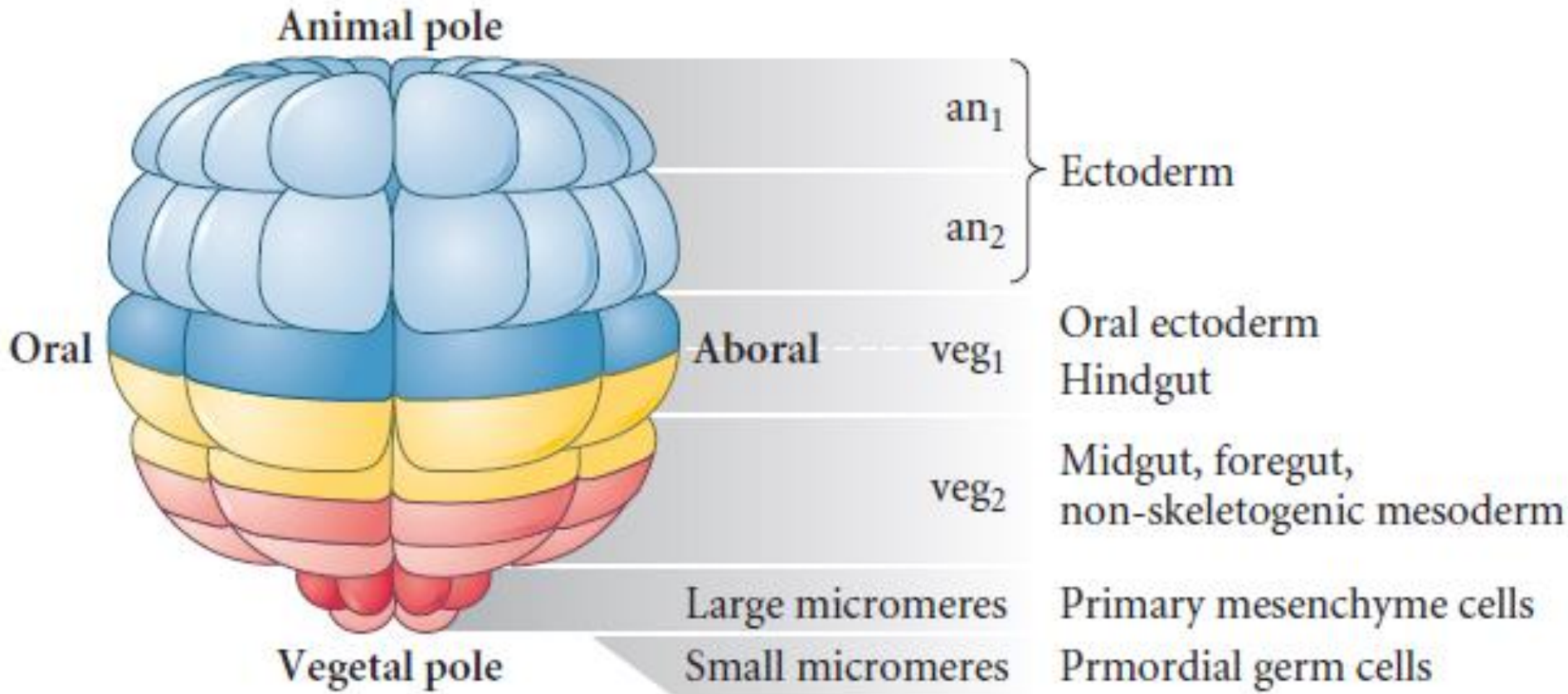
(D) Stage 10

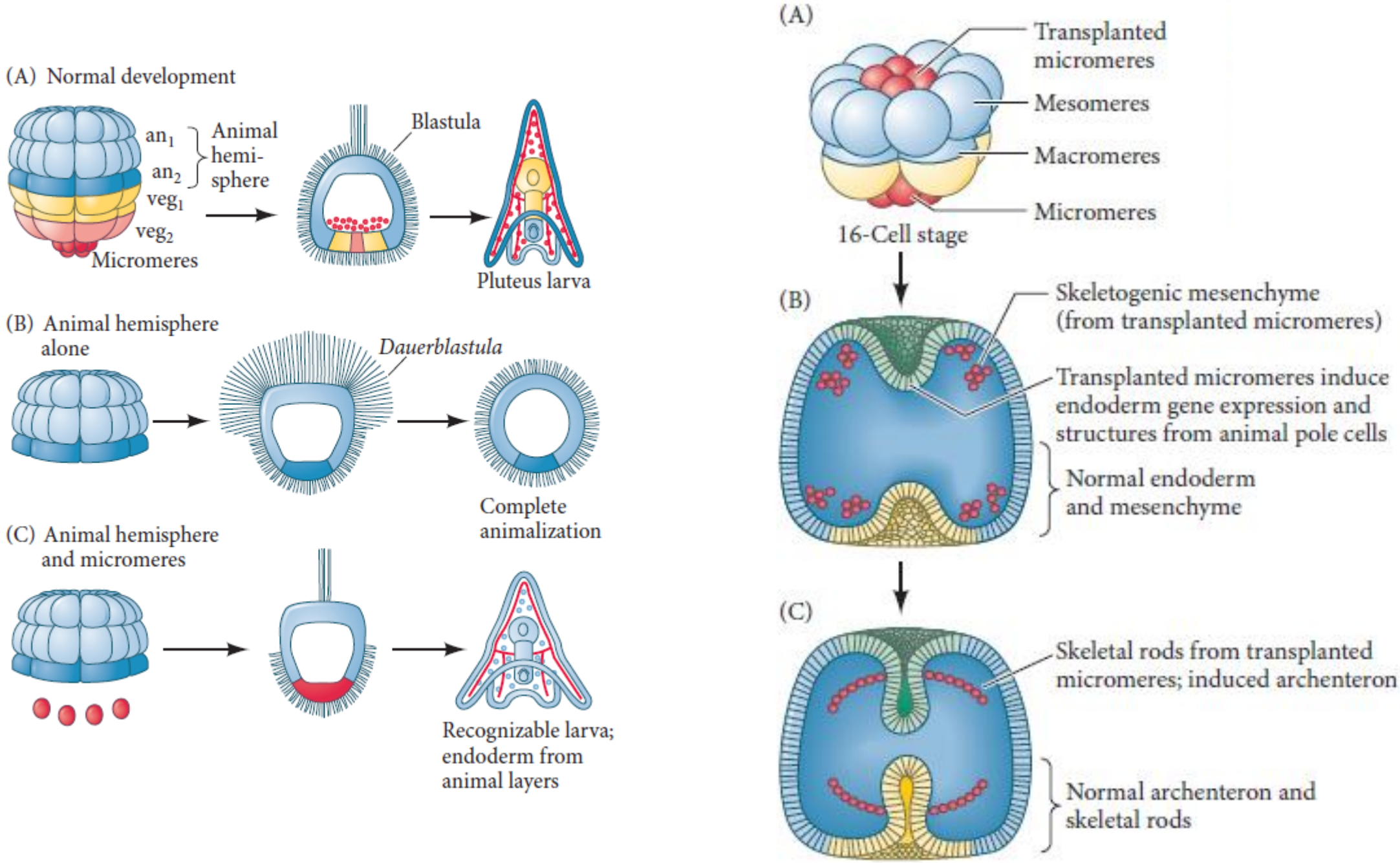




Erizo de mar


(A)
Animal pole
Vegetal pole
Animal half
Vegetal half
Mesomeres
Micromeres
Macromeres
an1
an2
an1-derived
an2-derived
veg1
veg2


Animal pole
Oral
Aboral
Vegetal pole
an1
an2
Ectoderm
veg1
Oral ectoderm
Hindgut
veg2
Midgut, foregut,
non-skeletogenic mesoderm
Large micromeres
Primary mesenchyme cells
Small micromeres
Prmordial germ cells


(A) Normal development
an1
an2
veg1
veg2
Micromeres
Animal hemi-sphere
Blastula
Pluteus larva
(B) Animal hemisphere alone
Dauerblastula
Complete animalization
(C) Animal hemisphere and micromeres
Recognizable larva; endoderm from animal layers
(A)
Transplanted micromeres
Mesomeres
Macromeres
Micromeres
16-Cell stage
(B)
Skeletogenic mesenchyme (from transplanted micromeres)
Transplanted micromeres induce endoderm gene expression and structures from animal pole cells
Normal endoderm and mesenchyme
(C)
Skeletal rods from transplanted micromeres; induced archenteron
Normal archenteron and skeletal rods

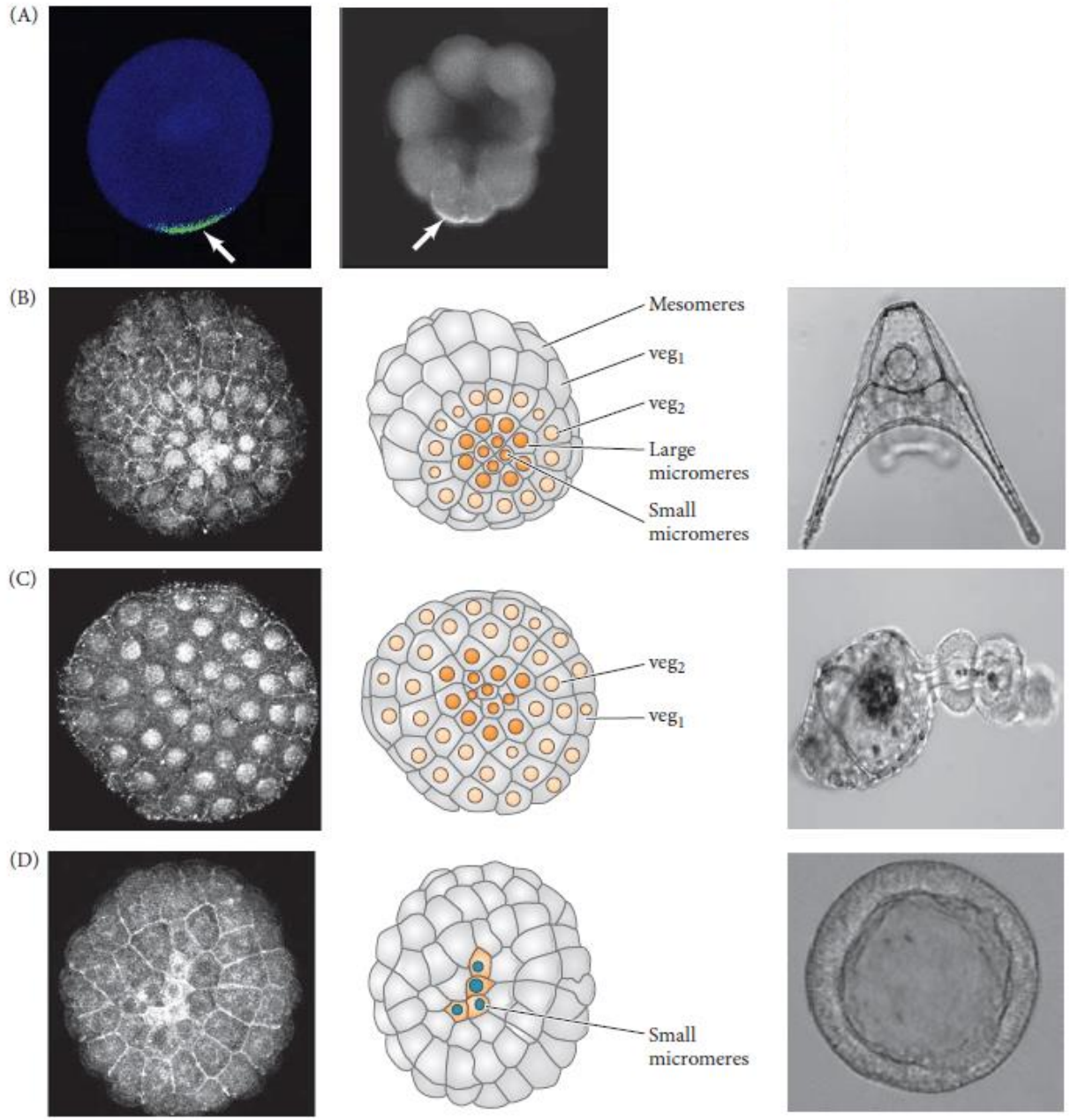
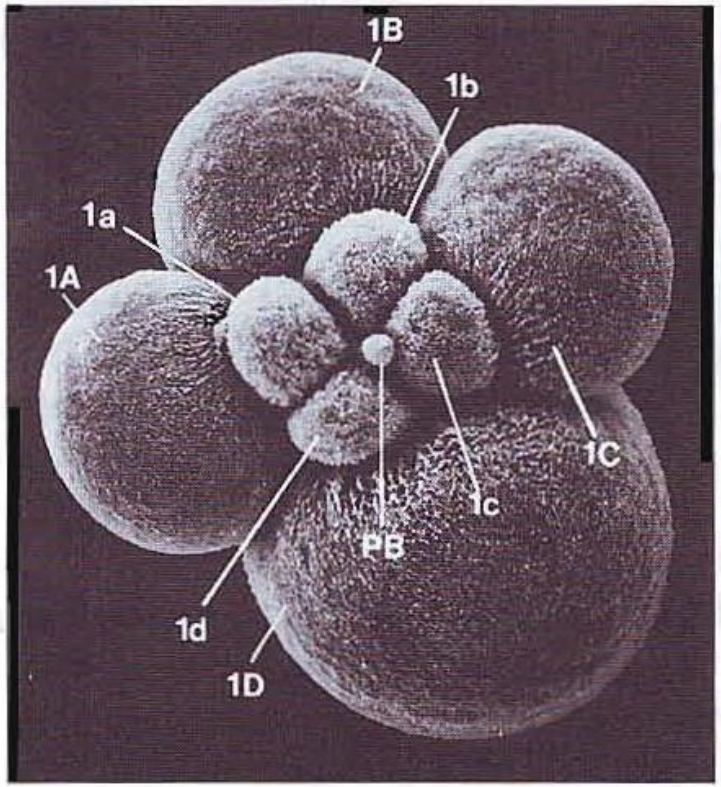
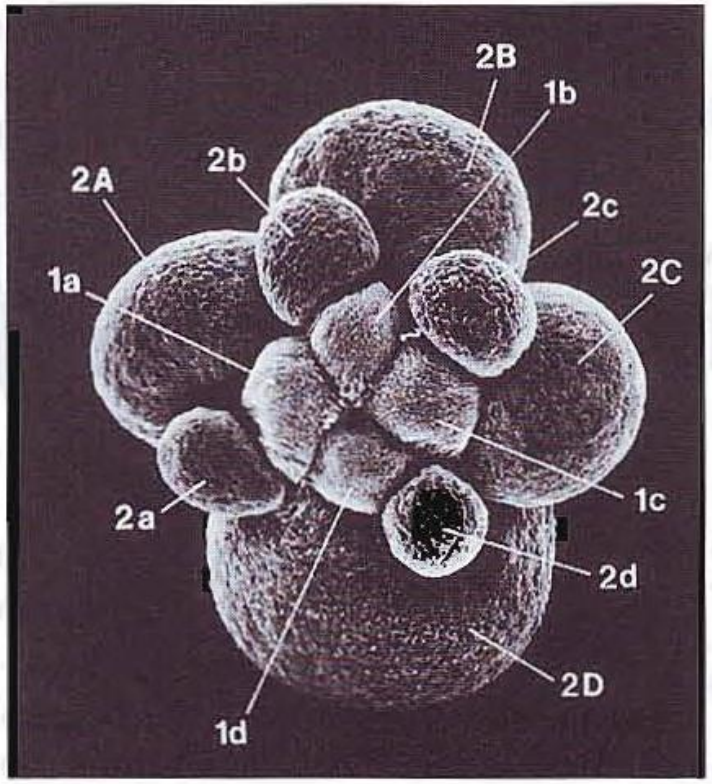


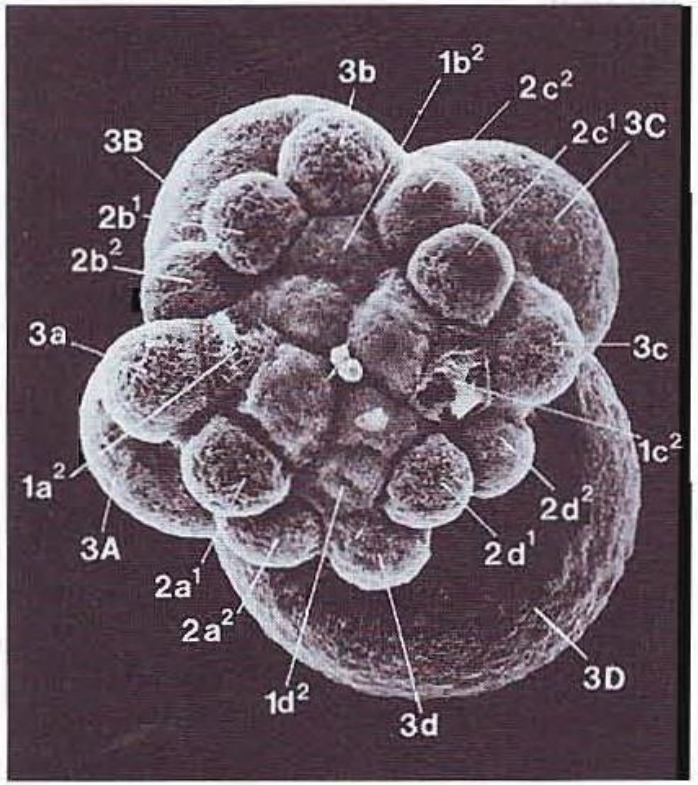
FIGURE 10.7 Role of the Disheveled and β-catenin proteins in specifying the vegetal cells of the sea urchin embryo. (A) Localization of Disheveled (arrows) in the vegetal cortex of the sea urchin oocyte before fertilization (left) and in the region of a 16-cell embryo about to become the micromeres (right). (B) During normal development, β-catenin accumulates predominantly in the micromeres and somewhat less in the veg_2 tier cells. (C) In embryos treated with lithium chloride, β-catenin accumulates in the nuclei of all blastula cells (probably by LiCl's blocking the GSK3 enzyme of the Wnt pathway), and the animal cells become specified as endoderm and mesoderm. (D) When β-catenin is prevented from entering the nuclei (i.e., it remains in the cytoplasm), the vegetal cell fates are not specified, and the entire embryo develops as a ciliated ectodermal ball. (From Weitzel et al. 2004, courtesy of C. Ettensohn, and from Logan et al. 1998, courtesy of D. McClay.)

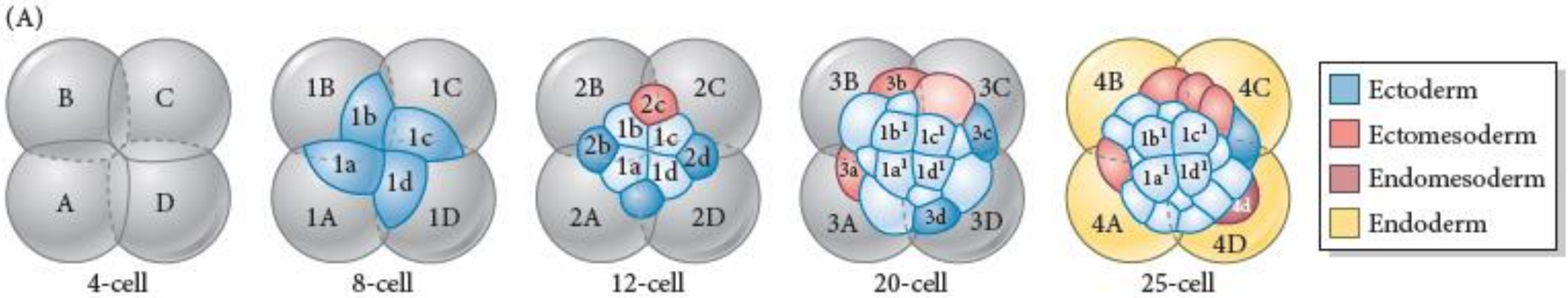
Overexpression of a synthetic mRNA encoding the transmembrane and intracellular domains of LvG-cadherin

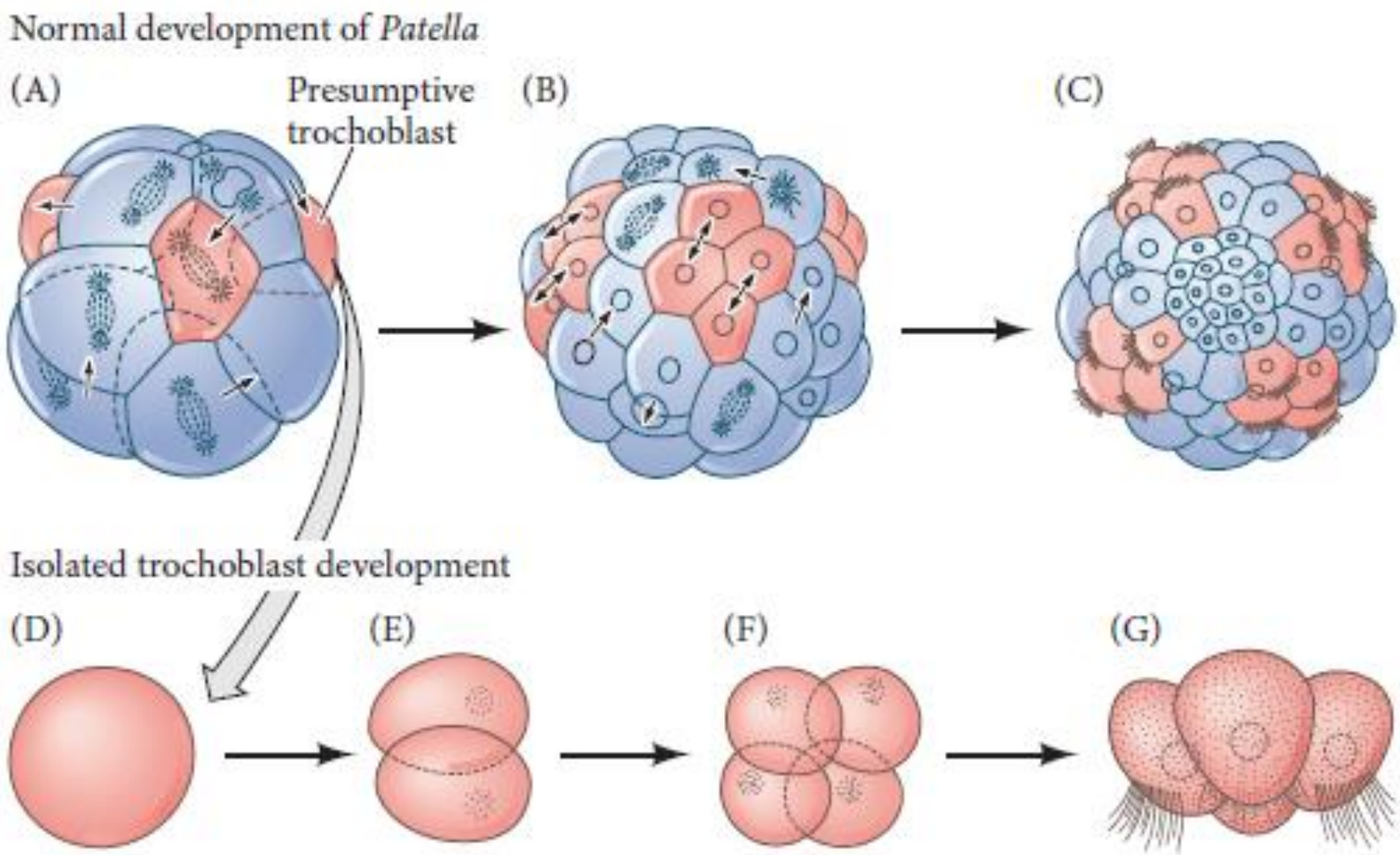
Desarrollo espiral – Moluscos, Anélidos, y amigos

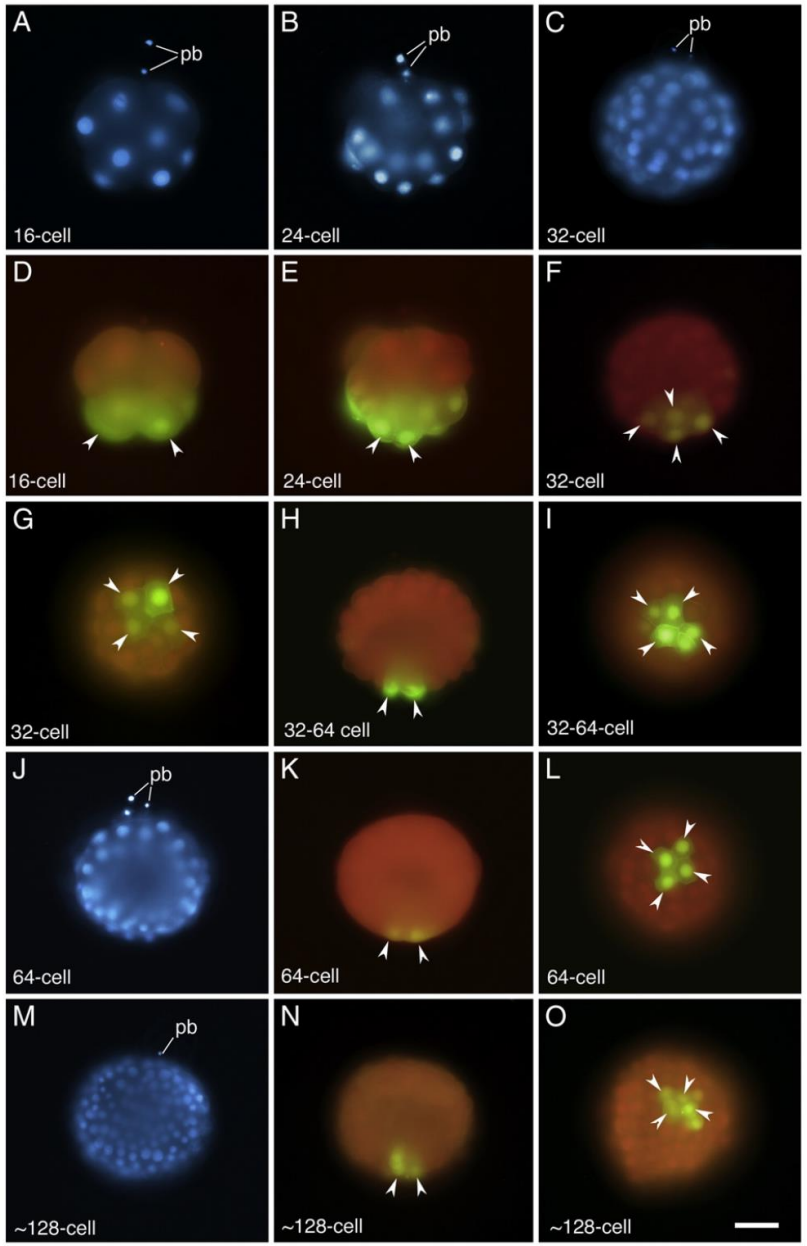




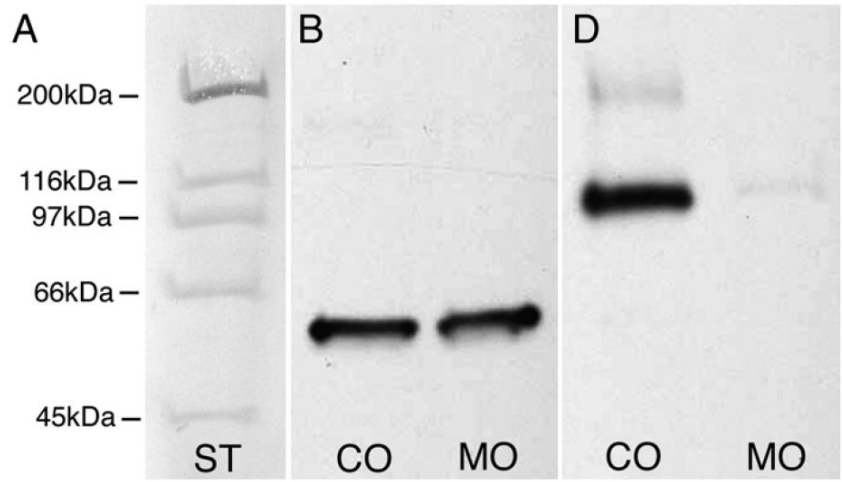


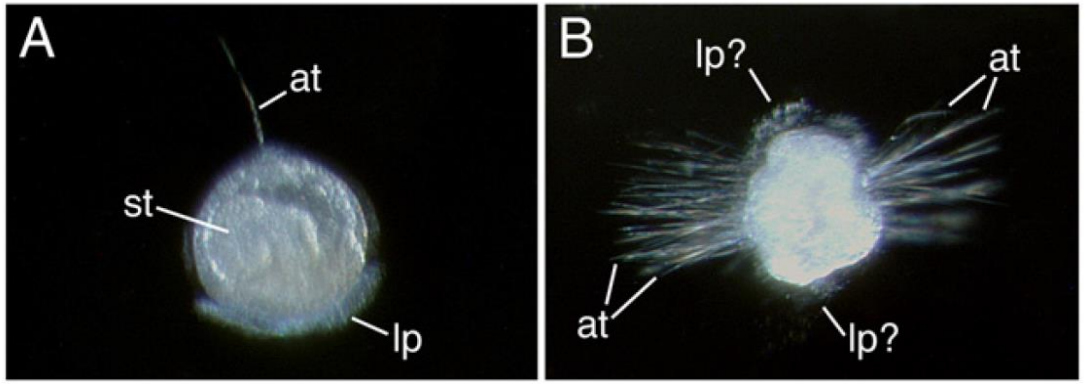

(A)
B
C
A
D
4-cell
1B
1C
1b
1c
1a
1d
1A
1D
8-cell
2B
2C
2c
1b
1c
2b
2d
1a
1d
2A
2D
12-cell
3B
3b
3C
1b¹
1c¹
3c
3a
1a¹
1d¹
3A
3d
3D
20-cell
4B
4C
1b¹
1c¹
1a¹
1d¹
4d
4A
4D
25-cell
Ectoderm
Ectomesoderm
Endomesoderm
Endoderm


Normal development of *Patella*
(A)
Presumptive trochoblast
(B)
(C)
Isolated trochoblast development
(D)
(E)
(F)
(G)

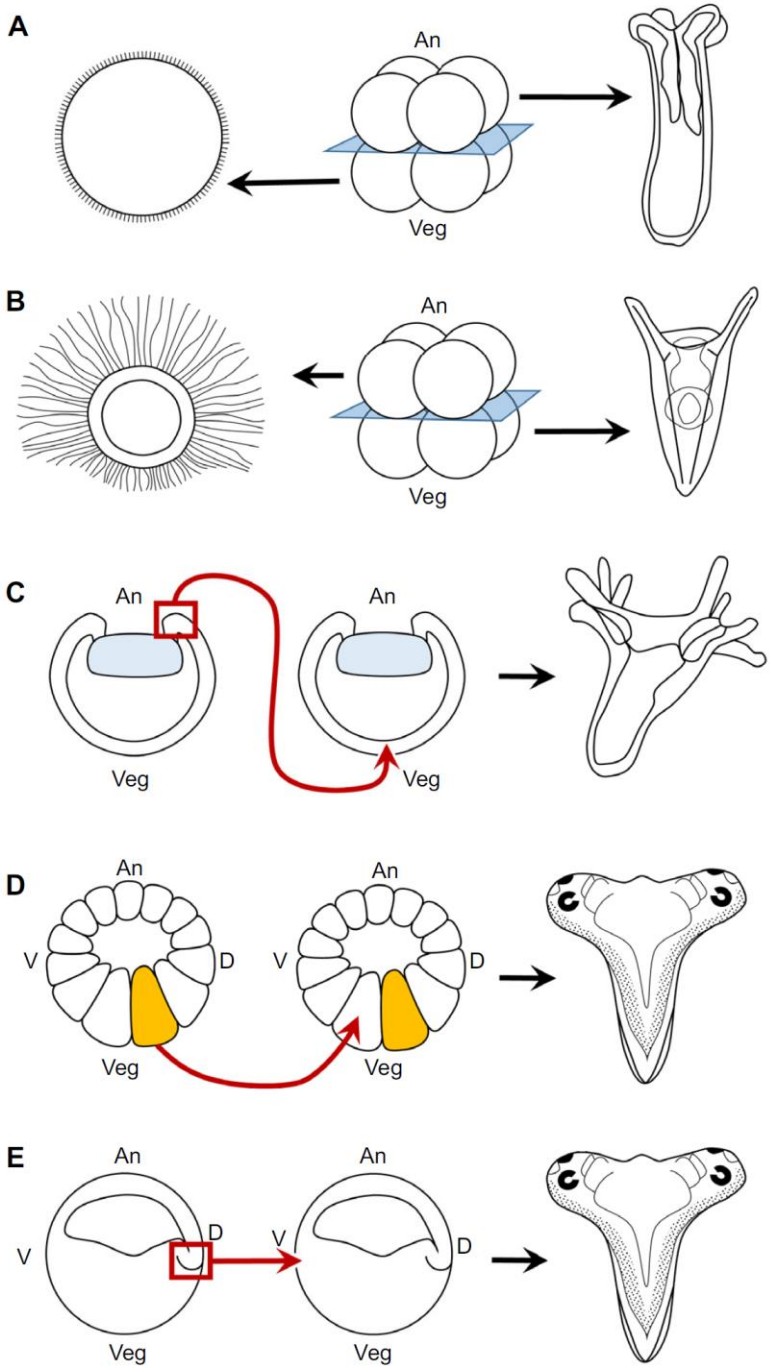


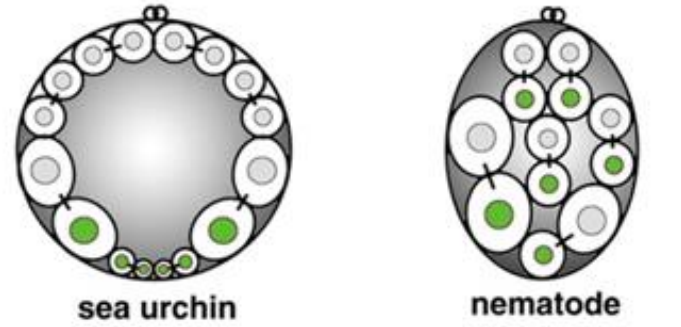
βcat-GFP mRNA

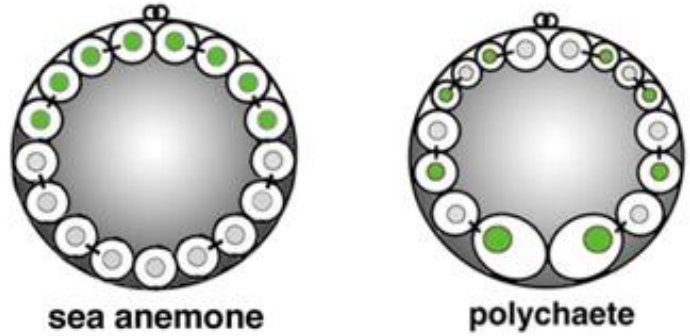


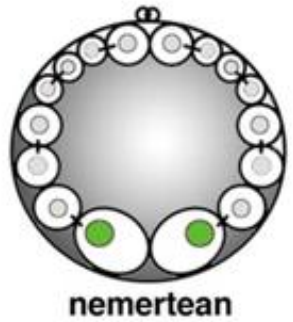


Henry et al 2008









Genikhovich 2017
Martindale & Hejnol 2009