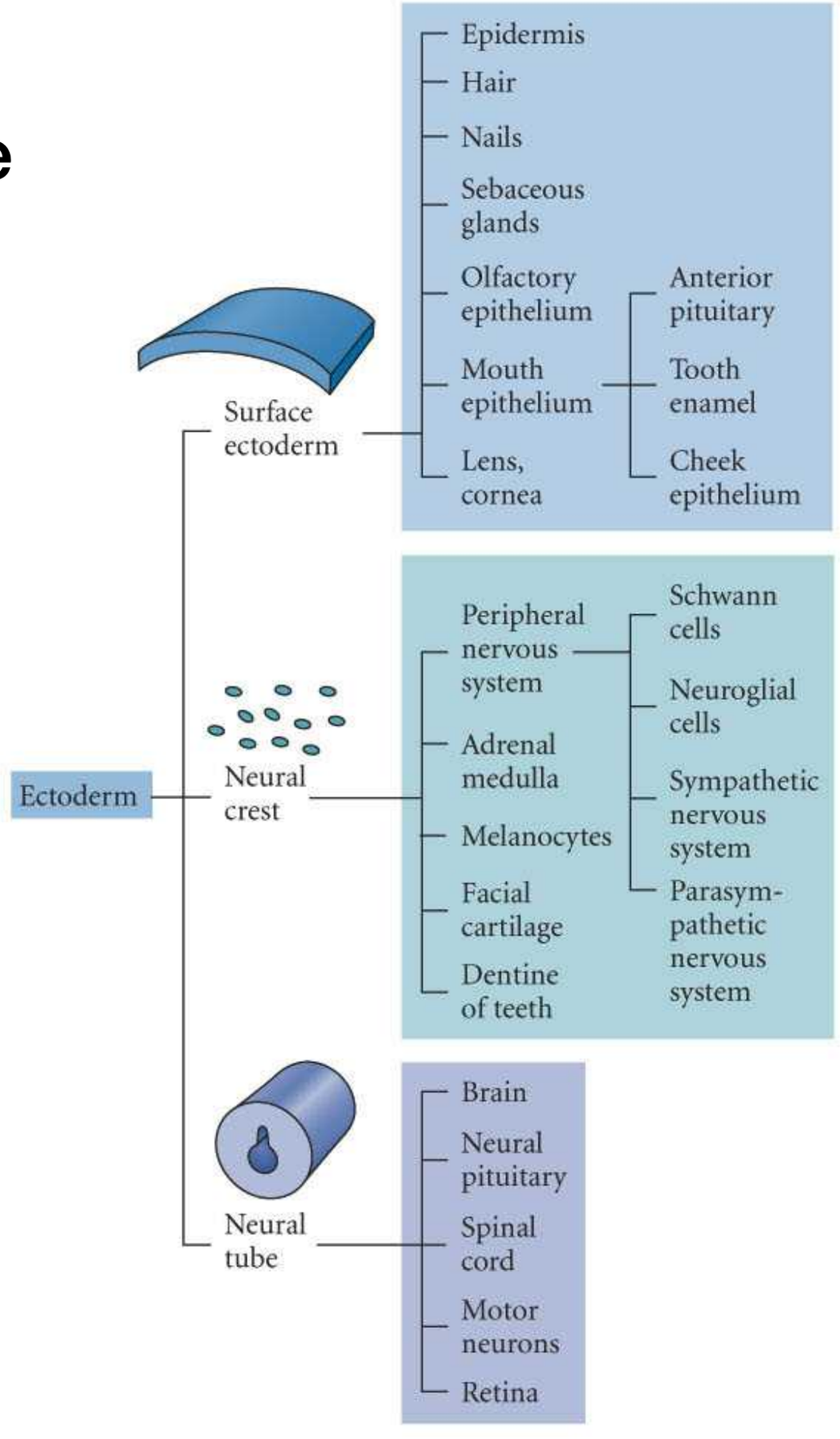
Neurulação e crista neural

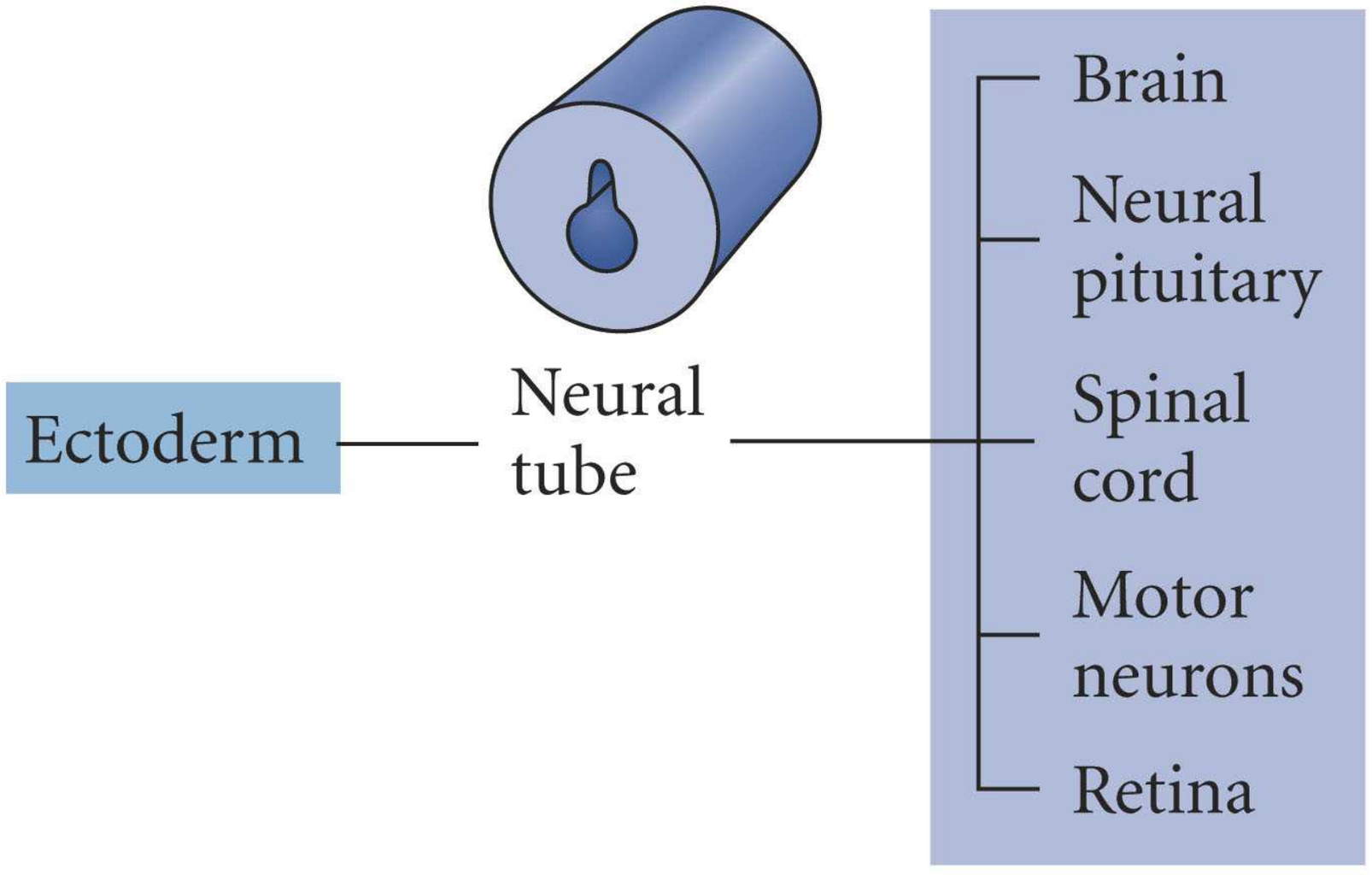
Felipe M Vieceli
Departamento de Biologia Celular e do Desenvolvimento
Instituto de Ciências Biomédicas USP

Derivados da ectoderme



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O tubo neural forma todo o sistema nervoso central



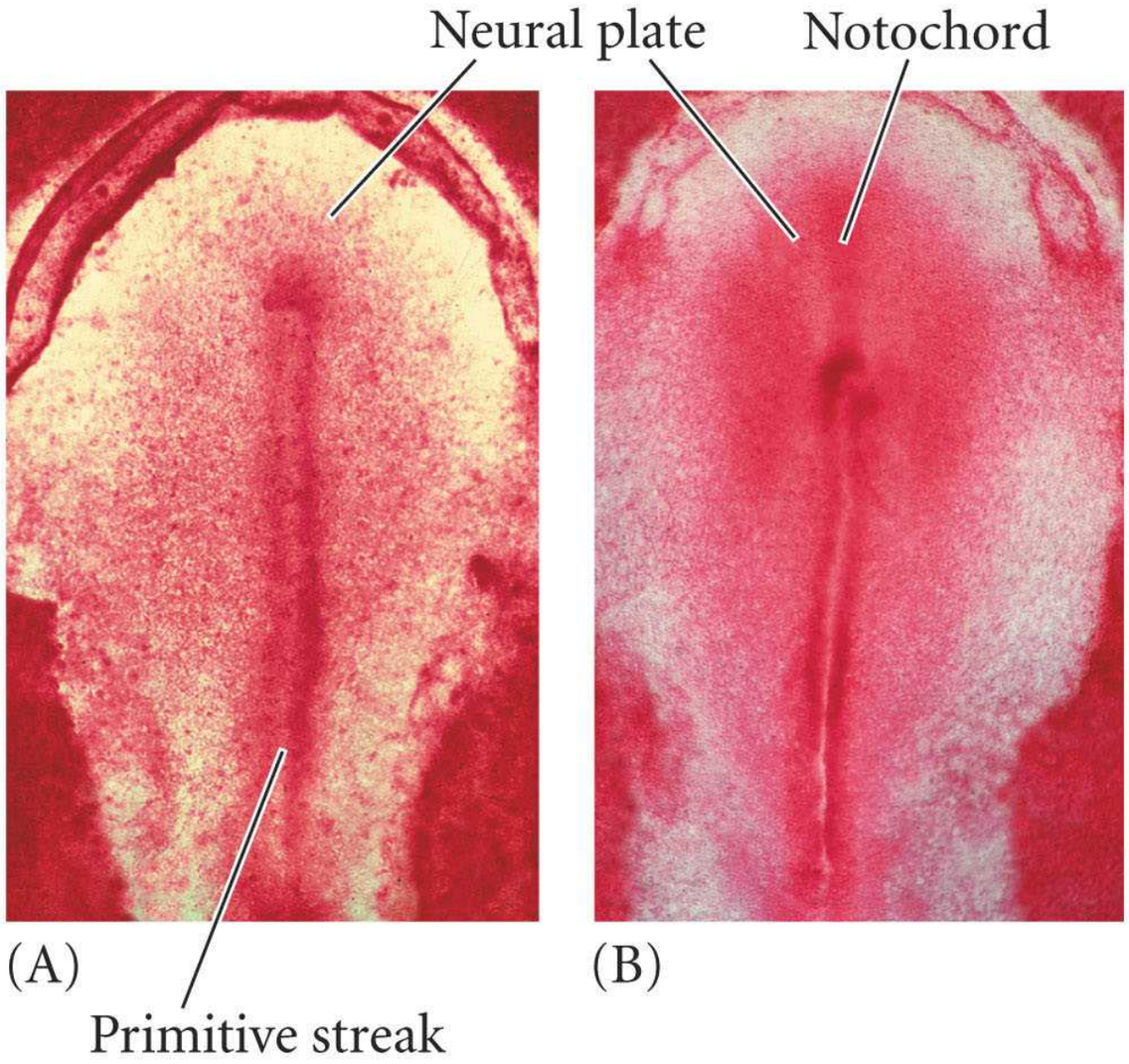
***DEVELOPMENTAL BIOLOGY, Eighth Edition,* Figure 12.1 (Part 3)** © 2006 Sinauer Associates, Inc.

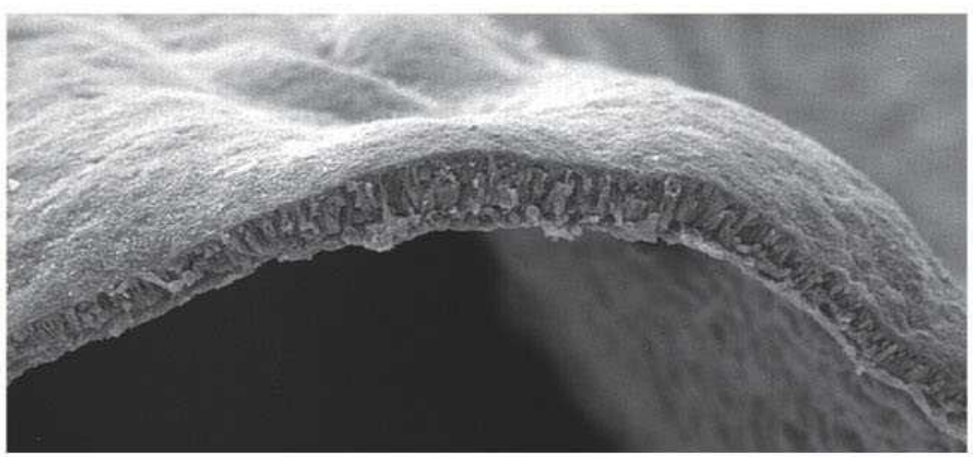


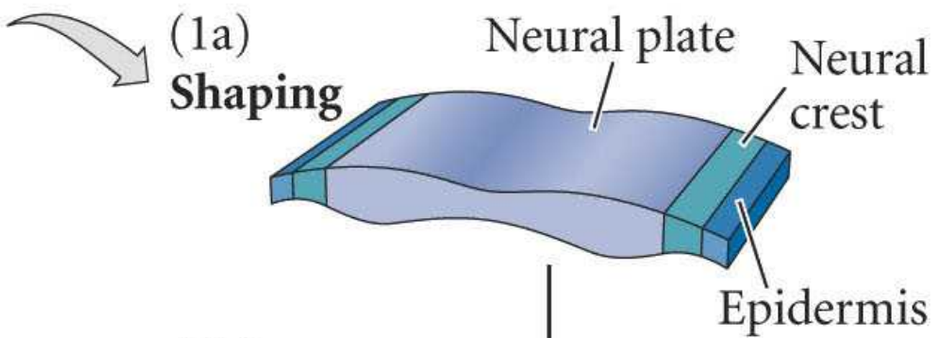
Neurulação no embrião de galinha

Formação da placa neural

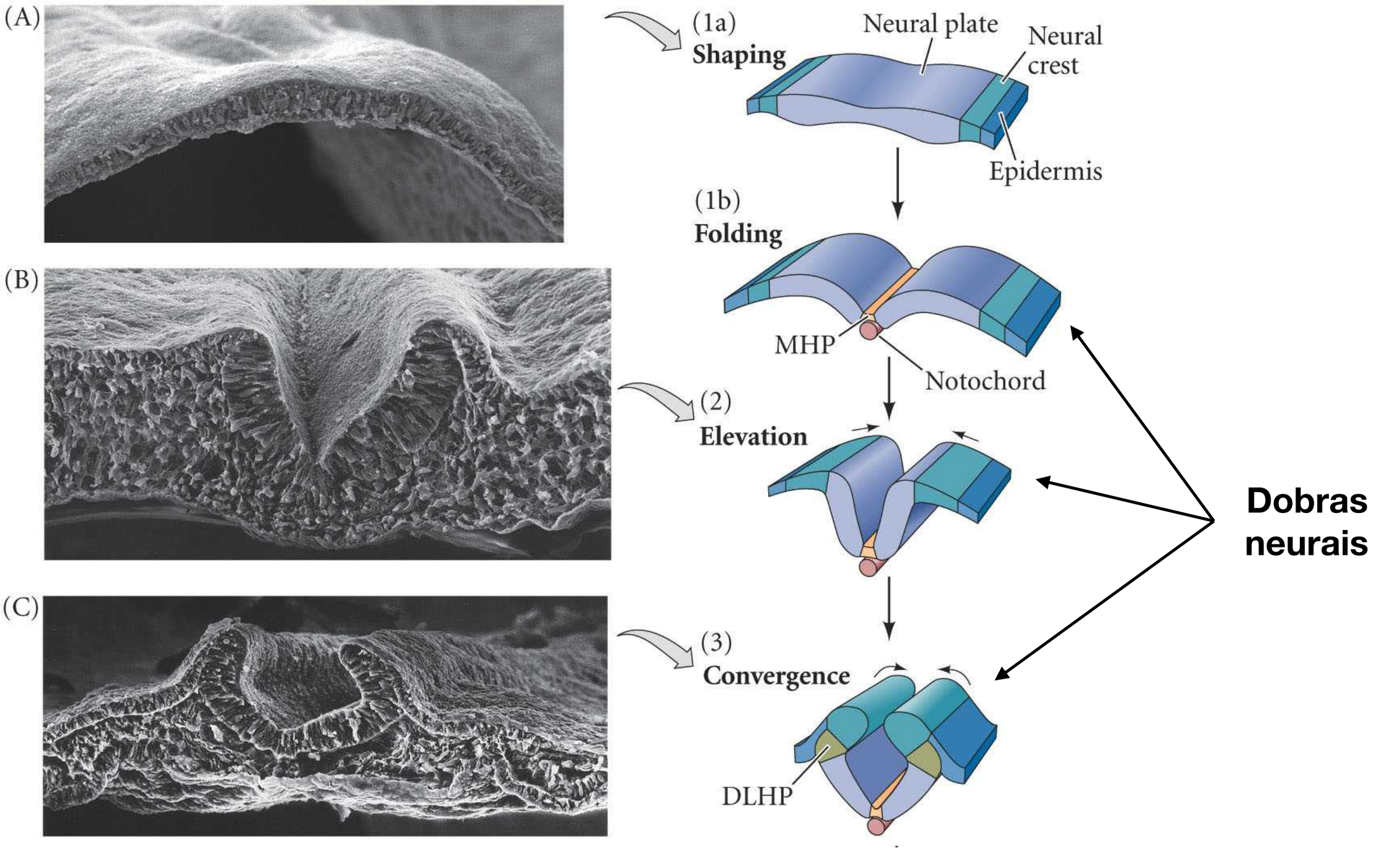
- Especificada na região central da ectoderme
- FGFs do hipoblasto e antagonistas de BMPs da notocorda
- Espessamento do neuroepitélio



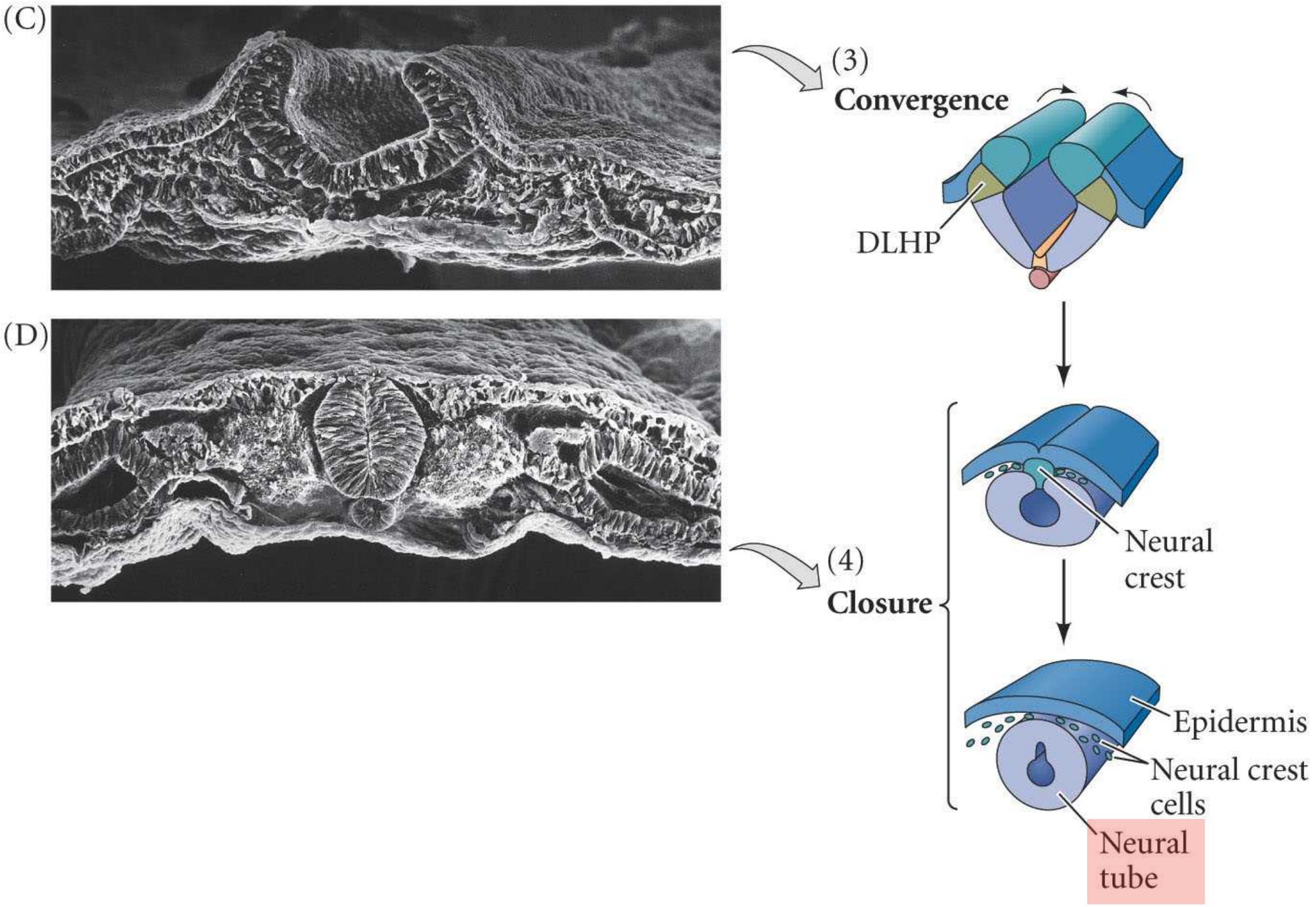




Neurulação primária: dobras neurais

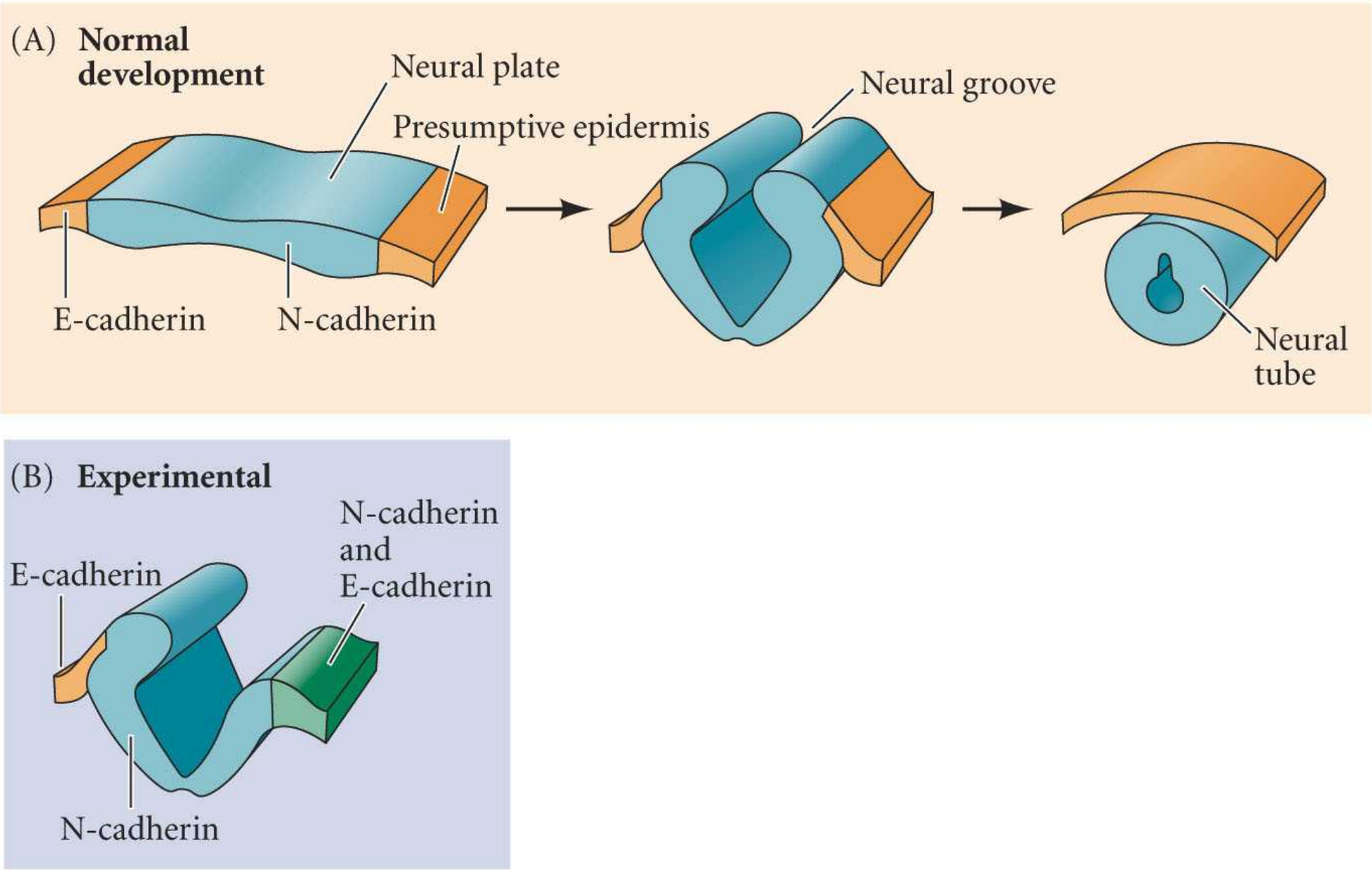


Neurulação primária: tubo neural



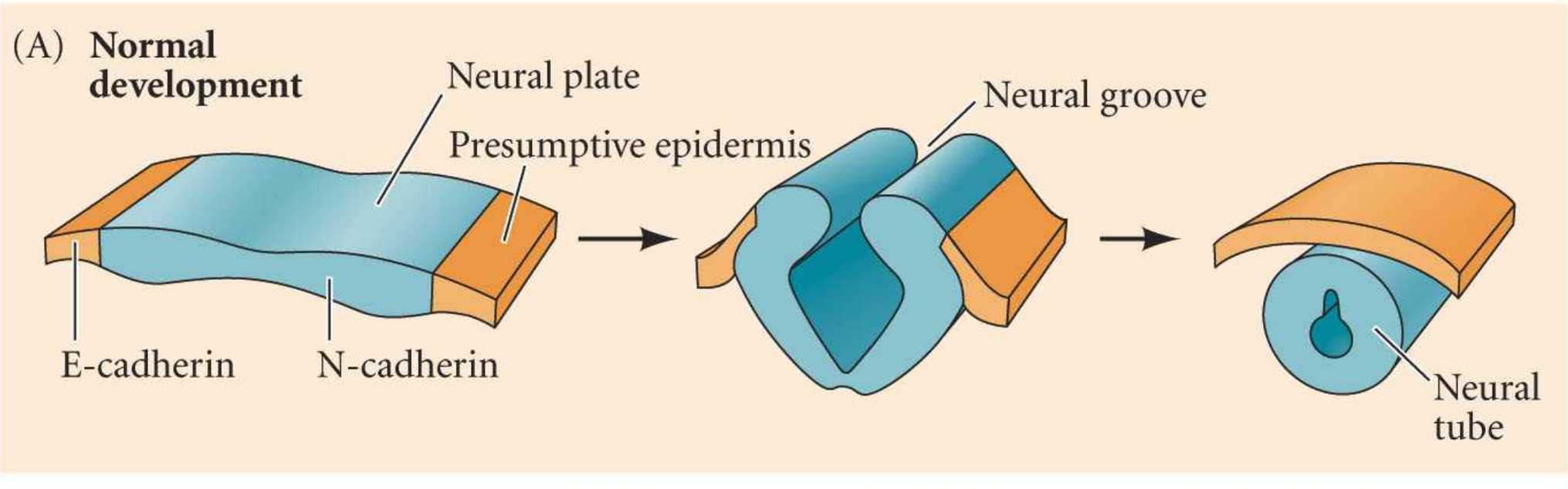
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.3 (Part 2)** © 2006 Sinauer Associates, Inc.

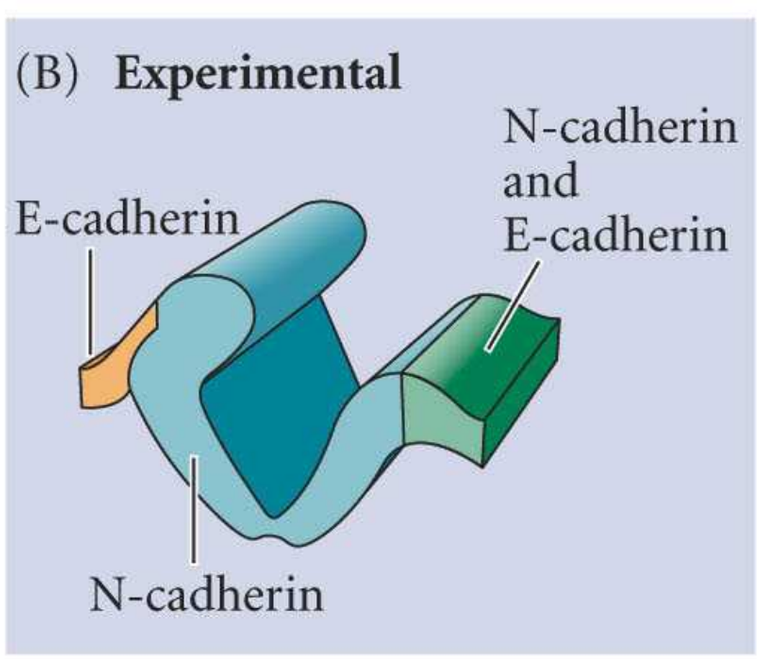
Segregação do neuroepitélio



DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.6** © 2006 Sinauer Associates, Inc.

Segregação do neuroepitélio

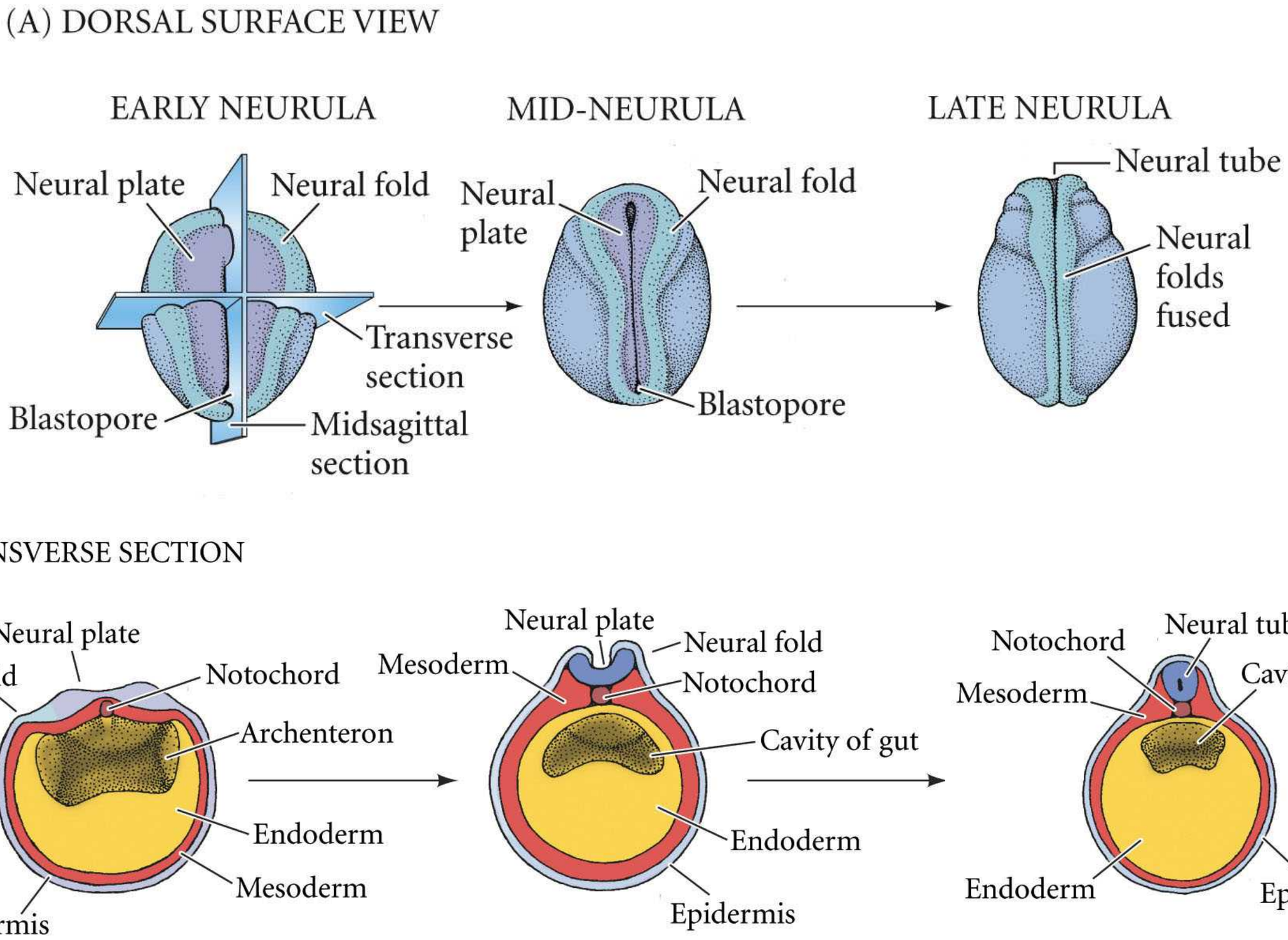




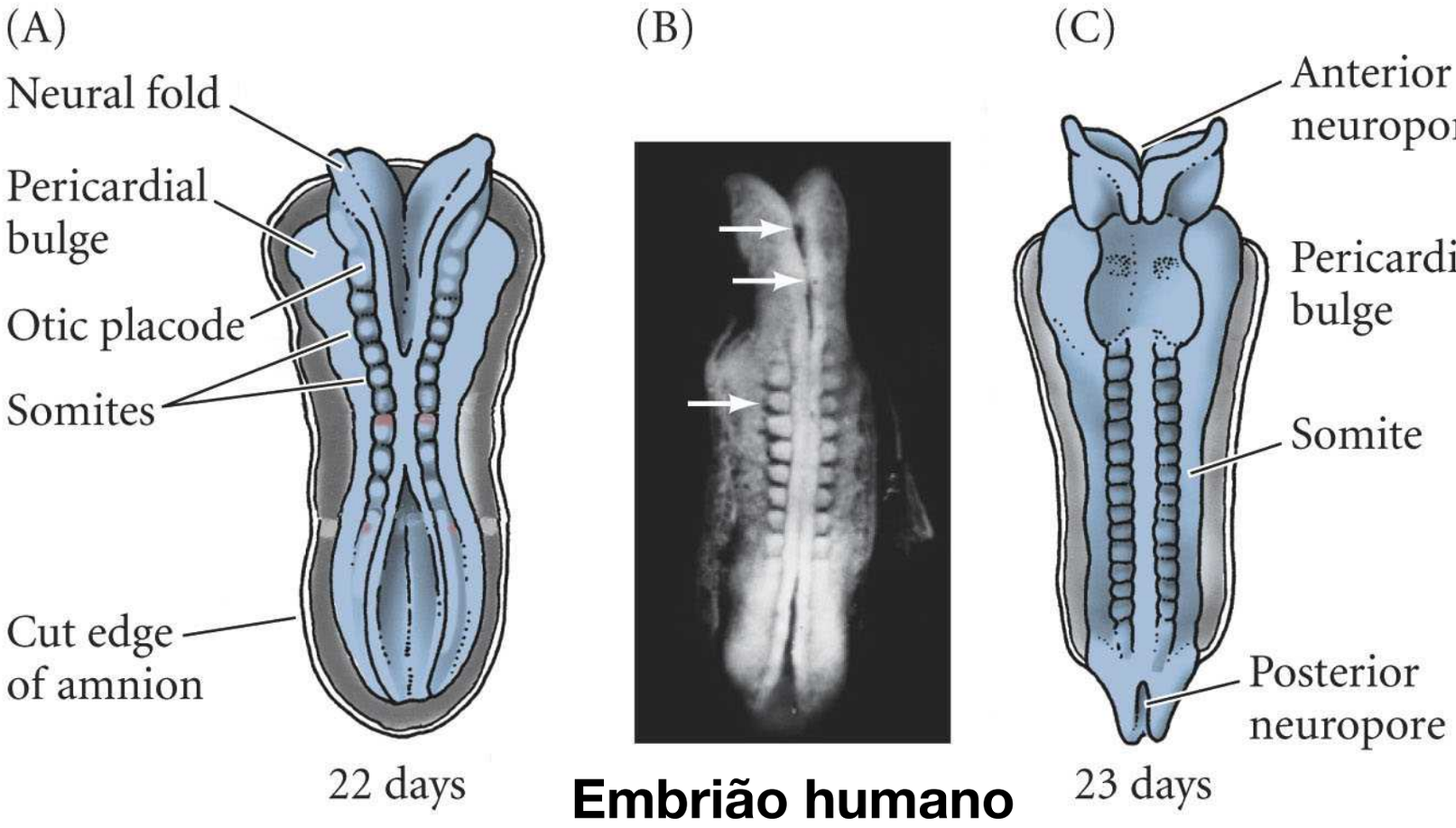
Separação do tubo mediada pela troca na expressão de **E-caderina** por **N-caderina**

DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.6** © 2006 Sinauer Associates, Inc.

Neurulação em anfíbios

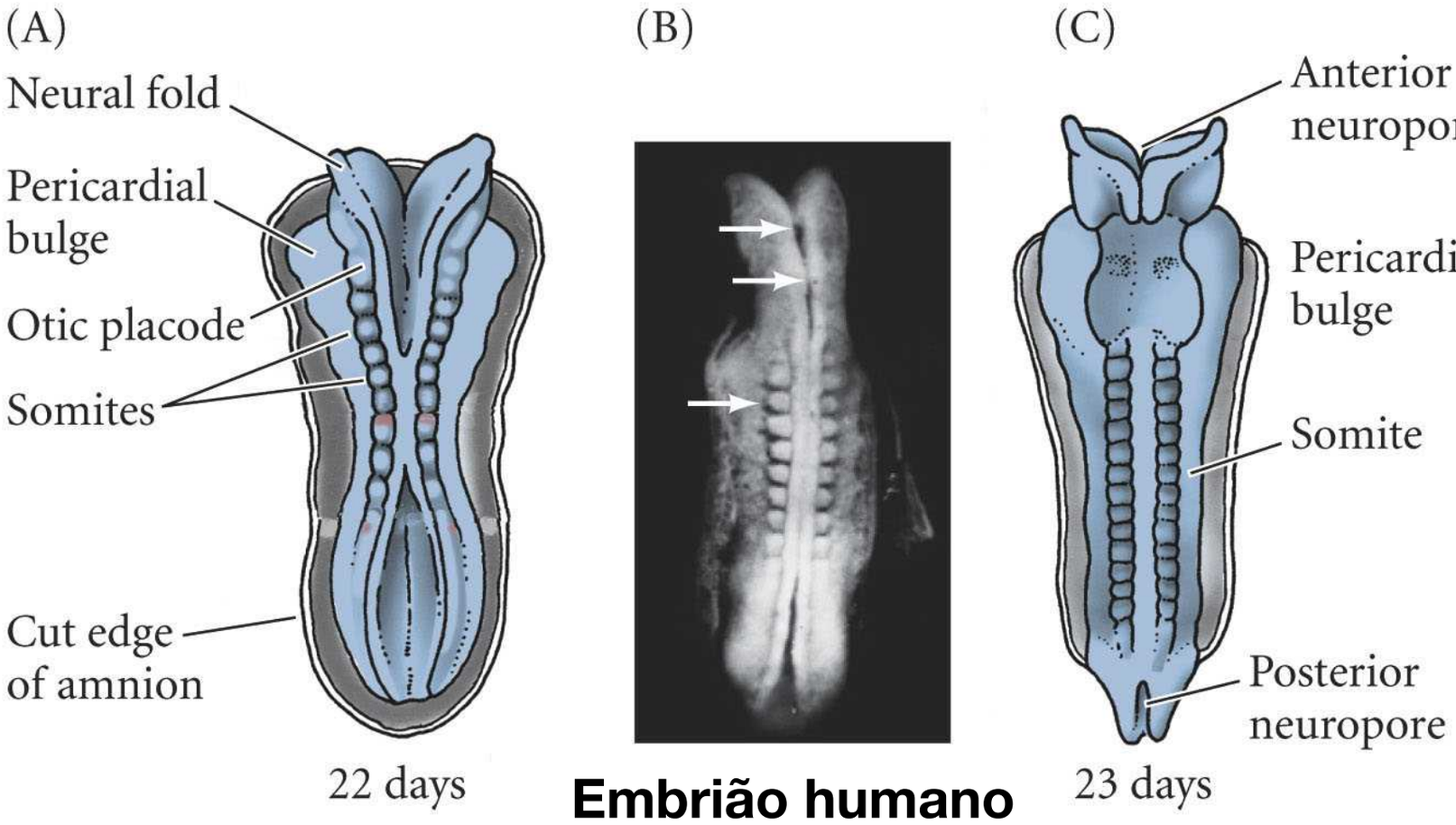


Neurulação em mamíferos



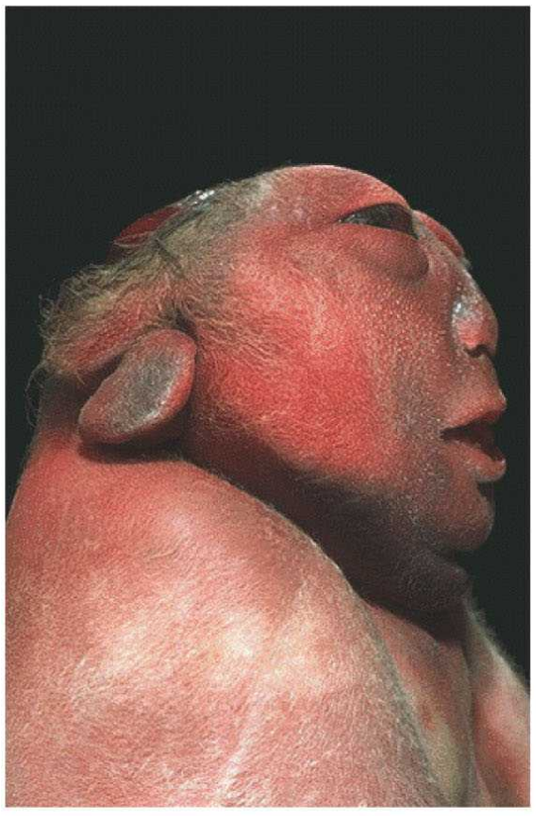
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.5 (Part 1)** © 2006 Sinauer Associates, Inc.

Neurulação em mamíferos



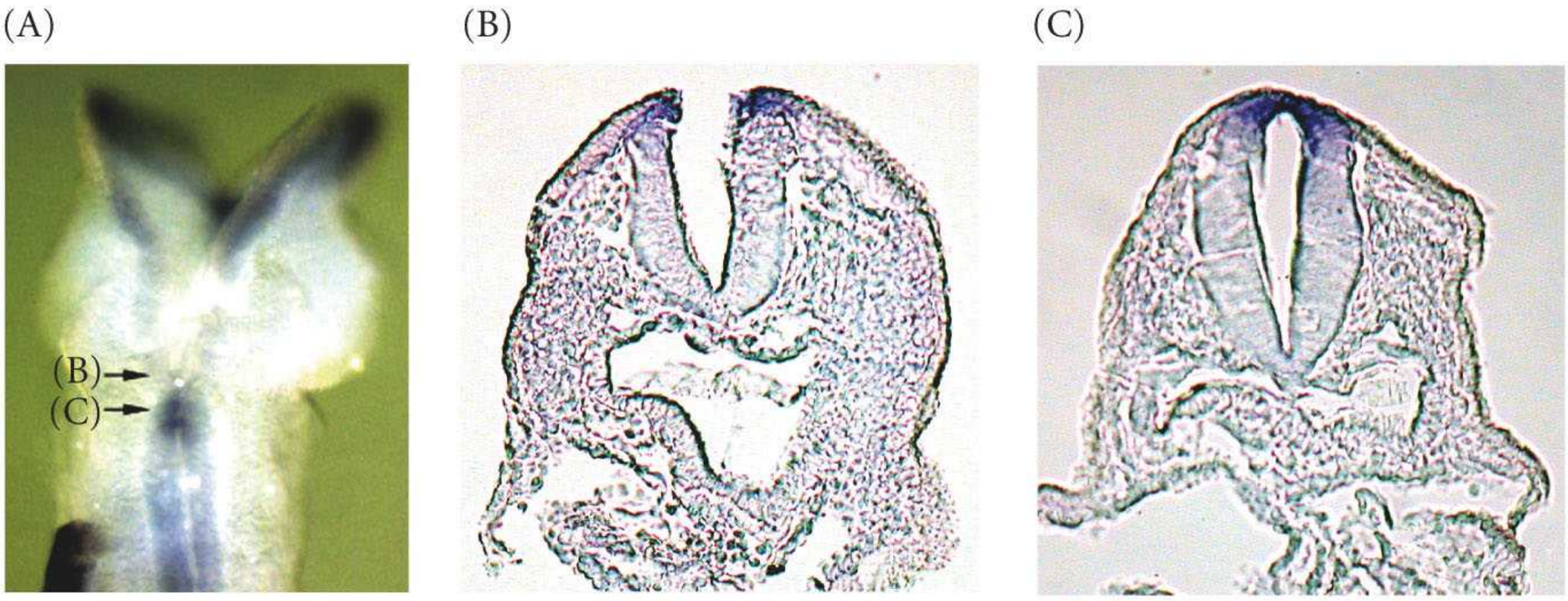
Embrião humano

Anencefalia causada pelo não fechamento do tubo neural cefálico



DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.5 (Part 1)** © 2006 Sinauer Associates, Inc.

Ácido fólico é essencial para o fechamento do tubo neural



Camundongo 10 somitos **RNAm de folate-binding protein 1 (FBP1)**

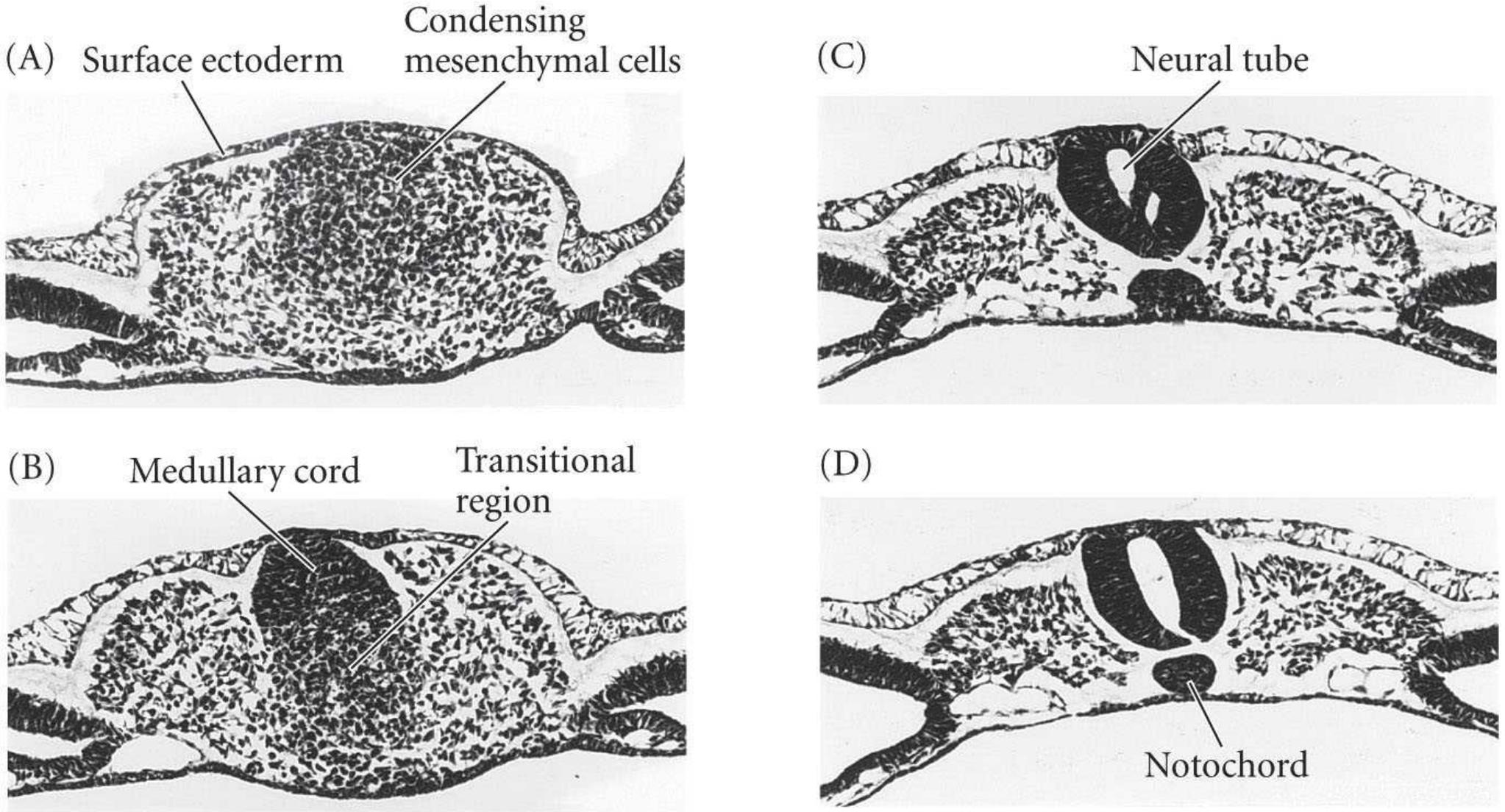
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.7** © 2006 Sinauer Associates, Inc.

Neurulação secundária

posterior

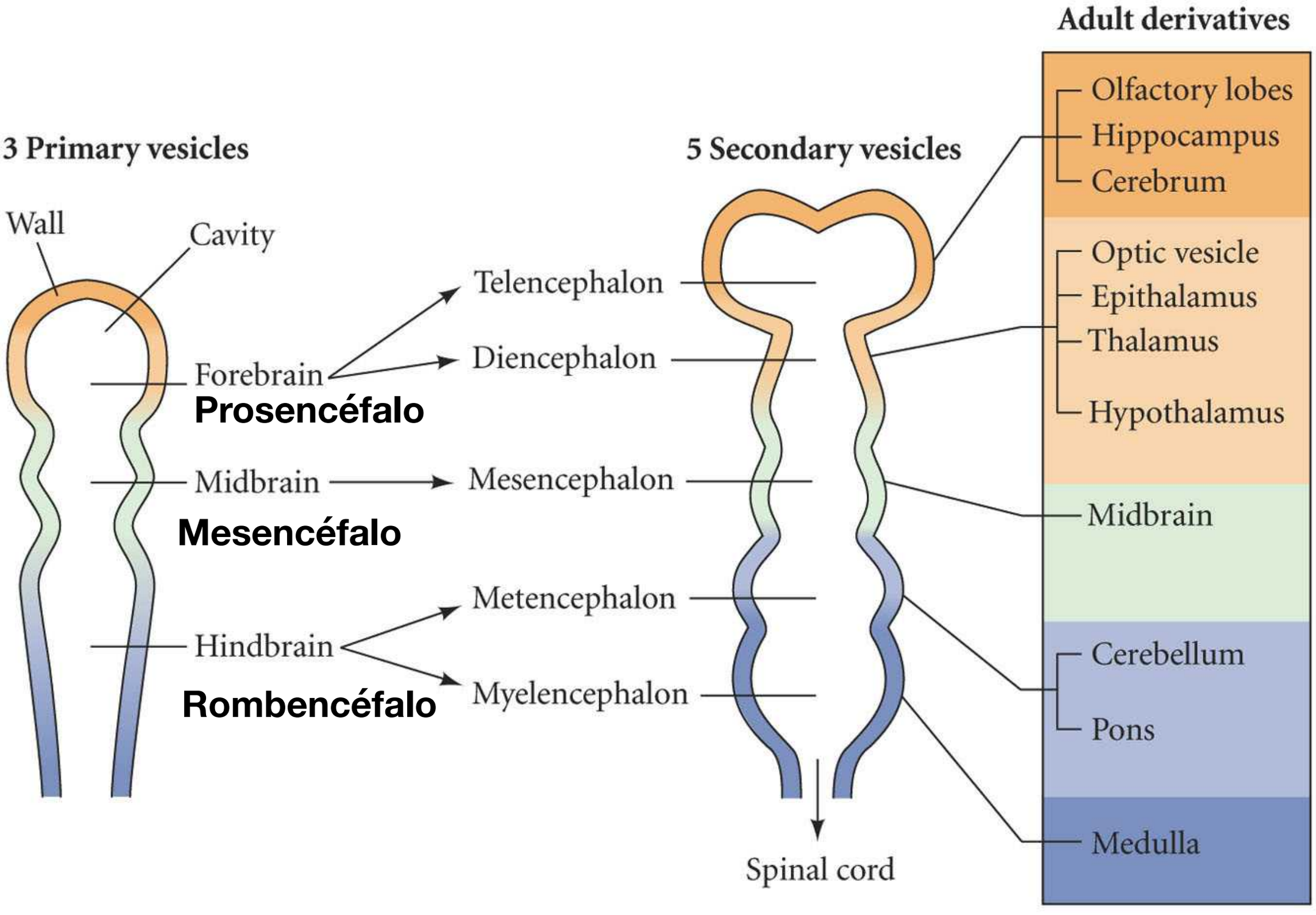
Galinha
Broto da cauda
25 somitos
(2,5 dias)

anterior



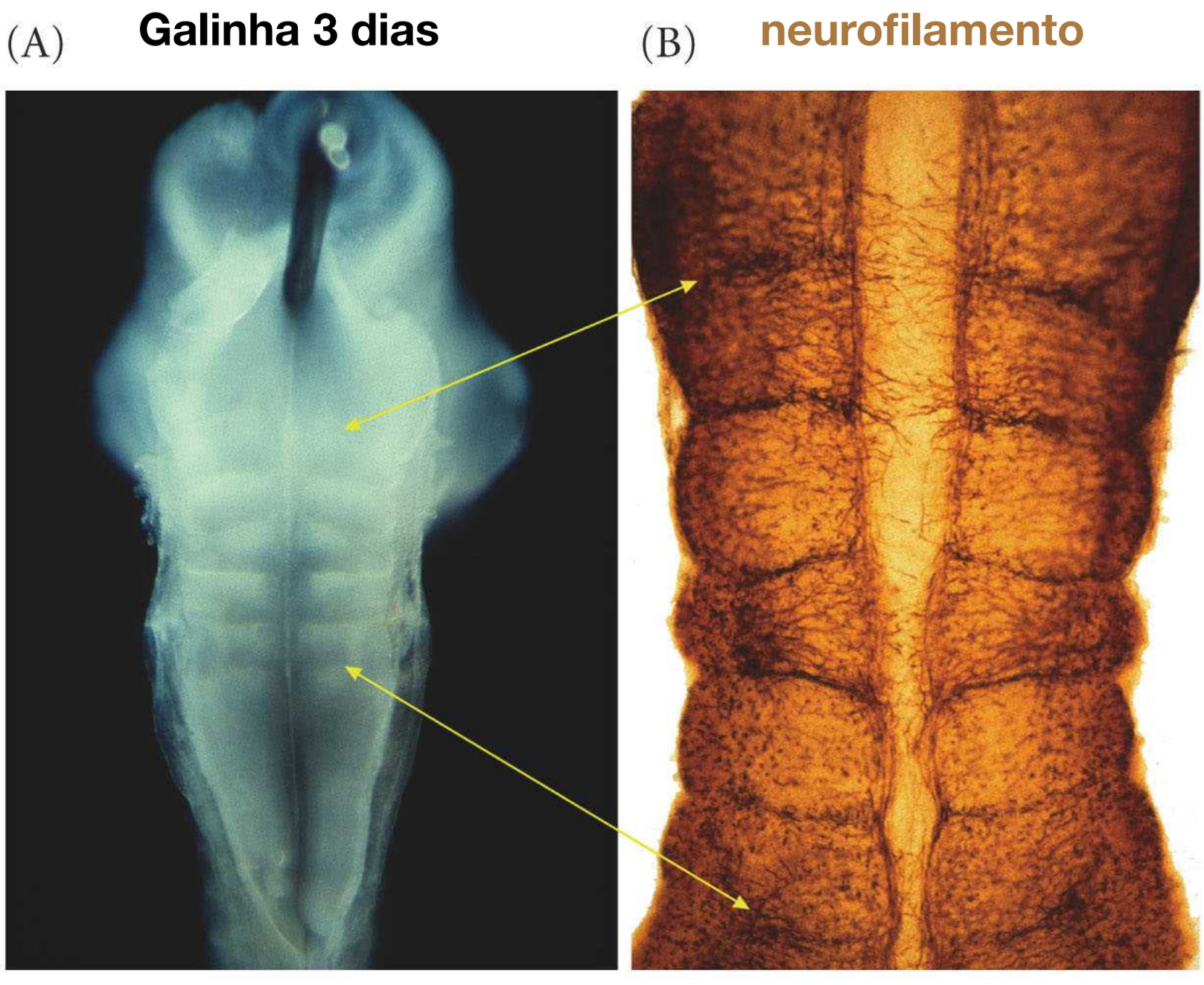
***DEVELOPMENTAL BIOLOGY, Eighth Edition,* Figure 12.8** © 2006 Sinauer Associates, Inc.

Divisões do tubo neural cefálico



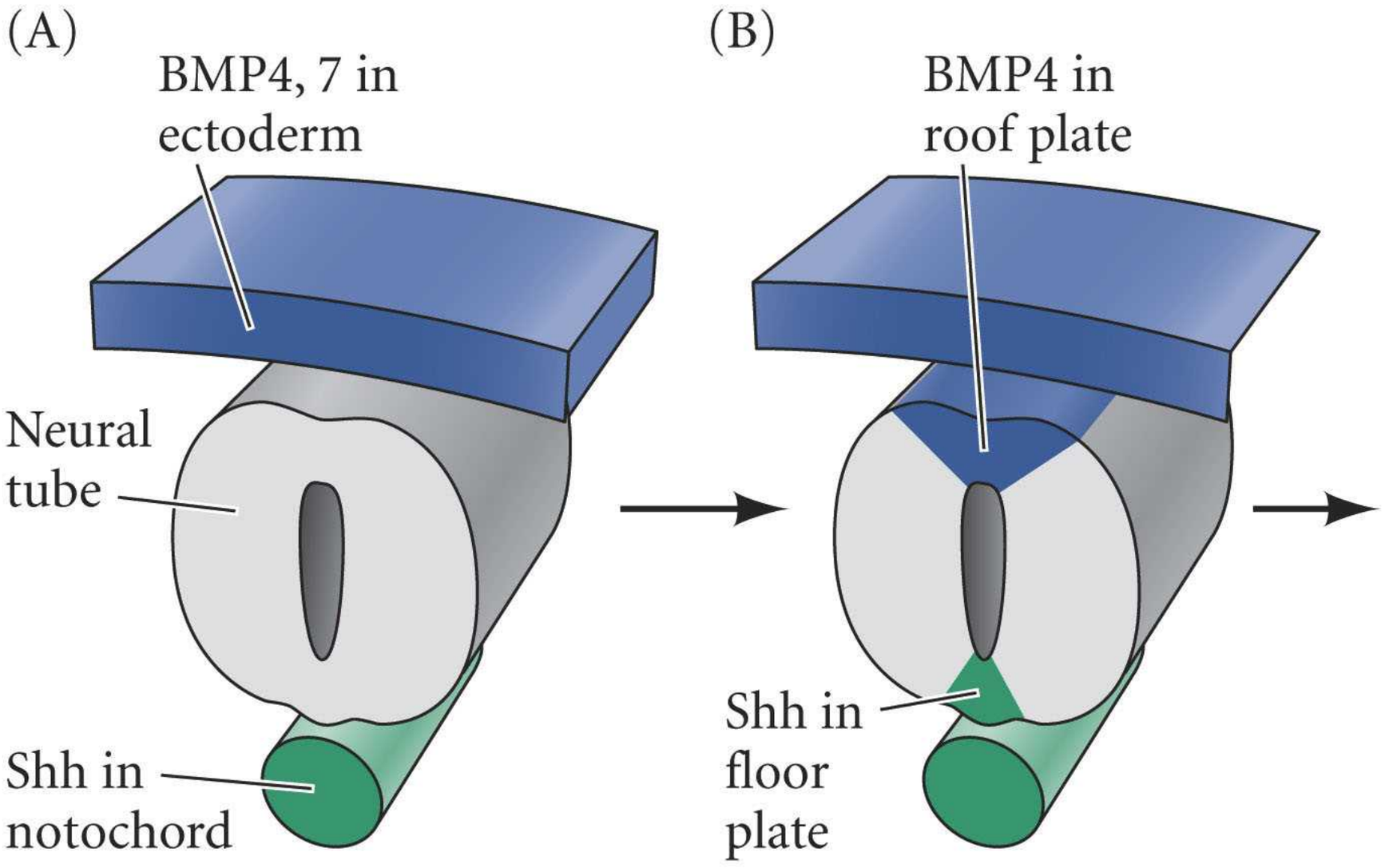
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.9** © 2006 Sinauer Associates, Inc.

Os rombômeros são divisões anatômicas e funcionais do rombencéfalo



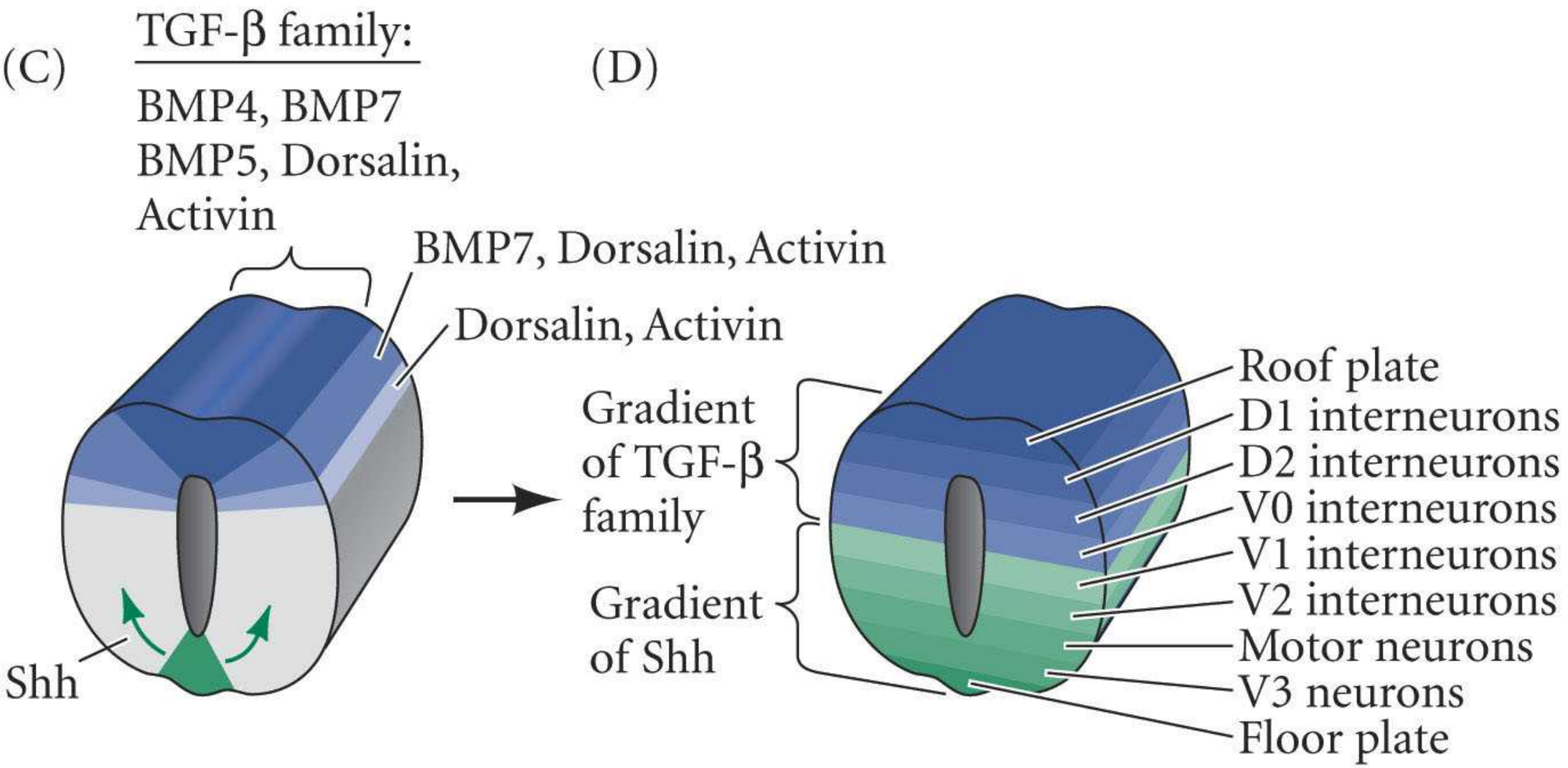
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.10** © 2006 Sinauer Associates, Inc.

Especificação de subtipos neuronais no eixo DV



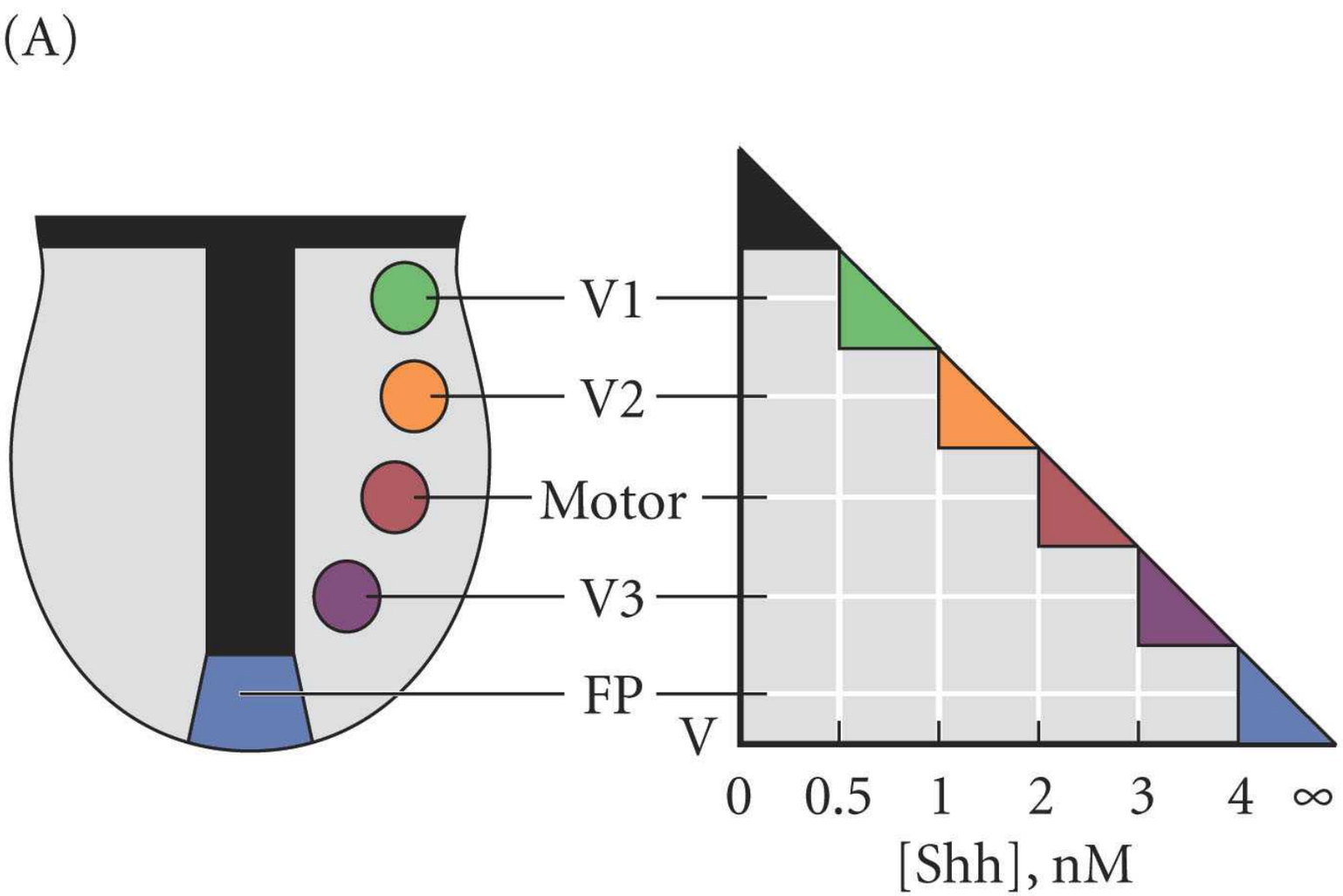
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.13 (Part 1)** © 2006 Sinauer Associates, Inc.

Especificação de subtipos neuronais no eixo DV



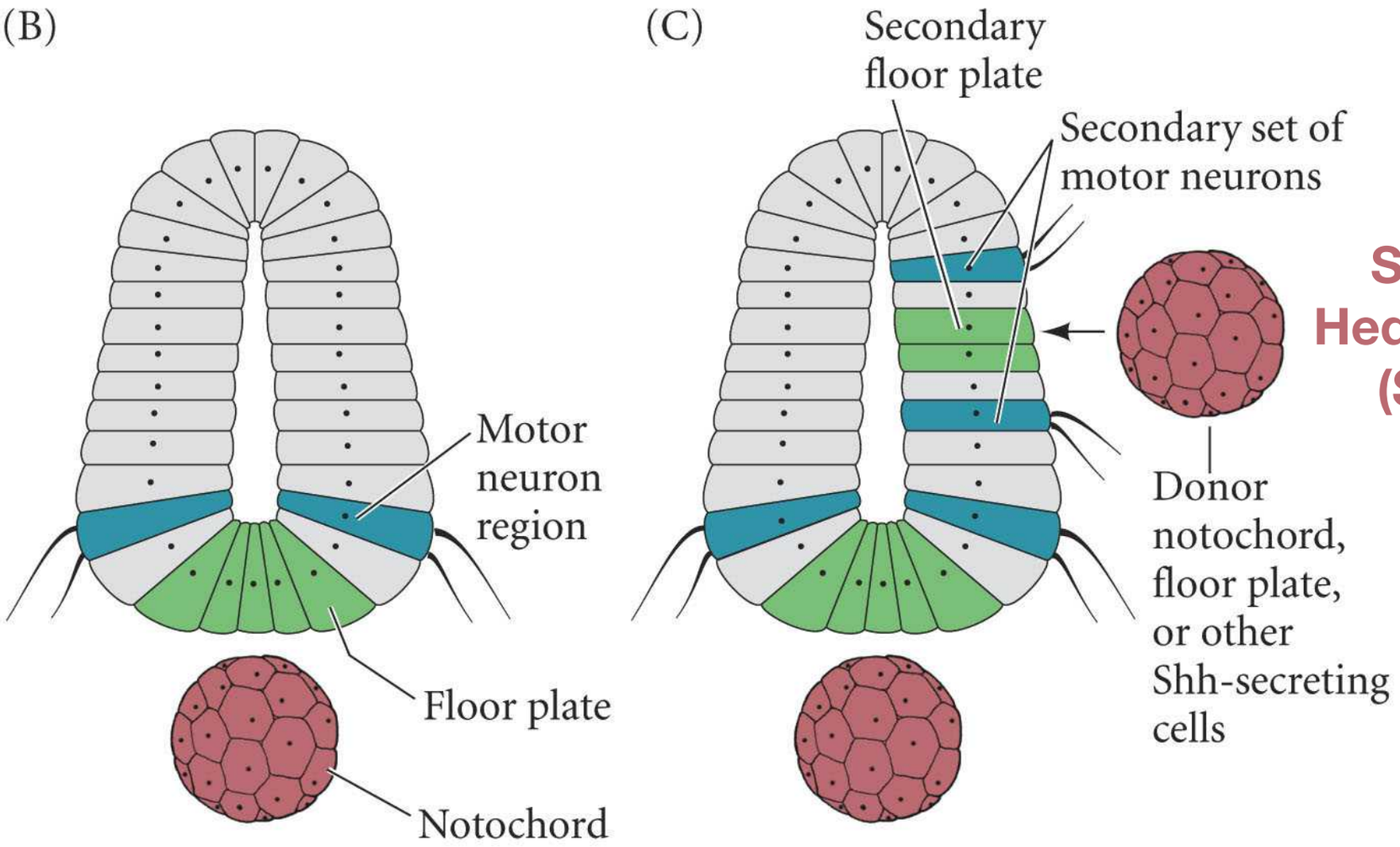
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.13 (Part 2)** © 2006 Sinauer Associates, Inc.

Indução dose-dependente de tipos neurais ventrais por Sonic (Shh)



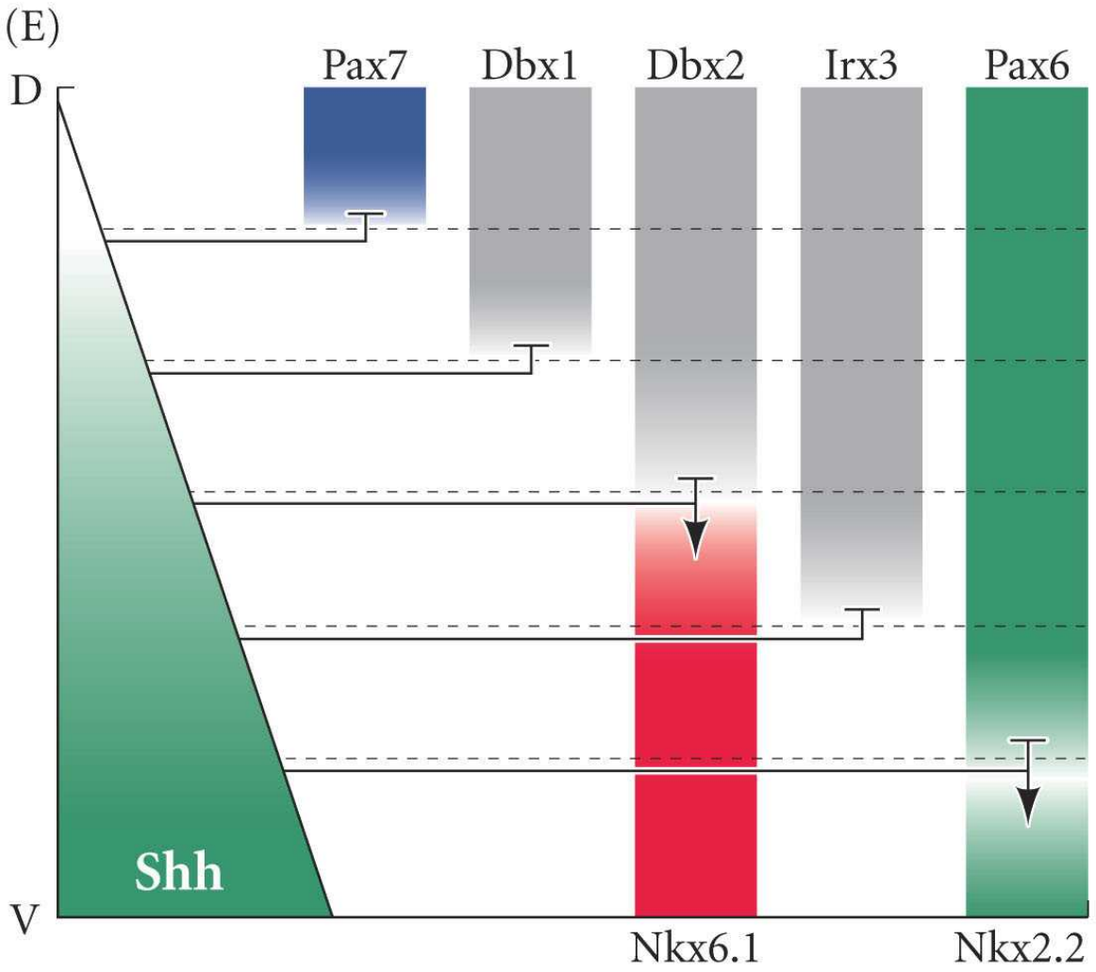
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.14 (Part 1)** © 2006 Sinauer Associates, Inc.

Shh é suficiente para induzir destinos ventrais em precursores não-especificados



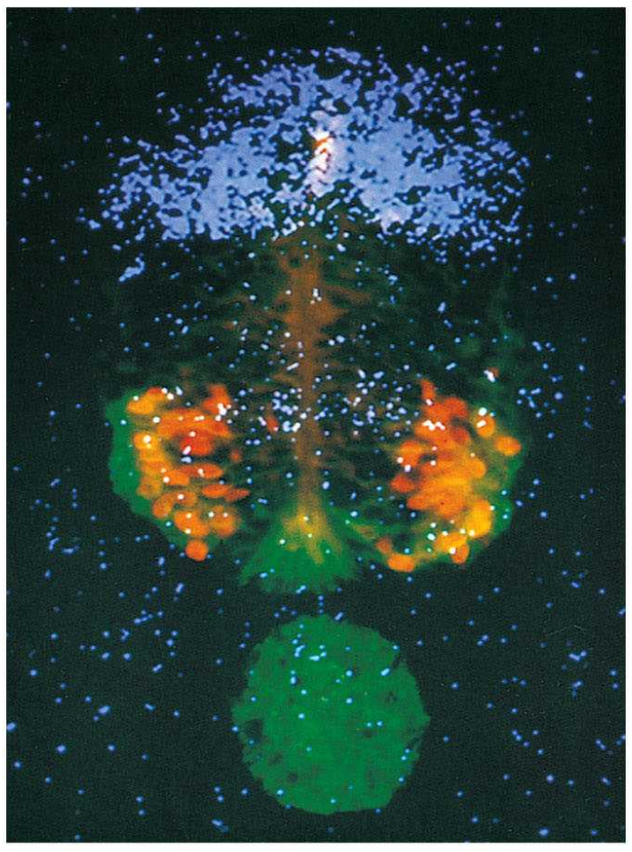
DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.14 (Part 2)** © 2006 Sinauer Associates, Inc.

A padronização funcional do tubo neural é mediada por fatores de transcrição específicos dos subtipos neurais

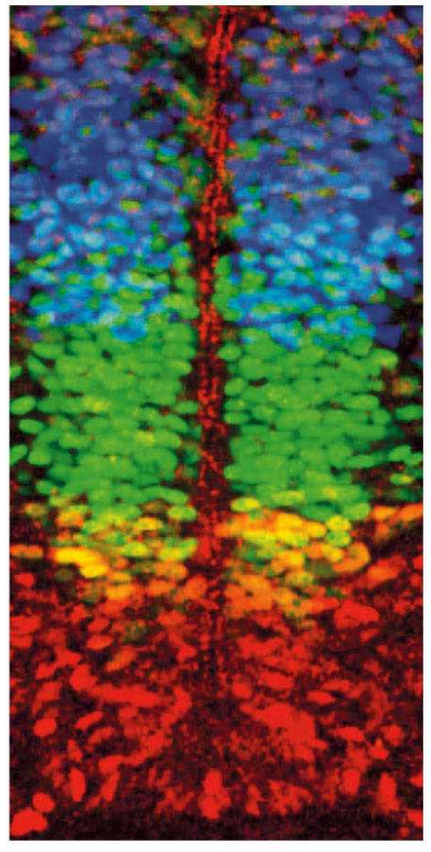


Pax7
Pax6
Nkx6.1

(F)



(G)

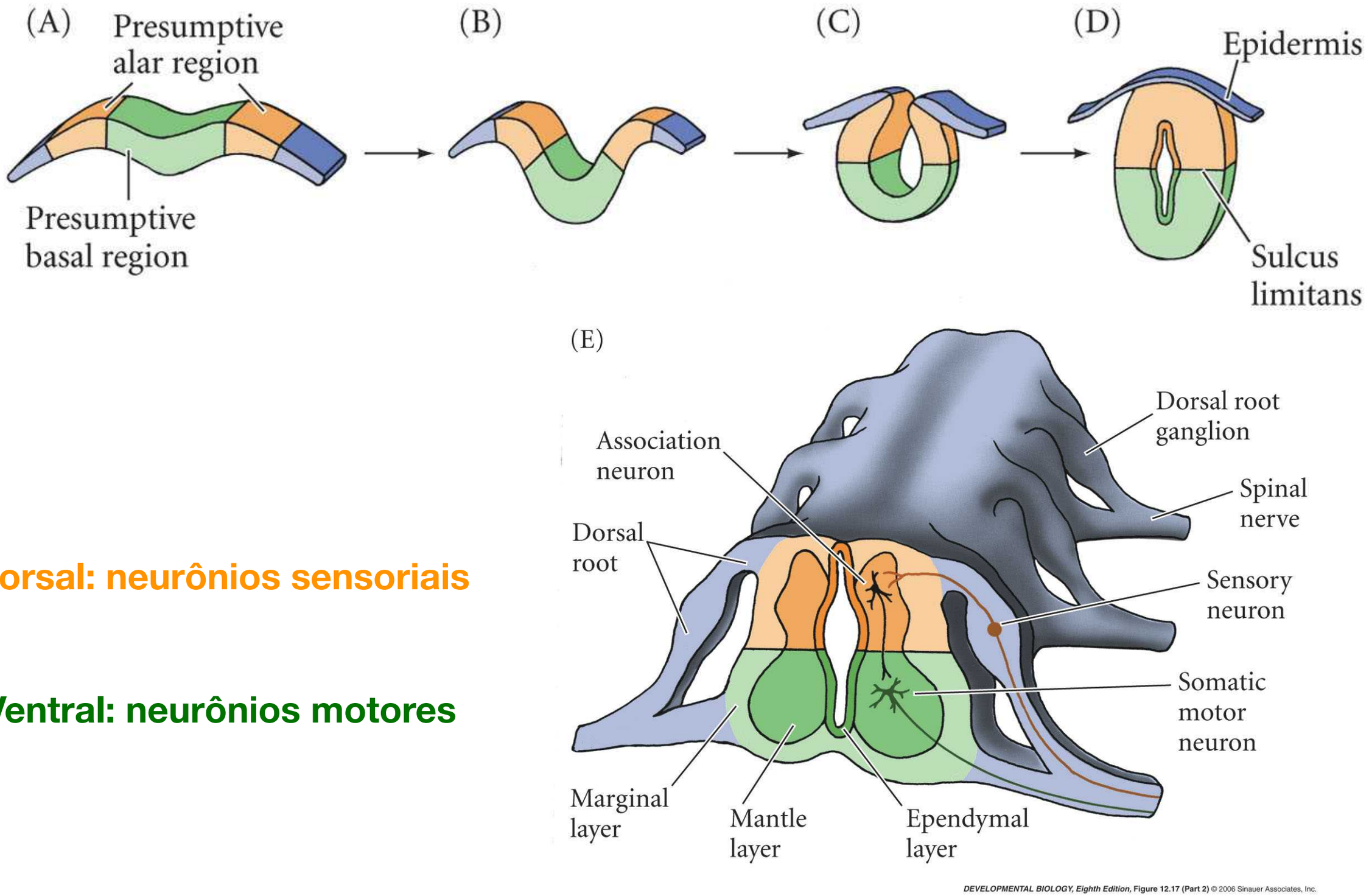


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Placa basal: neurônios motores (ventral)
Placa alar: neurônios sensoriais (dorsal)

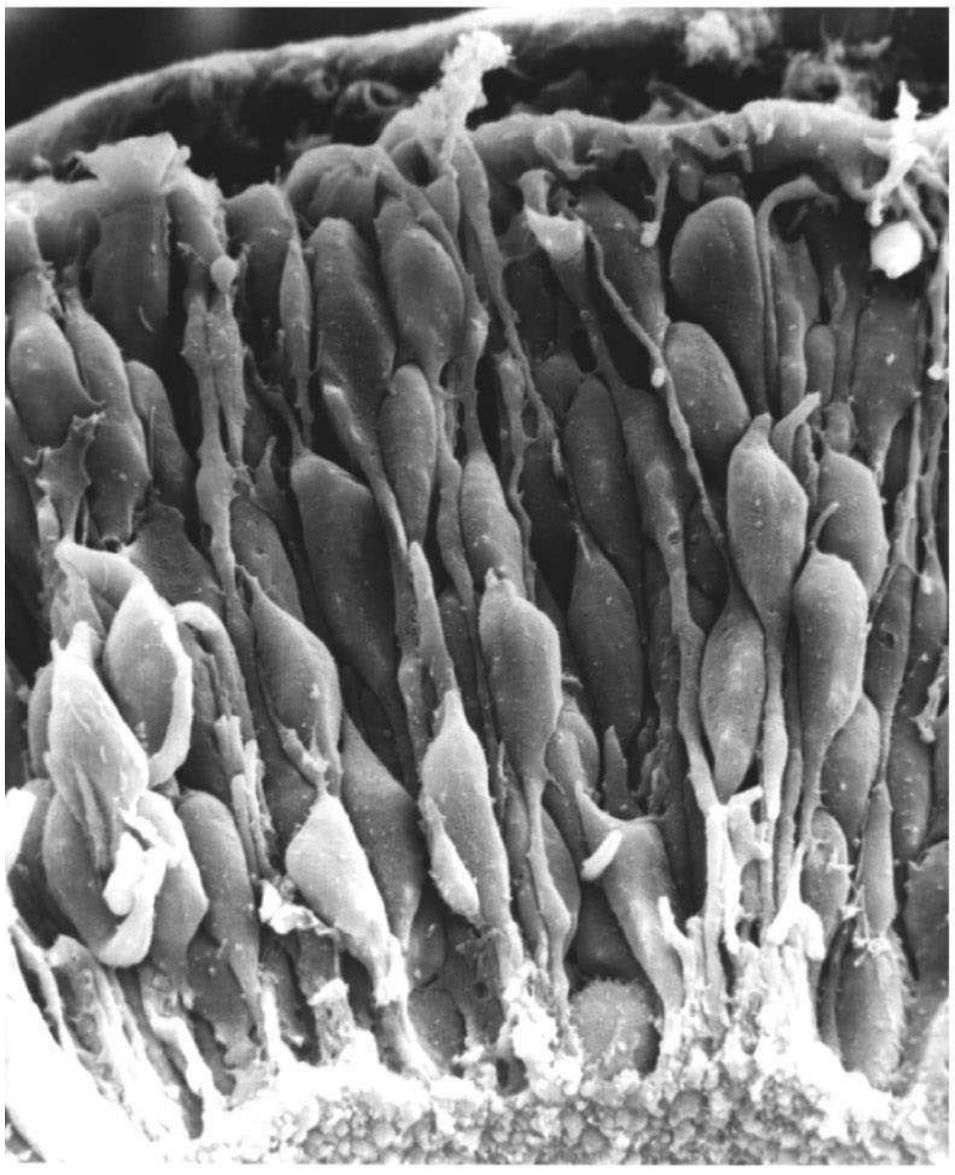
Dorsal: neurônios sensoriais

Ventral: neurônios motores

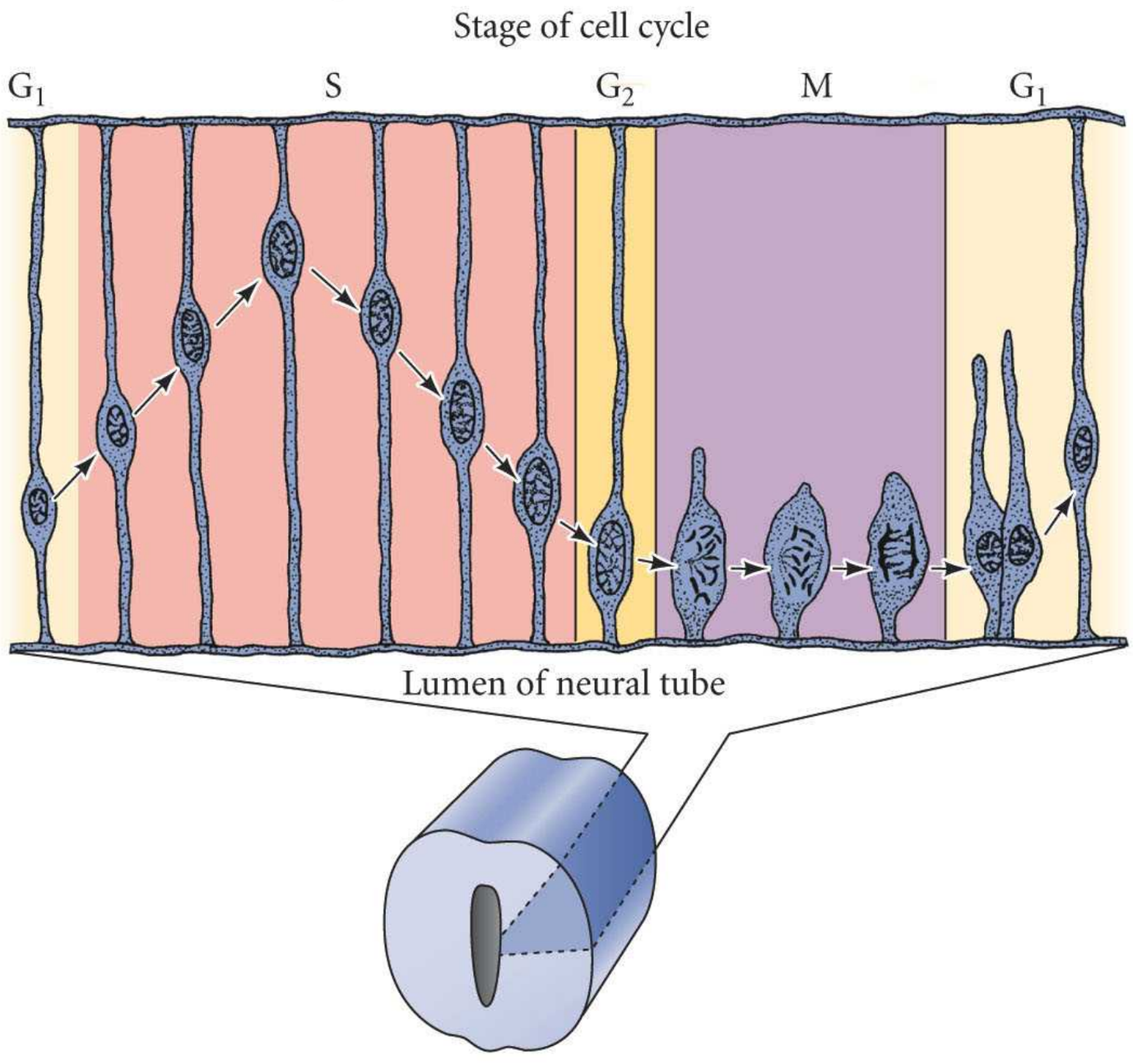


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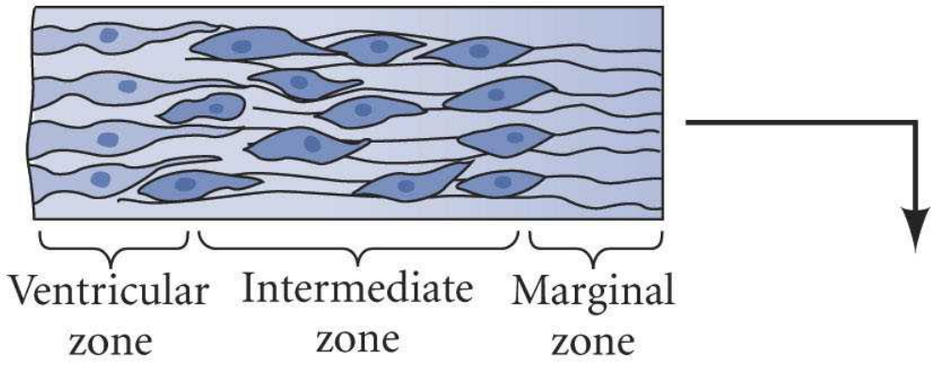
O neuroepitélio proliferativo é pseudoestratificado



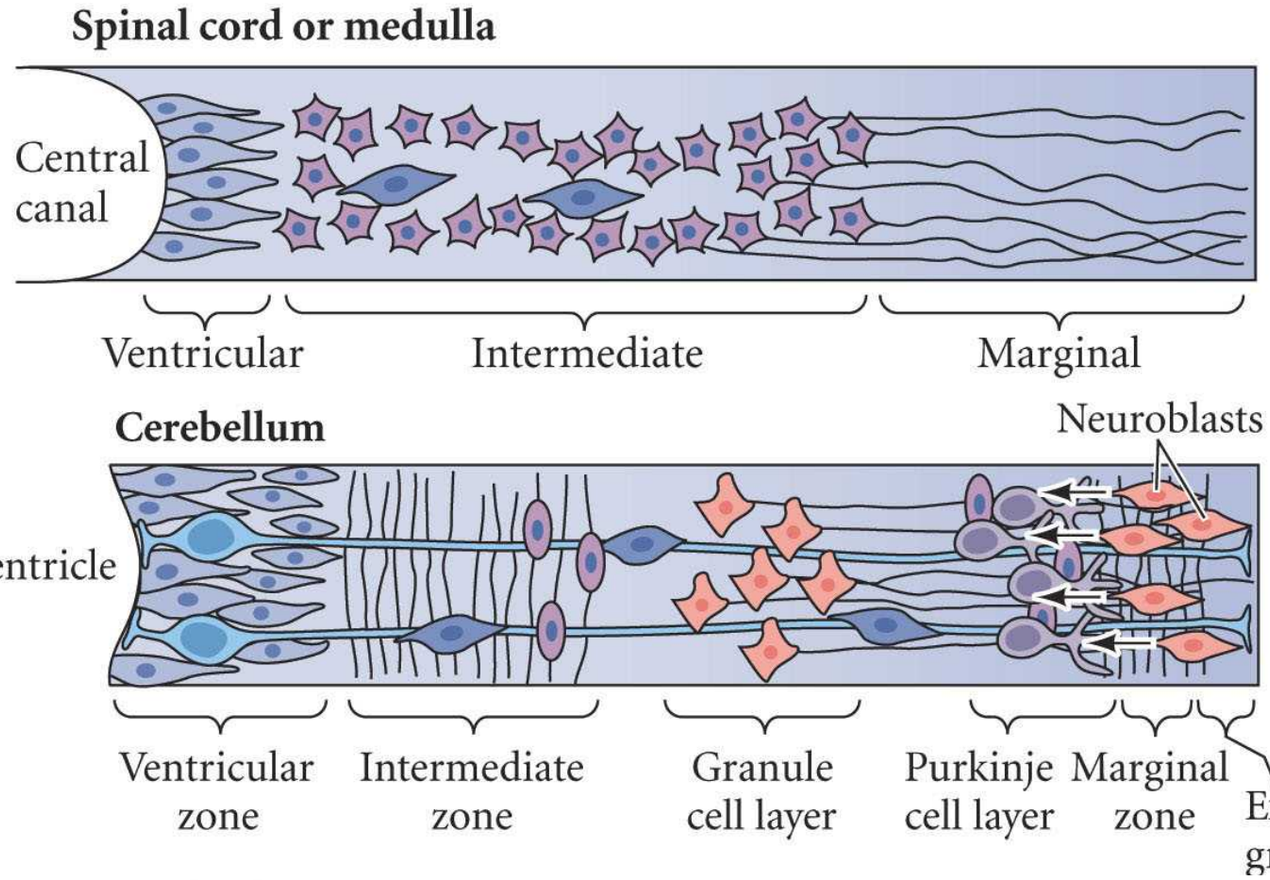
Migração intercinética nuclear



DEVELOPMENTAL BIOLOGY, Eighth Edition, **Figure 12.15 (Part 2)** © 2006 Sinau

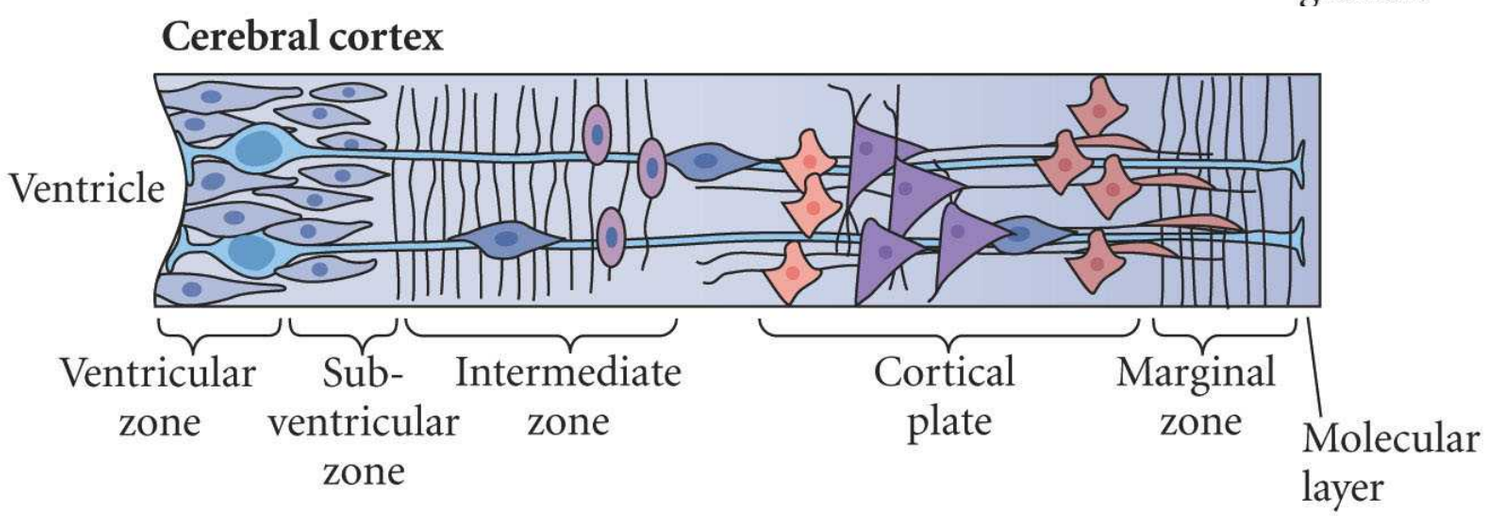


Precursores neurais pós-mitóticos migram e se diferenciam na periferia



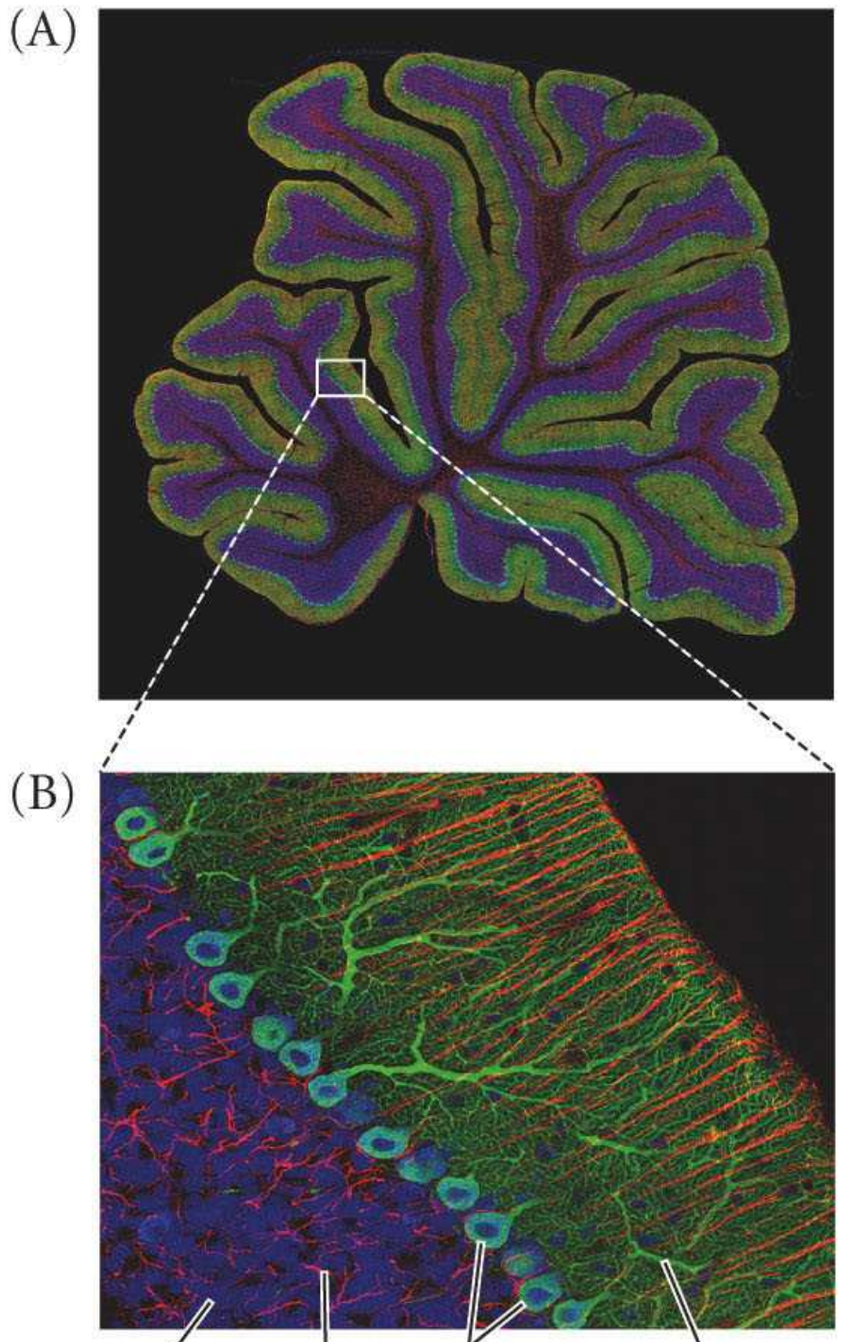
Medula espinhal (1 camada)

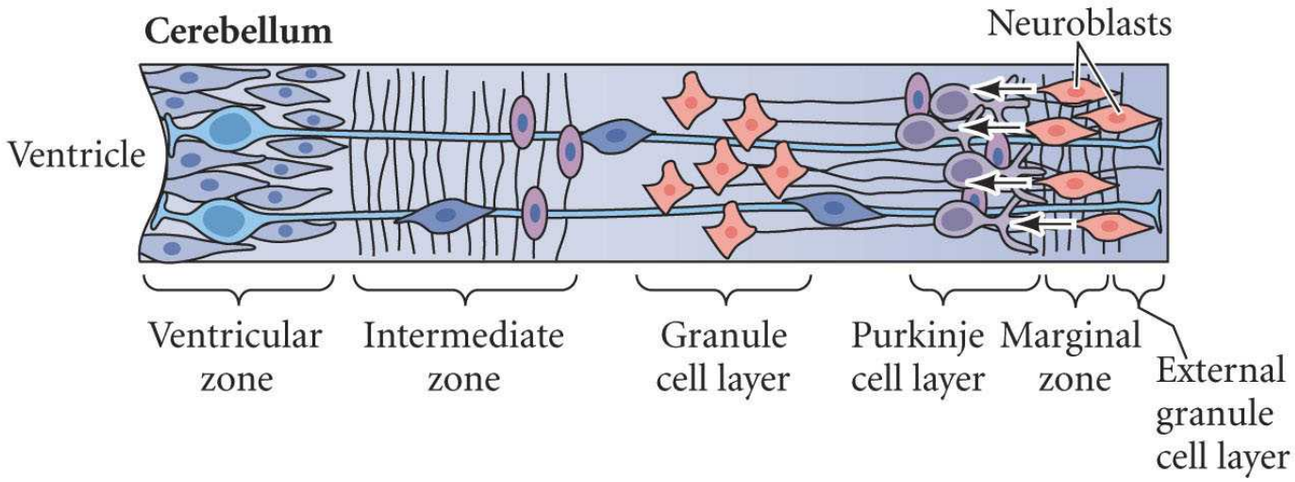
Cerebelo (3 camadas)



Cortex cerebral (6 camadas em mamíferos)

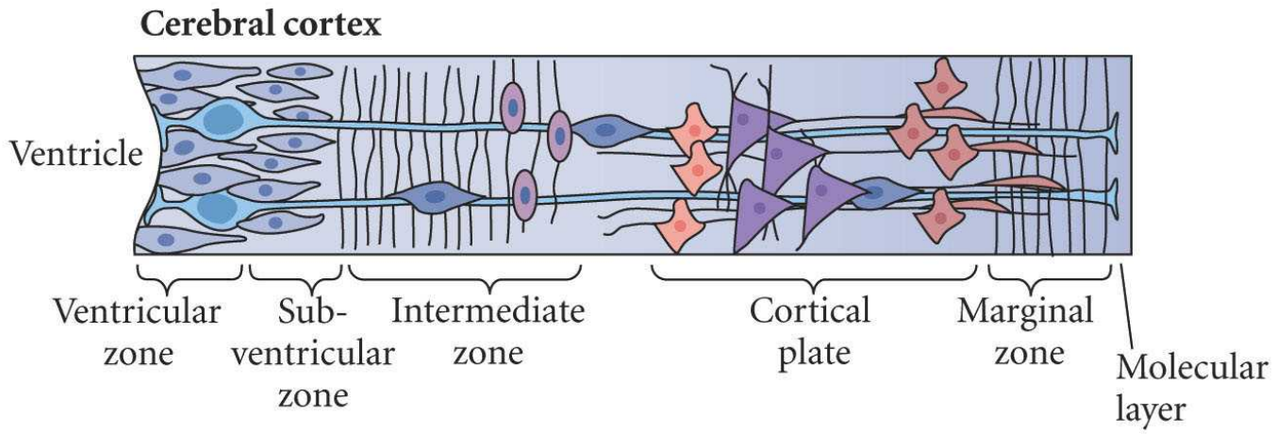
Mas, na zona marginal do cerebelo os neuroblastos se dividem novamente para formar os neurônios de Purkinje

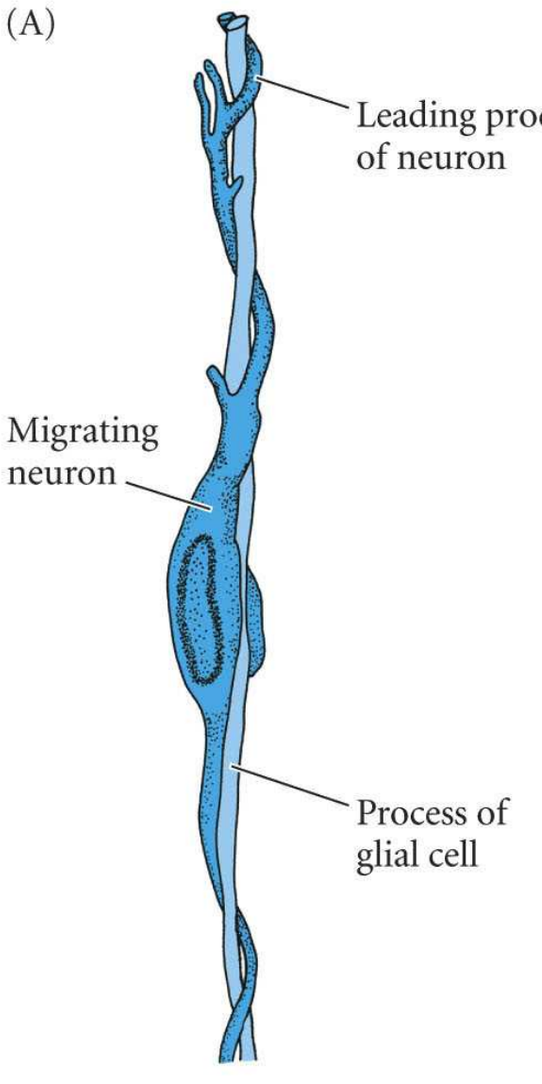


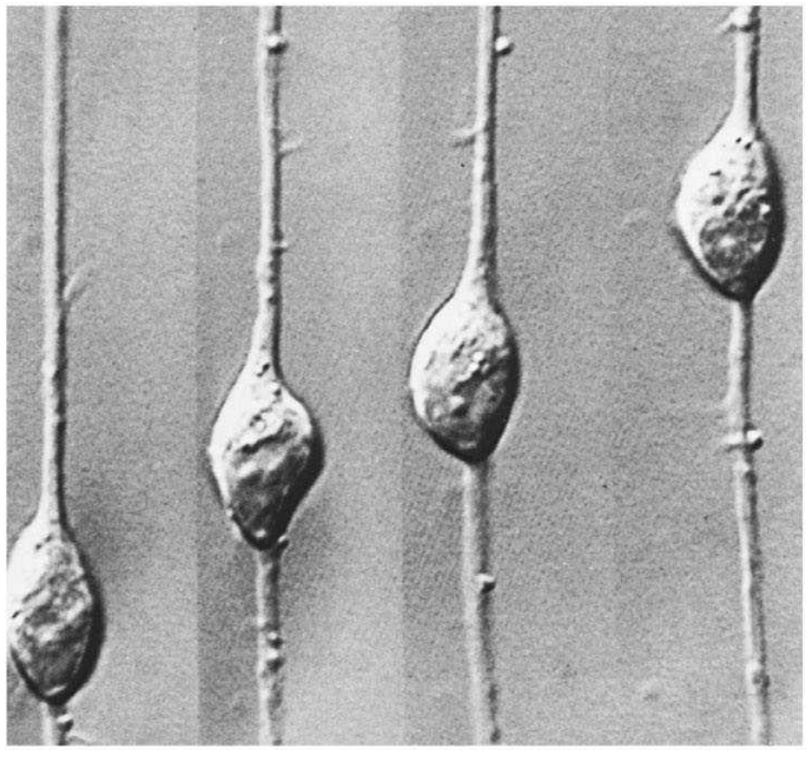


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Migração do neurônio pós-mitótico pela glia radial é essencial para a formação das camadas do neocortex



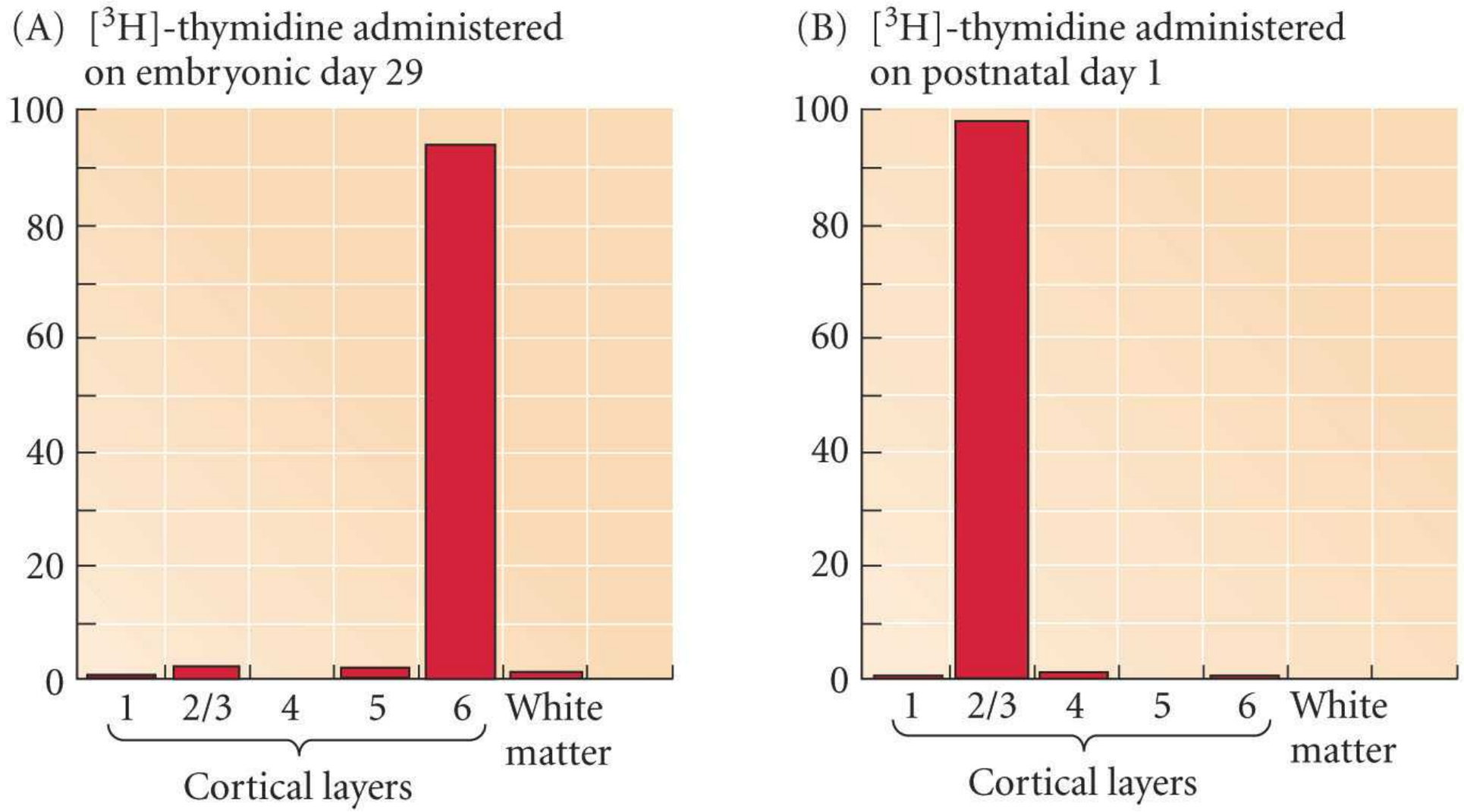


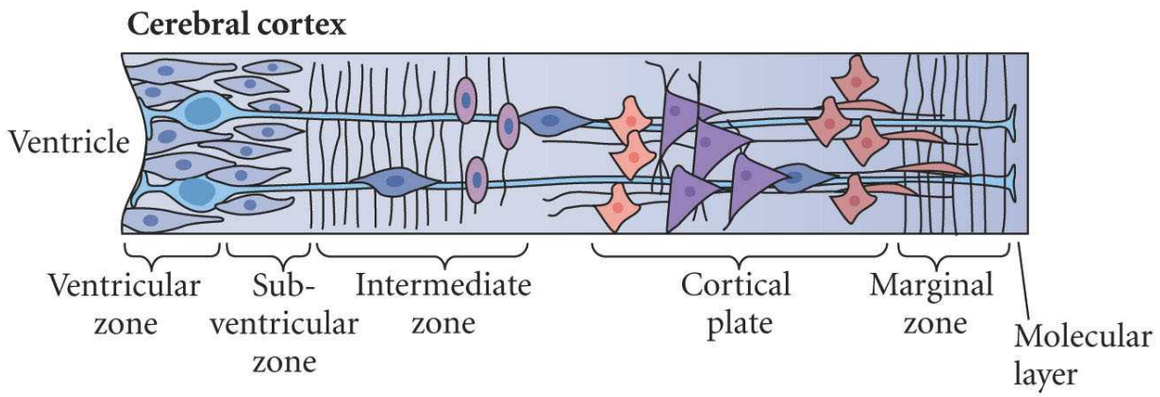


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Os primeiros neurônios que deixam o ciclo celular formam as camadas mais internas do neocortex

Ferret

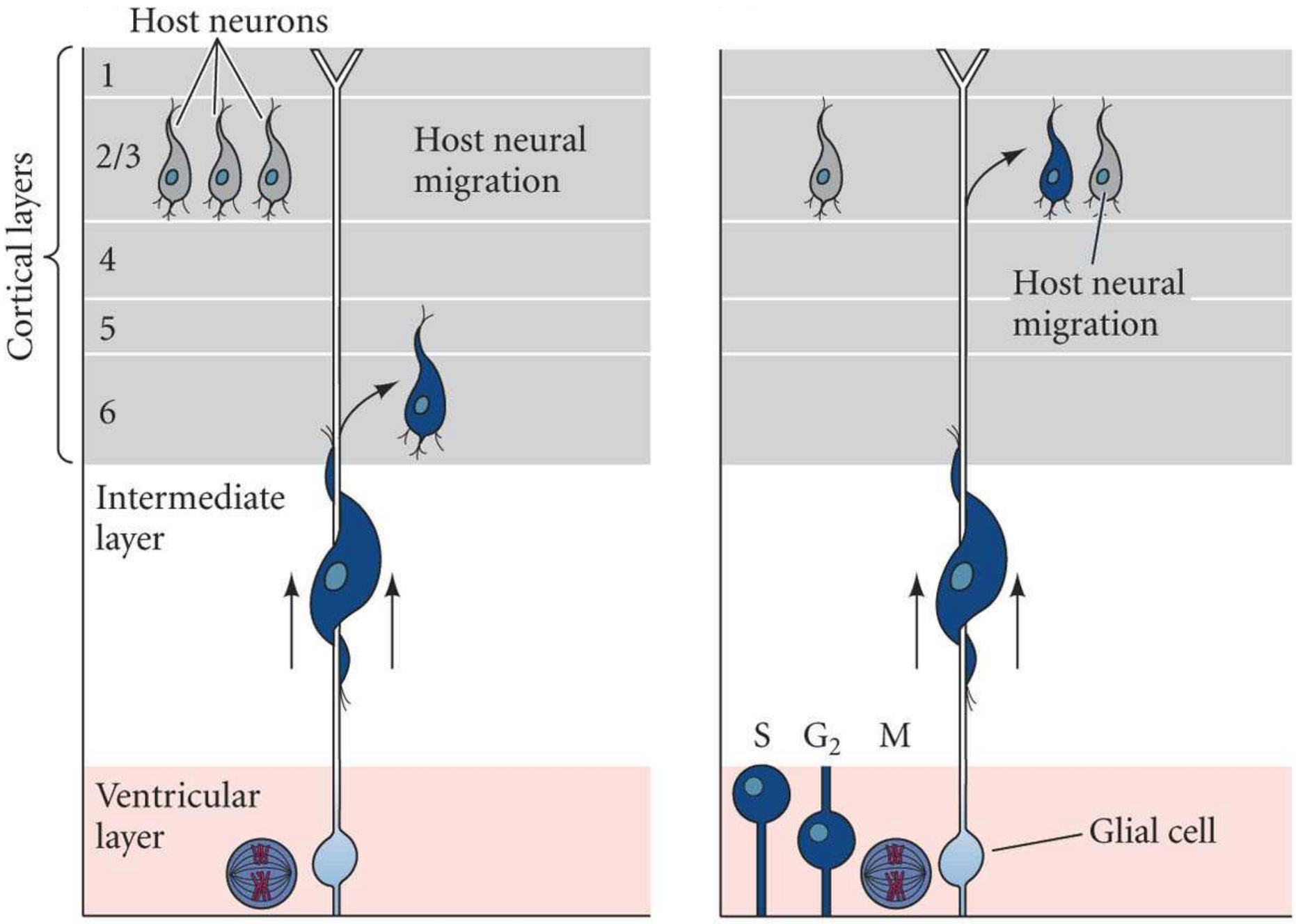




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As camadas externas são populadas por precursores tardios que migram através das camadas internas já formadas

A camada alvejada após a saída do ciclo celular é determinada por sinais recebidos durante a fase S

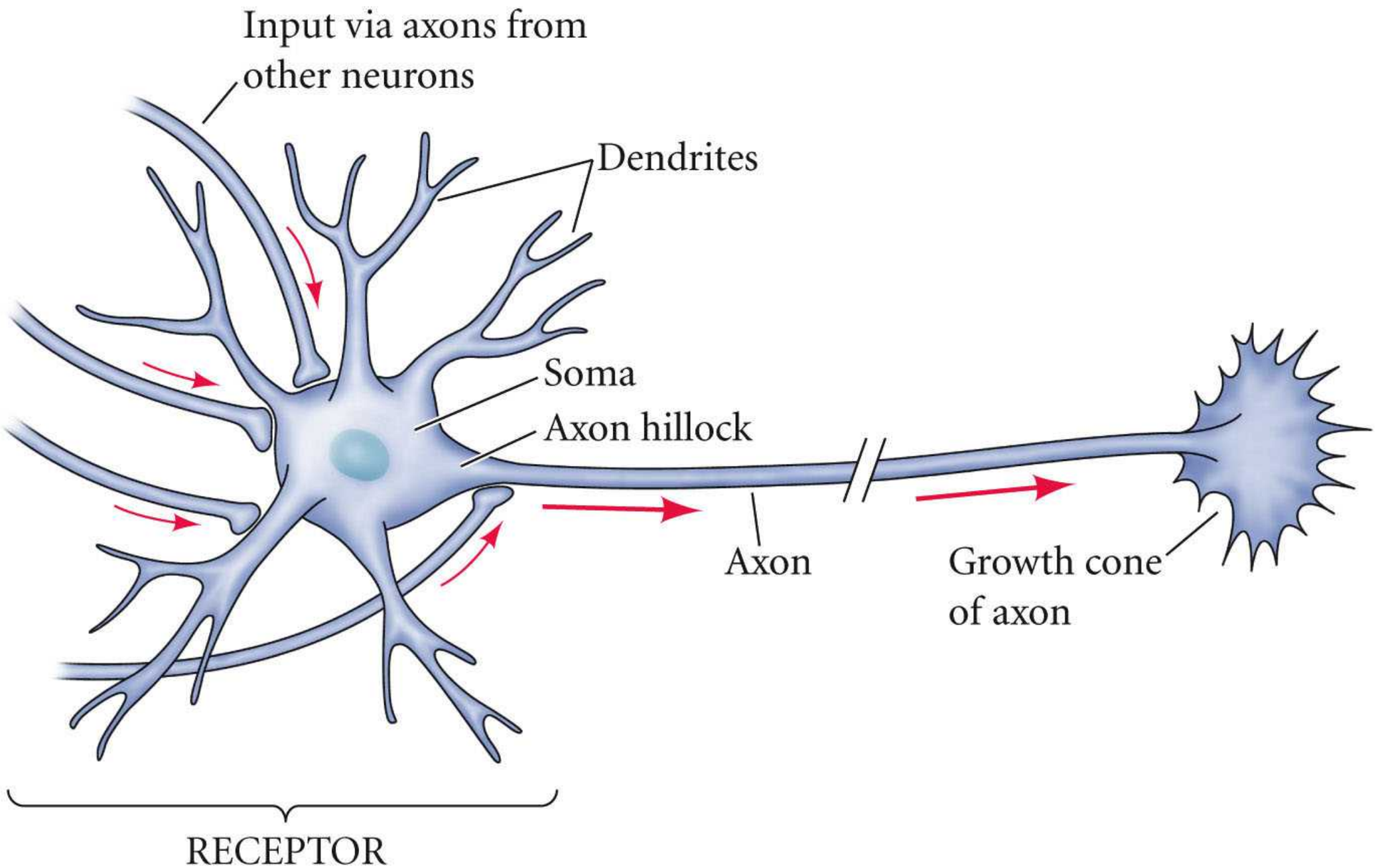


Cell-autonomous fate when transplanted after last S phase

Host fate when transplanted in S phase

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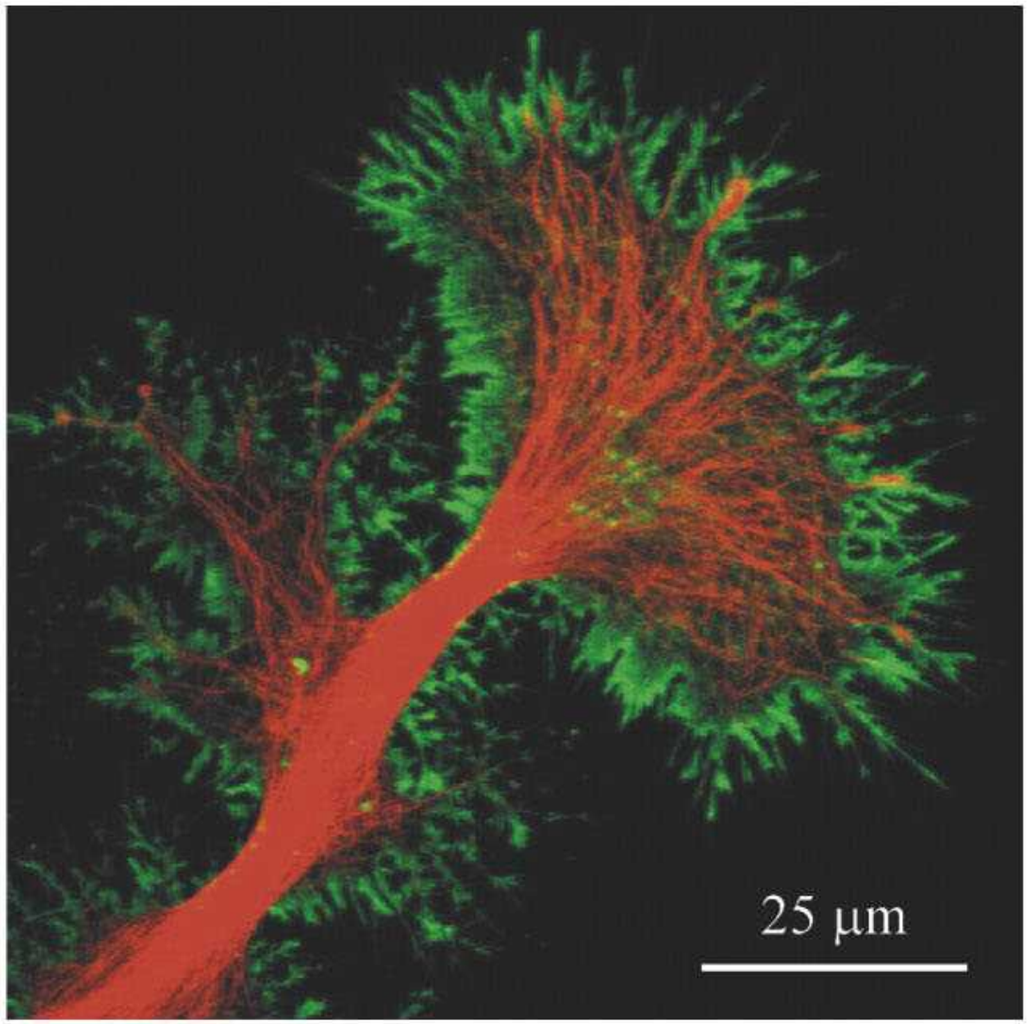
Após a migração, a diferenciação dos neurônios é concluída com o processo de neuritogênese



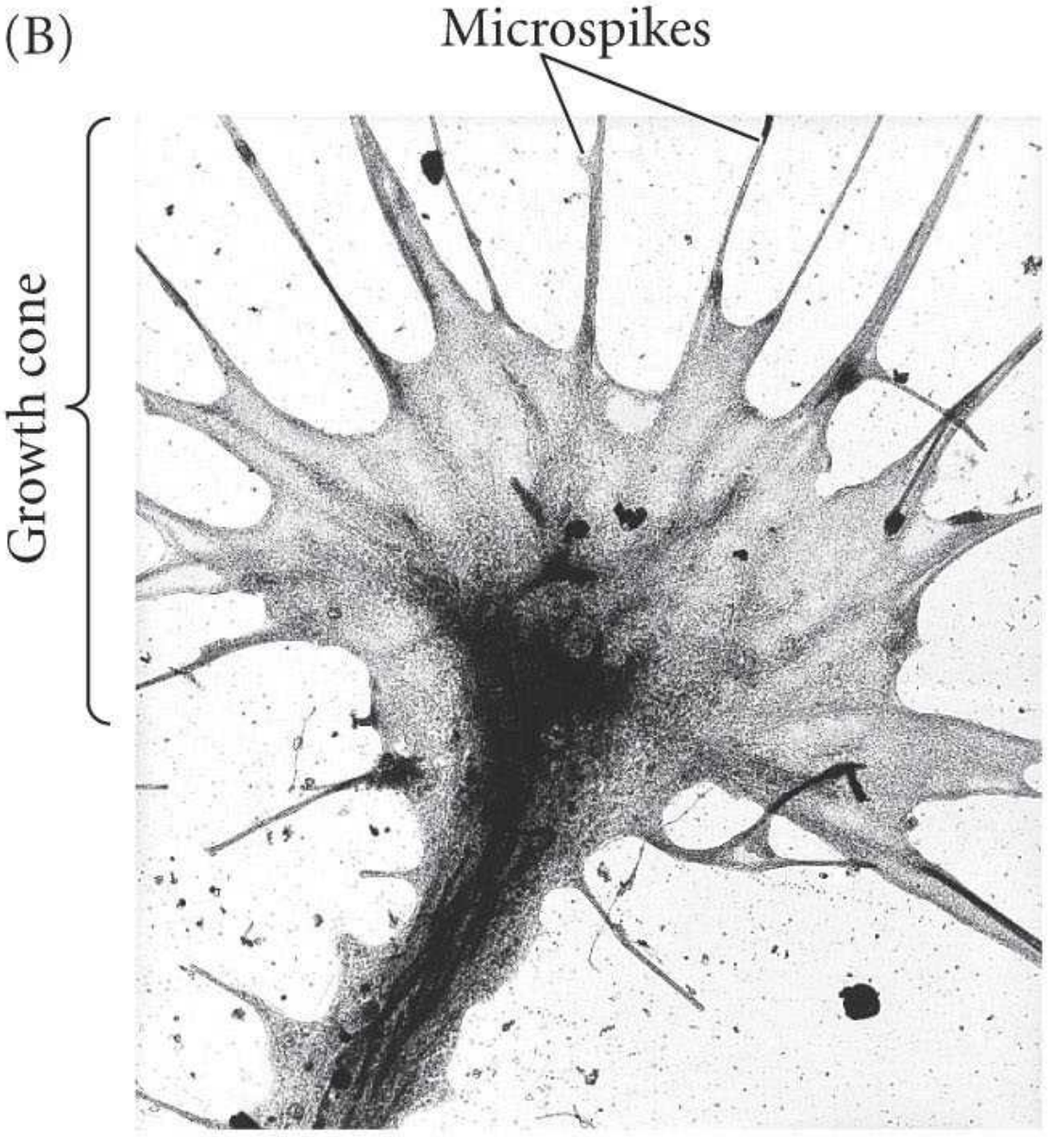
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O cone de crescimento guia o axônio até seus alvos sinápticos

(A)

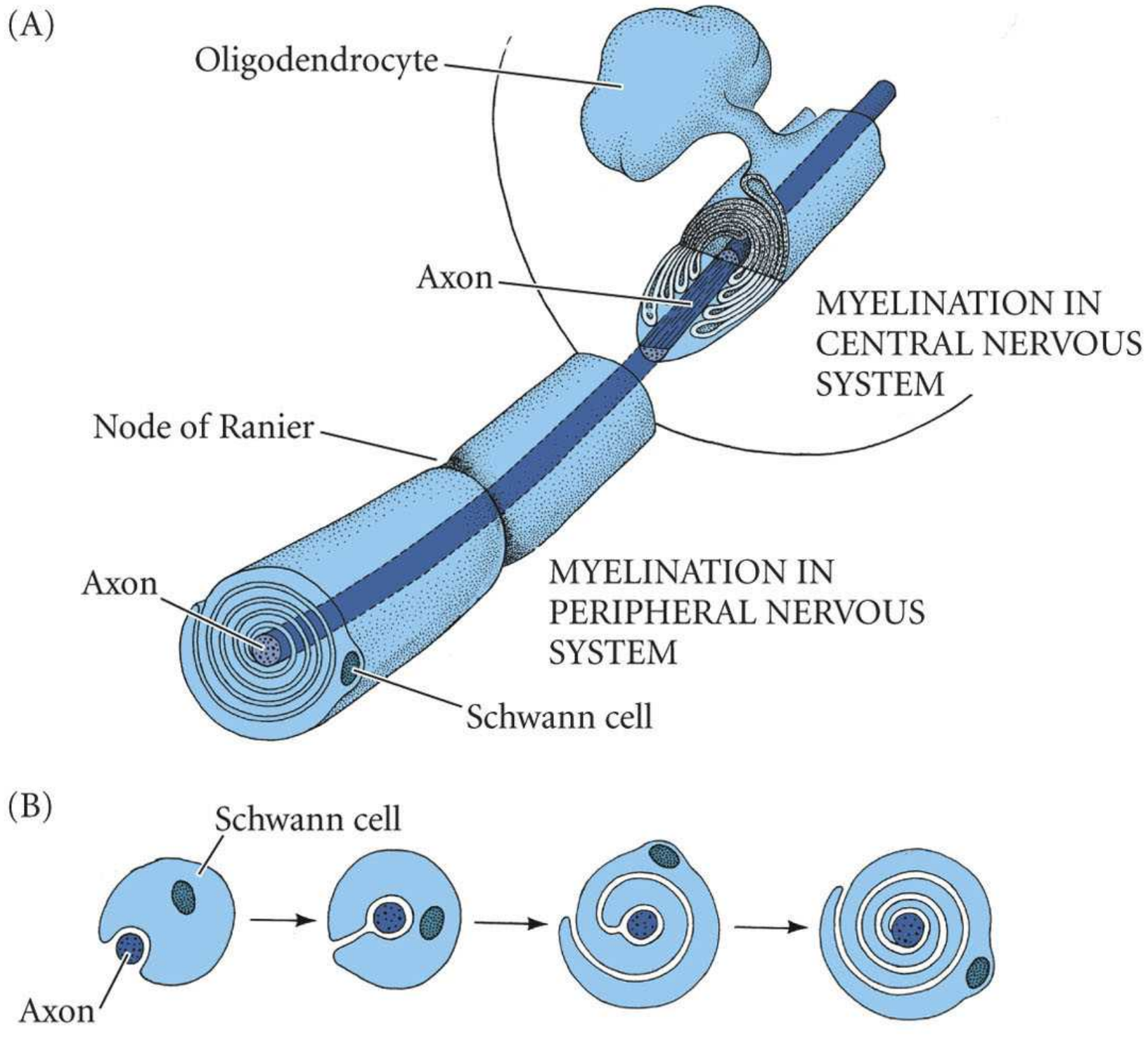


(B)



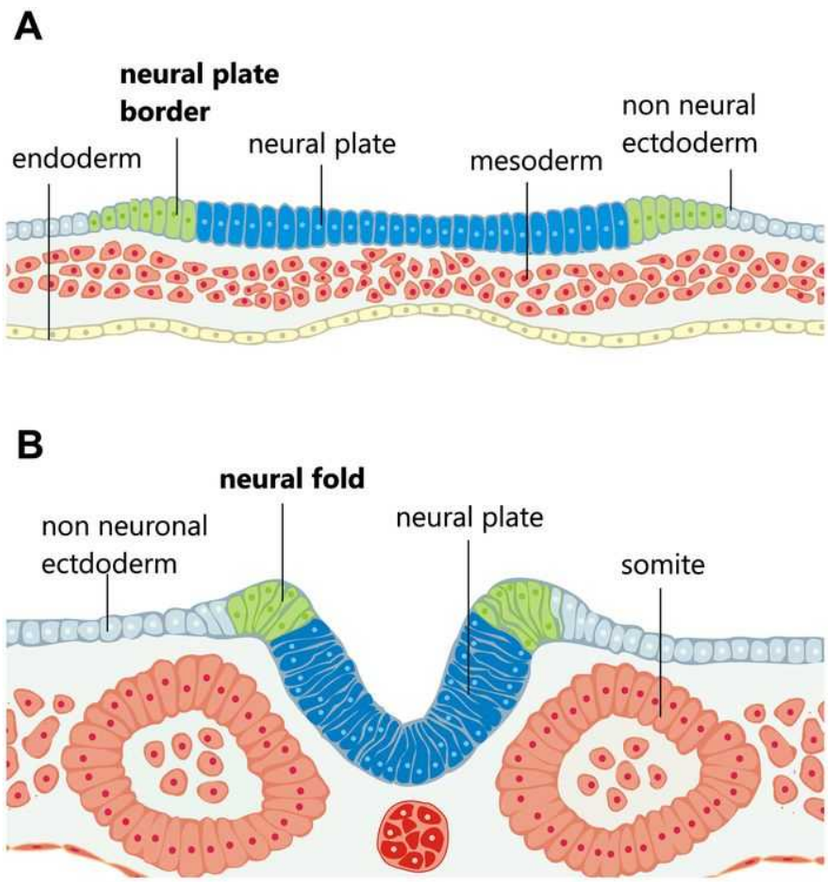
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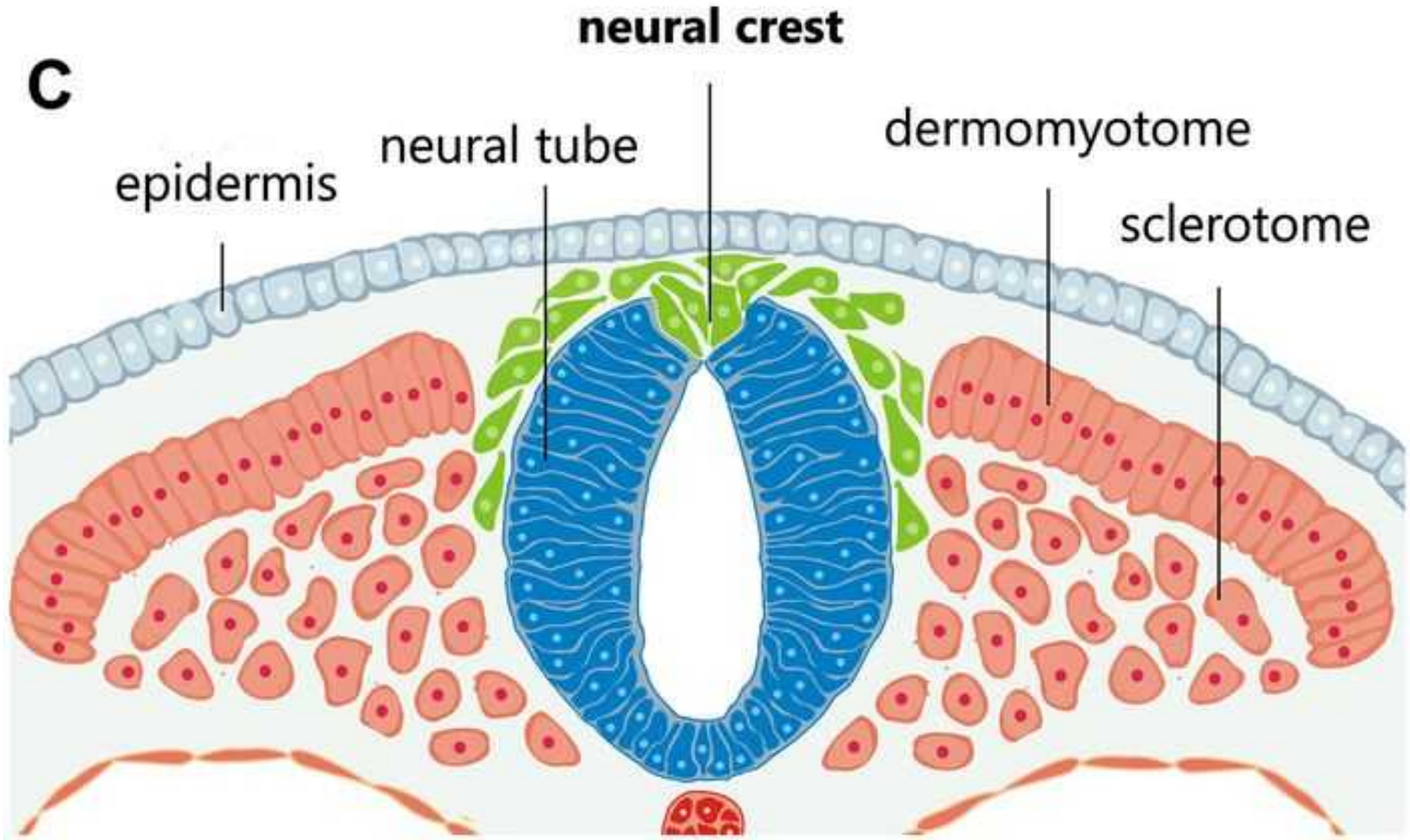
Os axônios são mielinizados por oligondendrócitos no SNC e células de Schwann no SNP



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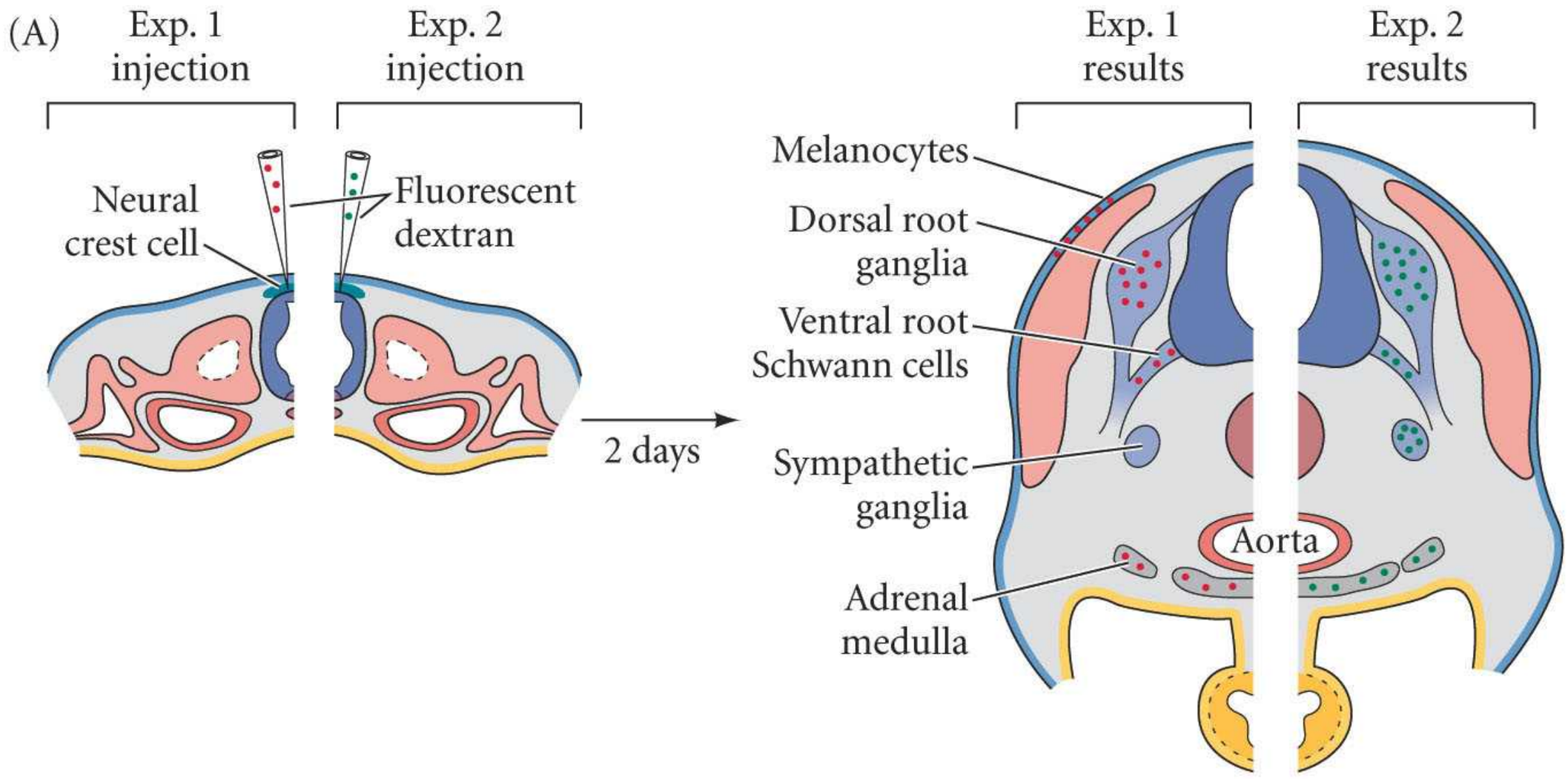
A crista neural se forma nas periferias da placa e migra a partir do tubo neural dorsal





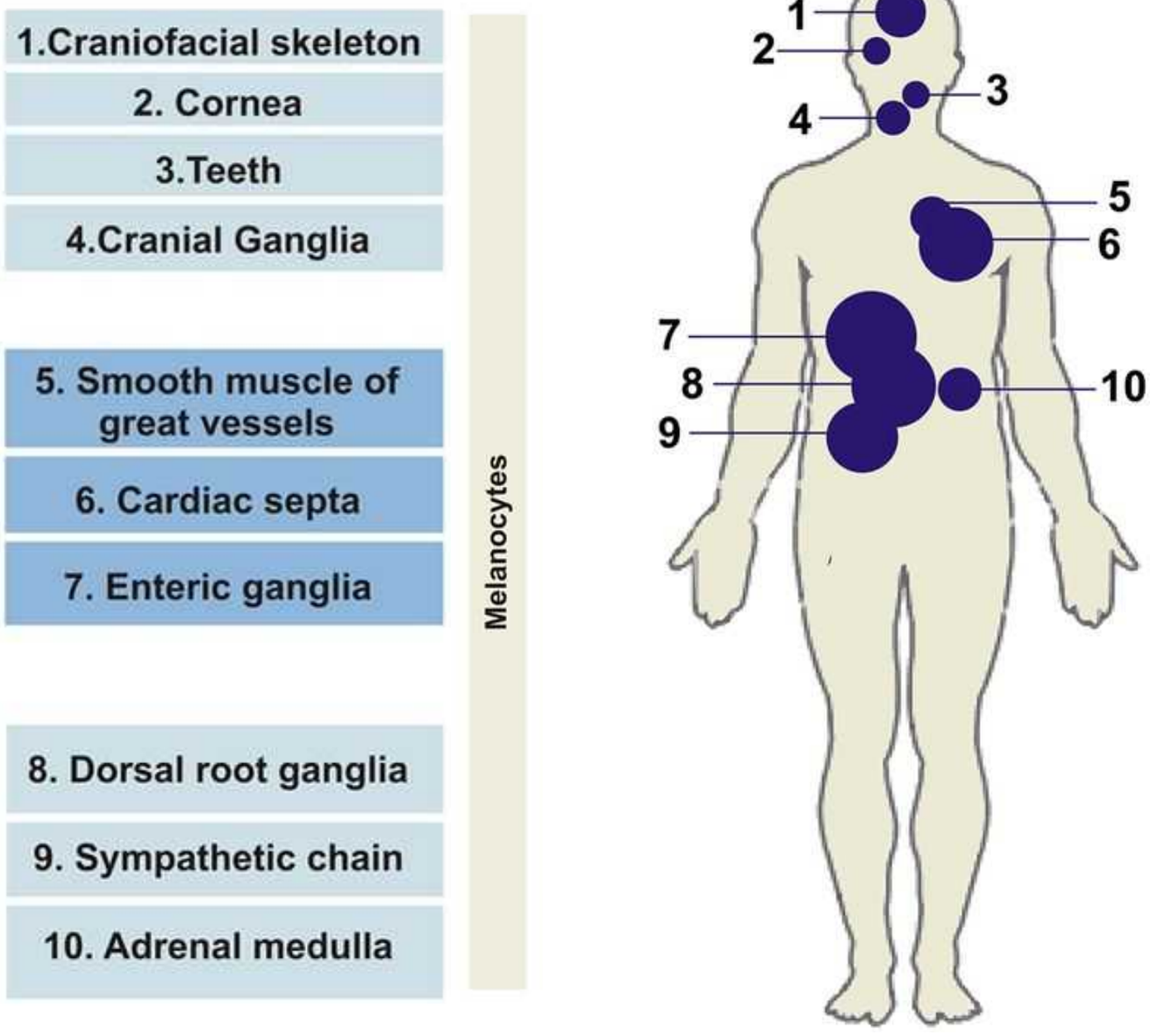
Simões-Costa e Bronner, 2013. Genome Research 23.

A crista neural é multipotente!



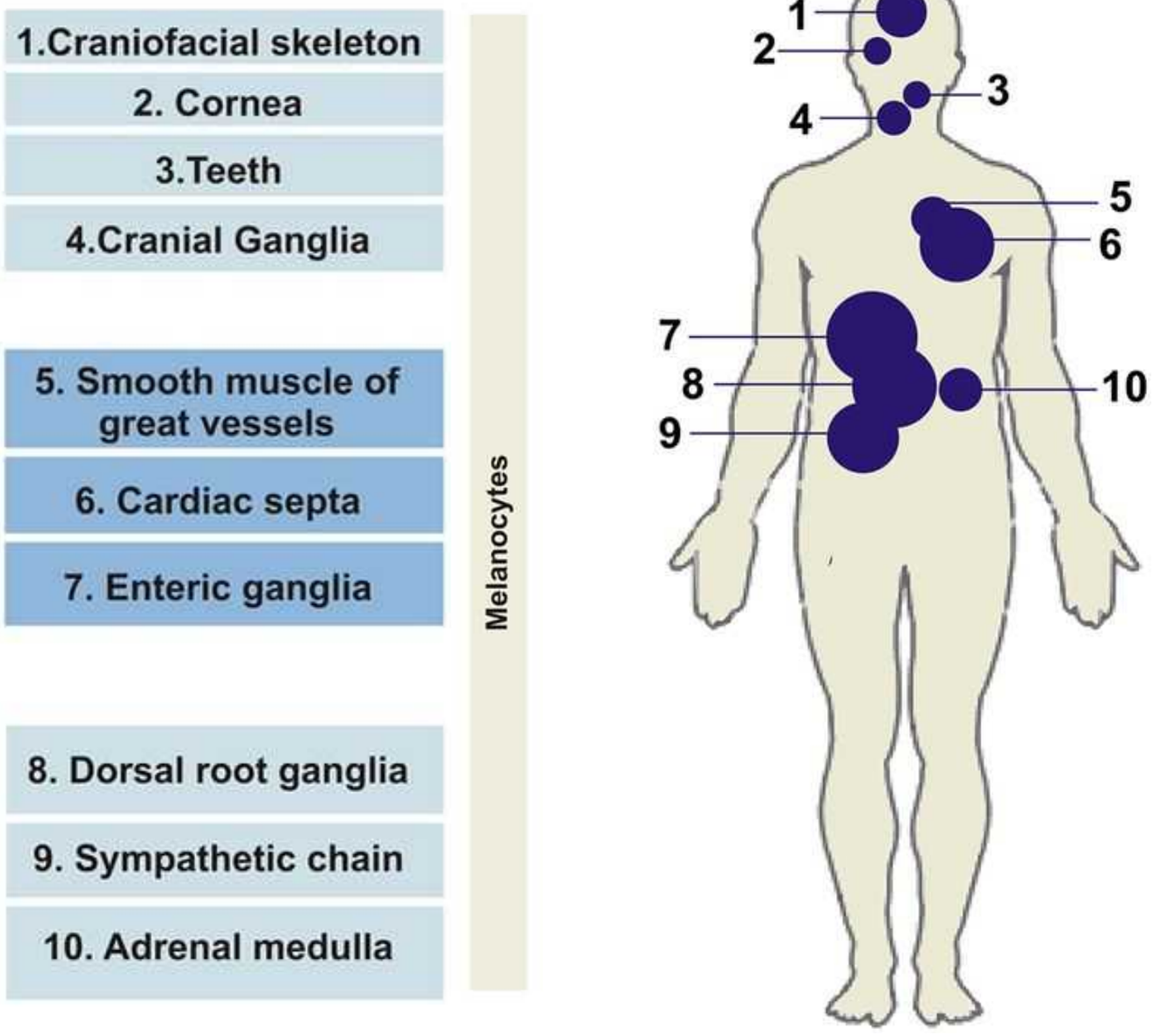
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Contribuições da crista neural ao adulto



Simões-Costa e Bronner, 2013. Genome Research 23.

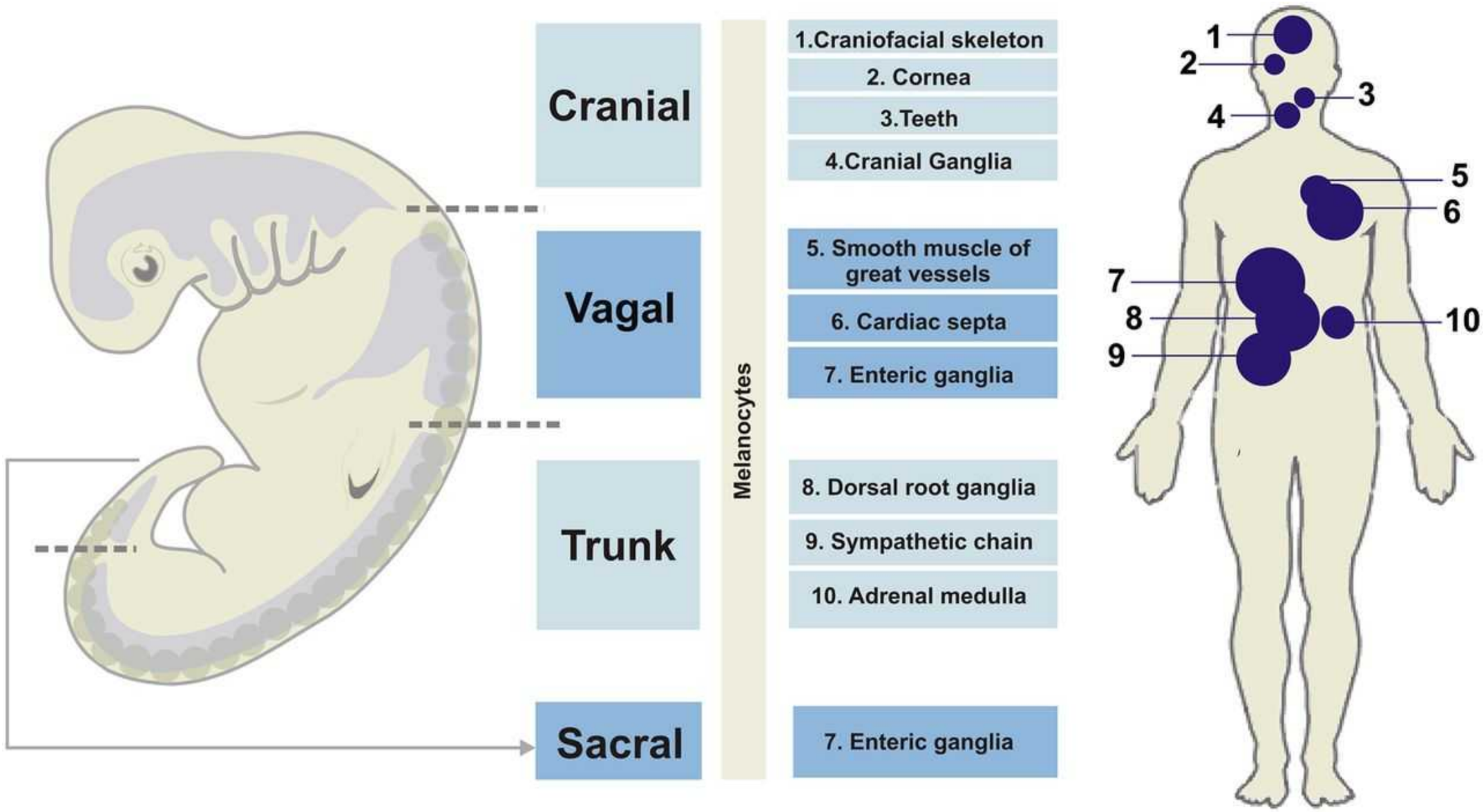
Importância de estudar a crista neural



- Sinapomorfia e contribuição extensa aos vertebrados
- Potencial único para formar estruturas de outro folheto
- Comportamento migratório semelhante ao do câncer
- **~30% das malformações congênitas** são relacionadas à crista neural.

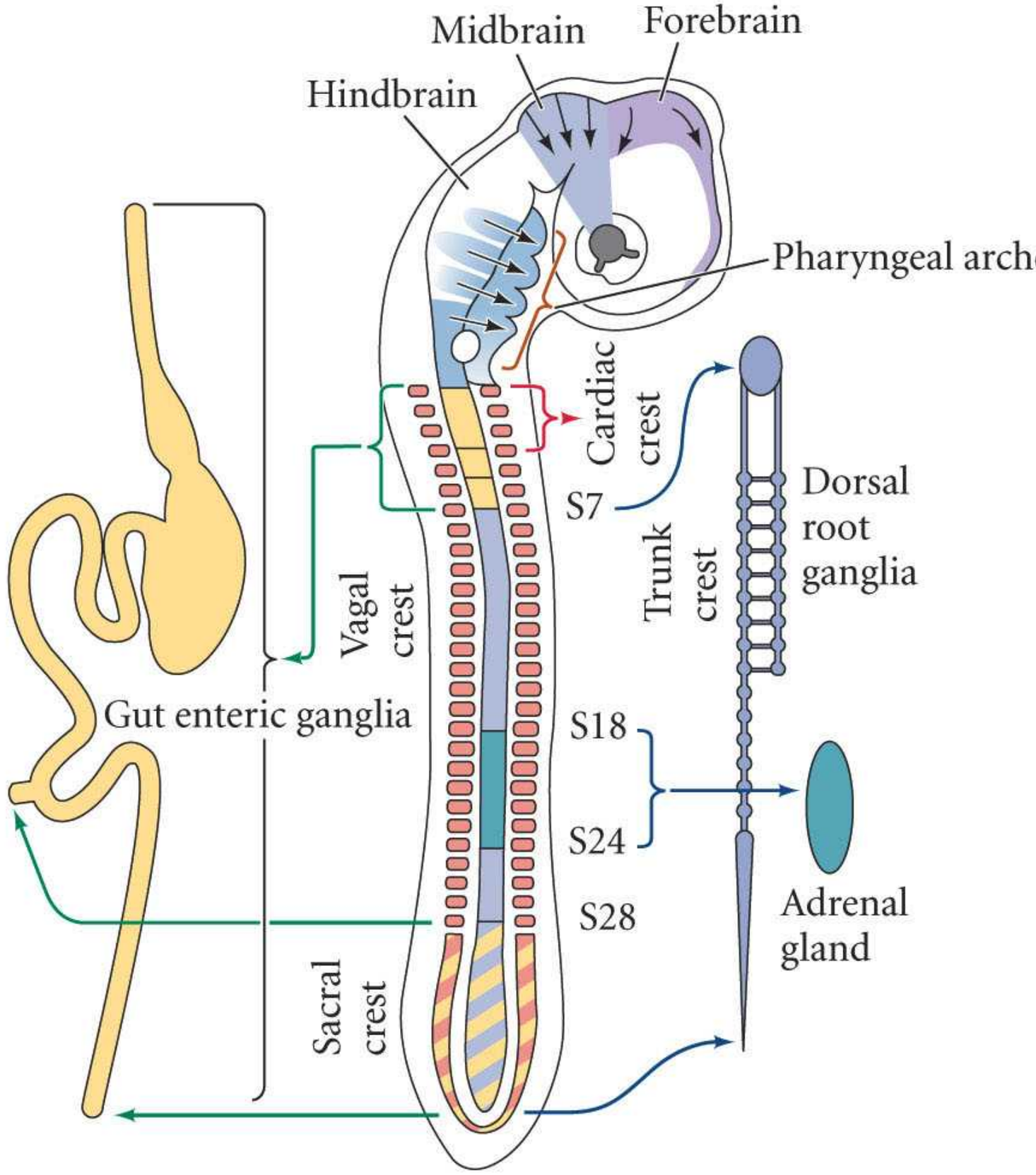
Simões-Costa e Bronner, 2013. Genome Research 23.

Populações da crista neural



Simões-Costa e Bronner, 2013. Genome Research 23.

Populações da crista neural no embrião de galinha



Transição epitélio-mesenquimal (TEM):

perda de adesividade e aquisição de motilidade

RhoB

↓

Mudanças no citoesqueleto (migração)

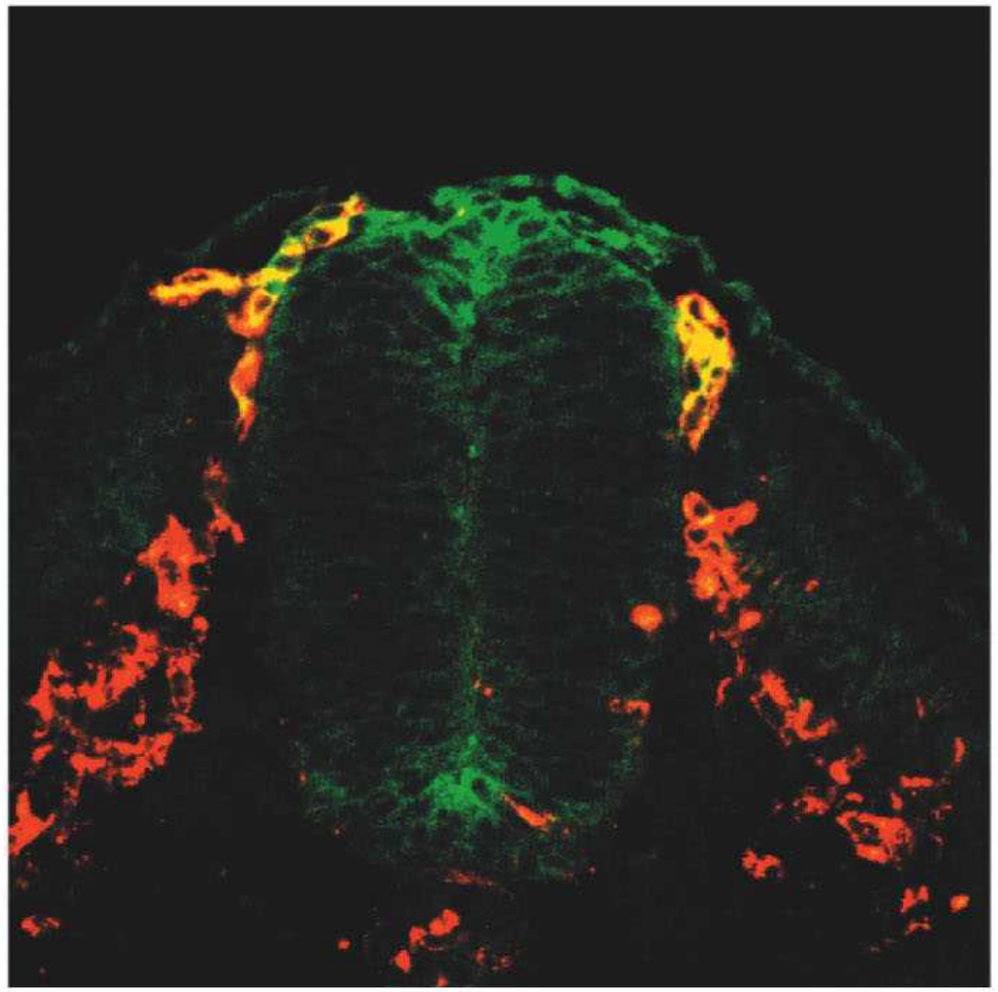
Snail

⊥

E-caderina

⊥

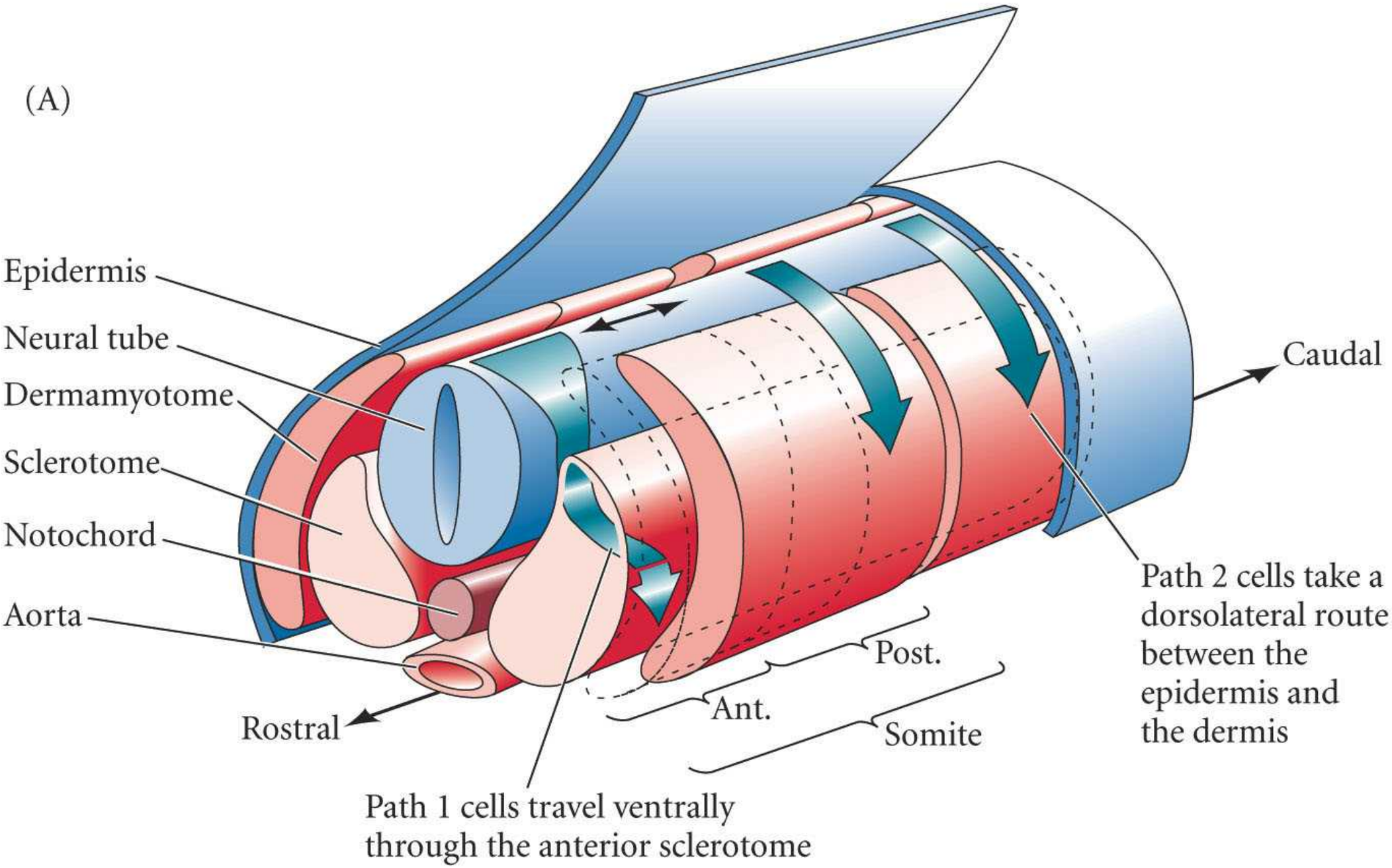
TEM



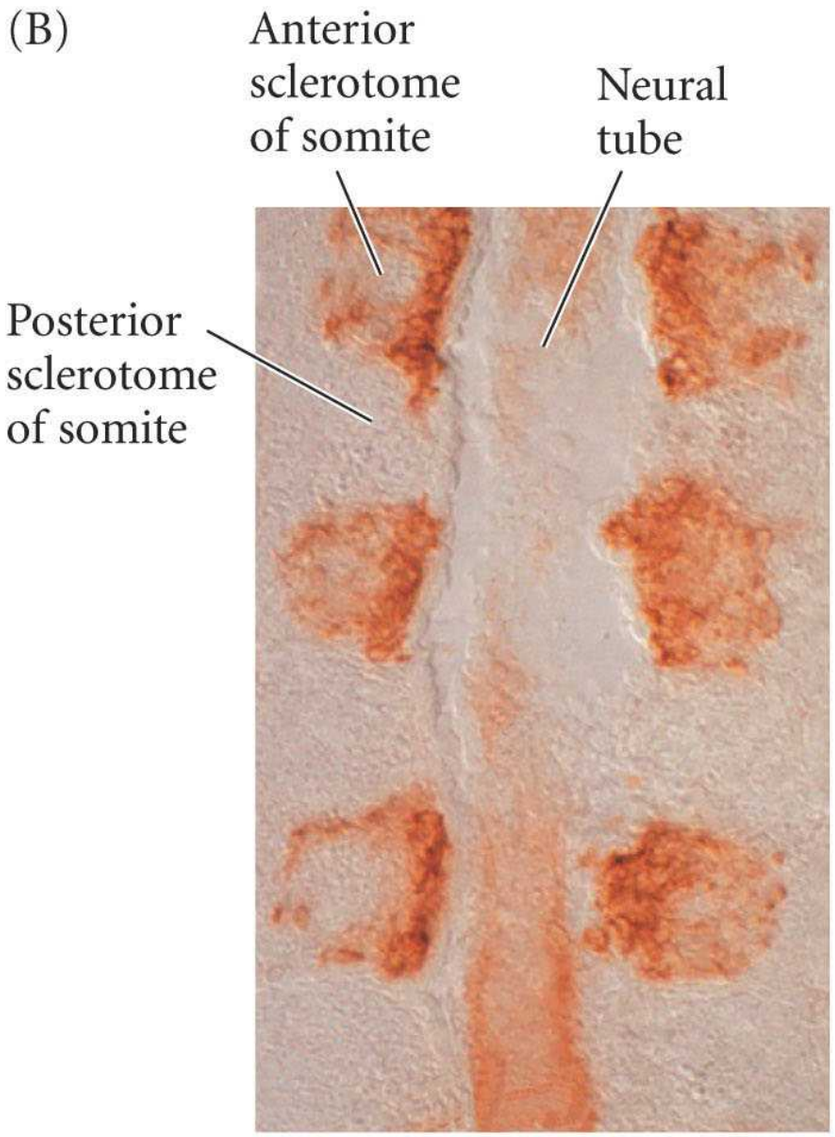
HNK-1 (crista neural migratória)

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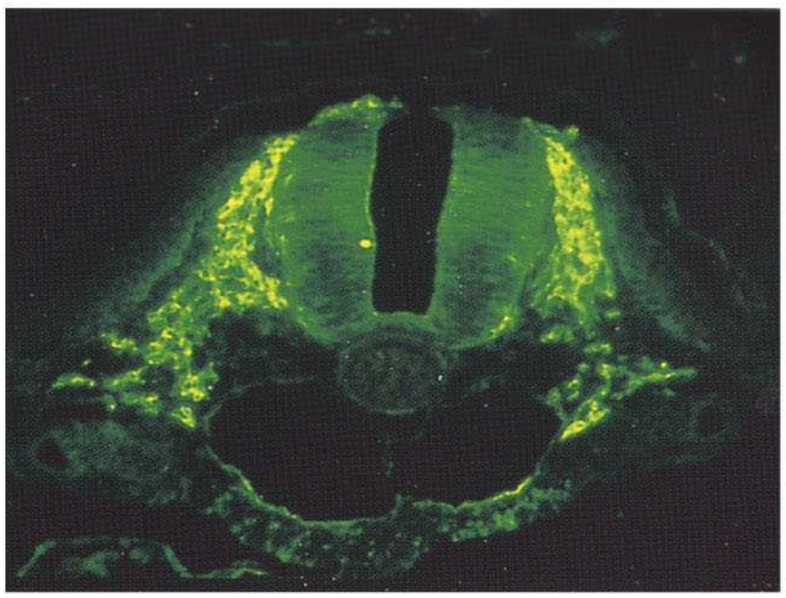
A crista neural migra por pelas vias ventral e dorsal



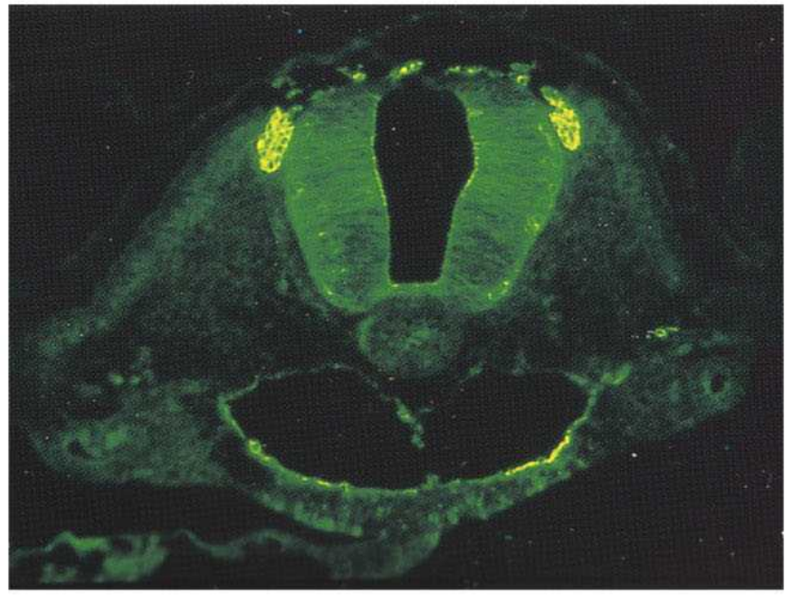
A crista neural truncal migra somente pela porção anterior do somito no embrião de galinha



Anterior

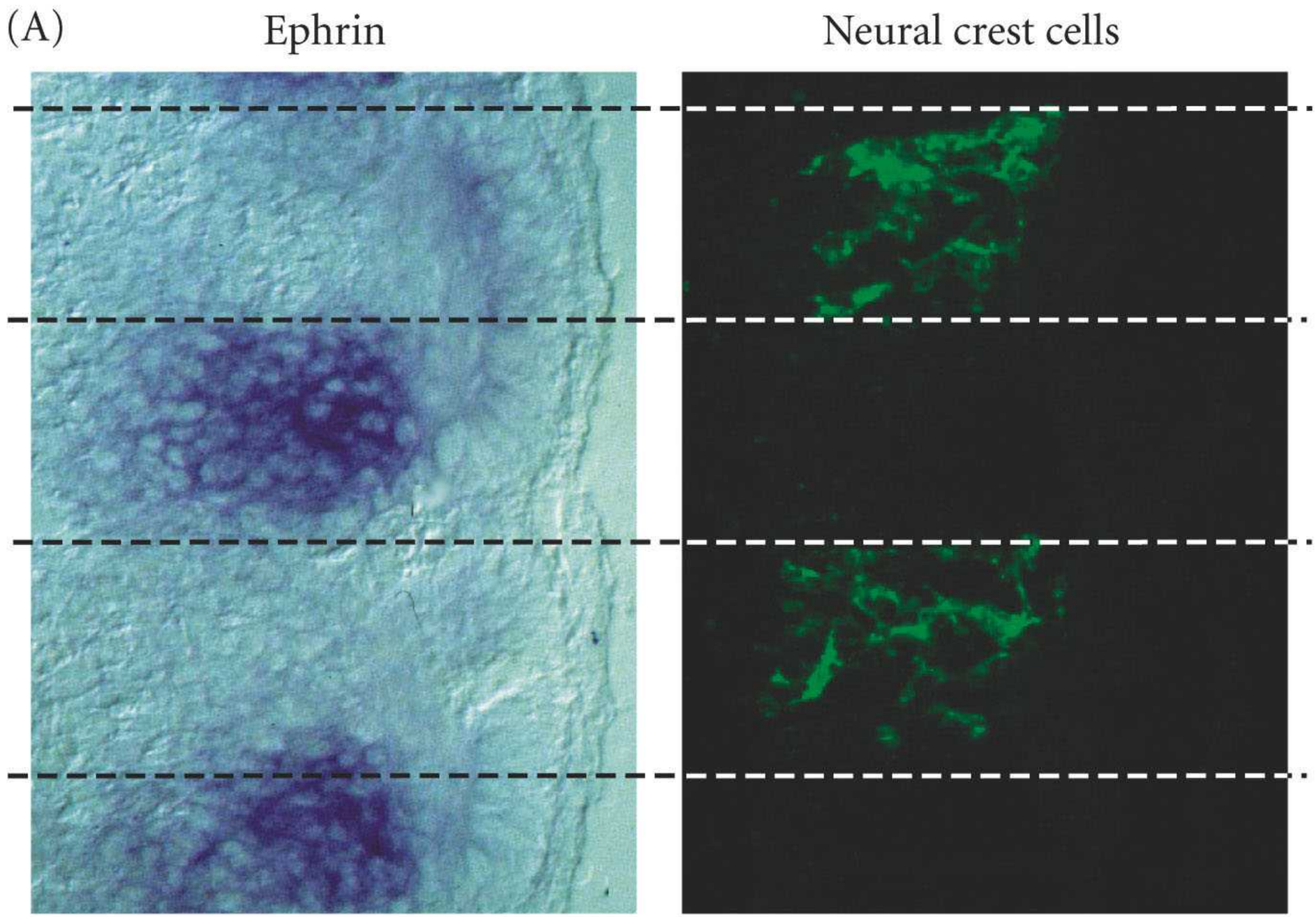


Posterior



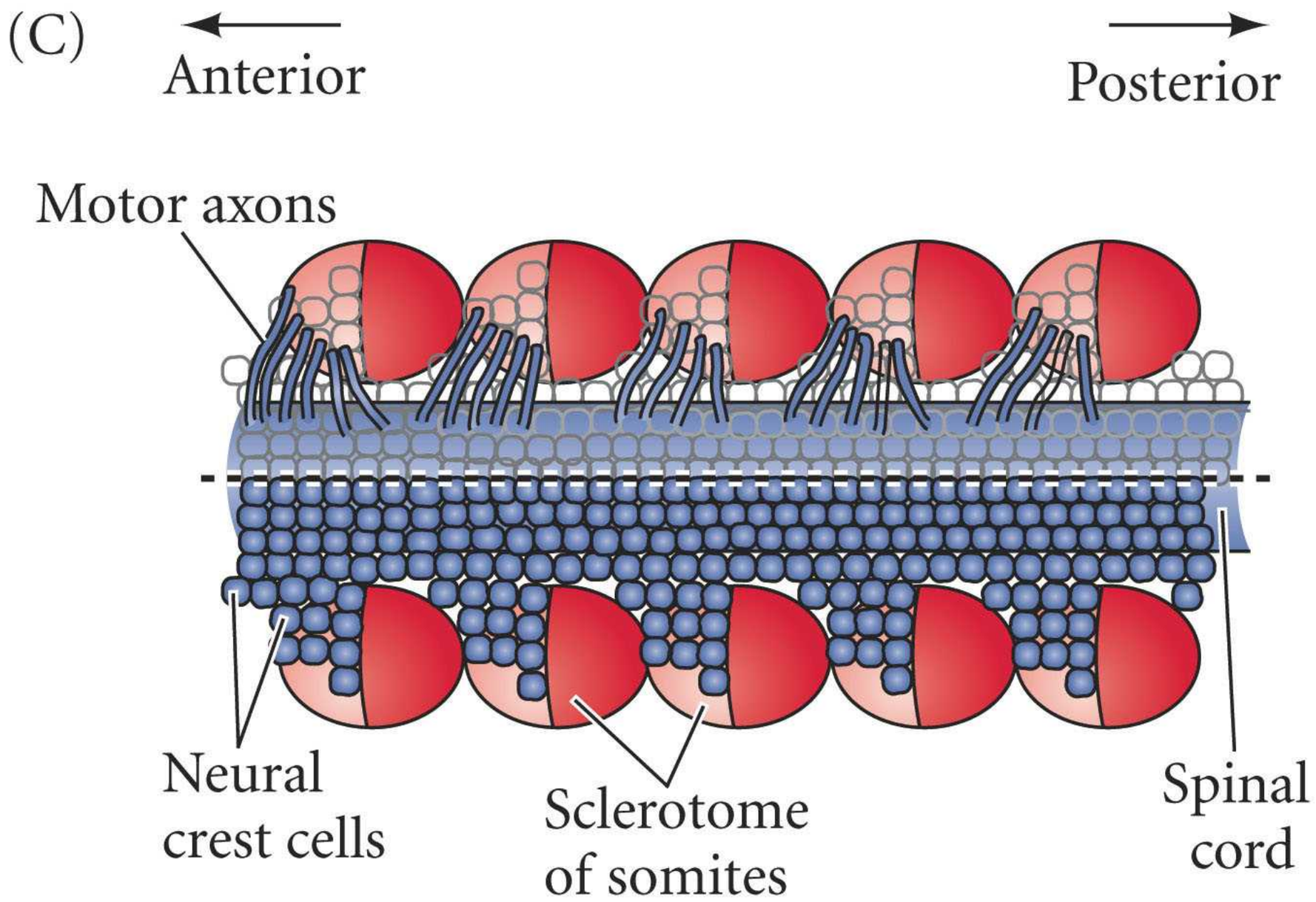
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Ephrinas repelem a crista neural de migrar pela metade posterior dos somitos



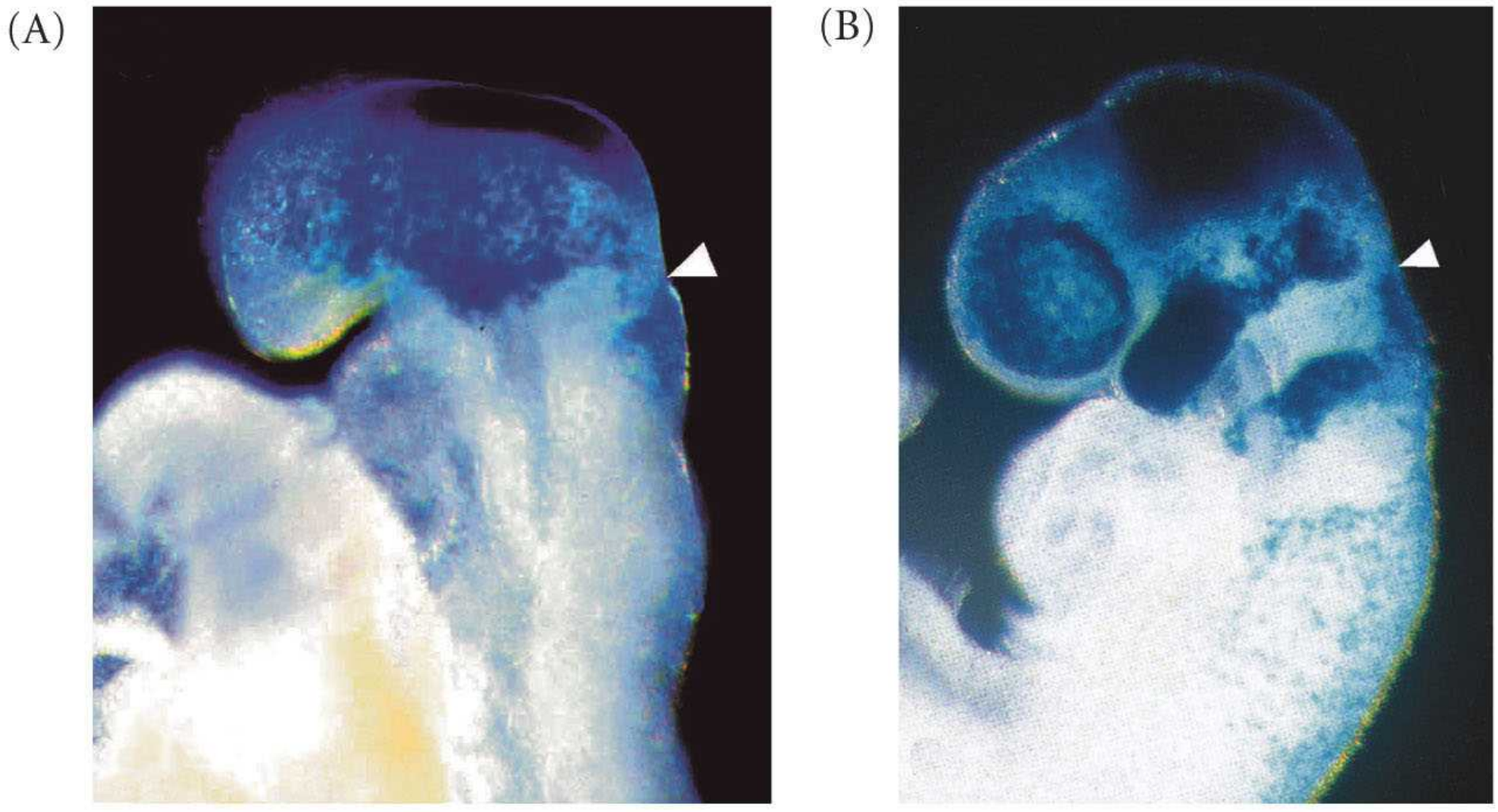
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A crista neural forma os gânglios da raiz dorsal ao lado do tubo neural no mesmo padrão segmentado dos somitos



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Fate-mapping da crista neural cranial no embrião de camundongo



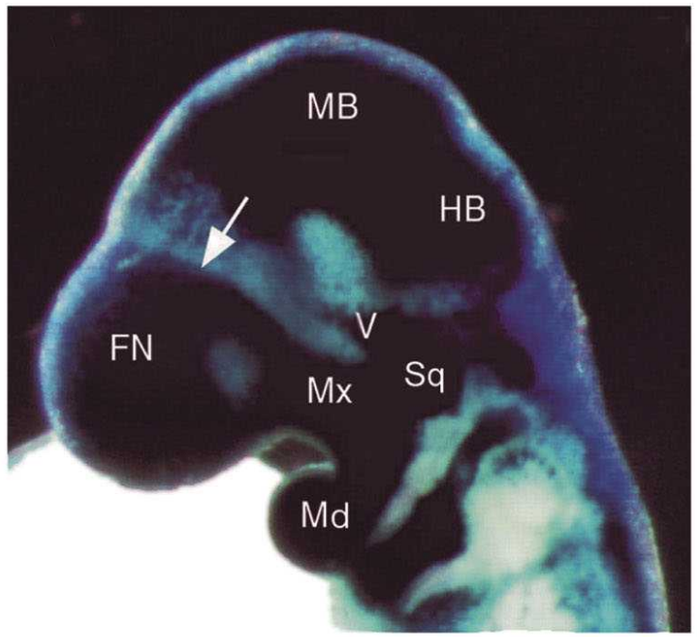
beta-galactosidase específica na crista neural

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Fate-mapping da crista neural cranial no embrião de camundongo

beta-galactosidase específica na crista neural

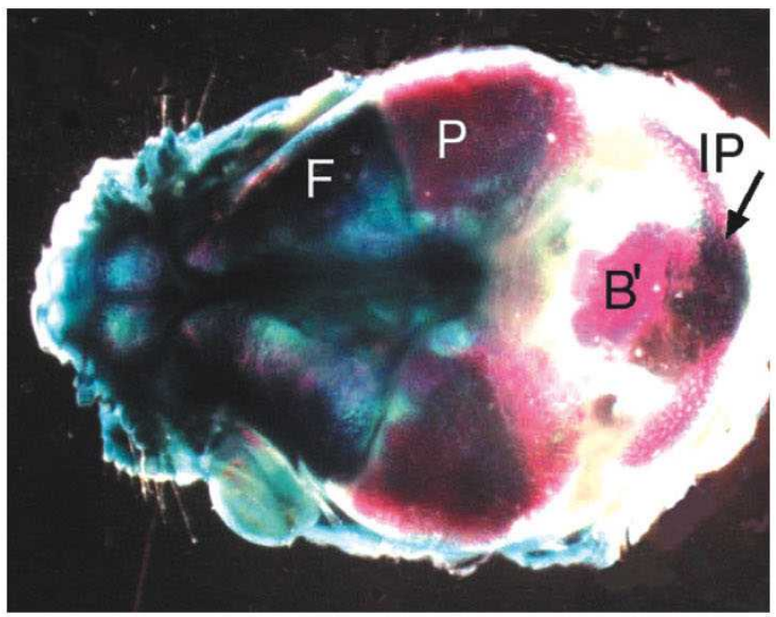
(C)



FN, frontal nasal process
MB, midbrain
HB, hindbrain
Mx, maxilla
Md, mandible
Sq, squamosal bone
F, frontal bone
P, parietal
B, mineralized bone
IP, interparietal bone
V, trigeminal ganglion

A crista neural cranial forma os ossos da face

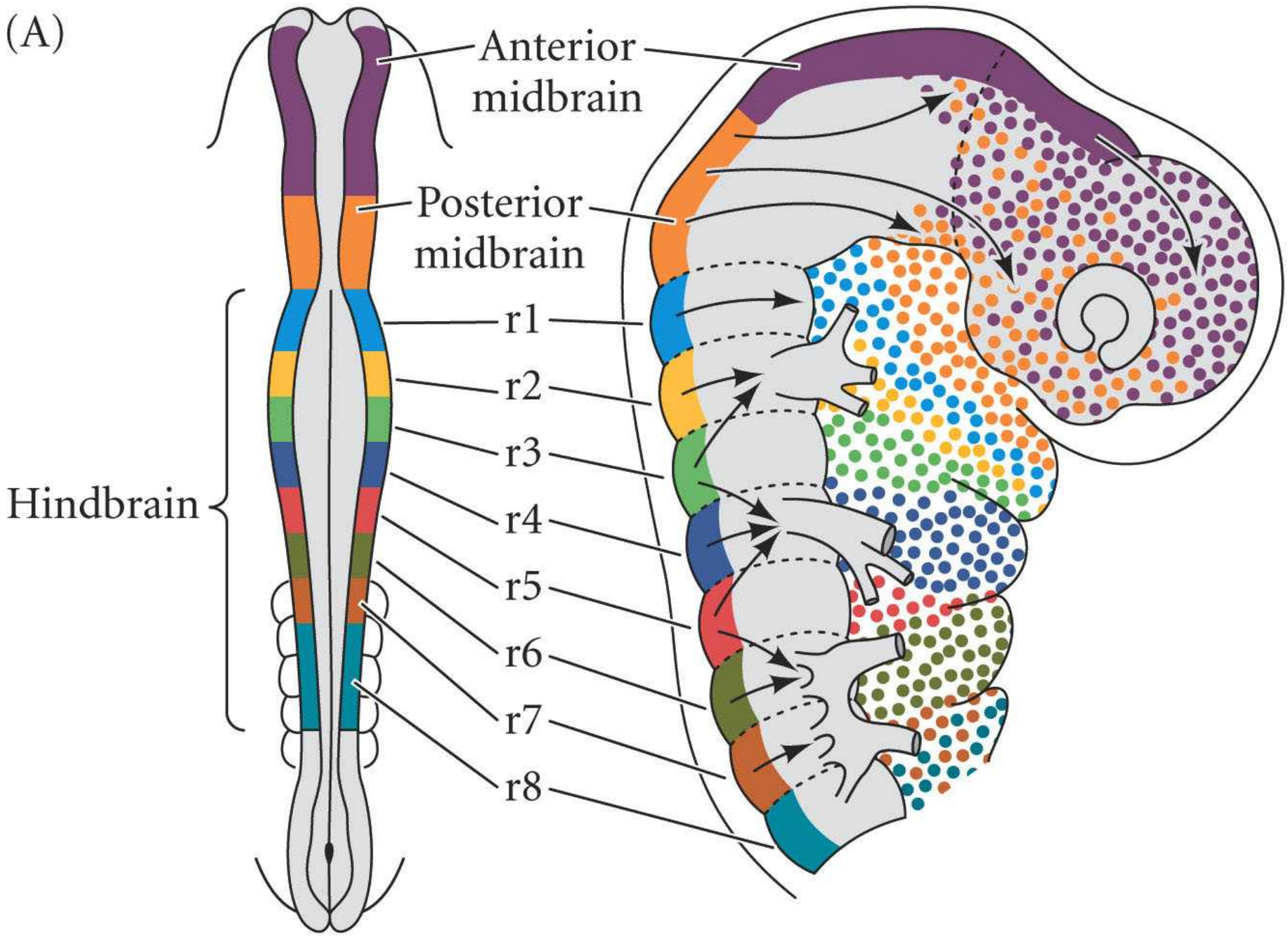
(D)



FN, frontal nasal process
B, midbrain
HB, hindbrain
Mx, maxilla
Md, mandible
Sq, squamosal bone
F, frontal bone
P, parietal
B, mineralized bone
IP, interparietal bone
V, trigeminal ganglion

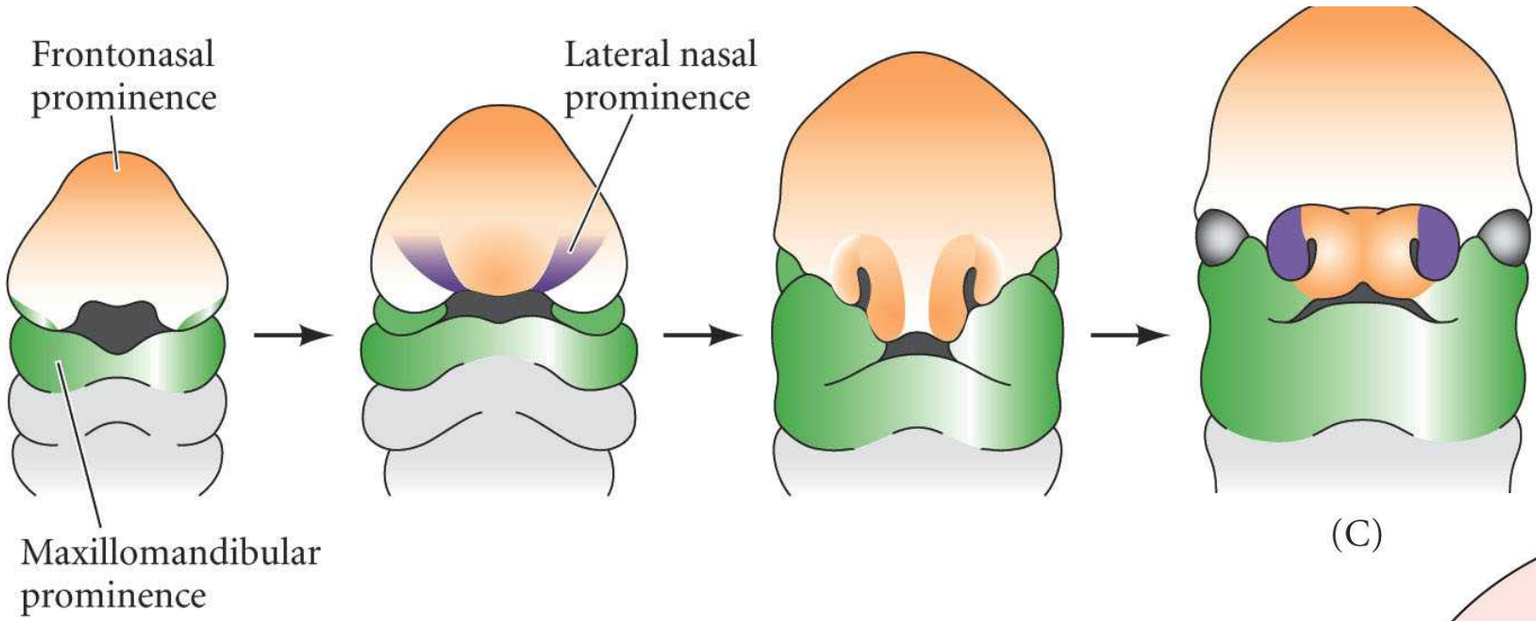
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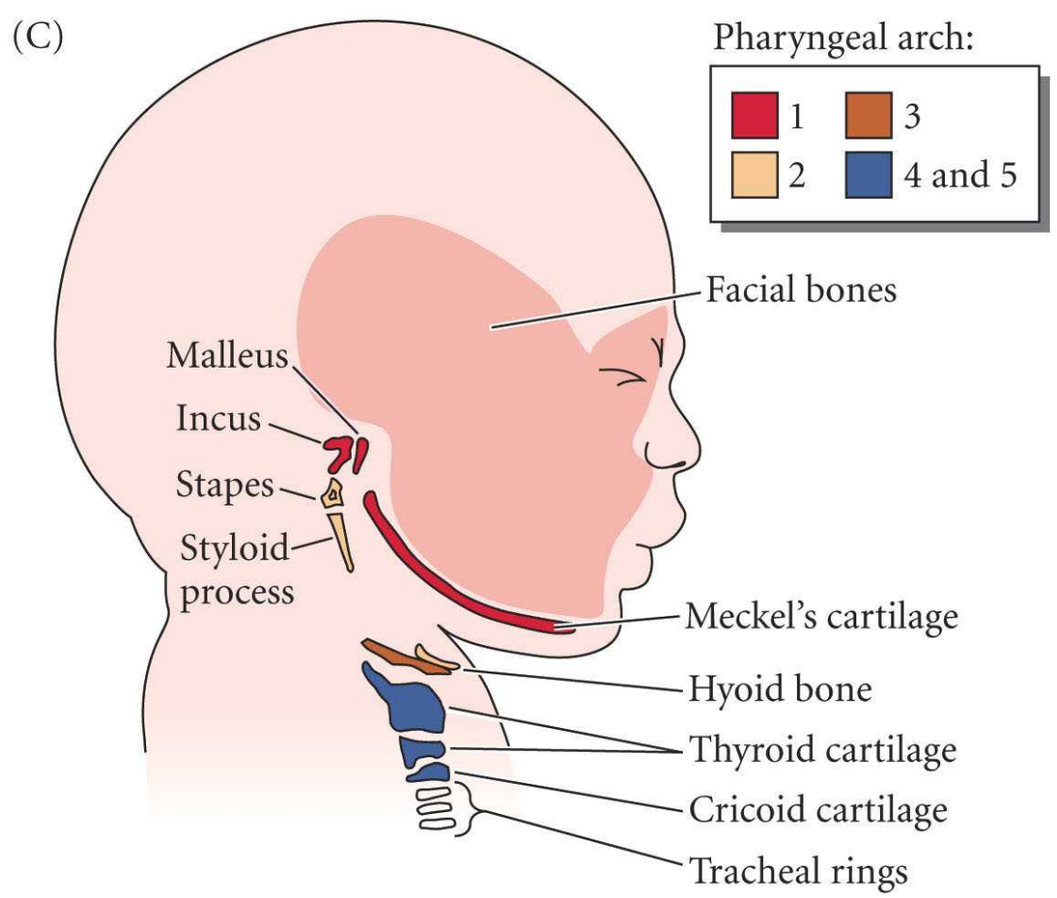
A crista neural cranial não migra pelos rombômeros 3 e 5



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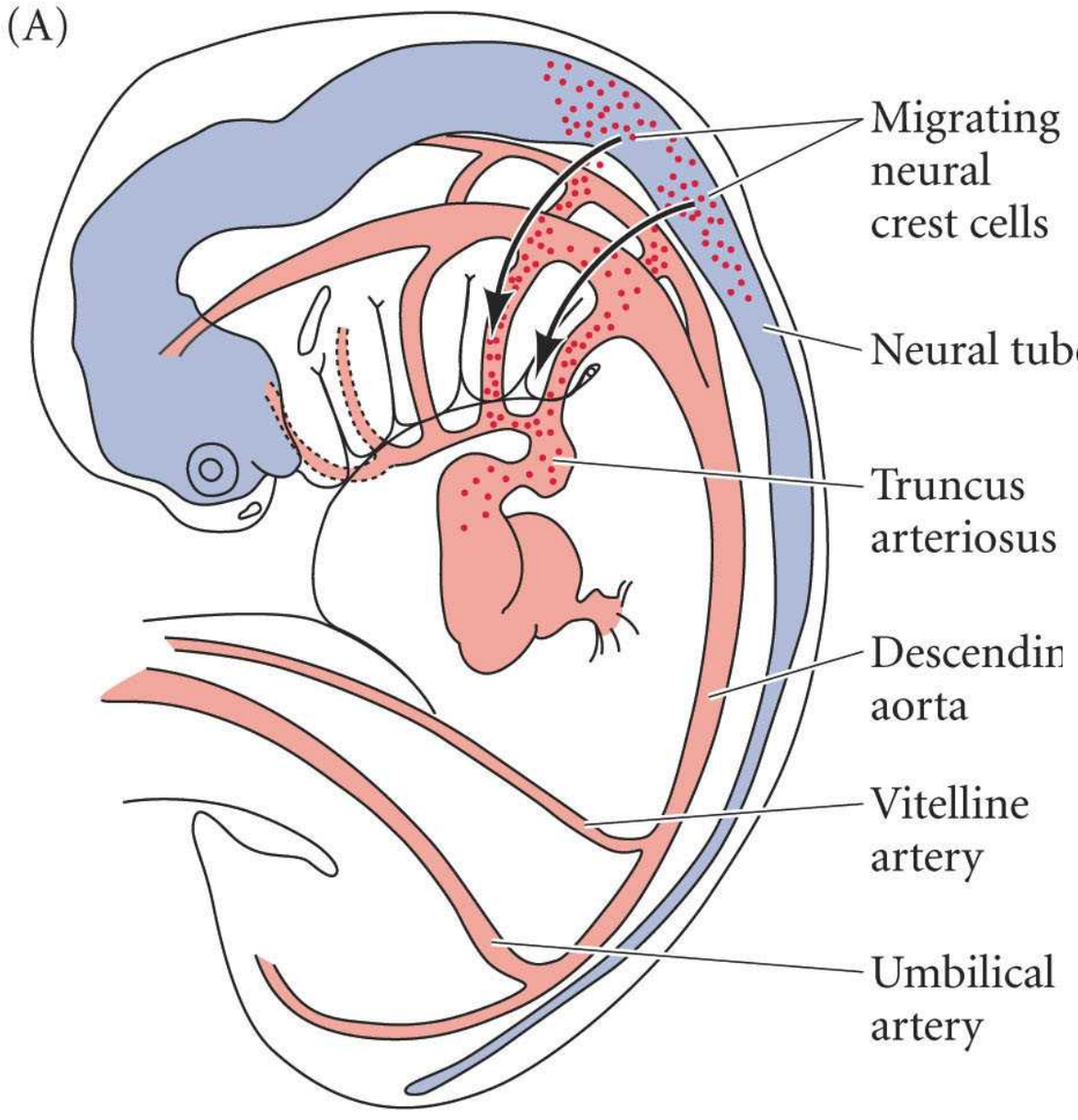
Ectomesênquima: os ossos e cartilagens derivados da crista neural cranial



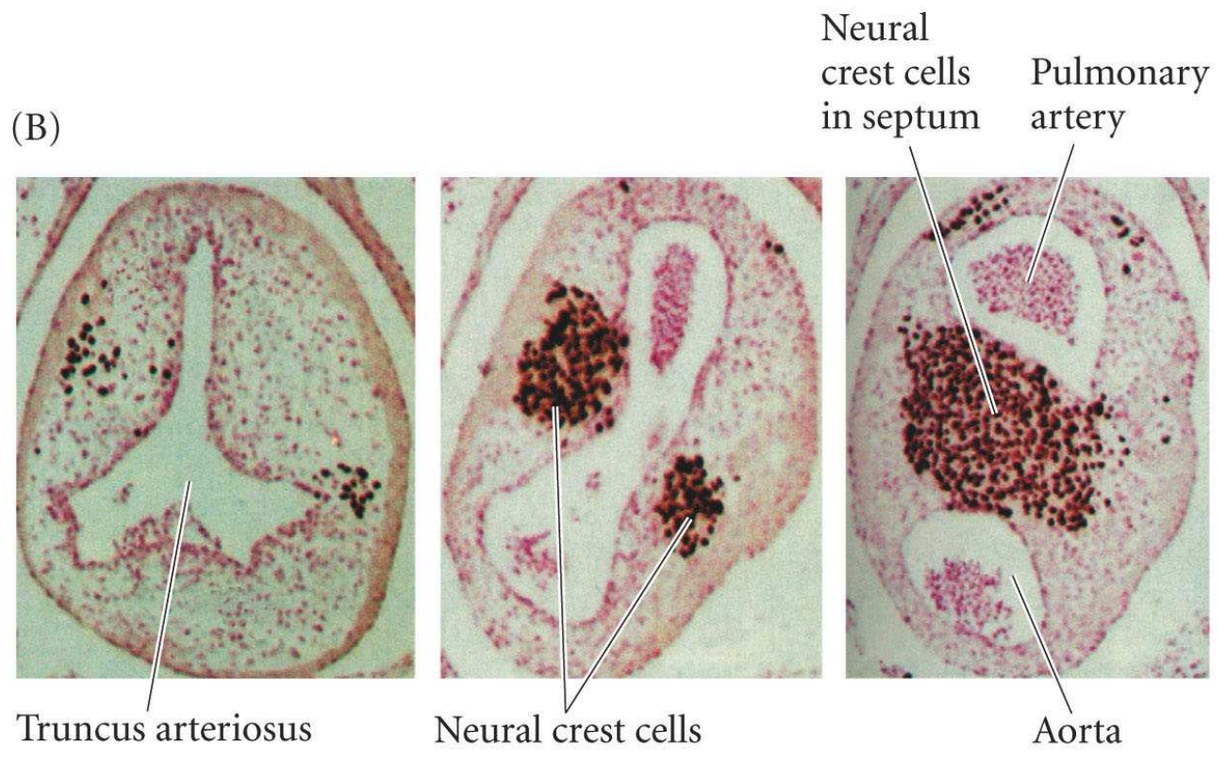


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A crista neural cardíaca

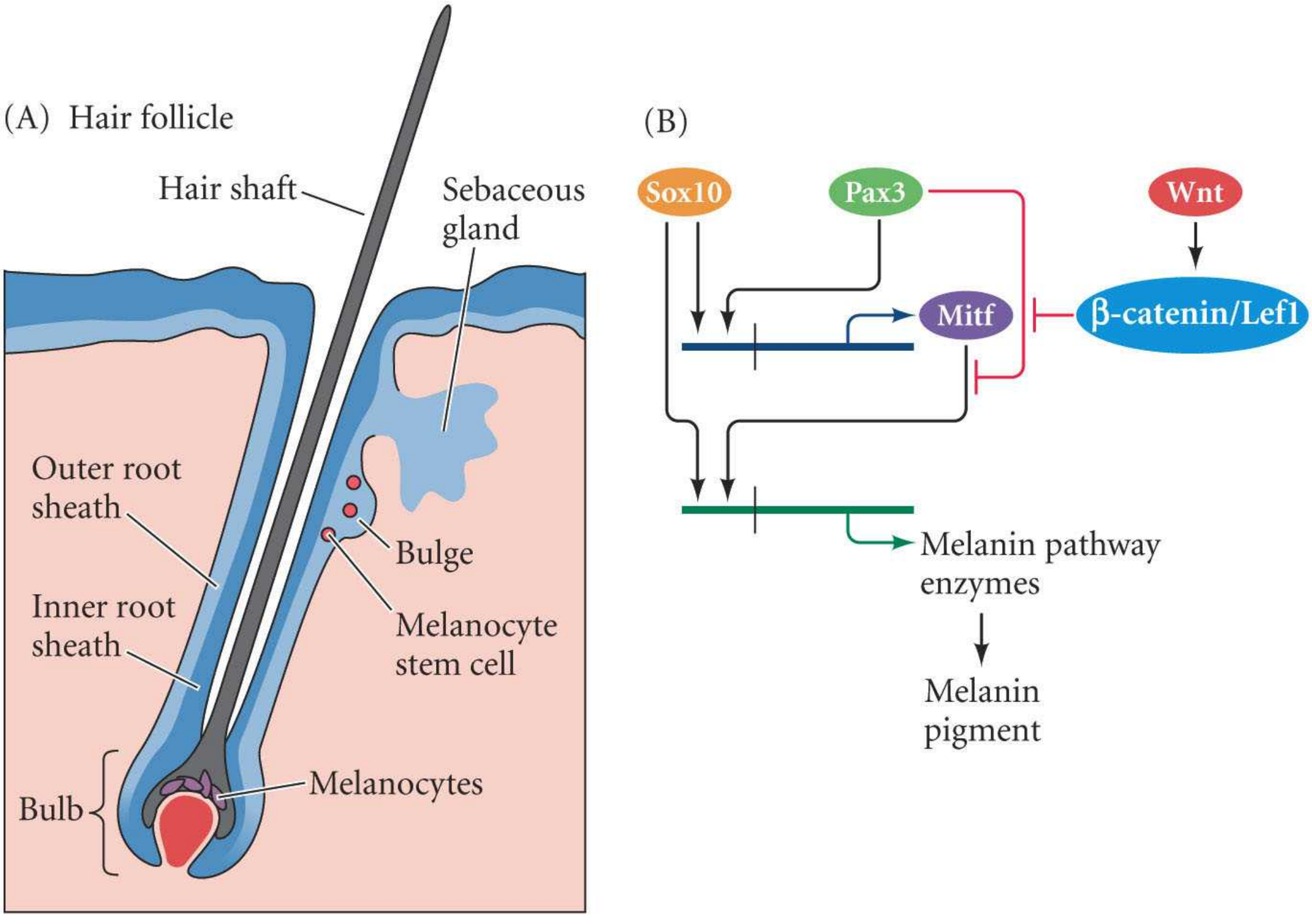


Septo aorta-artéria pulmonar



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Redes gênicas regulatórias:
diferenciação da crista neural em melanócitos



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