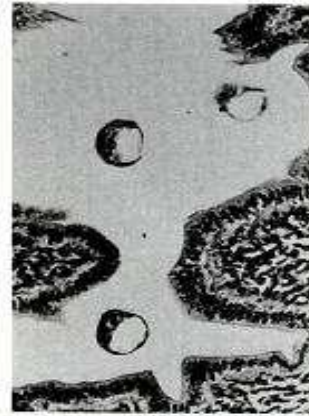
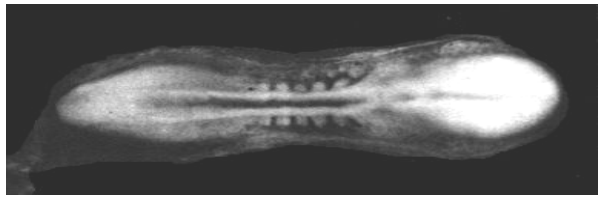
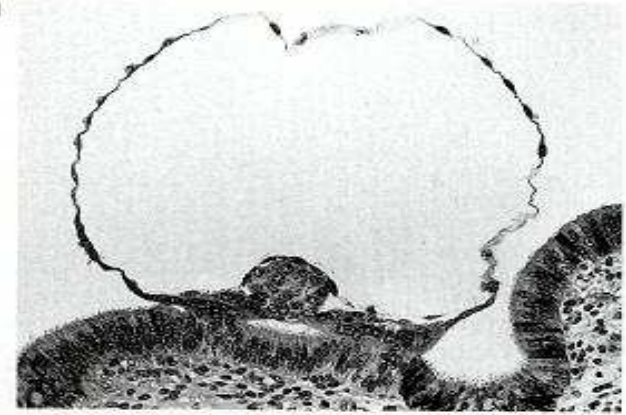


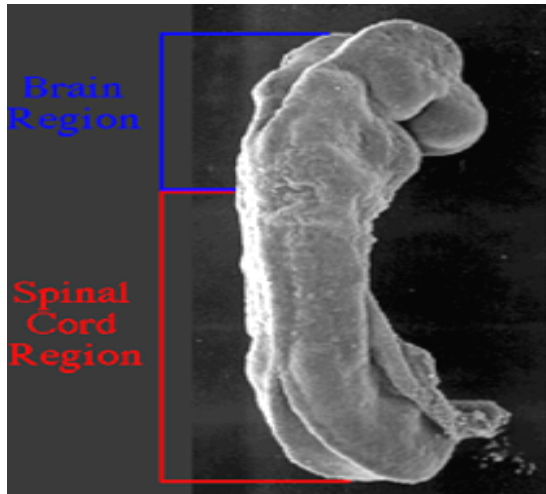
4,5 napos egér



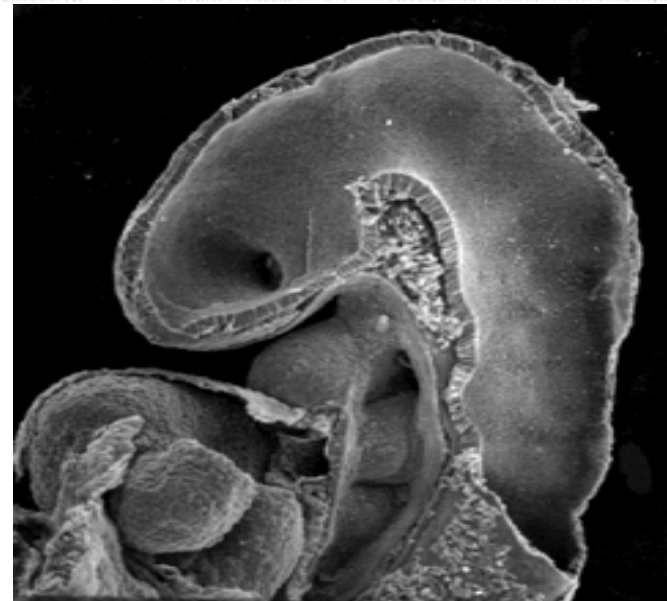
(B)



6 napos human

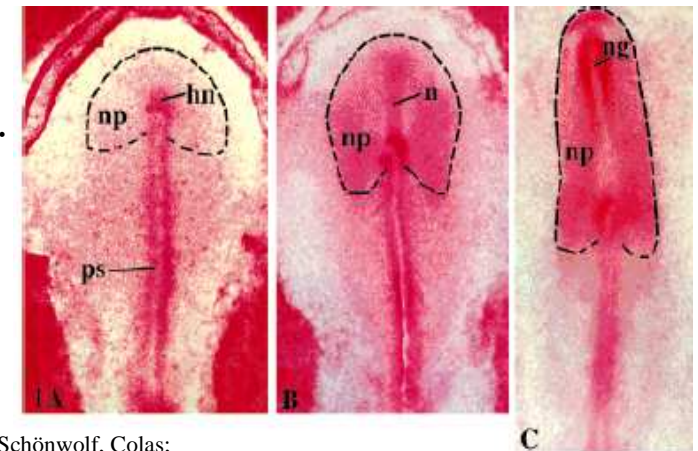
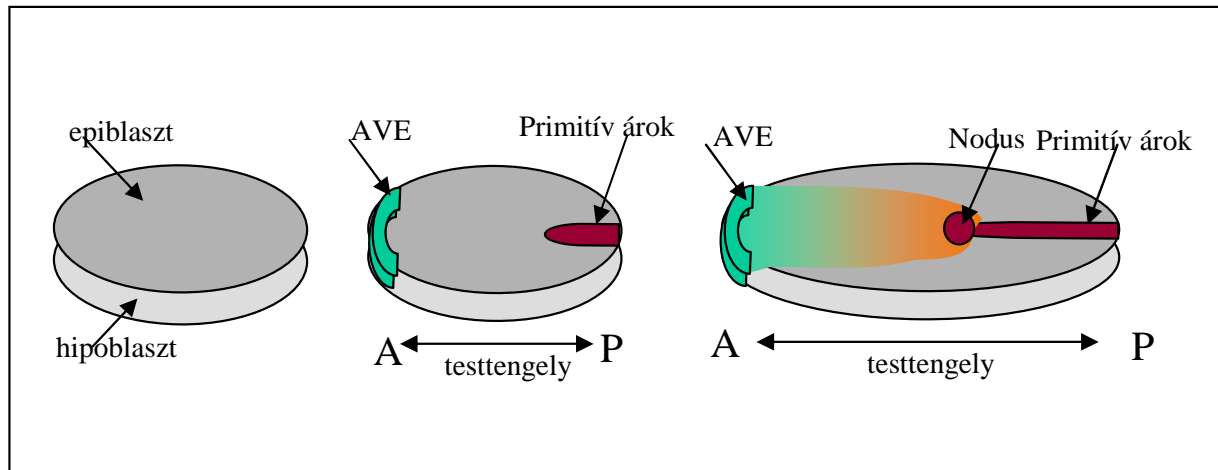


8 napos human



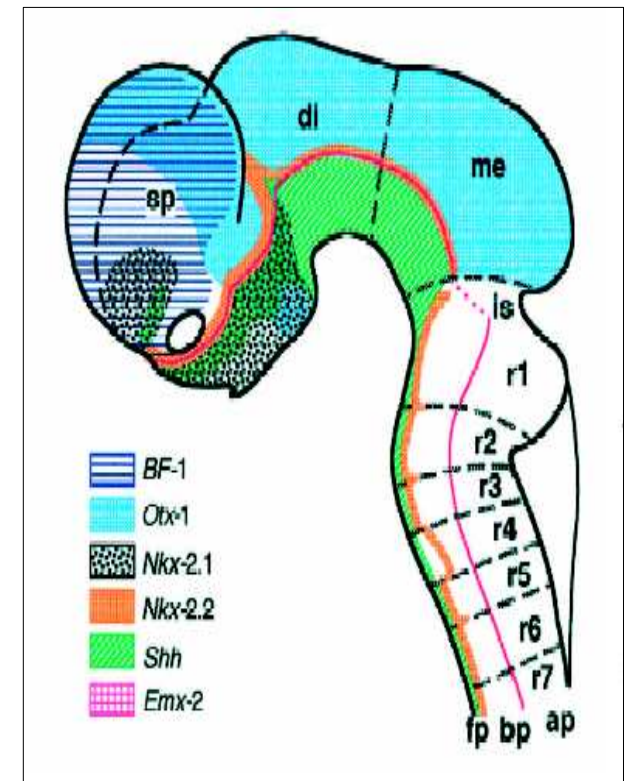
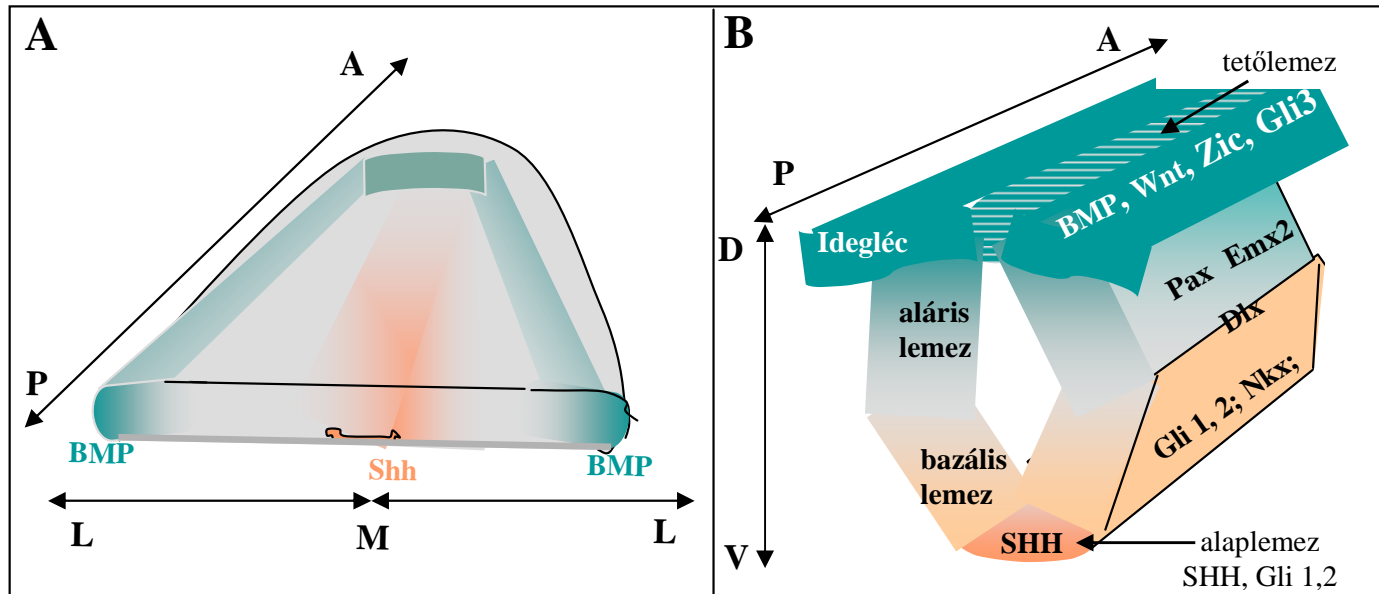
10 napos human

Az Anterio-Posterioralis testtengely „meghatározódik” a primitívárok és az antero-visceralis entoderma (AVE) kialakulásával.



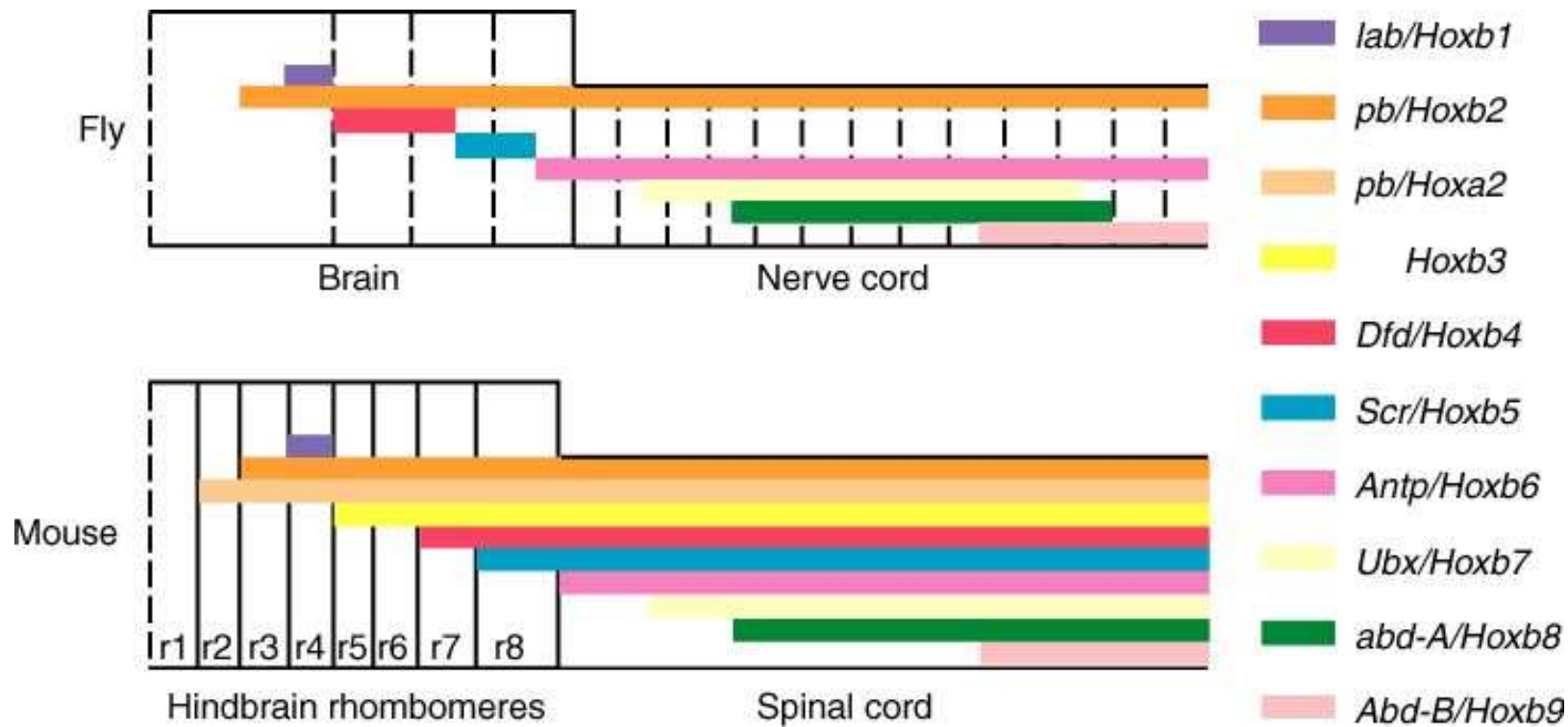
Schönwolf, Colas;
DEVELOPMENTAL DYNAMICS 221:117-145 (2001)

Dorso-ventralis tengely: Shh / Wnt



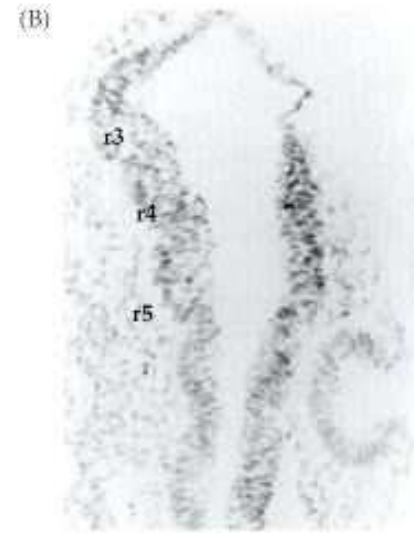
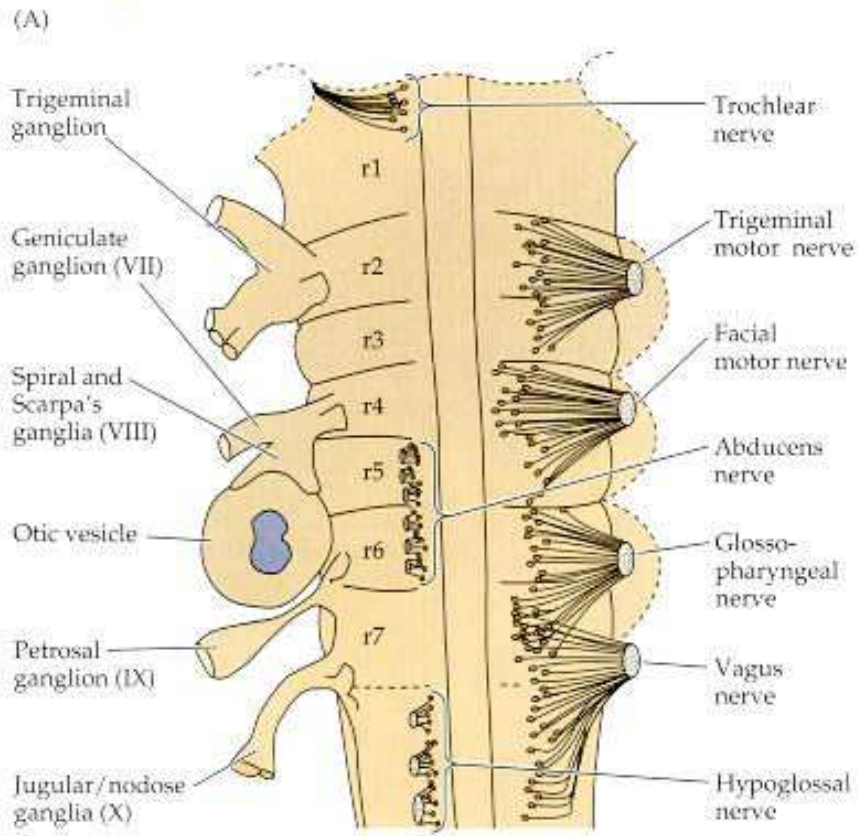
Shimamura, Rubenstein; 1995

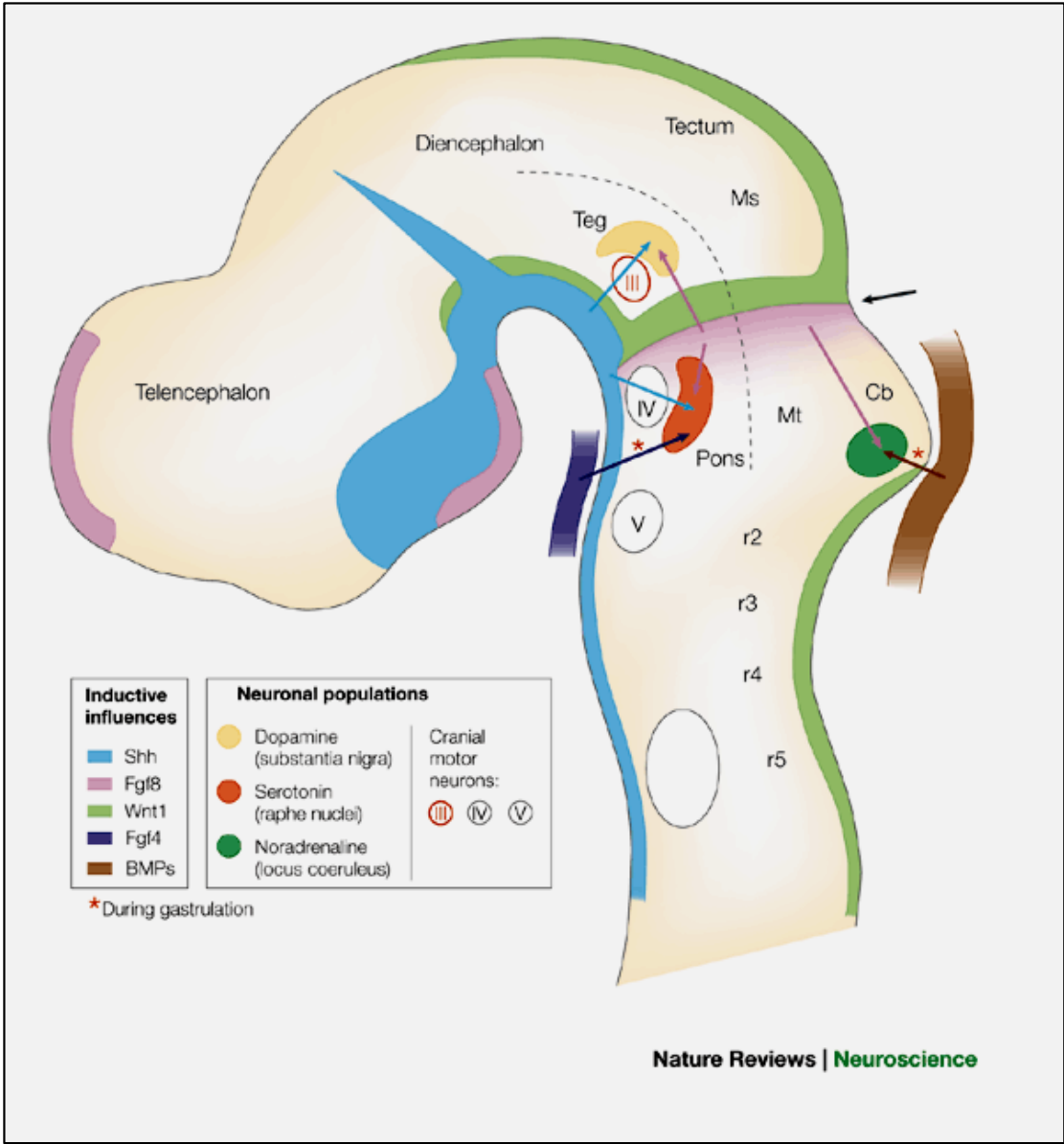
Hox gene expression domains in the CNS

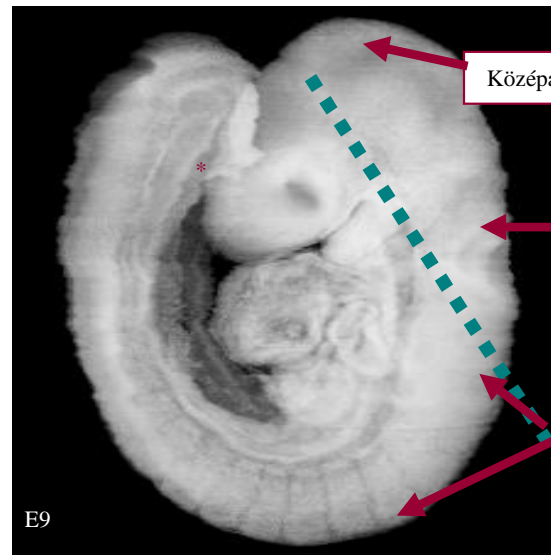


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Nested domains of homeotic genes along the AP axis of the *Drosophila* and mouse CNS. *Hox* genes specify a positional value along the AP axis, which is interpreted differently in fly and mouse in terms of downstream gene activation, resulting in neural structure; after Hirth *et al.*, (1998).





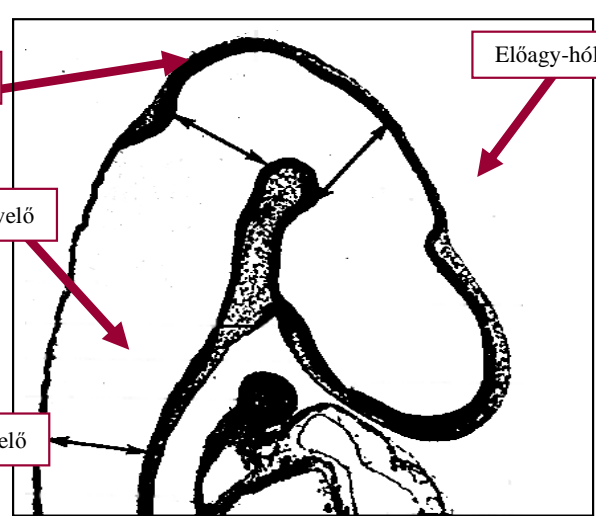


E9

Középgagy-hólyag

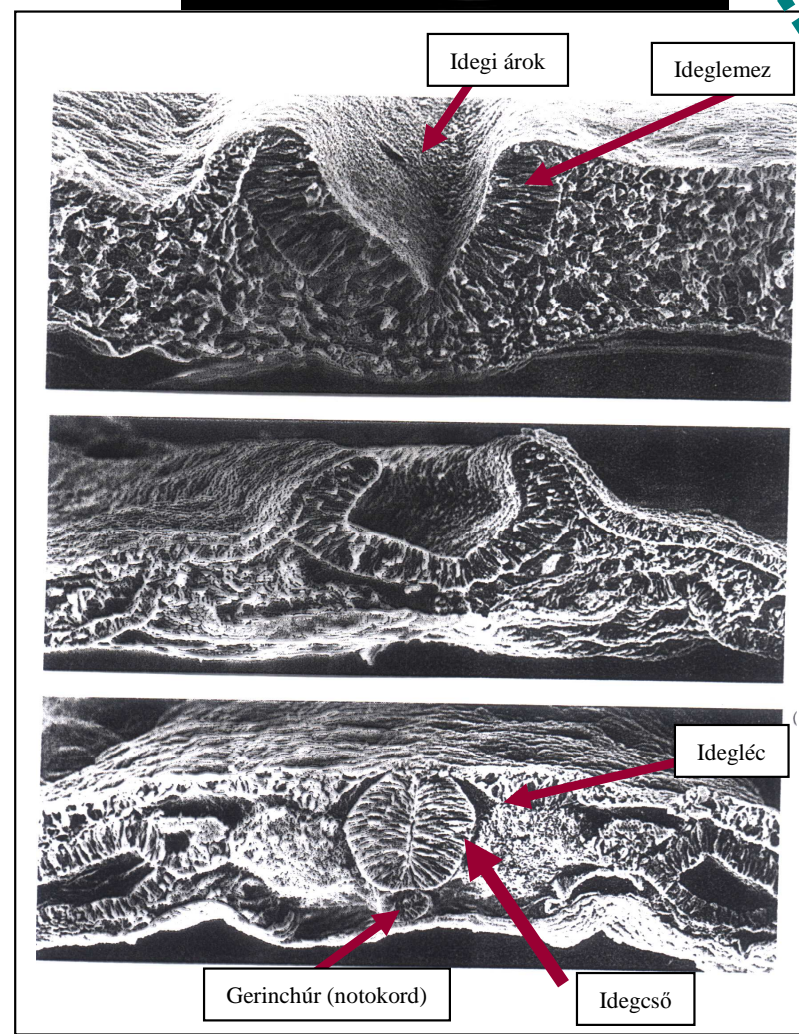
Nyúltvelő

Gerincvelő



Előagy-hólyag

Kilenc napos egér embrióban a központi idegrendszer-kezdemény a kamra falát alkotó osztódó sejtek rétegéből áll.



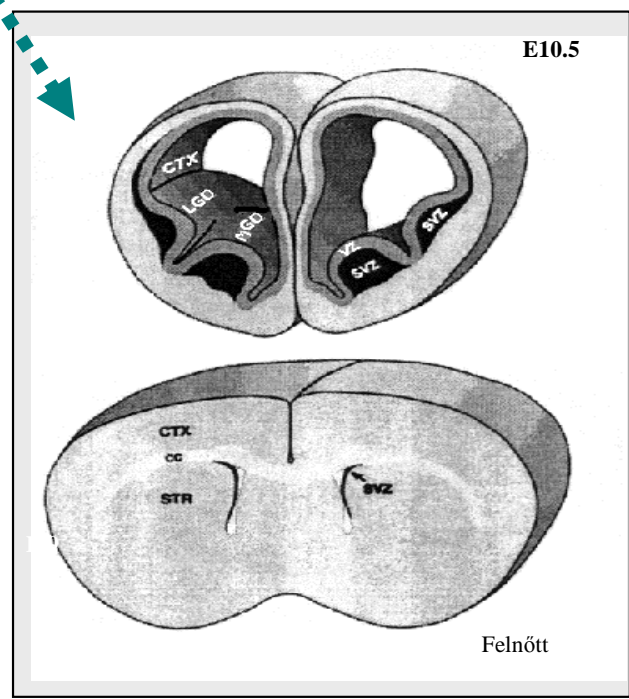
Idegi árok

Ideglemez

Idegléc

Gerinchúr (notokord)

Idegcső

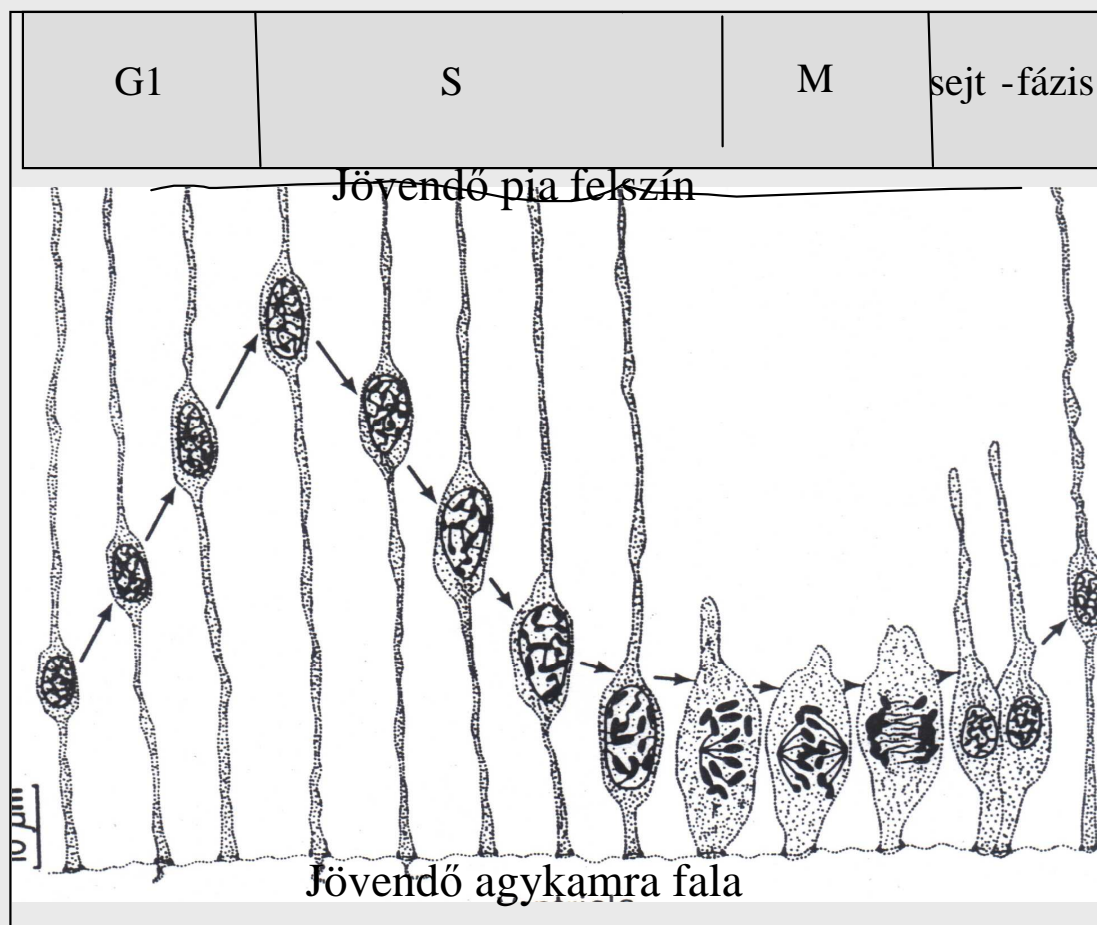
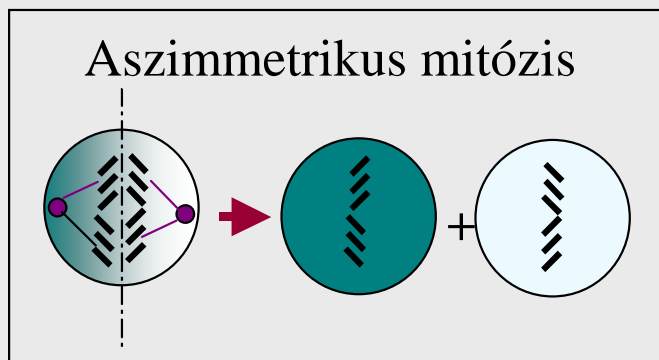
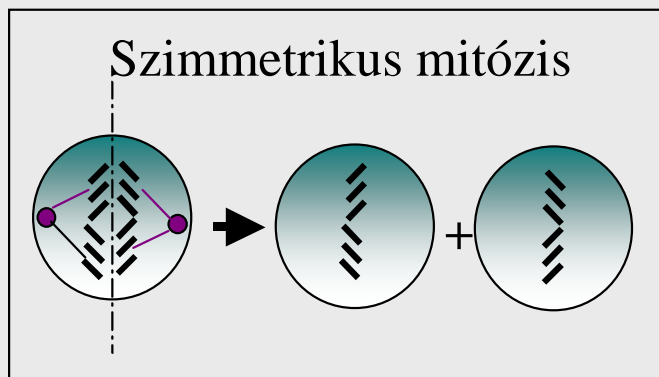
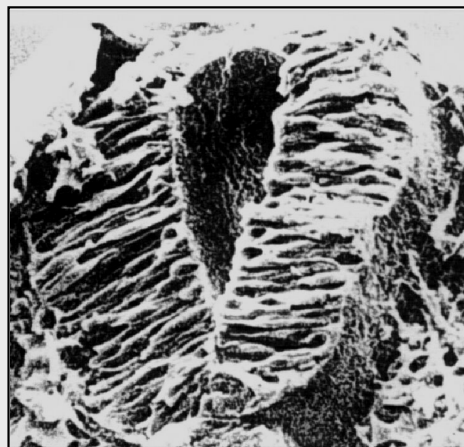


E10.5

Felnőtt

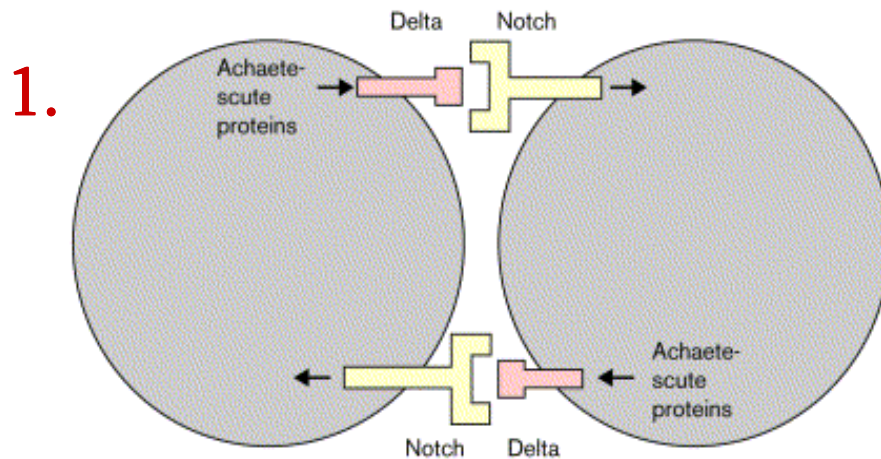
Az előagy-hólyag ventrális felületén alakulnak a gangliondombok (*). Ezek kamra felőli rétege felnőtt korban is képez idegsejteket.

Sejt-produkció és interkinetikus mag-vándorlás a primér ventrikuláris zónában

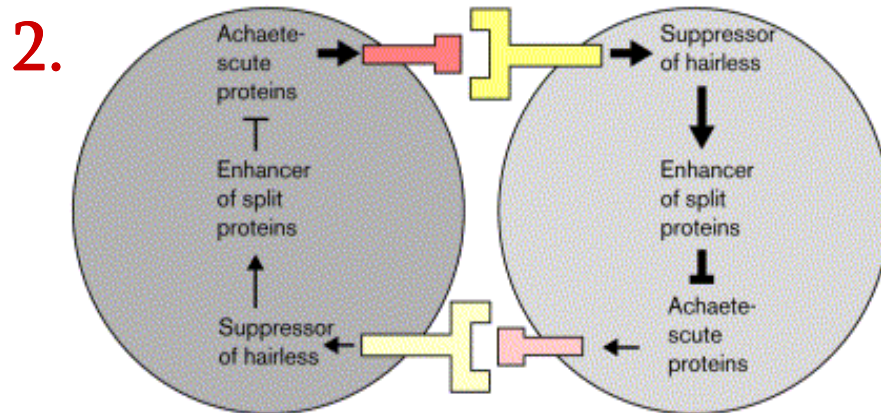


1. Notch/Delta rendszer

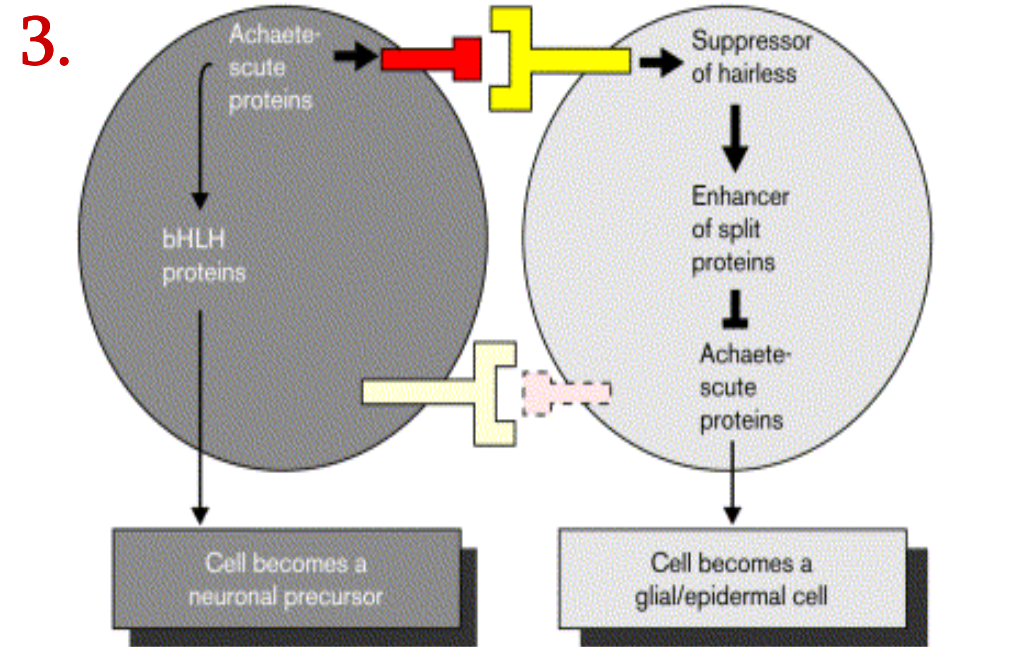
(a) Initially, Notch signaling between cells is balanced



(b) An imbalance in Notch signaling develops



(c) The imbalance is quickly amplified, leading to development of a neuronal precursor

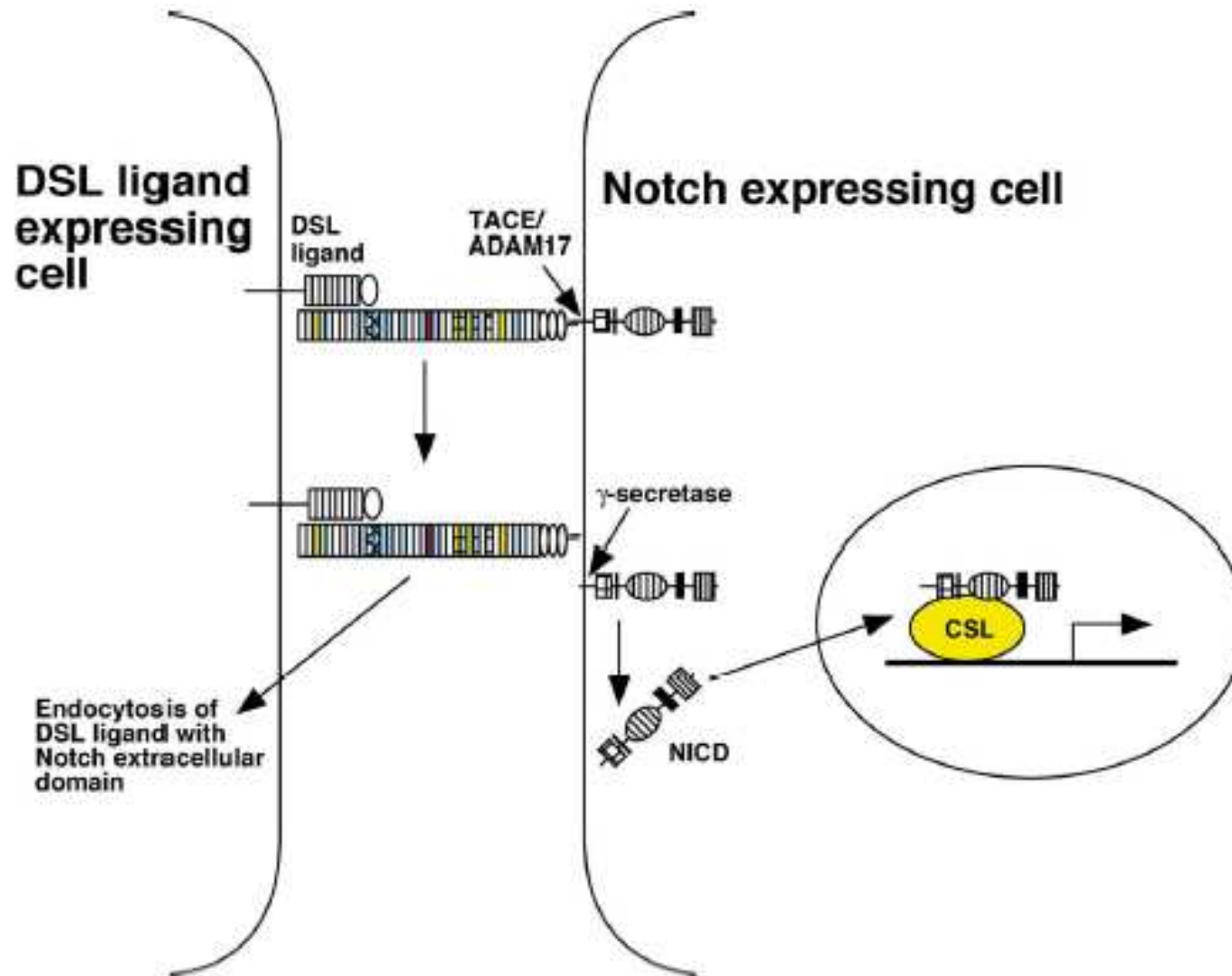


Current Opinion in Neurobiology

↓
Általánosságban:
differenciálódó sejt differenciálatlan sejt*

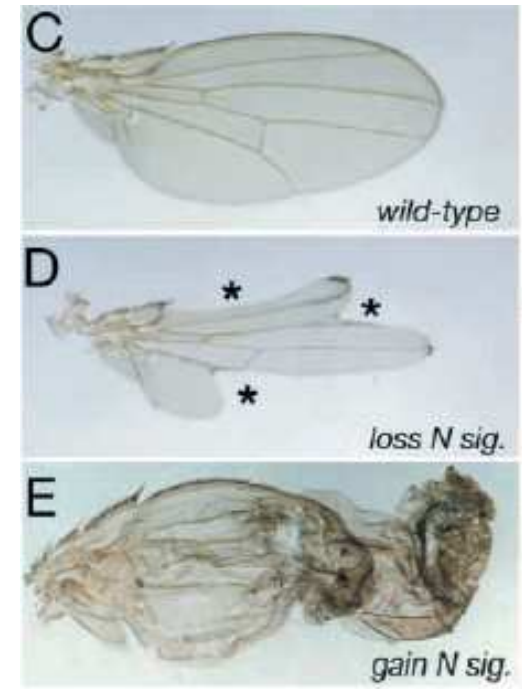
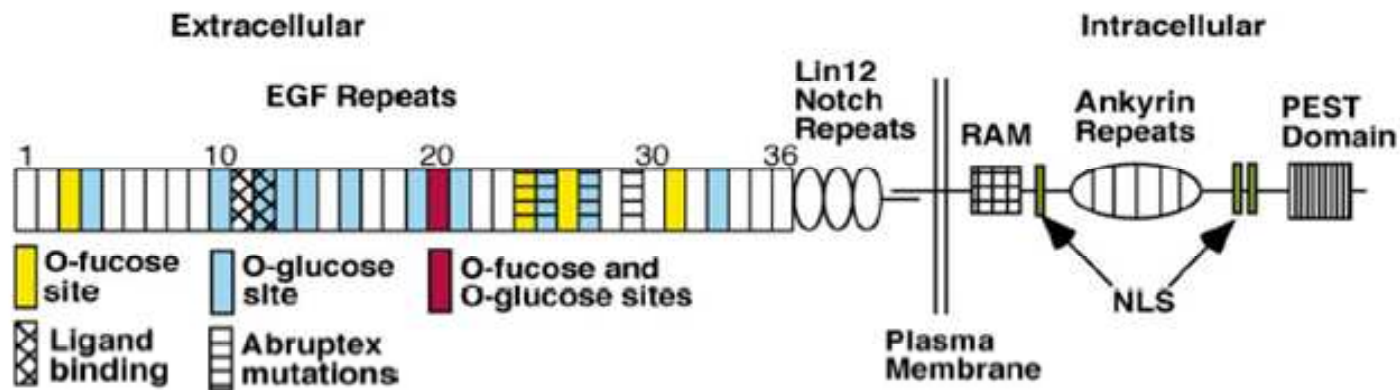
...differences between neighbor cells caused by stochastic events and intrinsic or extrinsic factors are stabilized or amplified through Notch and Delta signals...

1. Notch/Delta rendszer



DSL – Delta, Serrate, Lag-2
CSL – CBF1, Su(H), Lag-1
NICD – Notch Intracellular Domain
TACE/ADAM17 – TNF α Converting Enzyme
A Disintegrin And Metalloprotease

1. Notch



- Artavanis-Tsakonas, 1985: notch gén, ill. fehérje

- 300 kDa,

- 1 TM domén;

- **EC**: 36 tandem EGF-like repeat, 3 Notch/LIN-12 repeat: negatív regulátor;

- **IC**: 6 tandem ankyrin repeat, glutamingazdag domain, PEST-szekvencia (**NICD** = TF)

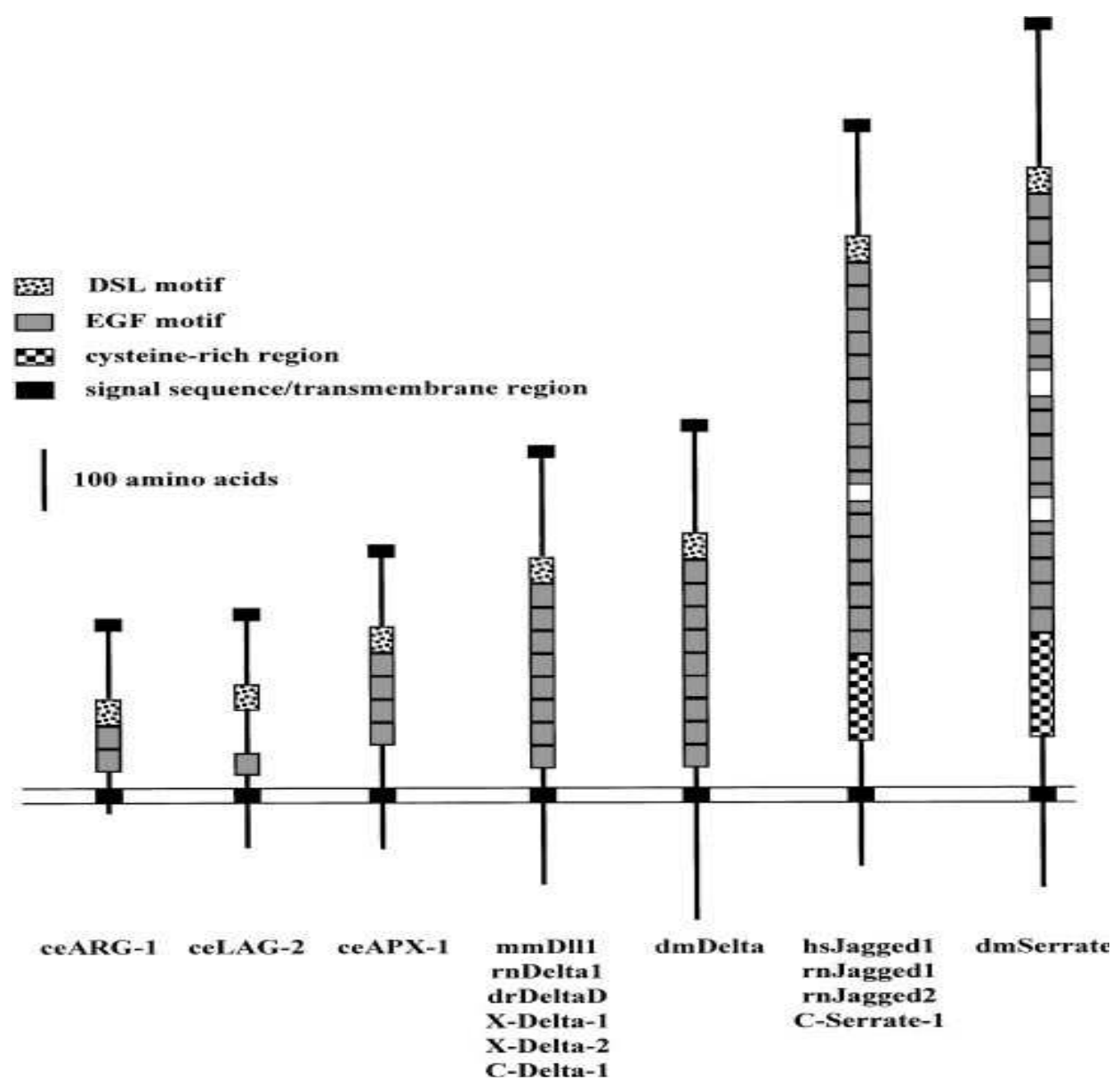
Előfordulás:

- az összes többsejtű állatban (*C. elegans*tól kezdve legalábbis),

- az összes szövetben

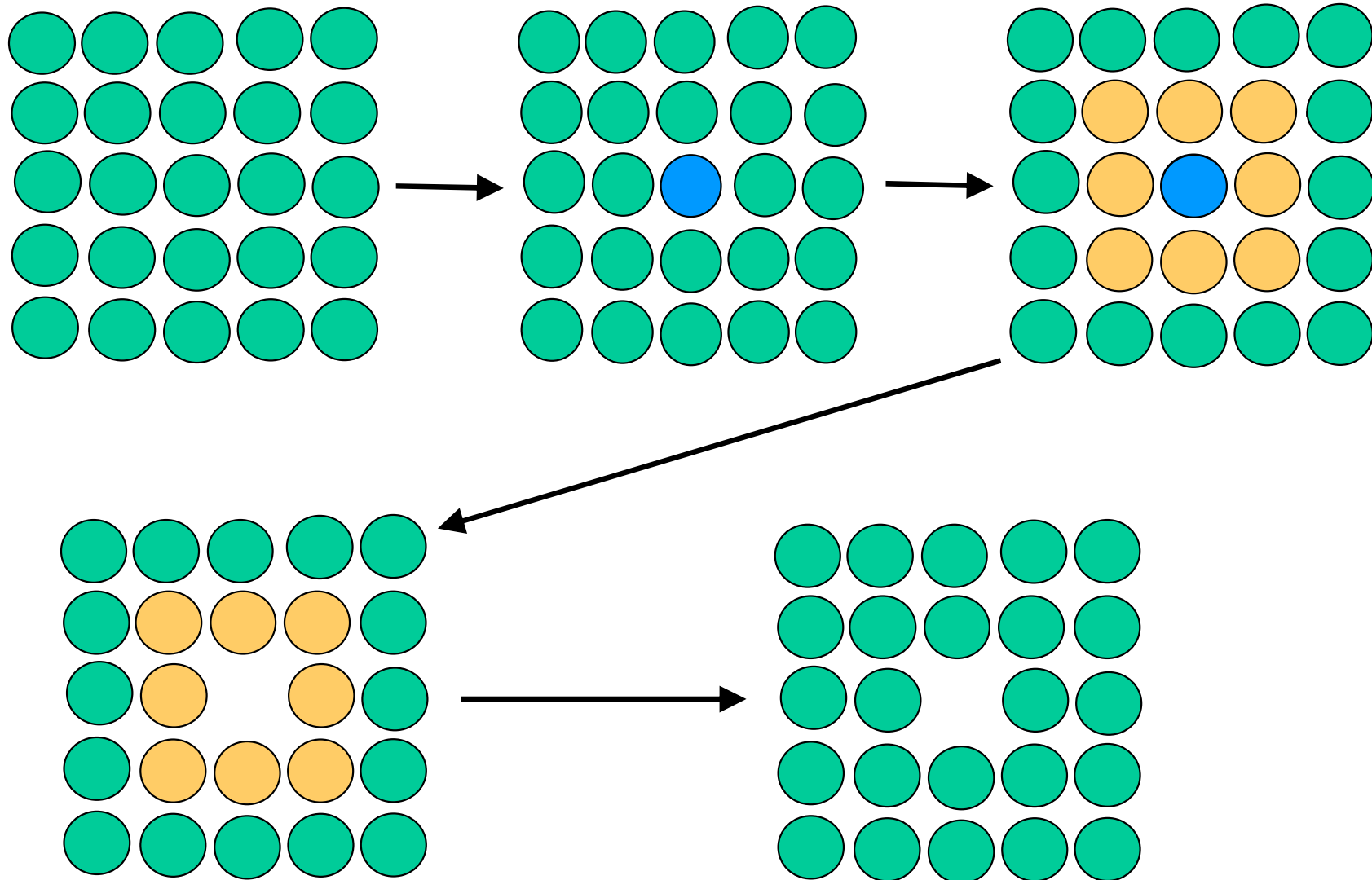
Funkció

- differenciálatlan (adott szinten!), osztódóképes populációk fennmaradása



1. Notch/Delta rendszer

Laterális gátlás (Drosophila proneurális cluster)

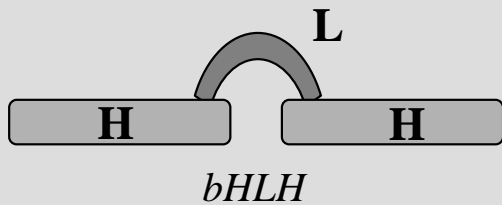


Notchrendszer

A szignalizáció legfontosabb elemei:

	<i>Drosophila</i>	<i>Emlős</i>
Receptor:	Notch	Notch1-4
Ligandum:	Delta, Serrate	Delta(-like) 1,3,4 Jagged1,2
Downstream effektor:	Su(H)	CBF1/RJBk
Primer target:	En(spl), Hairy (bHLH gének)	Hes1-...

Bázikus helix-loop-helix transzkripciós faktor fehérjék

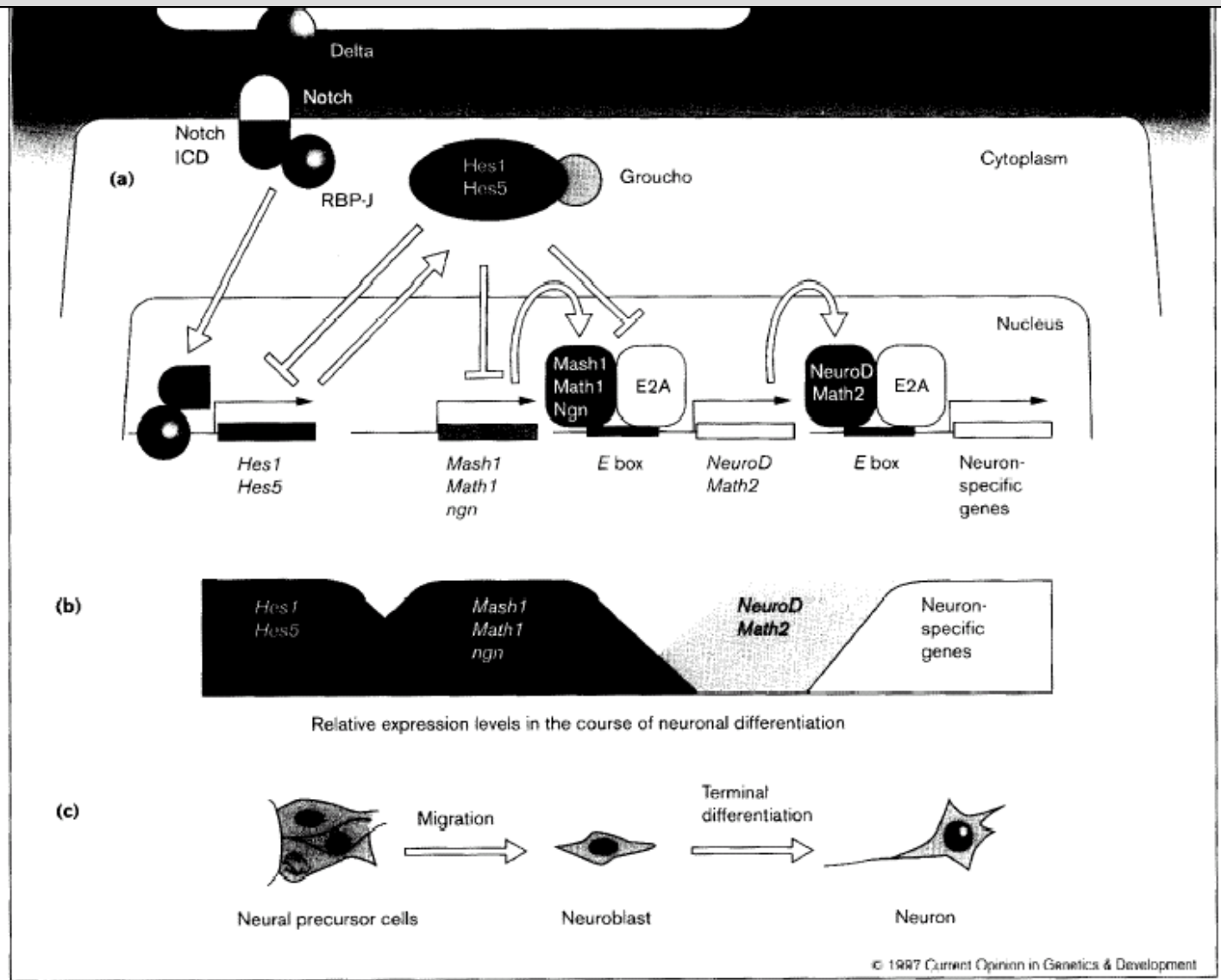


Pro-neurális

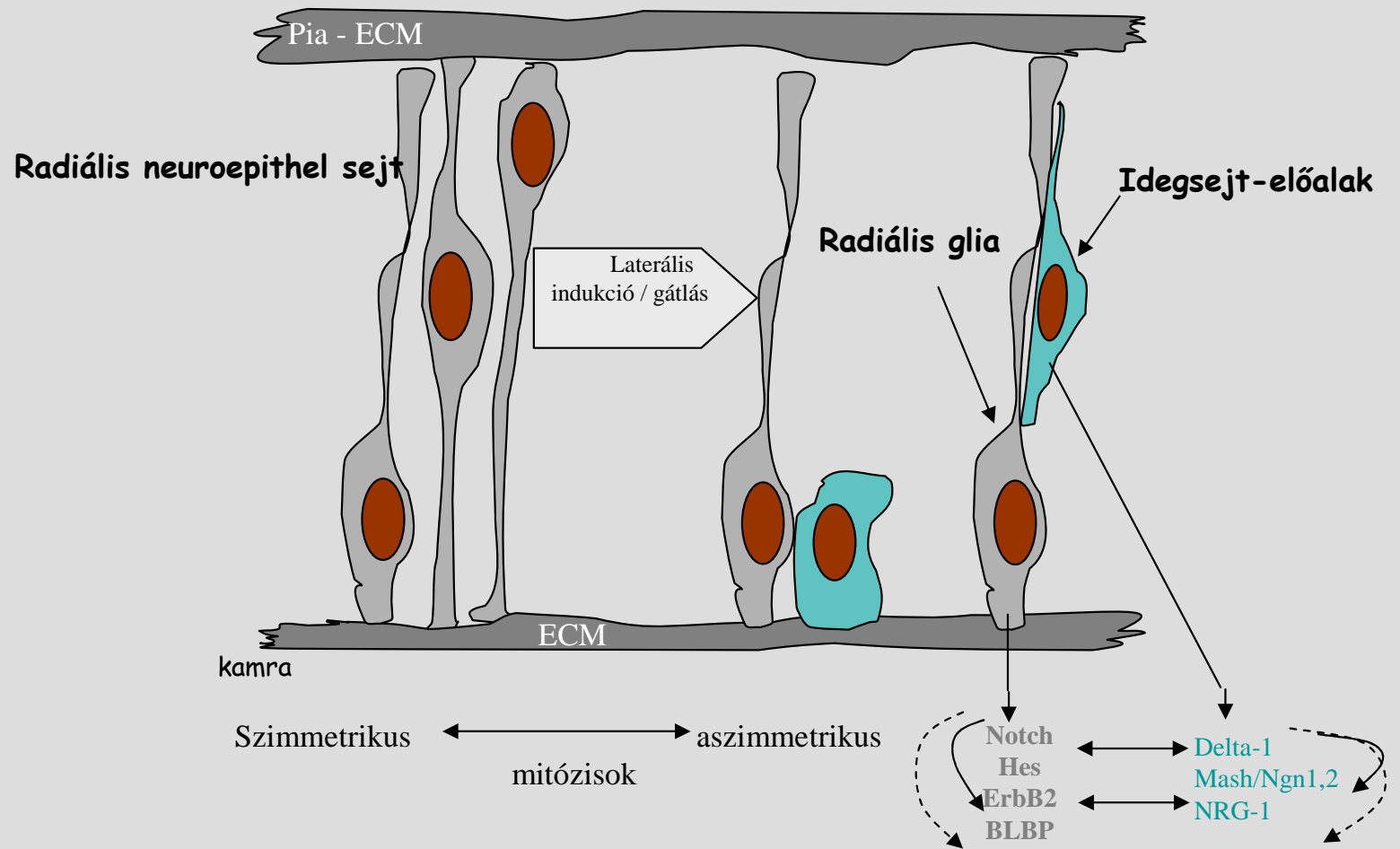
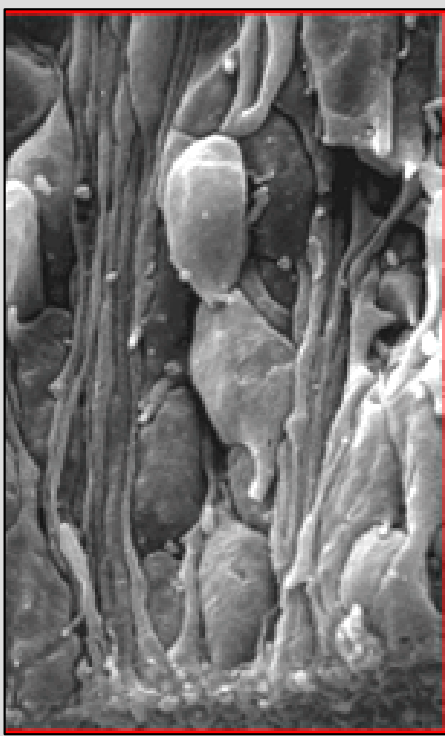
Mash 1..., Ngn 1,2,
Math 1

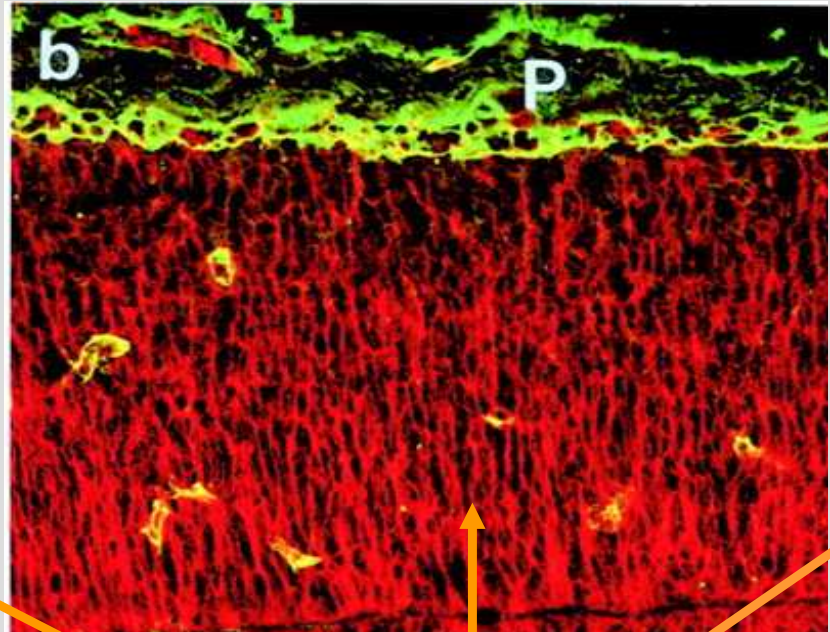
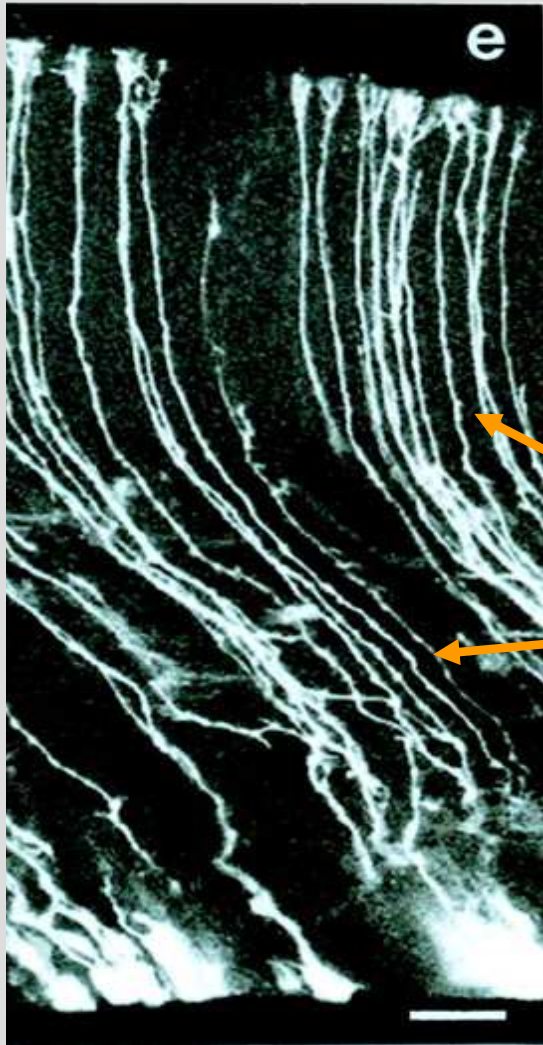
Neurális

Math 2, NeuroD



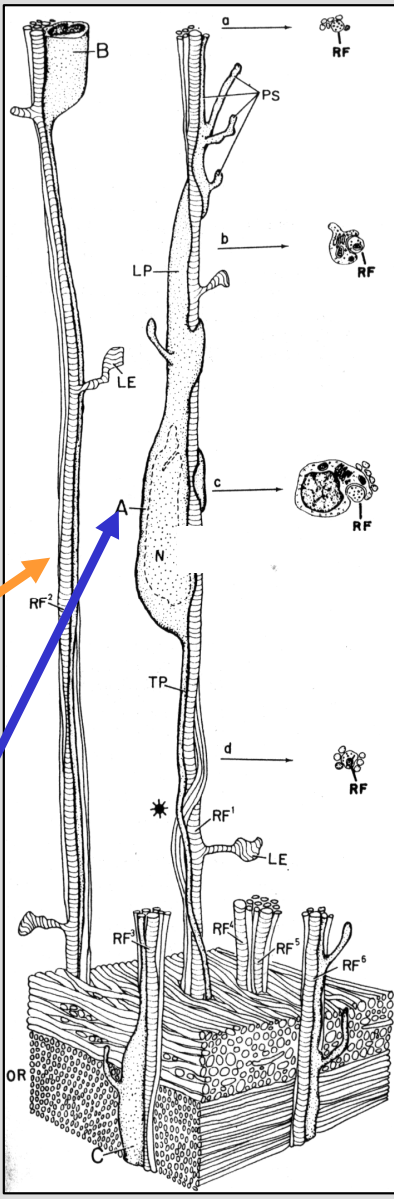
The Delta/Notch/RBP-J, Hes1/Hes5, Mash1/Math1/Ngn, NeuroD/Math2 pathway. (a) A model for antagonistic regulation of HLH genes under the control of the Delta/Notch pathway; (b) relative expression levels of HLH genes; and (c) corresponding stages of neural cells (from precursor cells to neuron) are shown. (a) When the transmembrane protein Notch is activated by its ligand Delta, proteolysis may occur and the intracellular domain of Notch (Notch ICD) complexed with RBP-J translocates to the nucleus. In the nucleus, the Notch ICD/RBP-J complex activates *Hes1* and *Hes5* transcription. Then *Hes1* and *Hes5* in association with the co-repressor Groucho homologue block the activity of *Mash1/Math1/Ngn* both by repressing their transcription and by depriving the functional complex of E2A. *Hes1* can also repress its own expression by binding to its promoter; *Hes1* induction by Notch could be a result of inhibition of *Hes1* negative autoregulation. When Notch is inactivated, *Hes1* and *Hes5* expression declines and neuronal HLH genes (*Mash1/Math1/ngn*) start functioning. Thus, *Hes1* and *Hes5* regulate the timing of neuronal differentiation. *Mash1/Math1/Neurogenin* then promote differentiation of precursor cells and upregulate late-expressing HLH genes (*NeuroD/Math2*), which direct the terminal differentiation of neurons. Whether these HLH factors either directly activate or repress others as shown in this figure remains undetermined.





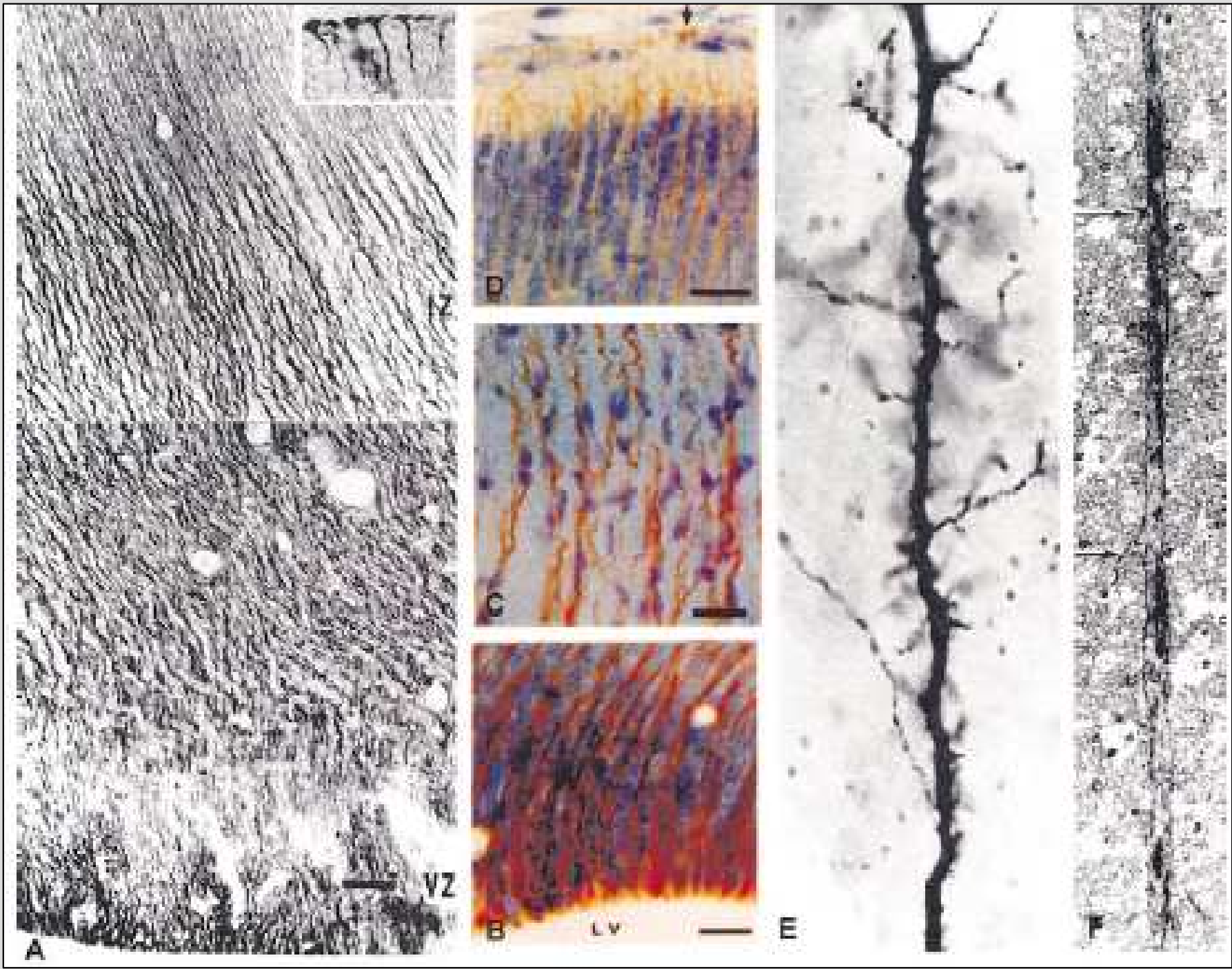
Radiális glia

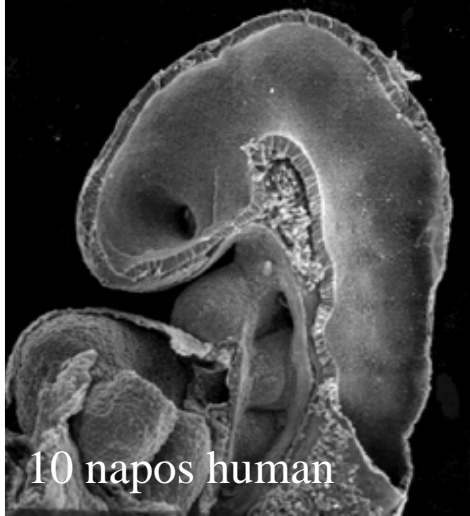
Vándorló idegsejt előalakok



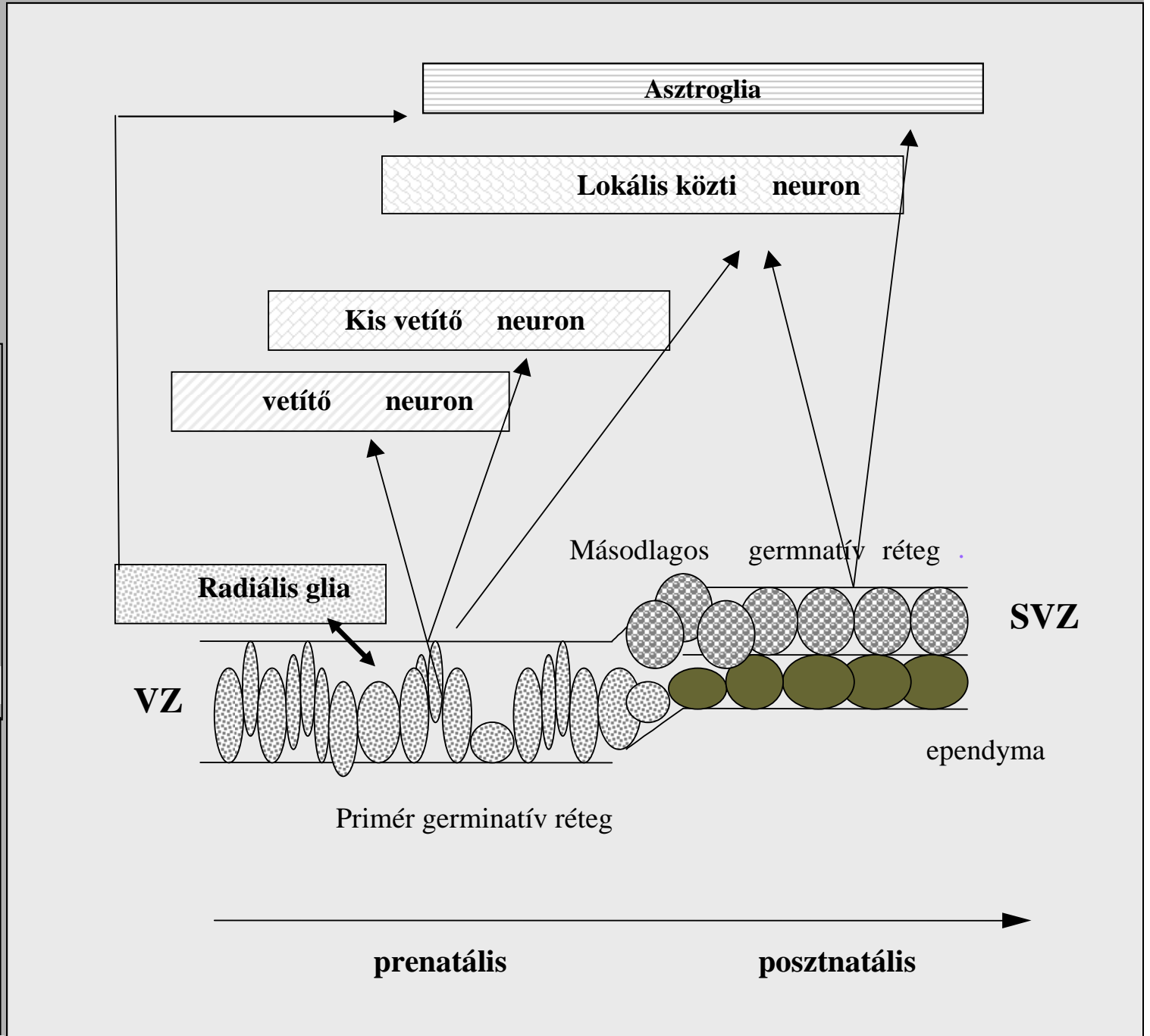
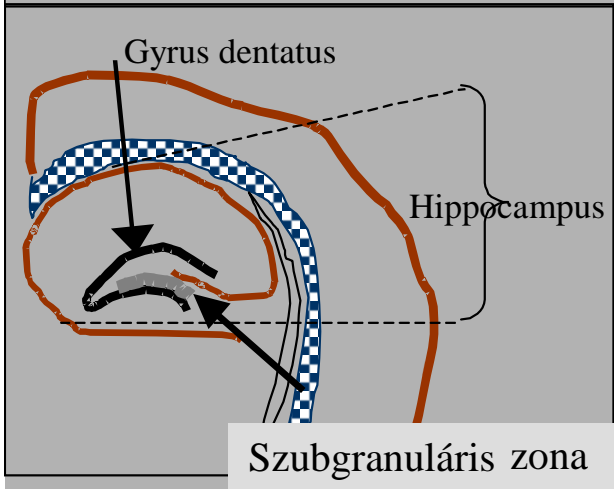
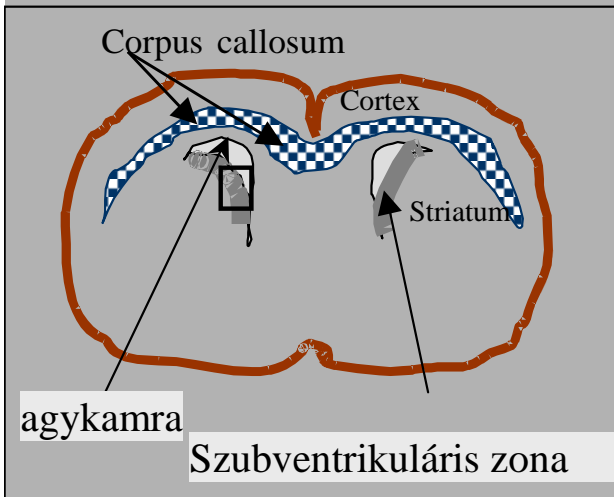
Halfter, W. et al. *J. Neurosci.* 2002;22:6029-6040

Rakic P. J. *Comp. Neurol.* 1972, 145: 61-84





10 napos human

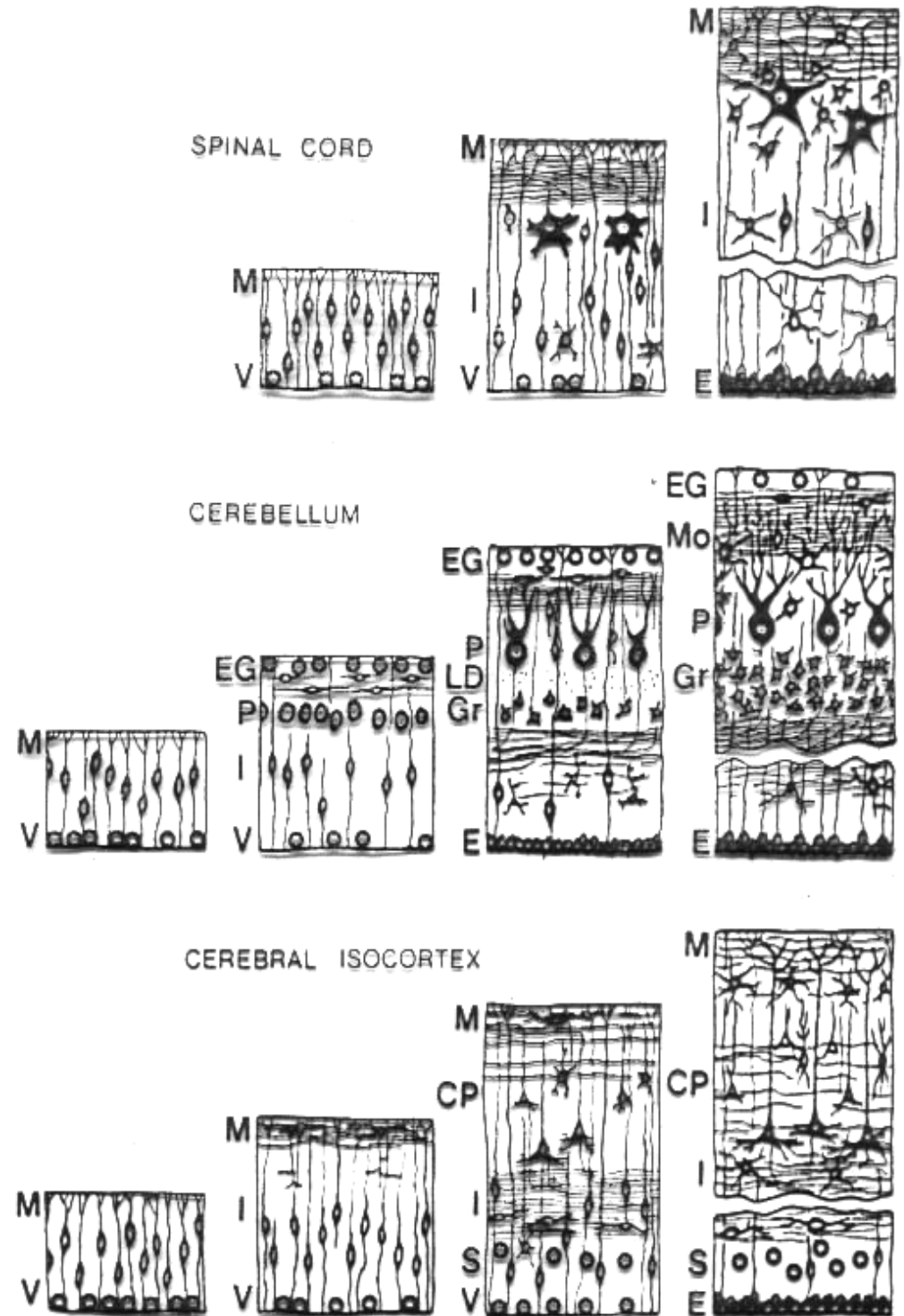


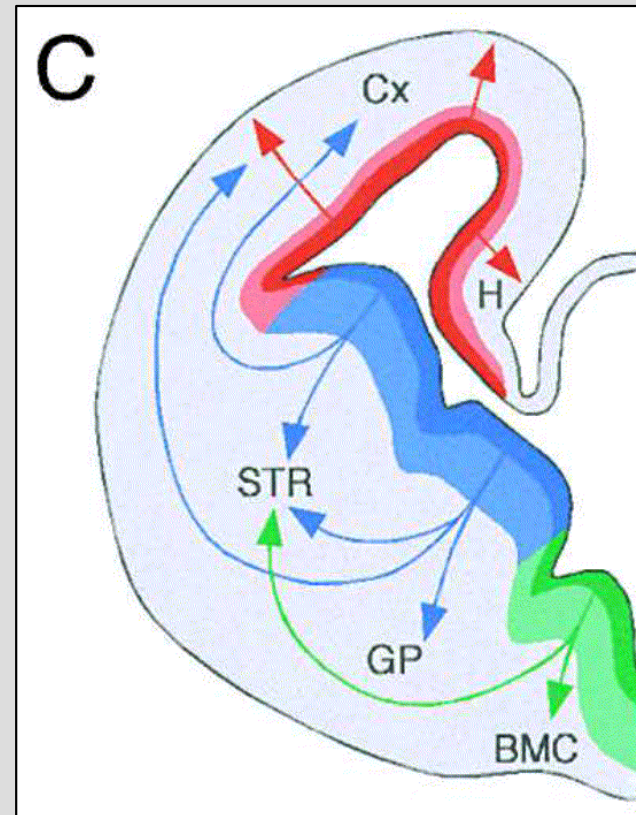
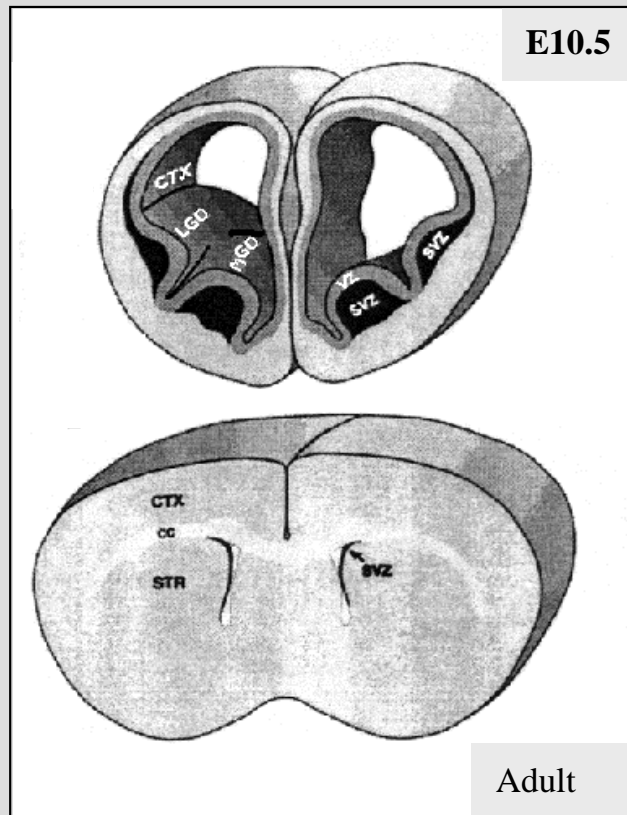
Primér idegi germinatív zóna:

- idegi őssejtek (különböző elkötelezettség)
- szimmetrikusan osztódó sokszorozó sejtek (tangenciális vándorlás)
- „megmerevedett” radiális glia (vezető felület)
- posztmitotikus idegsejt-előalakok (radiális irányban kifelé vándorló sejtek)

„Születésnapjuk”:

^3H -timidin, BrdU beépülés





Az agykéreg kialakításában primer és szekunder germinatív réteg eredetű, és eltérő régiókból származó idegsejtek sejtek vesznek részt