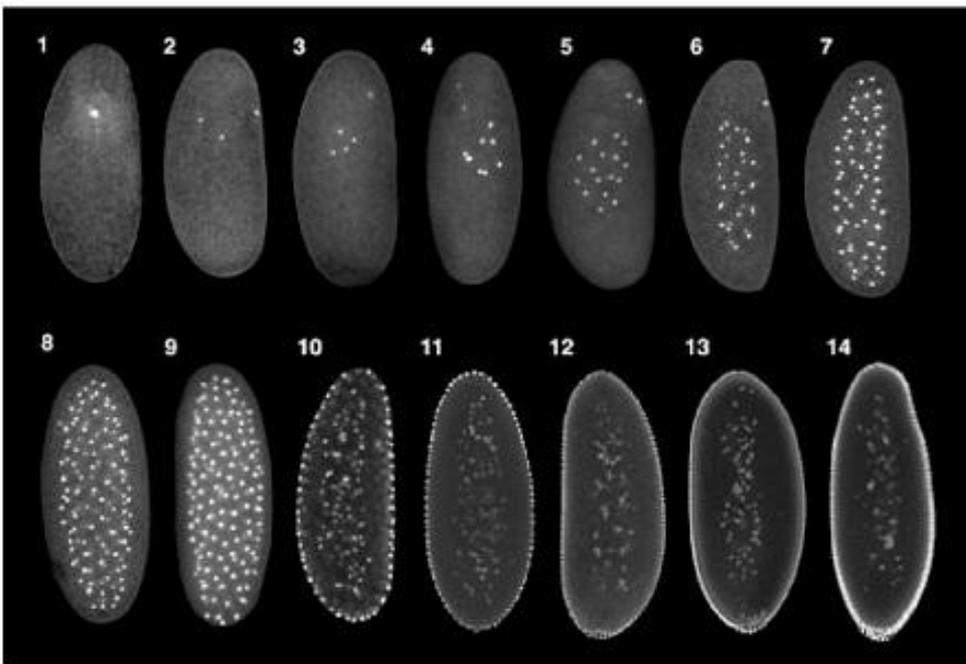


# La specificazione del sistema nervoso negli insetti



(b) Early embryonic stages in cross section

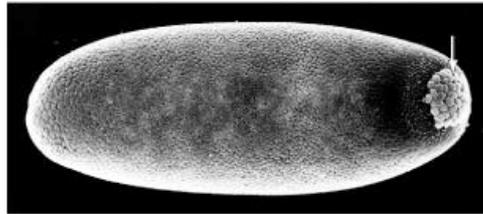


**Segmentazione  
Meroblastica superficiale**

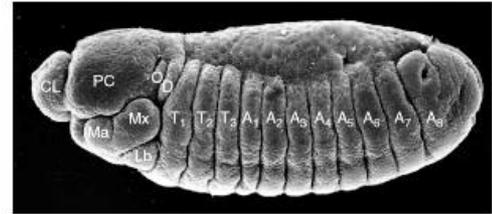
Blastoderma sinciziale  
Blastoderma cellulare (dal 14° ciclo mitotico)

**gastrulazione**

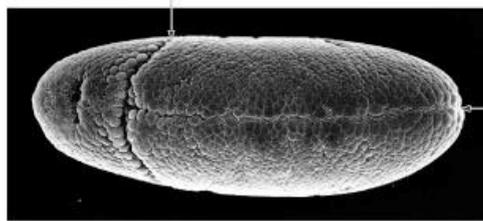
(a) Cellular blastoderm



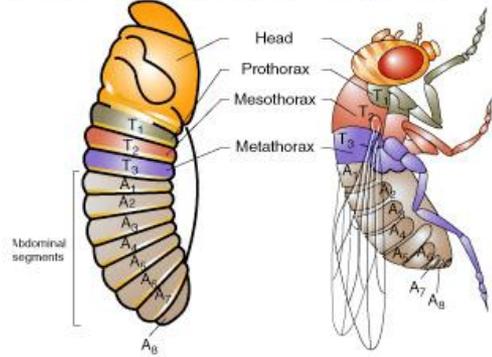
(c) Segmentation



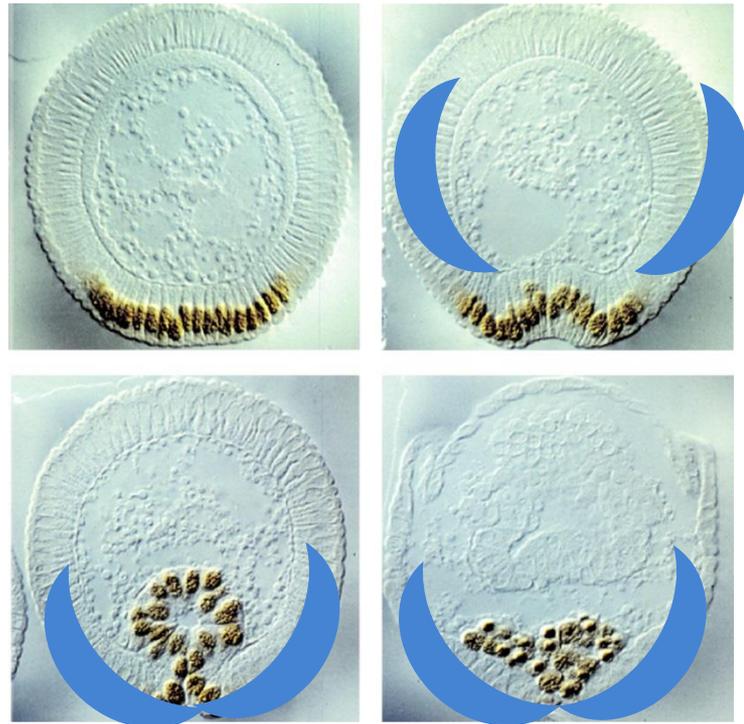
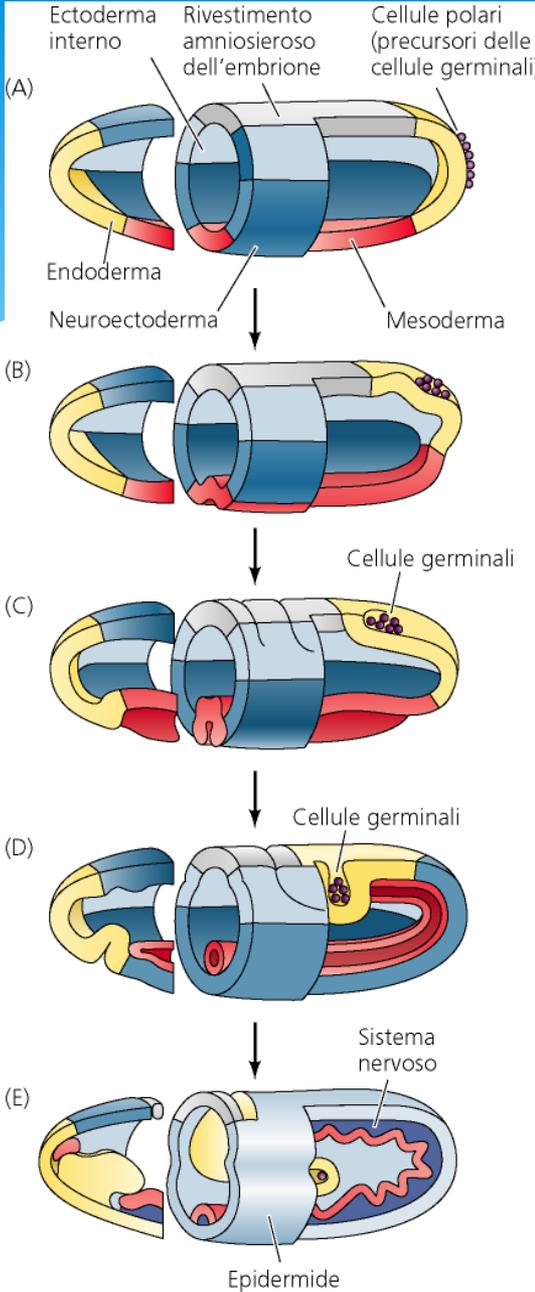
(b) Gastrulation



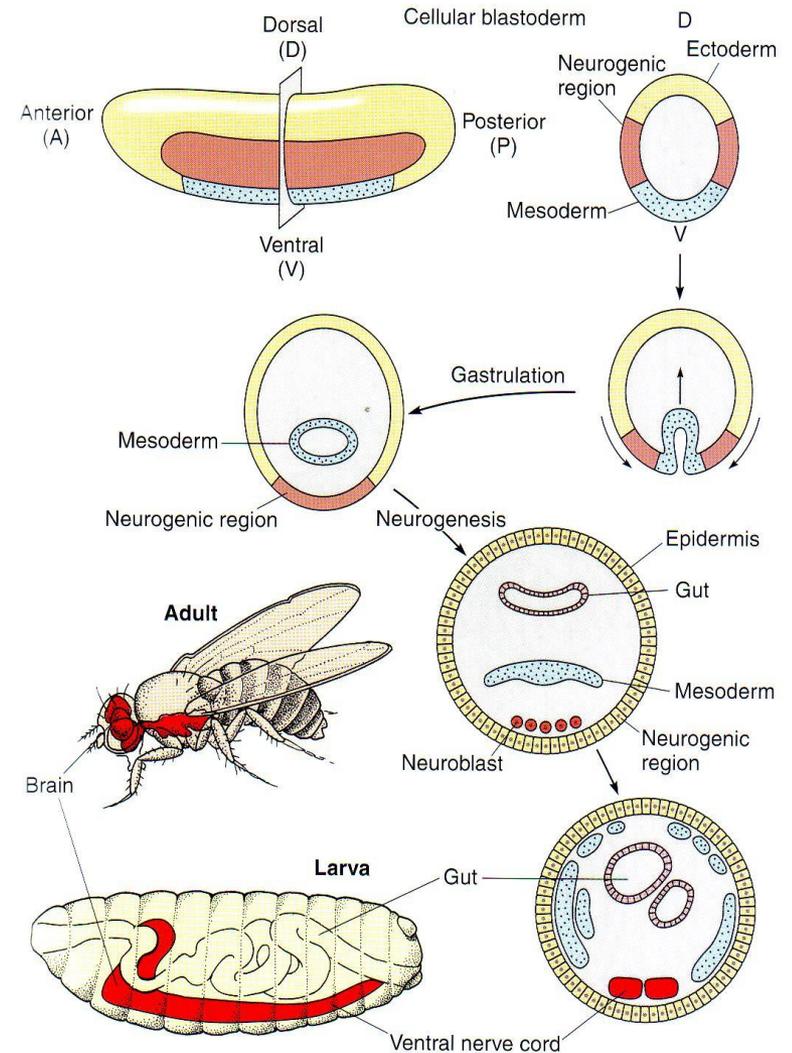
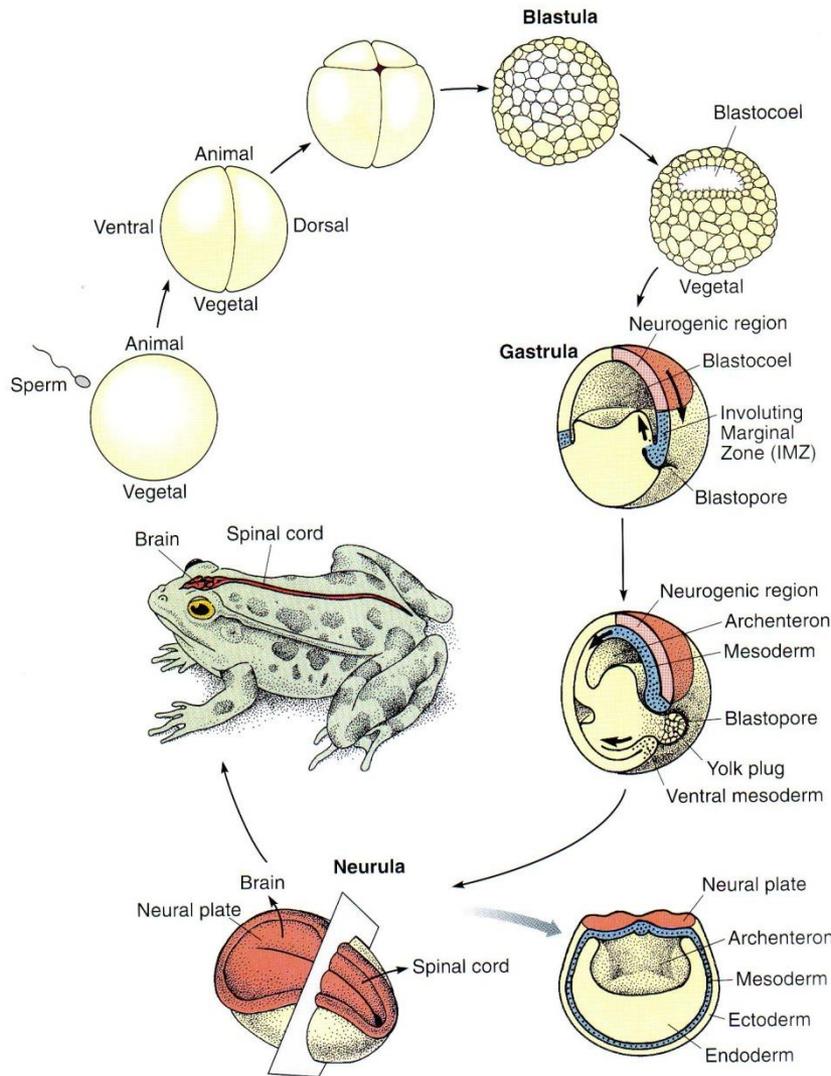
(d) Segment identity is preserved throughout development.



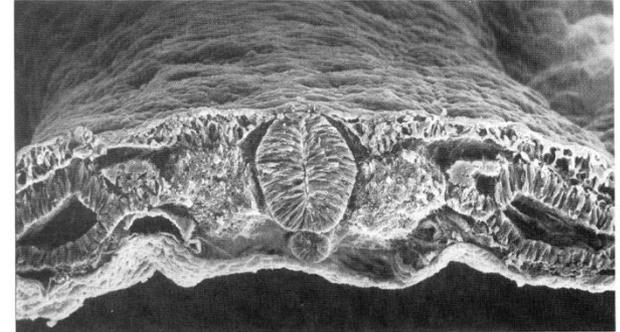
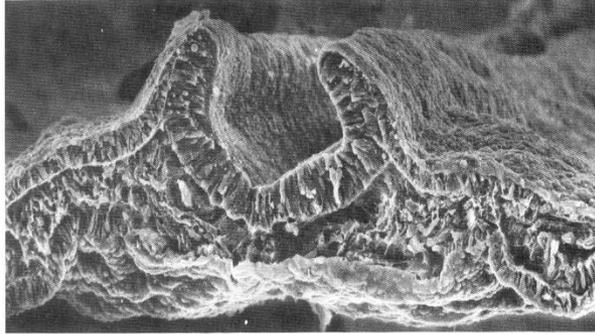
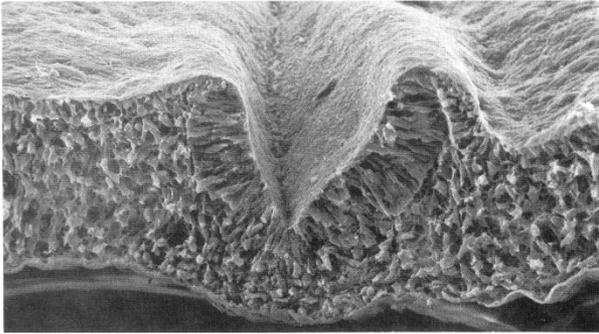
# Territori presuntivi e gastrulazione in Drosophila



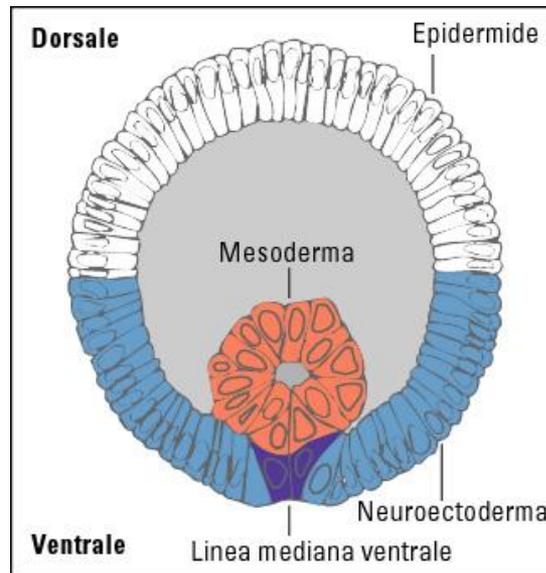
# Comparazione tra SN anfibii e artropodi

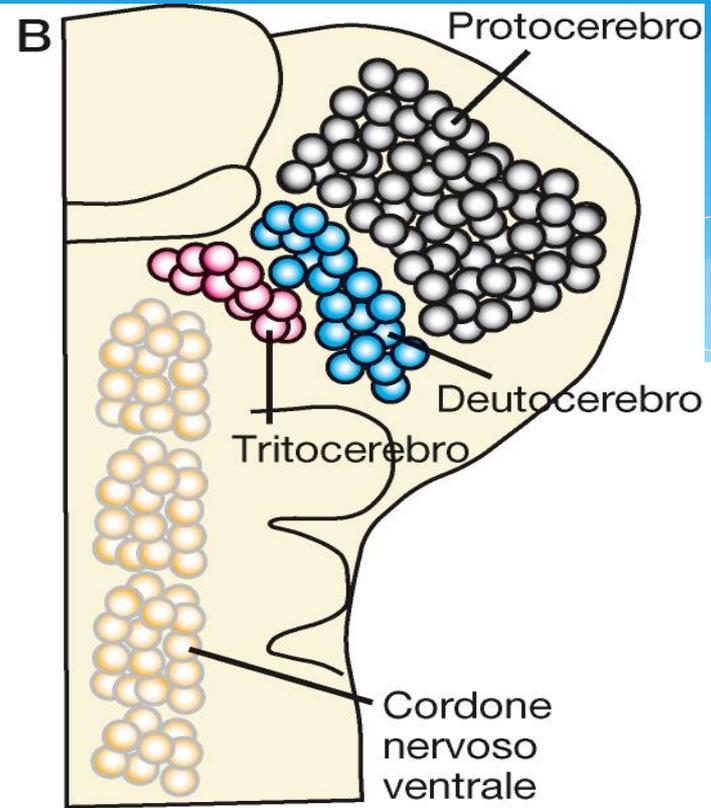


# Dorsale nei Vertebrati



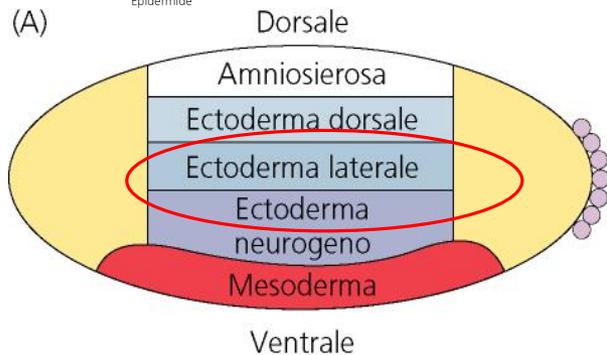
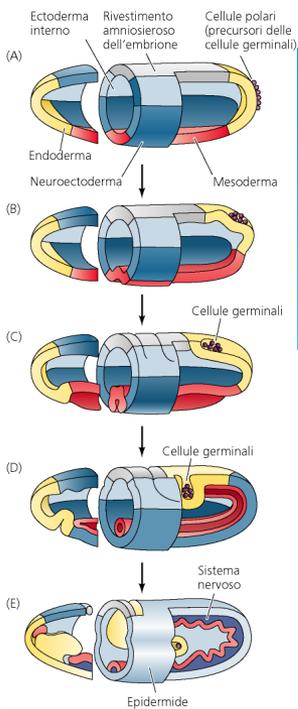
## VENTRALE nell'insetto



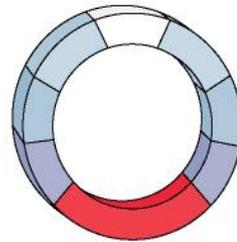


Negli invertebrati non c'è un Tubo Neurale  
Ma sono presenti strutture gangliari ripetute  
nei vari segmenti e nella testa

# Fattori materni guidano la specificazione dei territori ventrali

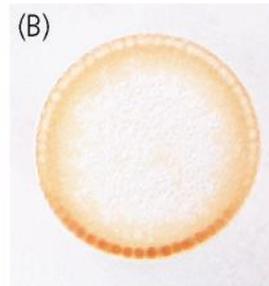


VISTA LATERALE

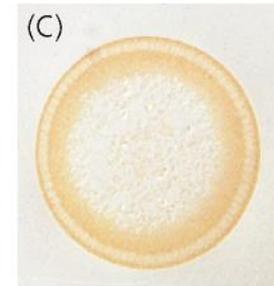


SEZIONE TRASVERSALE

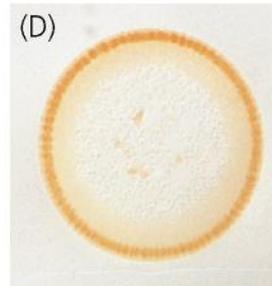
WT



d/d -/-

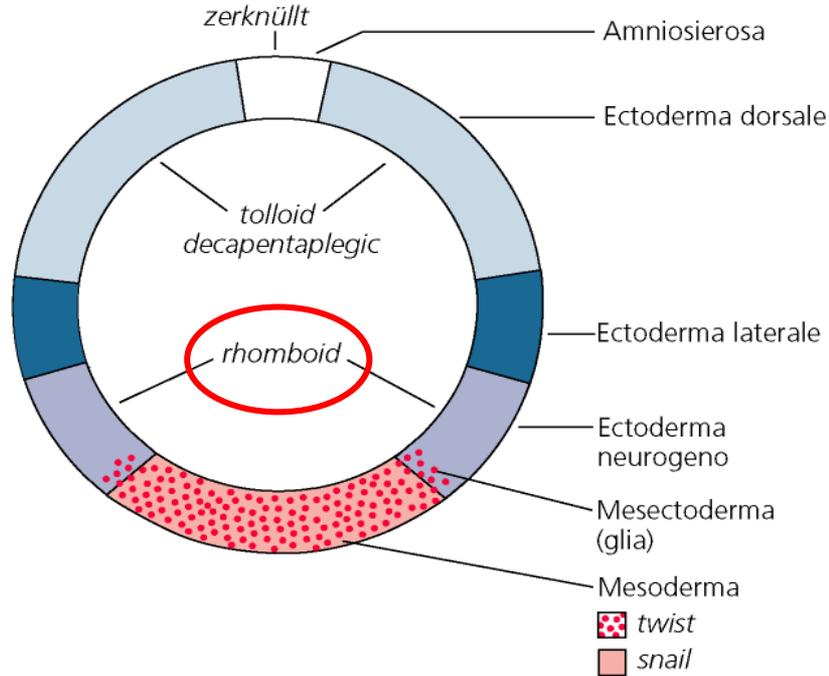


Over  
expression

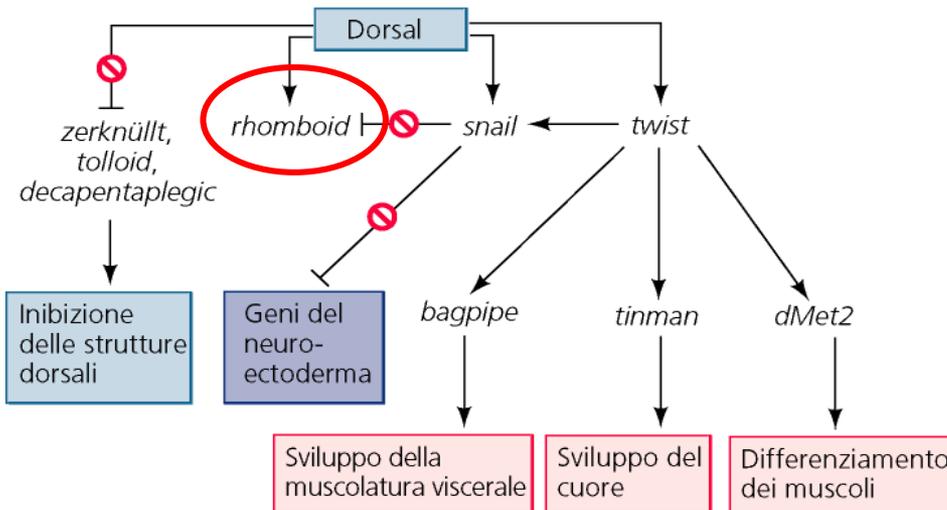


*Dorsal* è il gene ad effetto materno responsabile della definizione dell'asse dorso ventrale di *Drosophila*

(A) PIANIFICAZIONE DORSALE



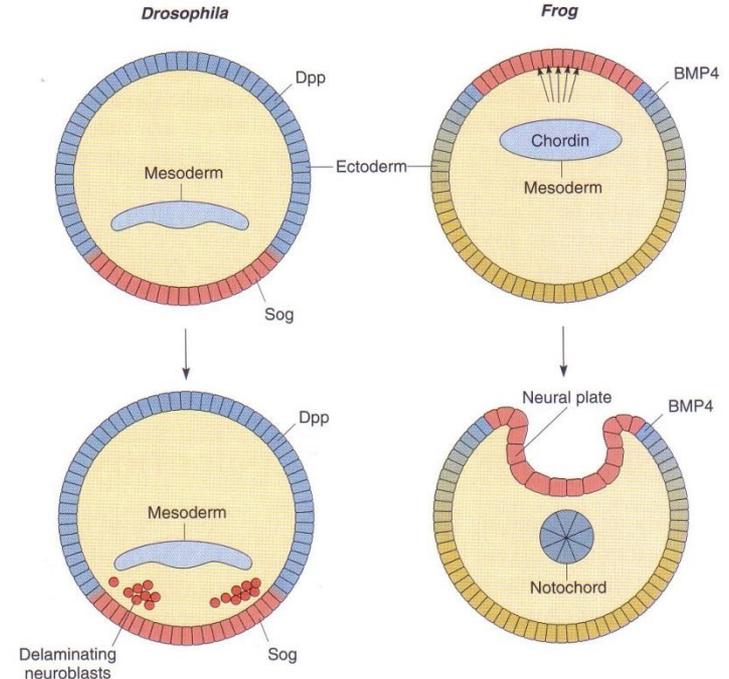
(B) PIANIFICAZIONE VENTRALE



Funzioni di Dorsal

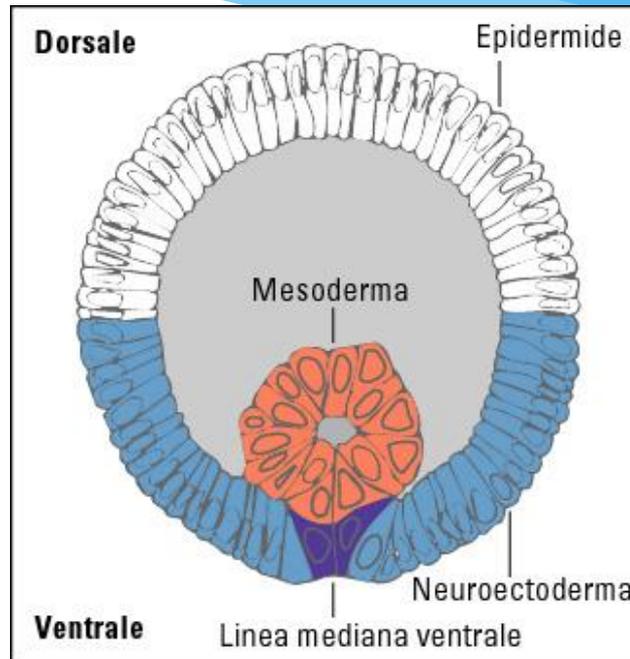
Geni ventrali ↑

Geni dorsali ↓

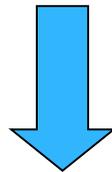


Sog omologo di cordina

Dpp omologo di TGFβ



***rhomboid***



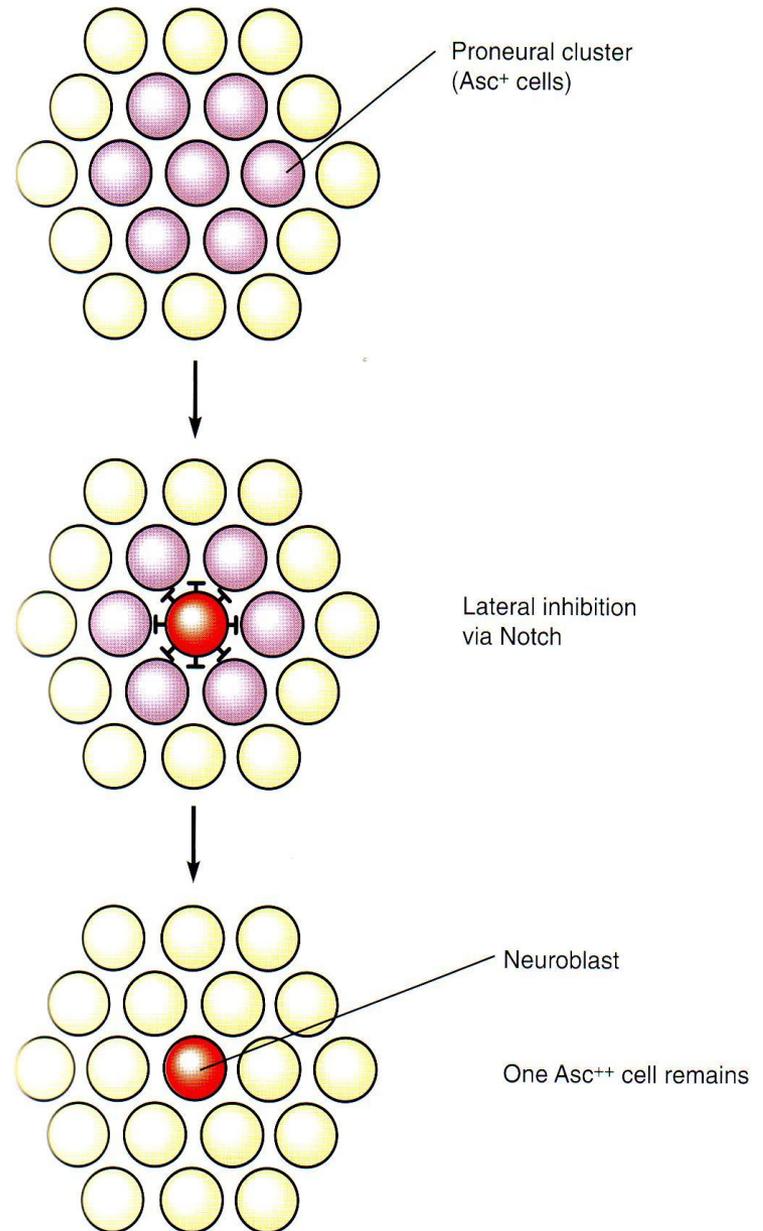
***complesso achete-scute***

# INIBIZIONE LATERALE

- Il complesso achaete –scute è costituito da geni che codificano per fattori di trascrizione HLH
- Funzionano in forma di eterodimeri, quando in presenza di partner attivi
- Sono espressi all'interno di clusters cellulari detti *clusters pro-neurali*

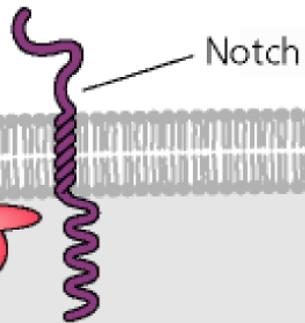


**Accensione del sistema Delta-Notch**



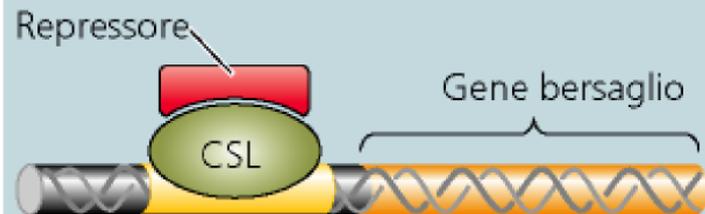
(A)

Cellula che invia il segnale



Proteasi

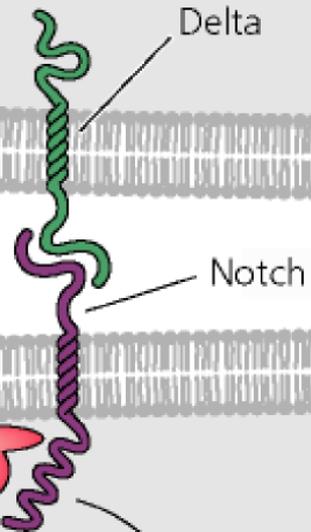
Cellula che riceve il segnale



Assenza di trascrizione

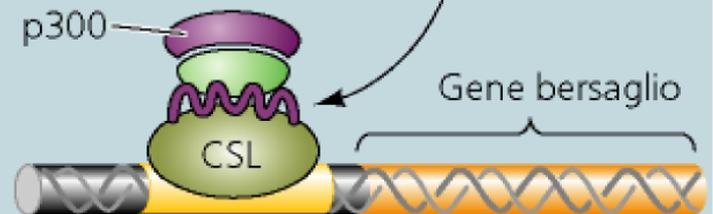
(B)

Cellula che invia il segnale



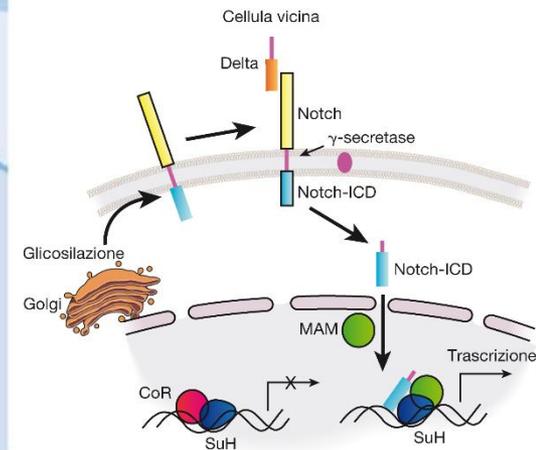
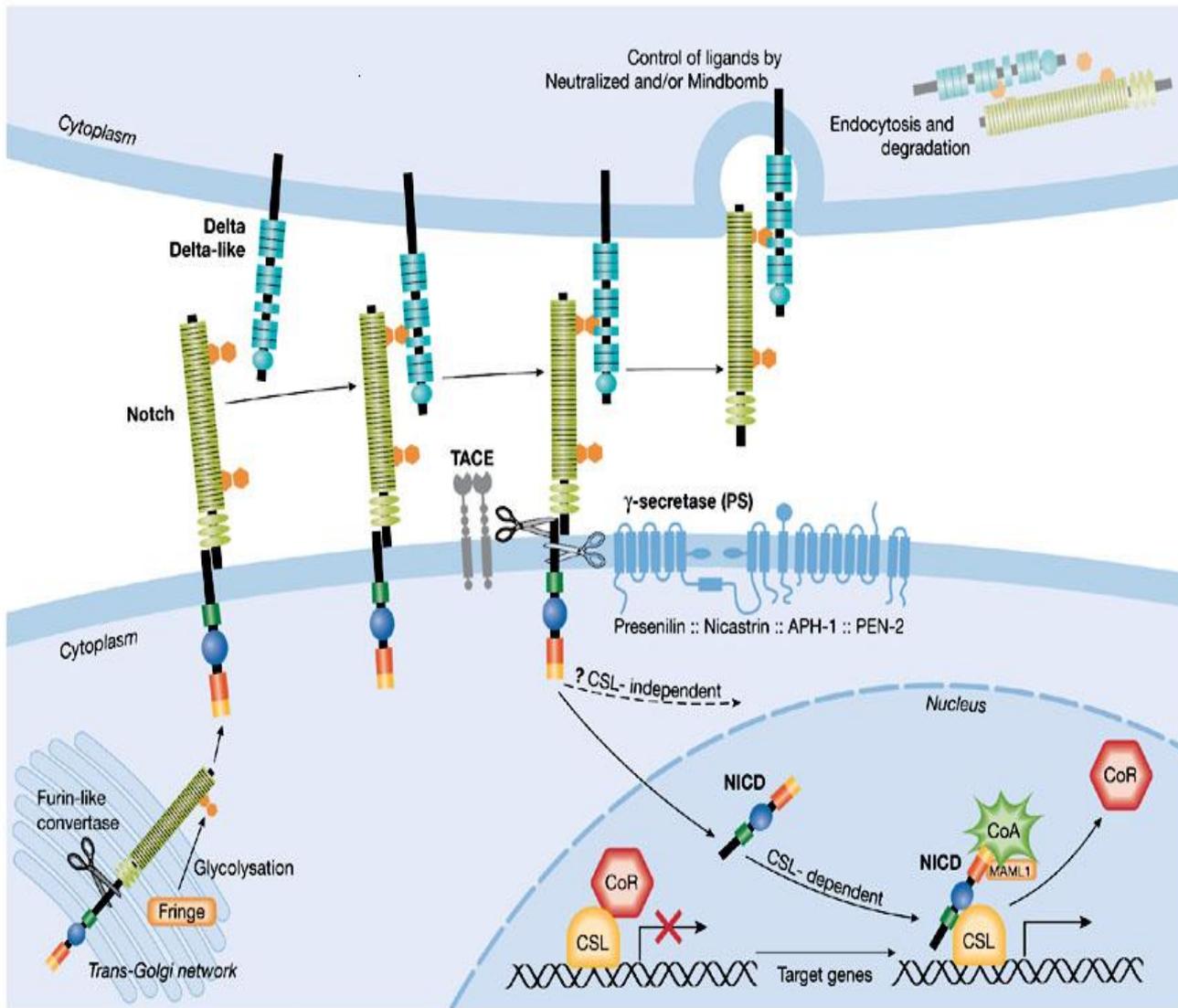
Proteasi

Cellula che riceve il segnale

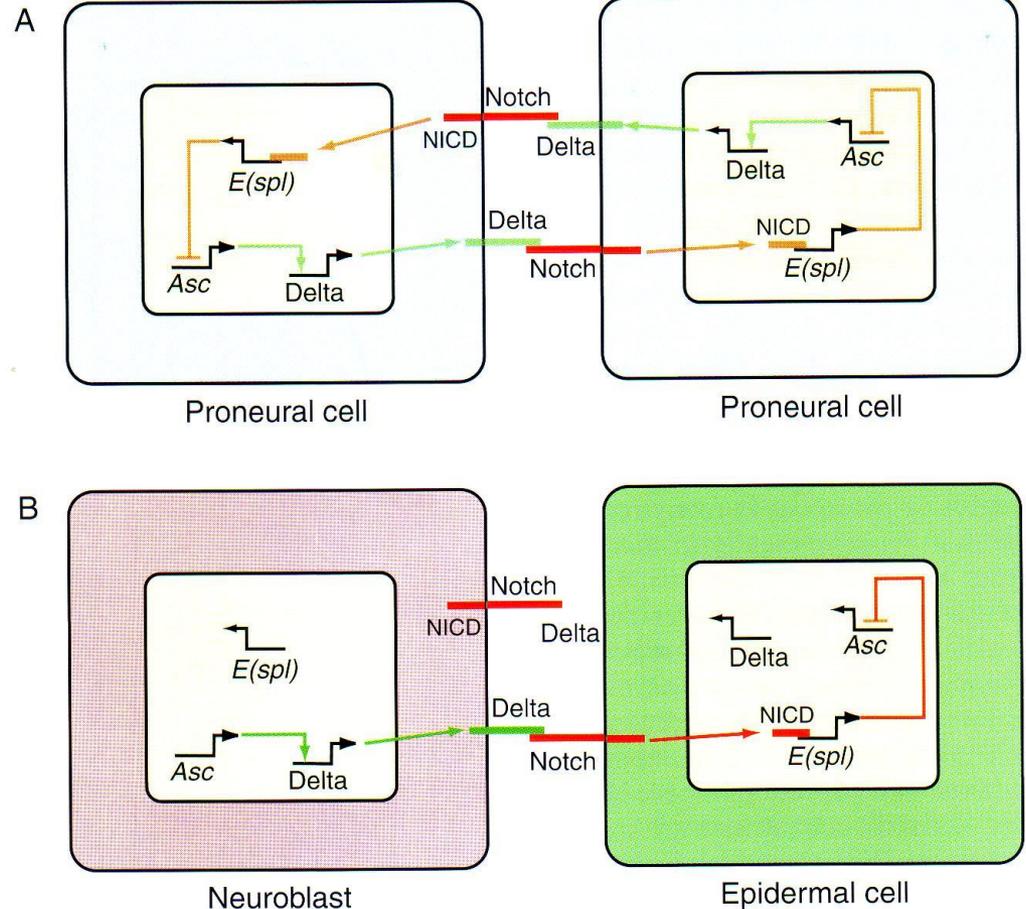
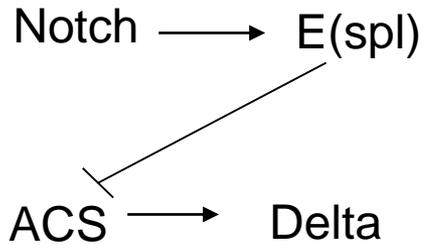
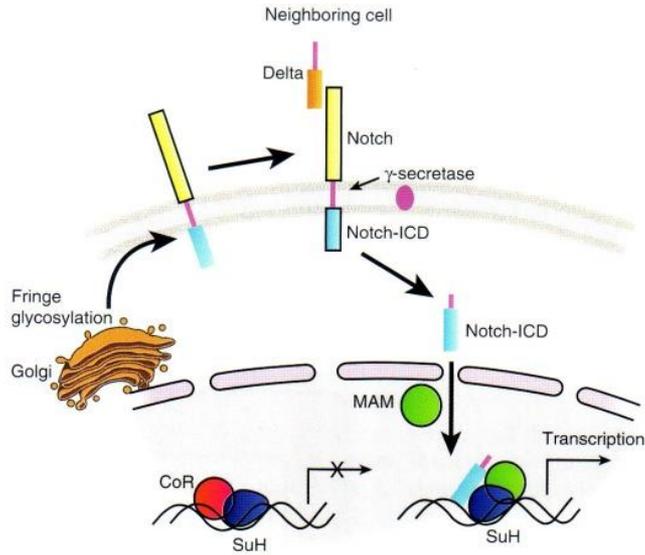


Trascrizione

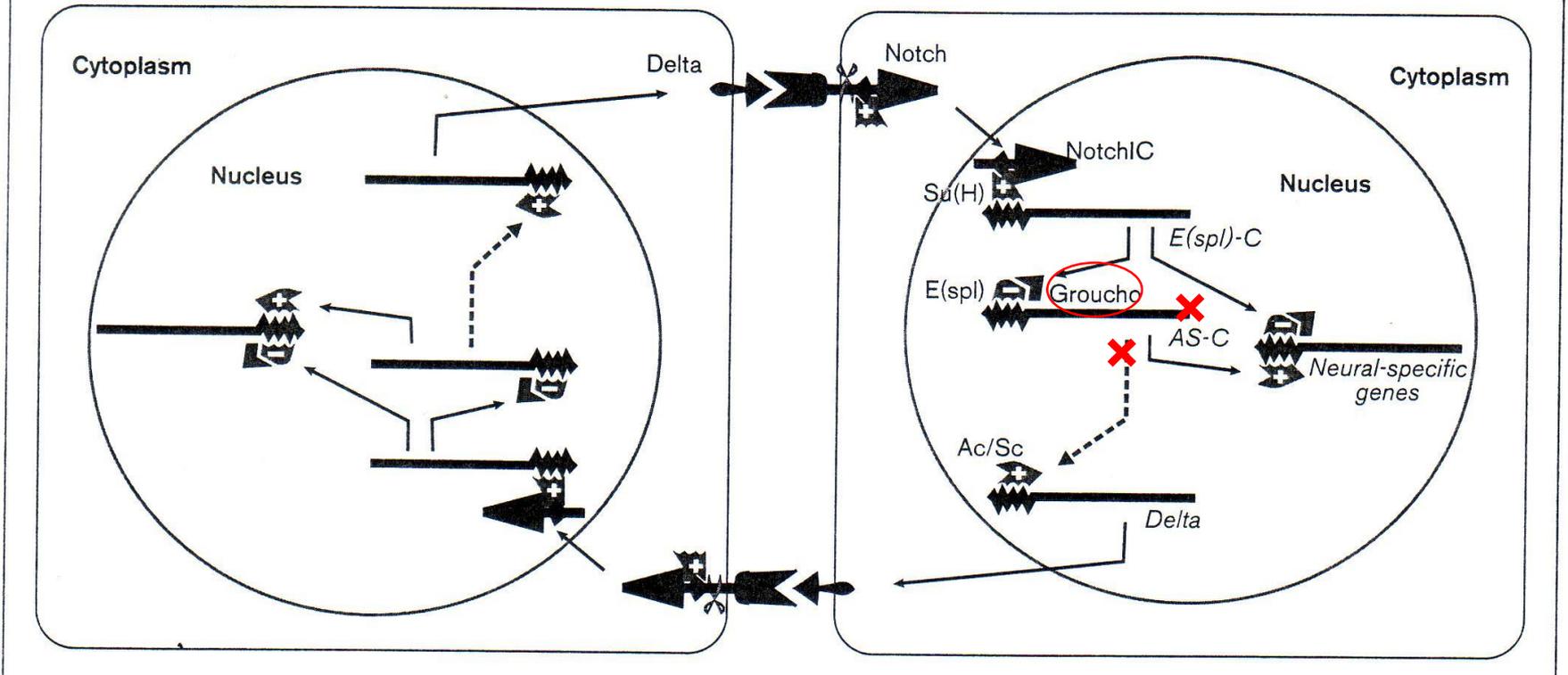
# L'interazione Delta-Notch



# Meccanismo di inibizione laterale



### Delta-Notch signalling between adjacent proneural cells

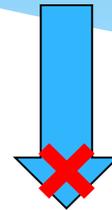


E (spl) è un fattore bHLH che è in grado di funzionare come omodimero.  
Funziona da repressore genico reclutando il co-repressore Groucho

Notch

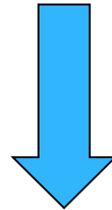


Enhancer of split (E/spl)



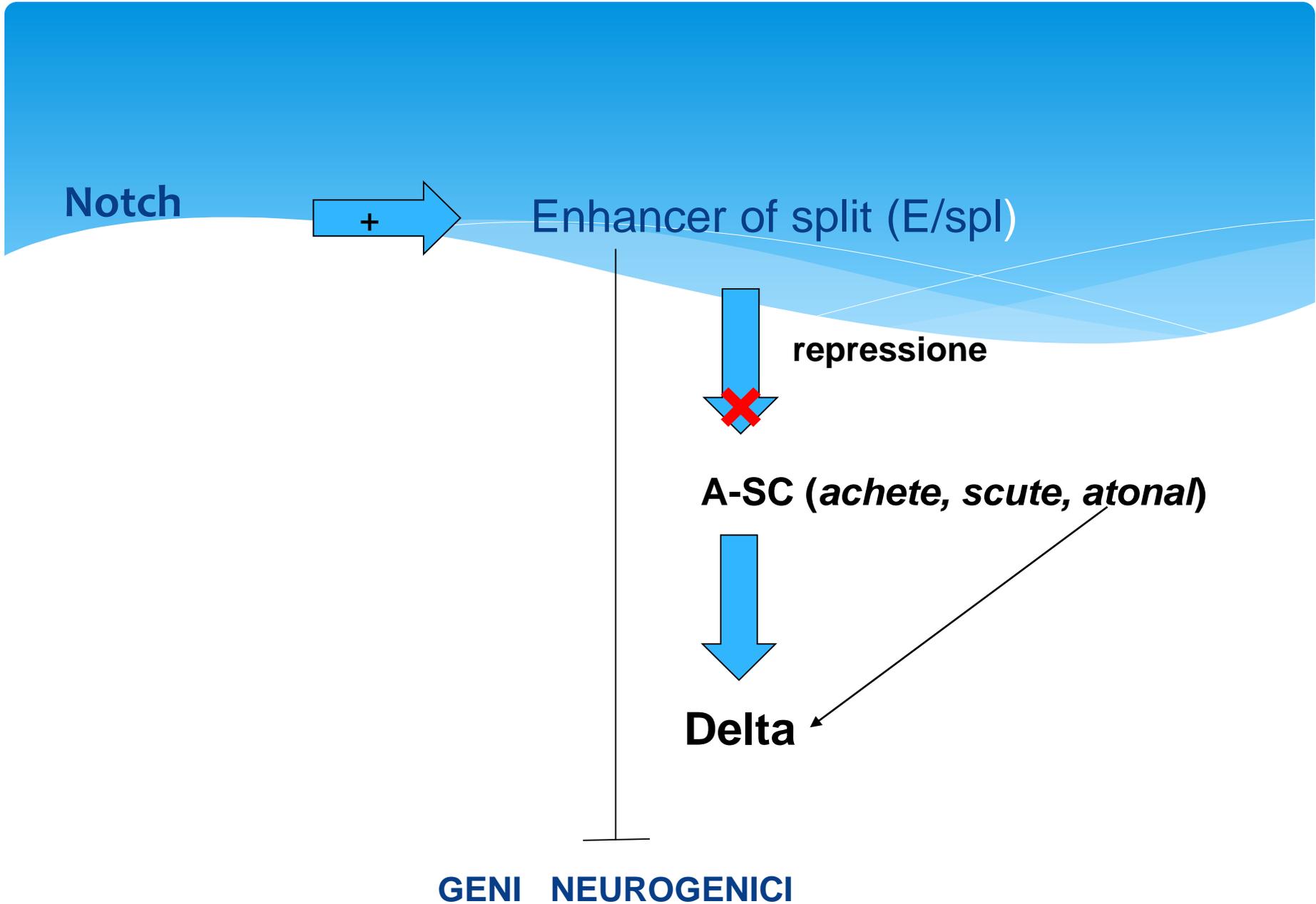
repressione

**A-SC** (*achete, scute, atonal*)

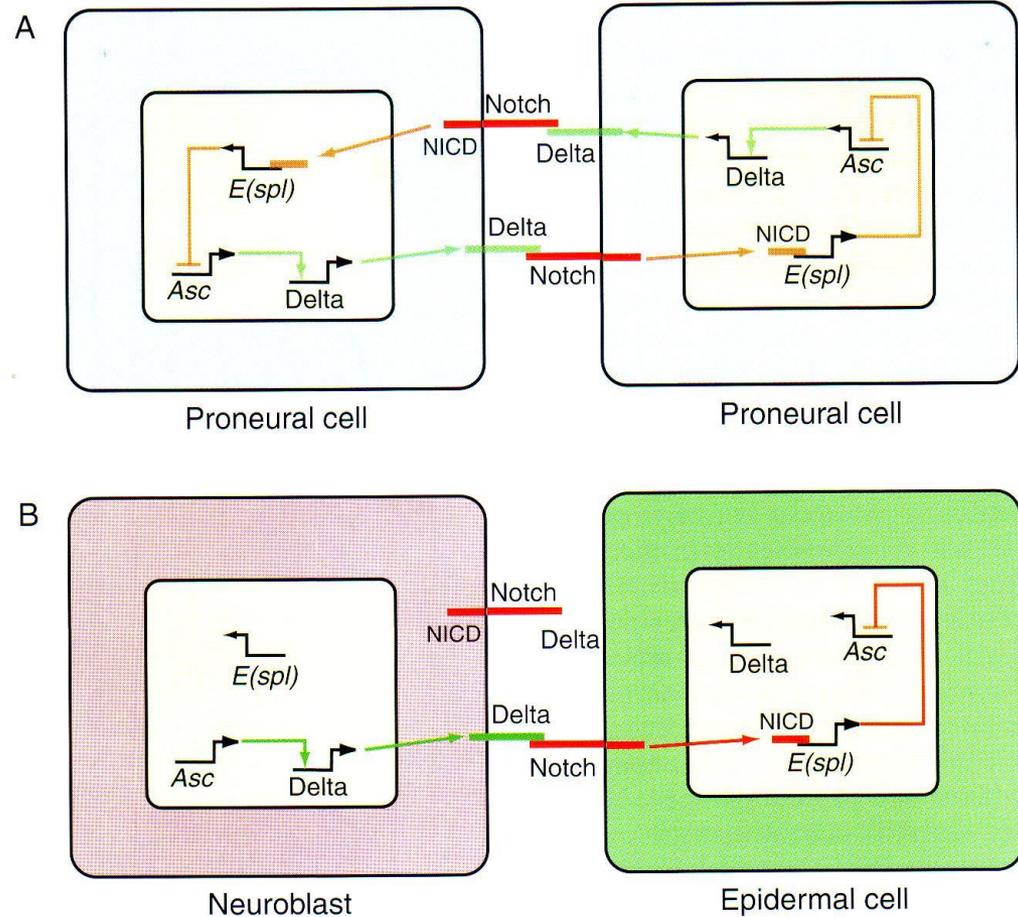
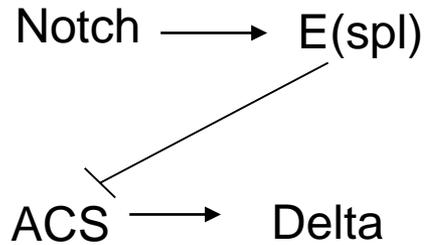
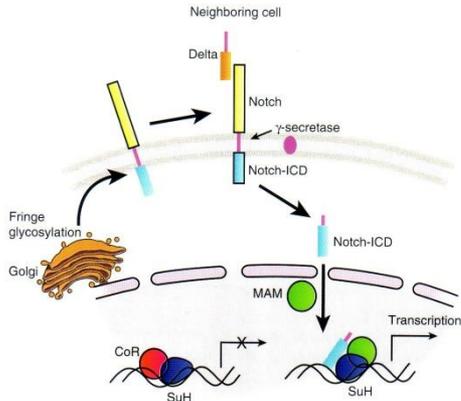


**Delta**

**GENI NEUROGENICI**

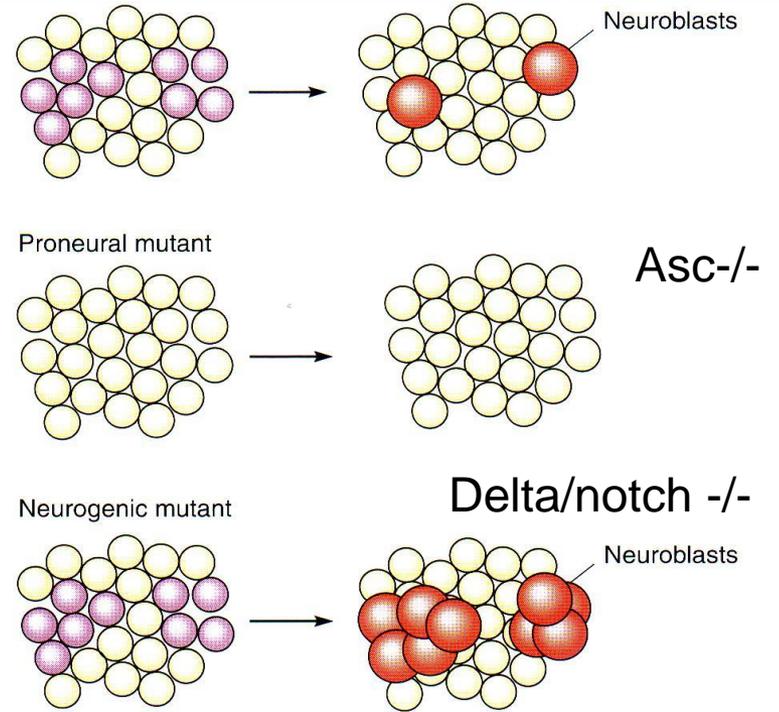
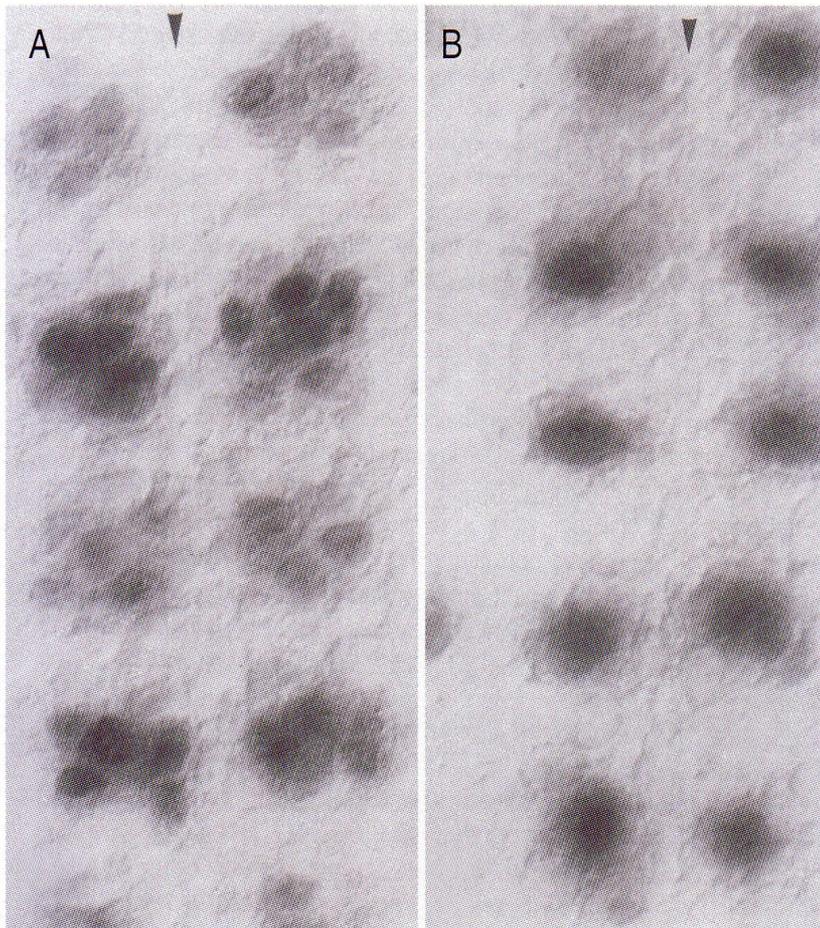


# Meccanismo di inibizione laterale



# Clusters pro-neurali

# Neuroblasti

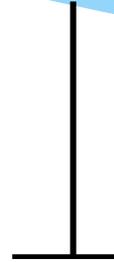


**Fig. 1.24** Neurogenic genes and proneural genes were first identified in the *Drosophila* due to their effects on neural development. In the wild type

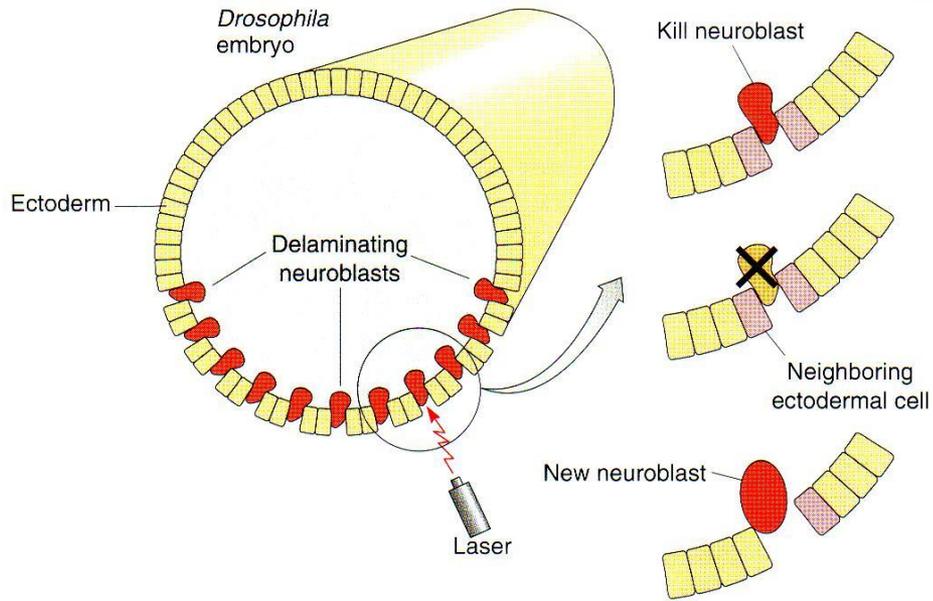
**Notch**



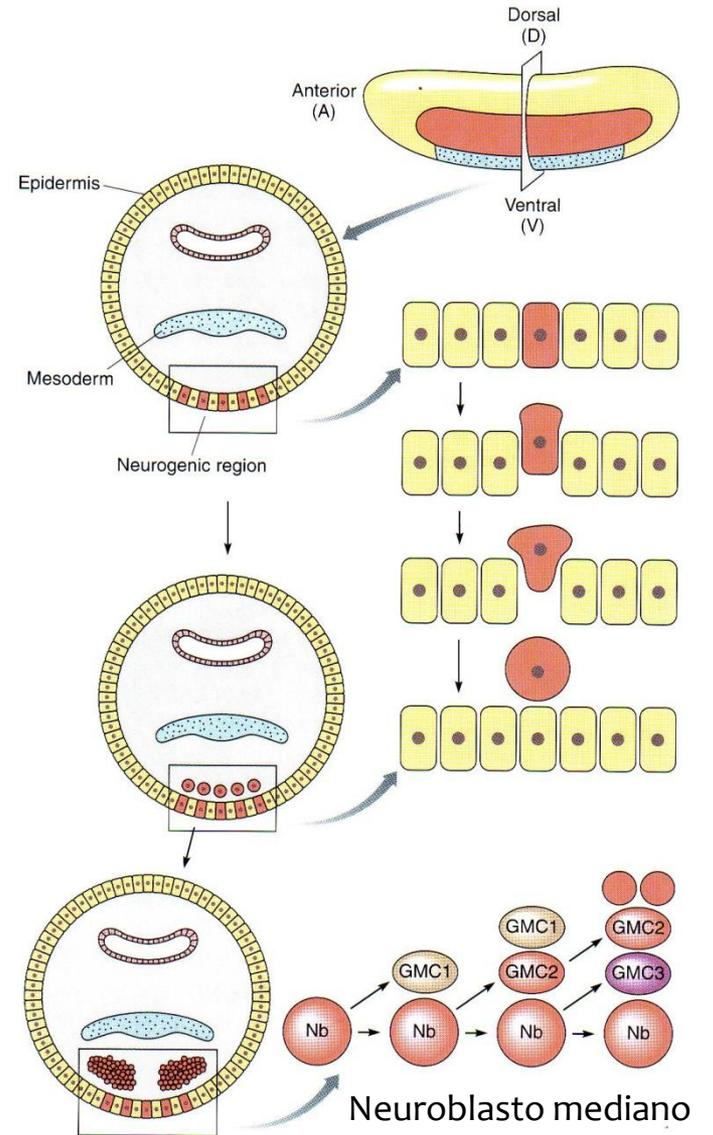
**Enhancer of split (E/spl)**



**GENI NEUROGENICI**



**Fig. 1.26** Ablation of the delaminating neuroblast with a laser microbeam directed to the ventral neurogenic region of the fly embryo causes a neighbor-



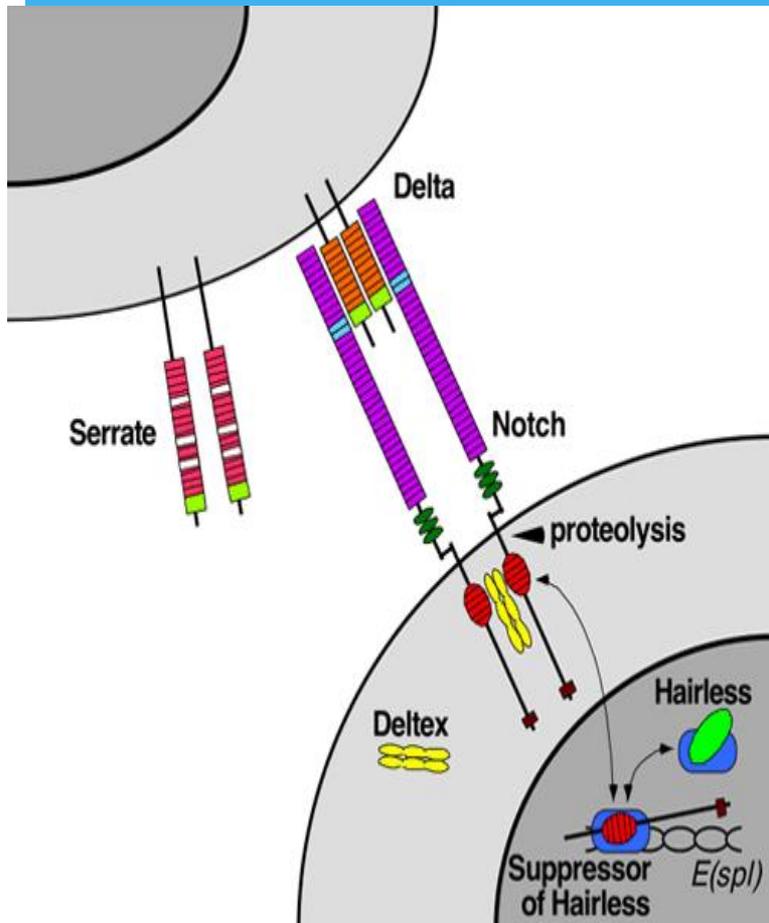


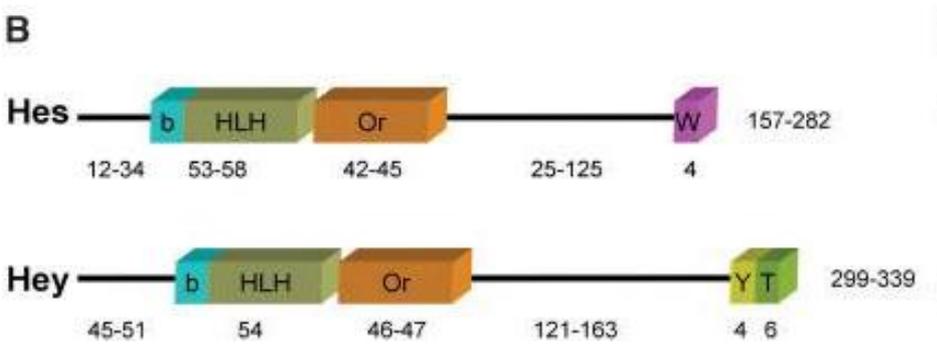
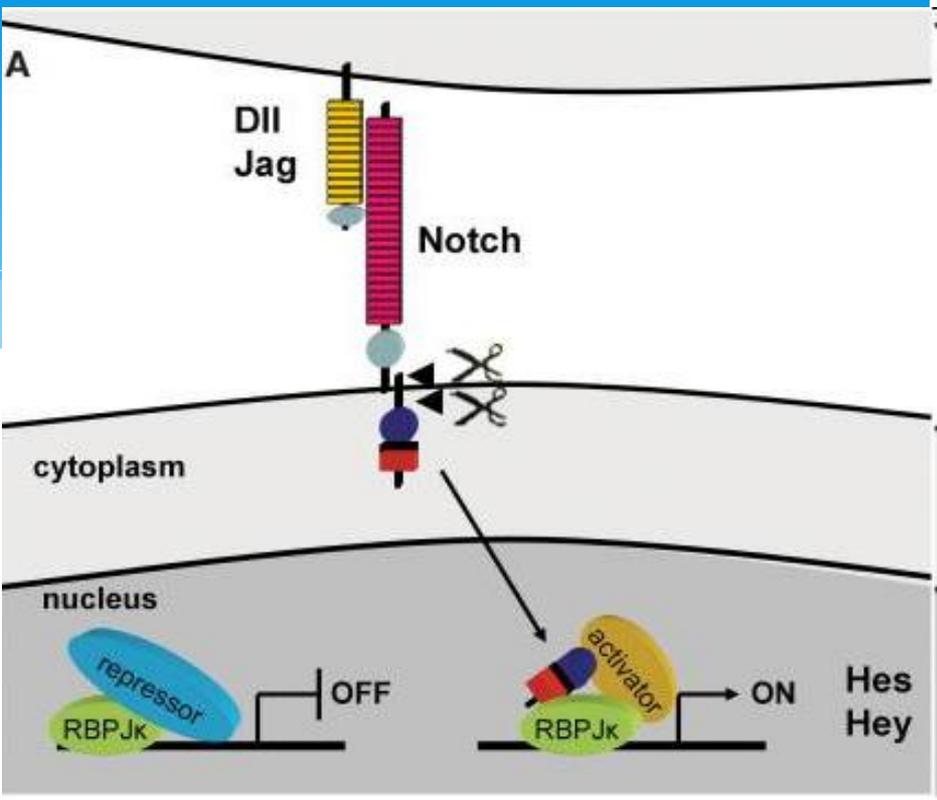
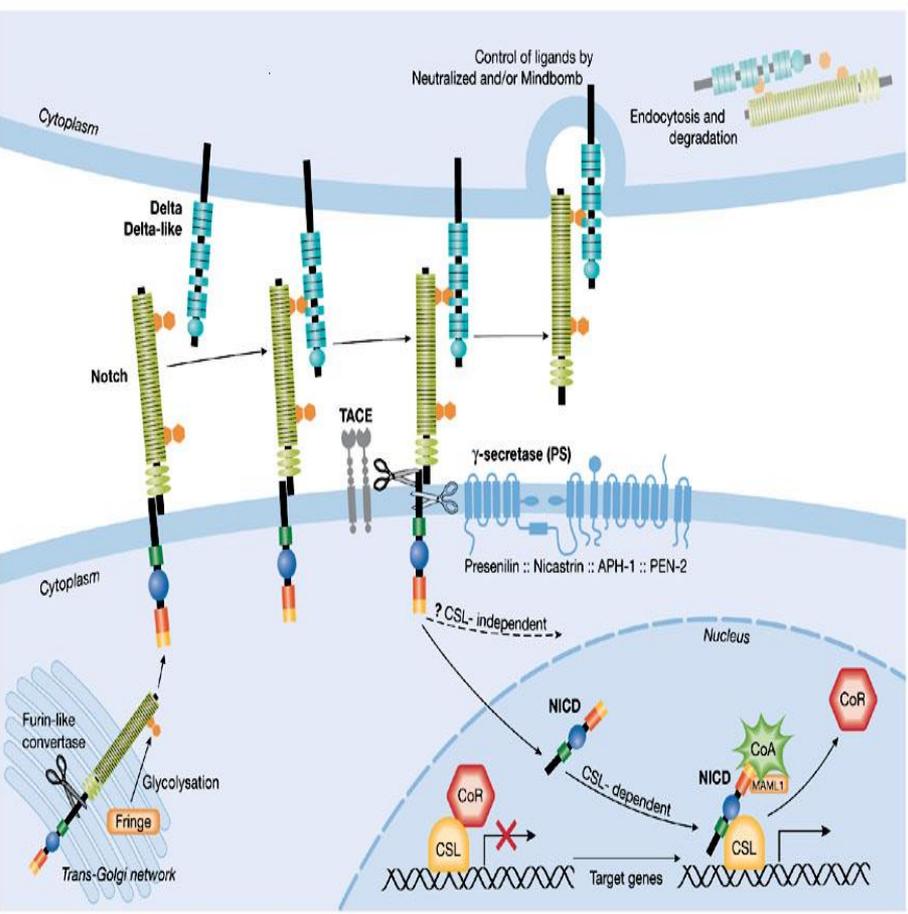
L'interferenza delle via TgfB è comune in  
anfibia e insetto

Il sistema Delta-Notch è presente nel vertebrato????

# Ligandi di Notch

1. Delta
2. Serrate (omologo di Delta)
3. Nel vertebrato Delta-1 e Jagged (omologo di Serrate, espresso in aree ristrette della zona ventricolare)





# HES Family: gli omologhi di E(spl)

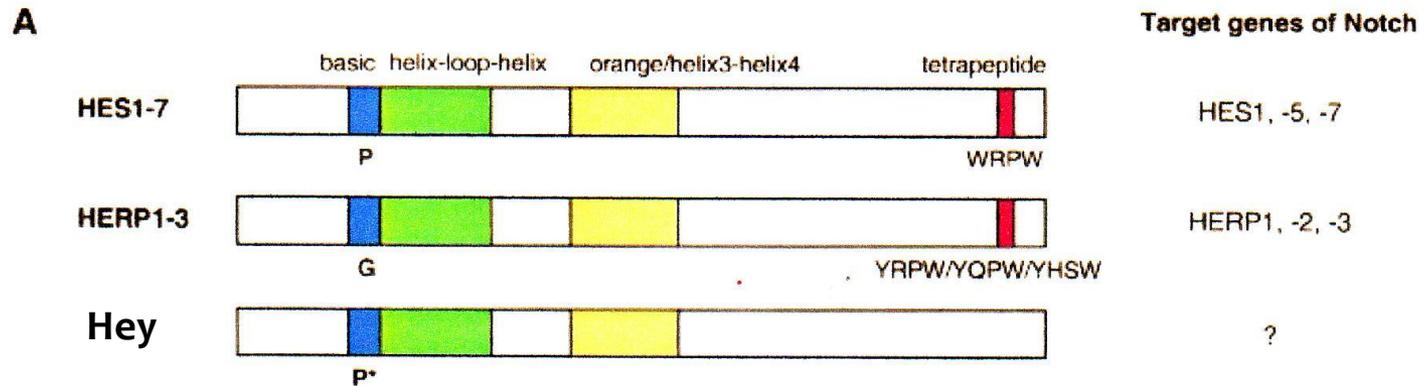
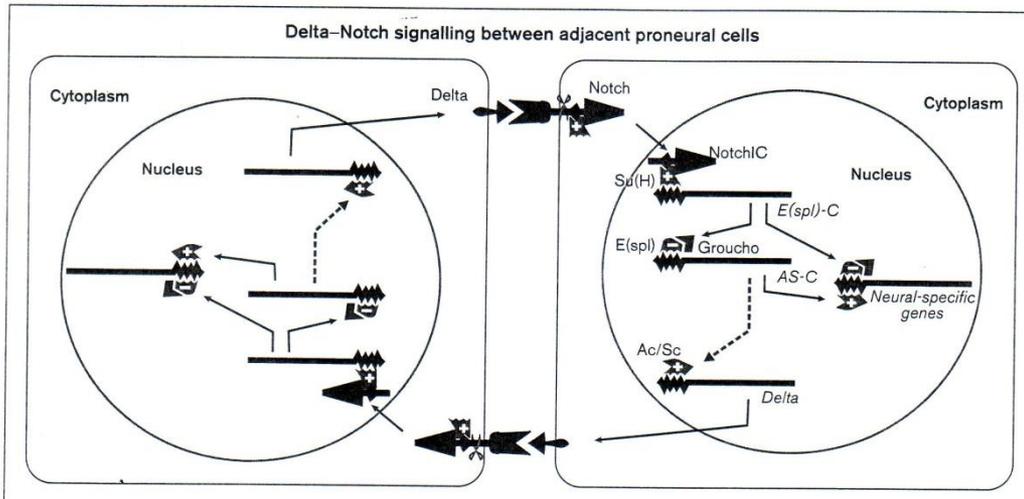


TABLE 2B. Consensus binding site **HLH transcription factors**

Classification		Consensus	Examples
Class A	Attivatori	CANCTG	CACCTG, CAGCTG
Class B		CANGTG	CACGTG, CATGTG
Class C	Repressori	CACGNG	CACGCG, CACGAG
E box		CANNTG	CACCTG, CAGCTG, CACGTG, CATGTG
N box		CACNAG	CACGAG, CACAAG

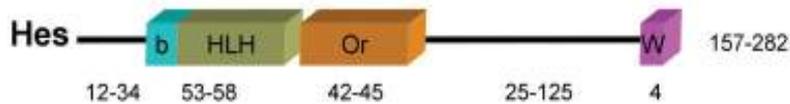
Class A and B are subtypes of E box. Class C and N box are mutually overlapping.

HLH di classe C (repressori trascrizionali) Comprende geni HES, HERP e Hey



## Meccanismi di repressione genica

HLH funzionano come dimeri

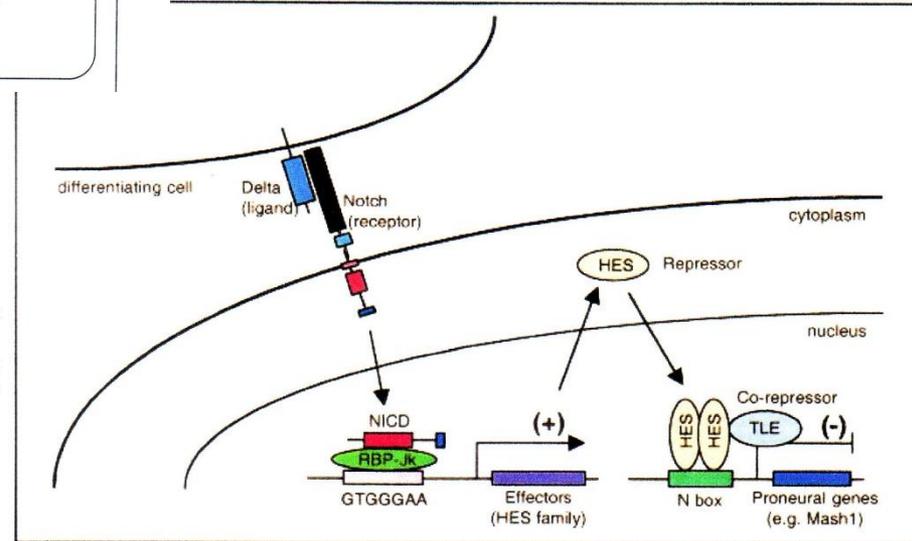


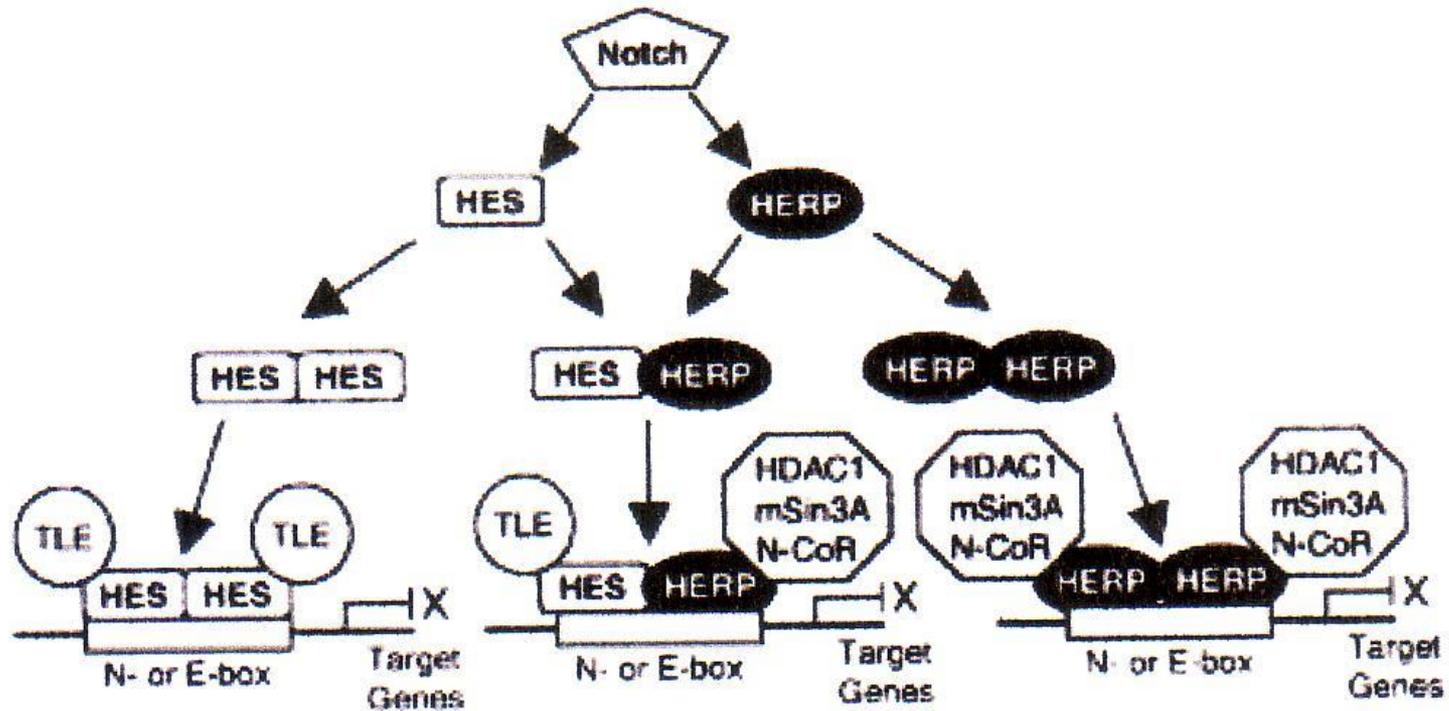
1. Hes può omodimerizzare

Recluta un omologo di Groucho (un co-repressore che viene reclutato da E (spl) ) che a sua volta recluta una istone deacetilasi

2. Repressione passiva: E(spl) eterodimerizza con E47 (bHLH) sottraendolo all'interazione con geni neurogenici

3. Dominio orange recluta un co-repressore diverso da Groucho





I geni Hes e Herp possono omodimerizzare o eterodimerizzare



Modificazione epigenetica del DNA

Phenotypes of *Hes* or *Hey* gene deficient mice

	Notch regulated	Mouse knockout phenotype	References
Hes1	Yes	Neurulation defects, premature differentiation of neural progenitor cells Eye and inner ear defects Pancreas defects and defective endocrine differentiation Disturbed T-cell differentiation, lack of thymus	(120–122) (123–125) (126) (127)
Hes3	No	Viable, fertile	(128)
Hes5	Yes	Viable, fertile Eye and inner ear defects Elevated myelin levels in central nervous system	(35,121) (129,104) (117)
Hes6	No	Viable, fertile	(24)
Hes7	Yes	Somitogenesis defects	(108)
Hes1/5		Enhancement of Hes1 <sup>-/-</sup> phenotype Defects in cranial and spinal nerves	(35,121,125,130) (131)
Hes1/3		Missing midbrain and anterior hindbrain due to premature neuronal differentiation	(128)
Hes1/3/5		More severe than Hes1/5 loss	(125)
Hey1	Yes	Viable, fertile	(132,133)
Hey2	Yes	Congenital heart defects Decreased arterial neointima formation	(134–138) (87)
HeyL	Yes	Viable, fertile	(47)
Hey1/2		Angiogenesis and arterial differentiation defects	(132,133)
Hey1/L		Congenital heart defects	(47)

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1. Aumentata espressione di Hes-1 inibisce la formazione di neuroblasti

2. KO Hes-1 si formano neuroni prematuri (anticipo del processo maturativo)