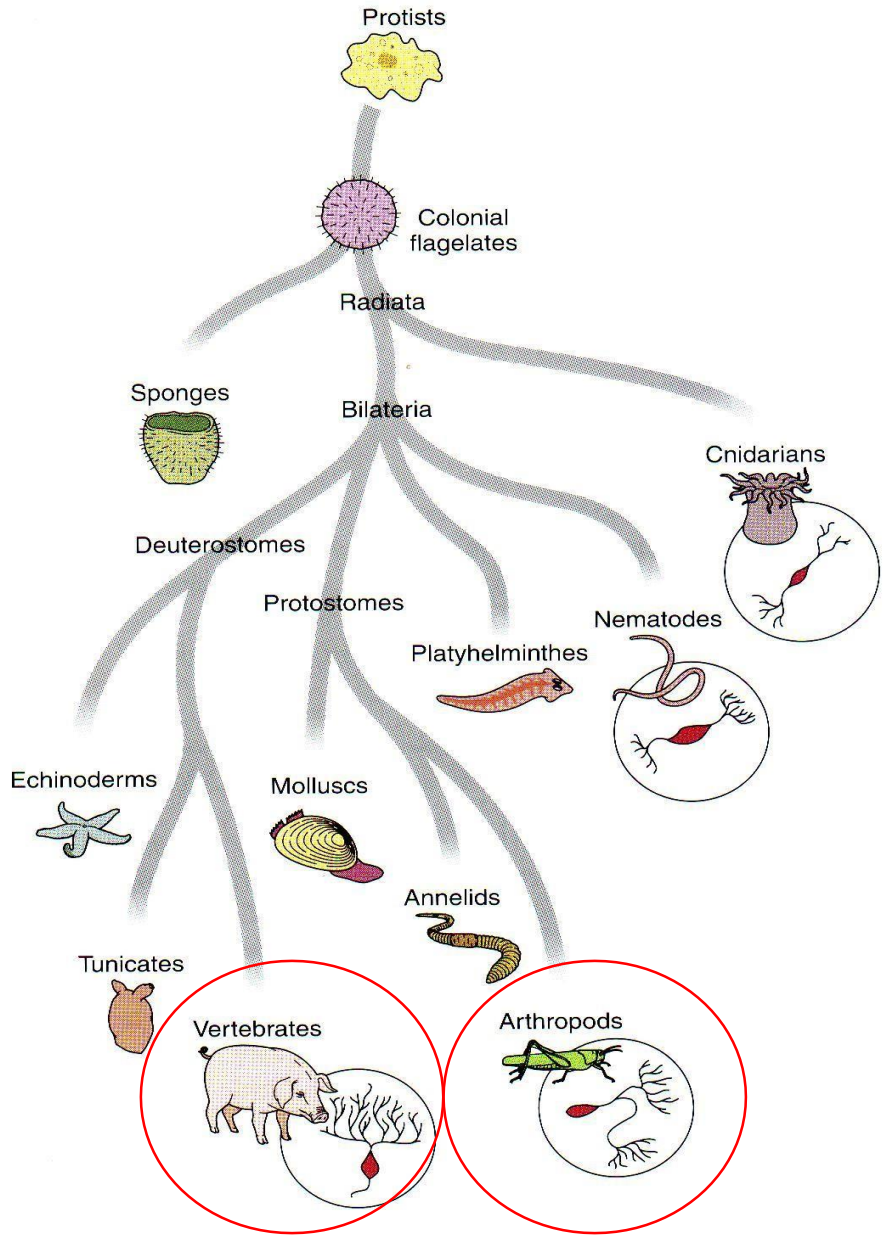
Specificazione del sistema nervoso nei Vertebrati



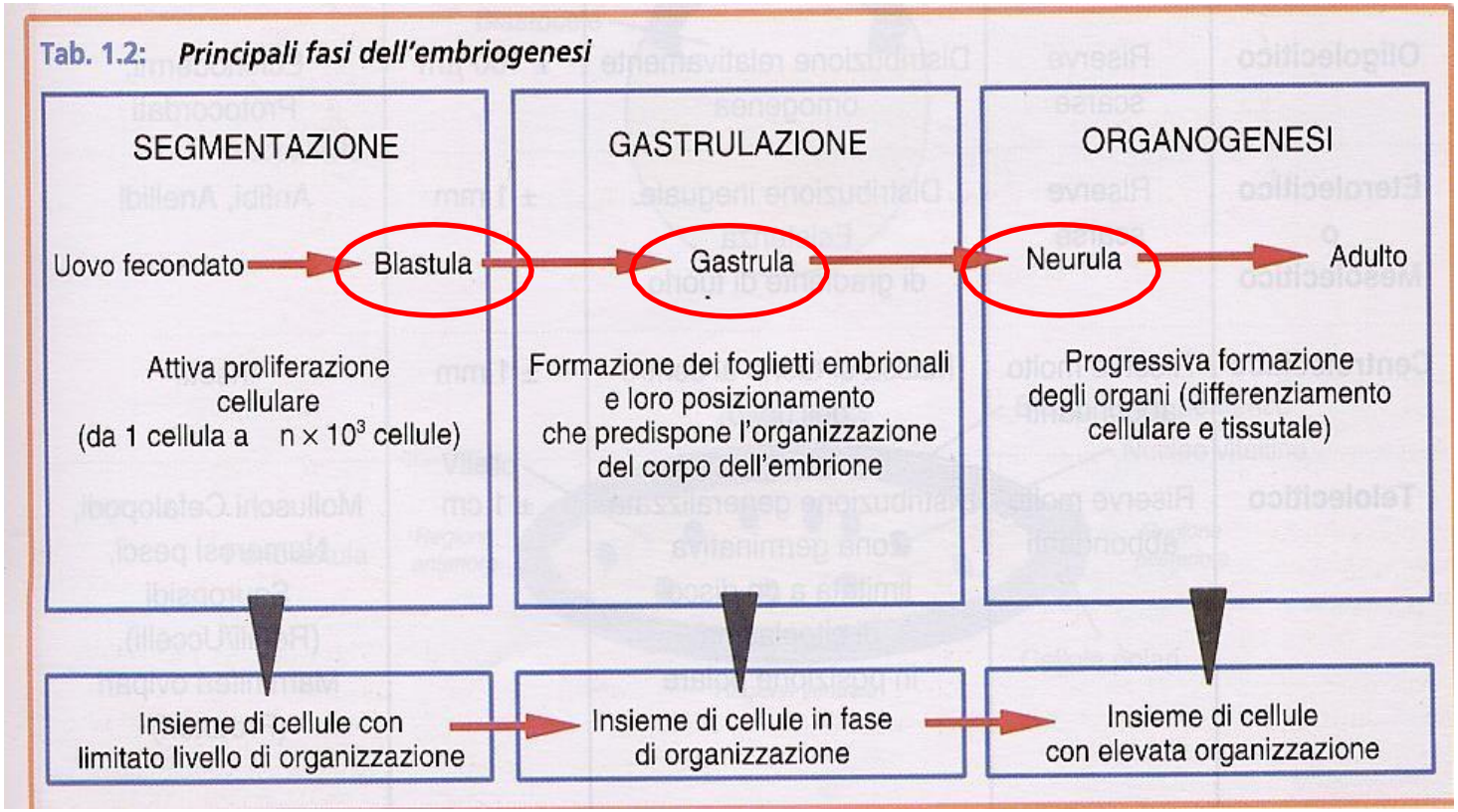
- Tutti gli organismi pluricellulari possiedono neuroni riconoscibili con lunghi processi e con attività elettrica simile

- Già dagli Cnidari è possibile trovare connessioni sinaptiche

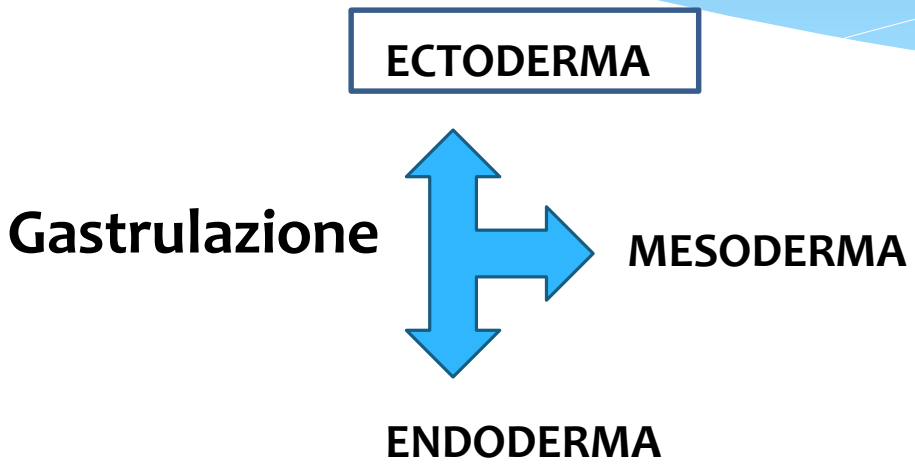
- Molti dei segnali molecolari che contribuiscono alla fisiologia e allo sviluppo del sistema nervoso sono conservati durante l'evoluzione.

Qualche breve cenno di embriologia

Embriologia dei Vertebrati



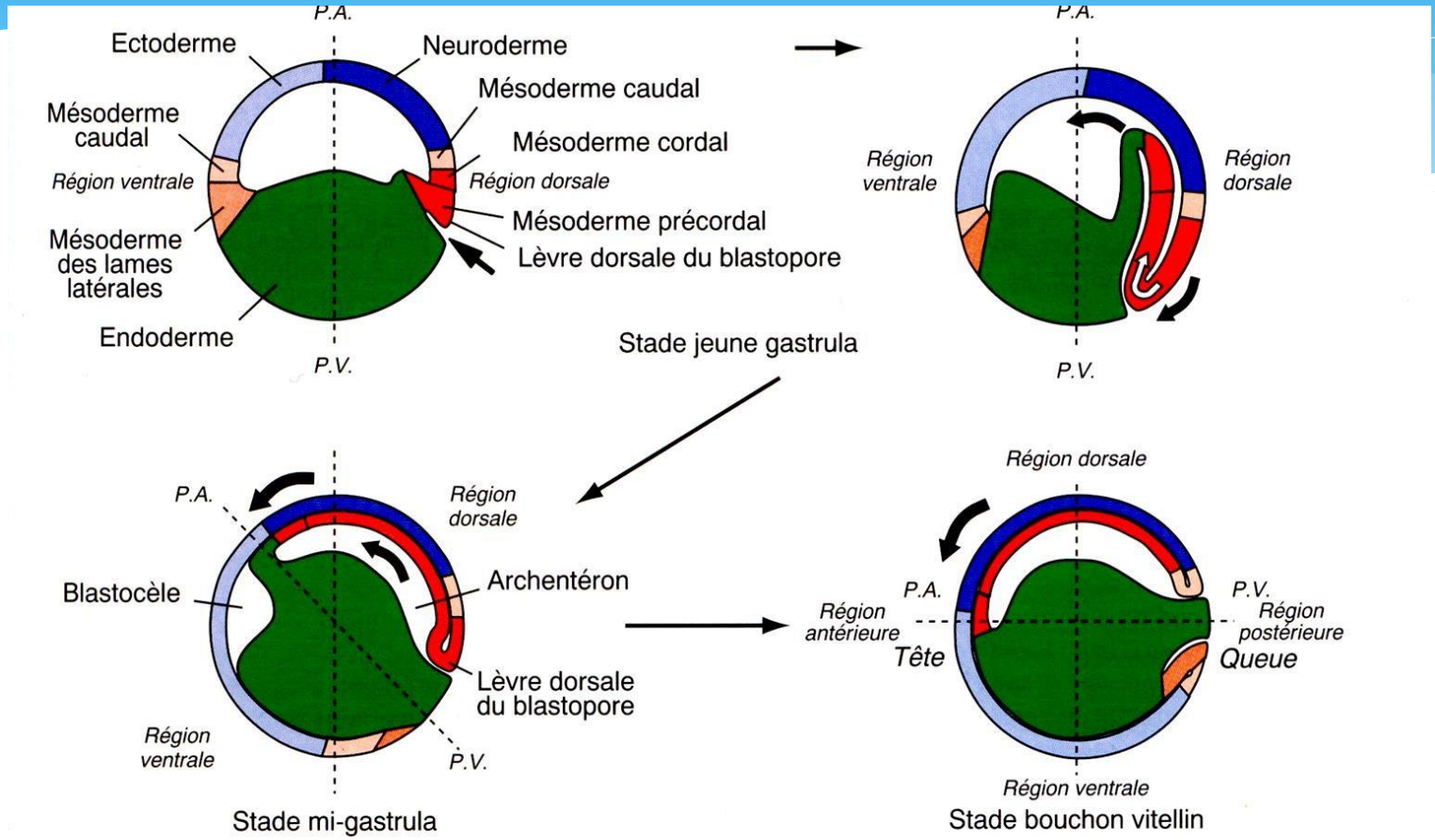
I Foglietti embrionali

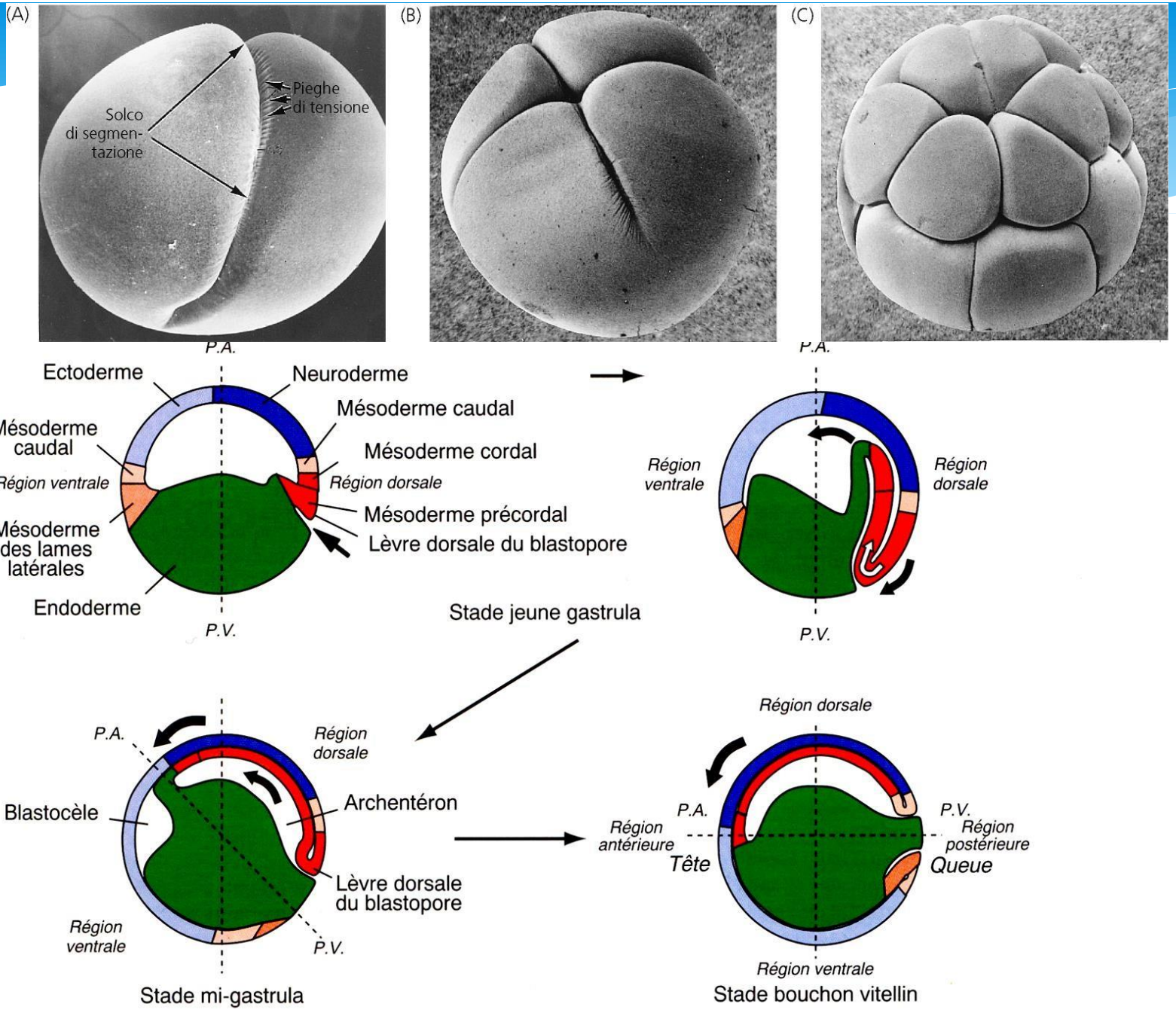


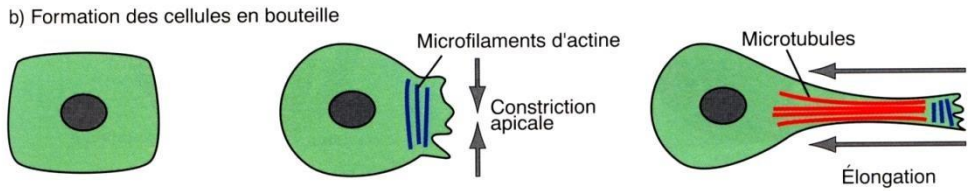
Organogenesi → **Sviluppo degli organi**

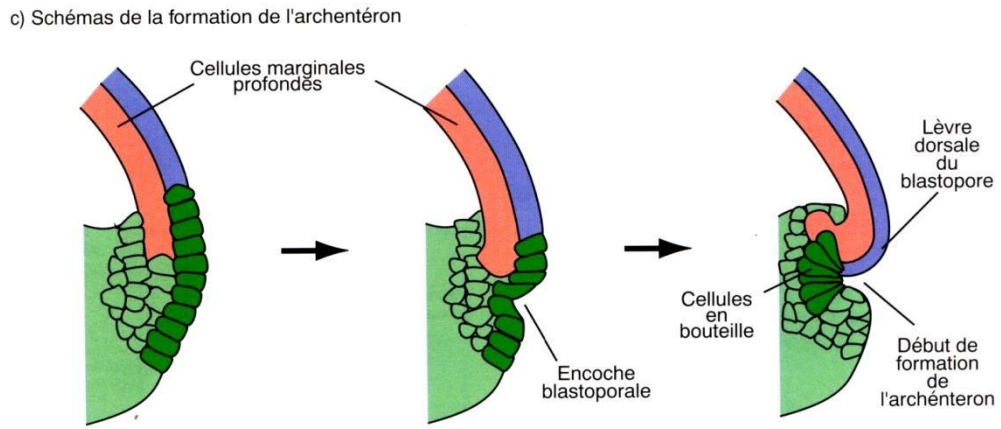
Neurulazione: Processo che favorisce l'iniziale sviluppo del sistema nervoso nei vertebrati

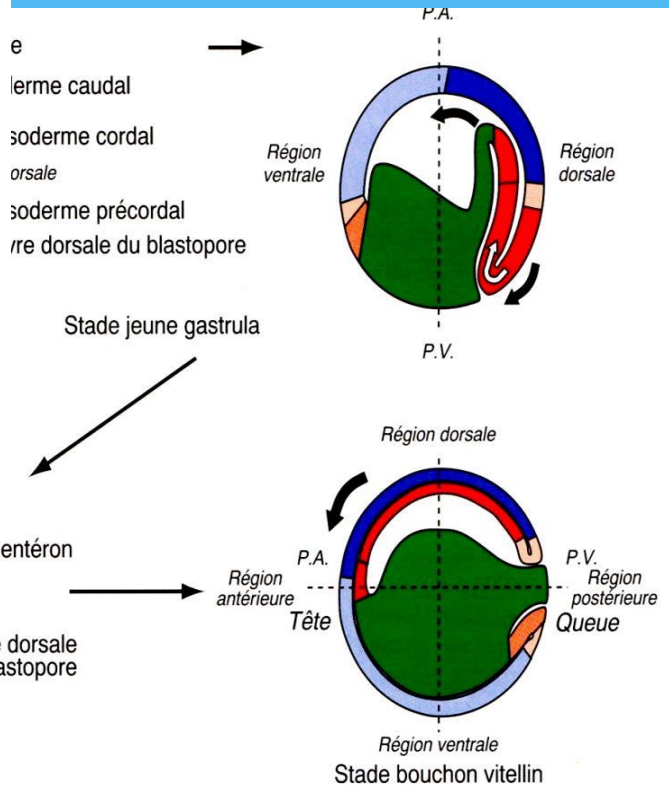
La mappa dei territori presuntivi ci indica il territorio presuntivo del sistema nervoso



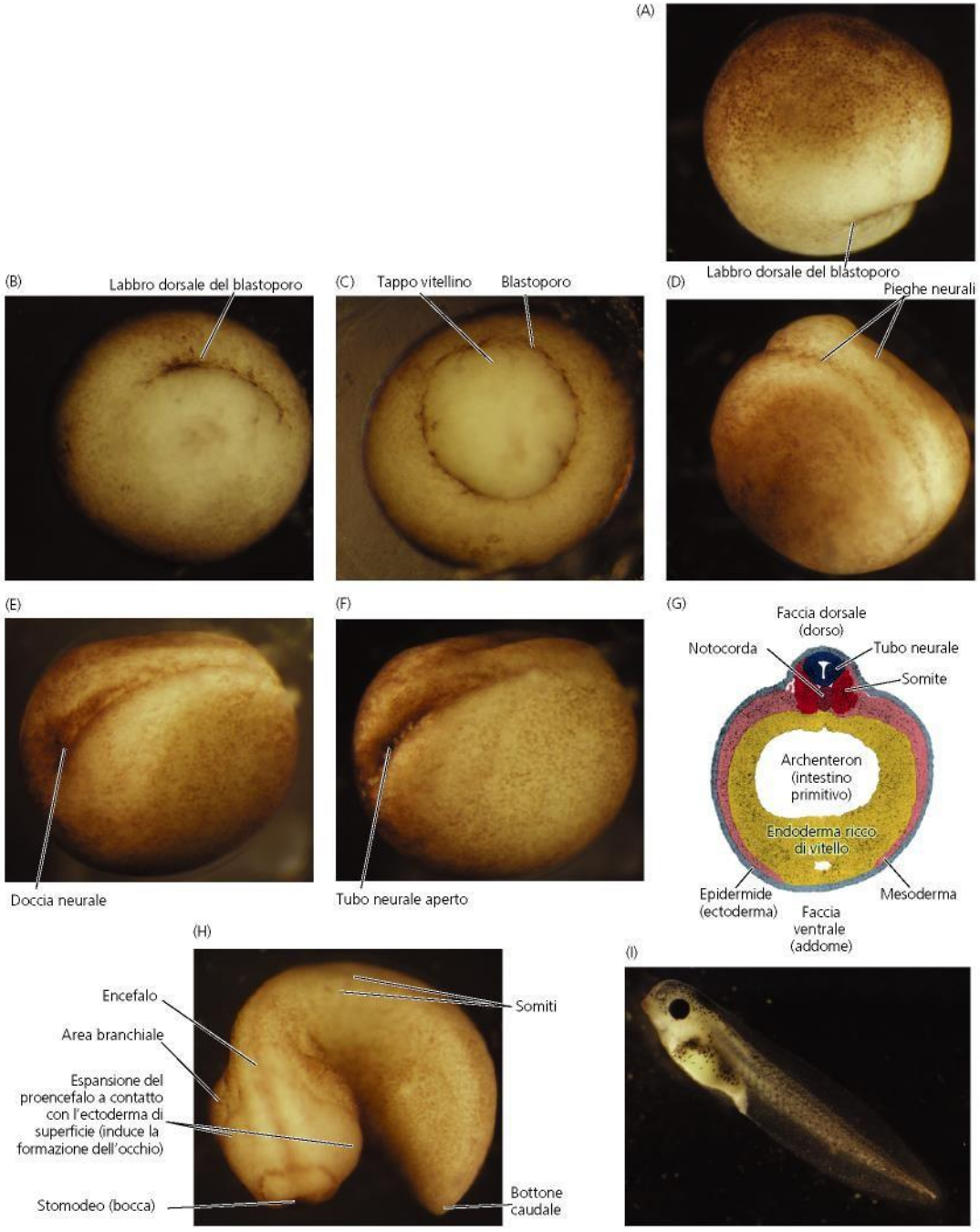

(A)
Solco di segmen-tazione
Pieghe di tensione
(B)
(C)
P.A.
Ectoderme
Neuroderme
Mésoderme caudal
Mésoderme caudal
Mésoderme cordal
Région ventrale
Région dorsale
Mésoderme précordal
Mésoderme des lames latérales
Lèvre dorsale du blastopore
Endoderme
P.V.
P.A.
Région ventrale
Région dorsale
P.V.
Stade jeune gastrula
P.A.
Région dorsale
Blastocèle
Archentéron
Lèvre dorsale du blastopore
Région ventrale
P.V.
Stade mi-gastrula
Région dorsale
P.A.
P.V.
Région antérieure
Région postérieure
Tête
Queue
Région ventrale
Stade bouchon vitellin





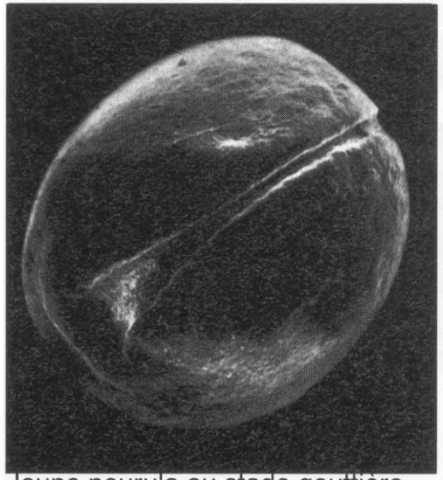


Involuzione del mesoderma al di sotto del neuroectoderma presuntivo

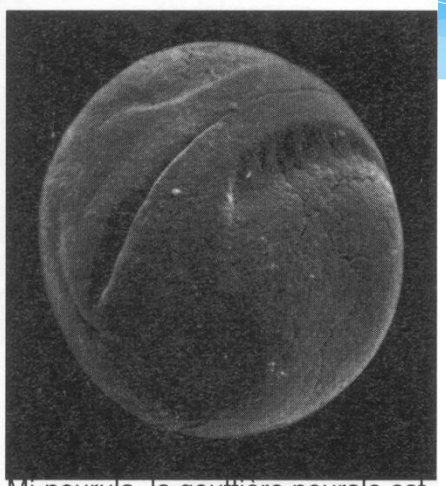


La neurulazione vista dall'esterno dell'embrione

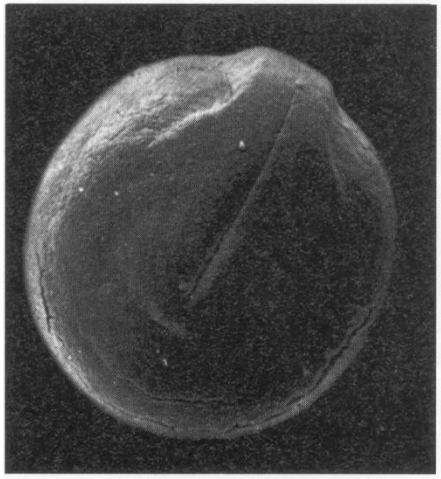
b) La neurulation, microphotographies d'embryons de xénope (les embryons sont dégangués et sans membrane de fécondation, x 50)



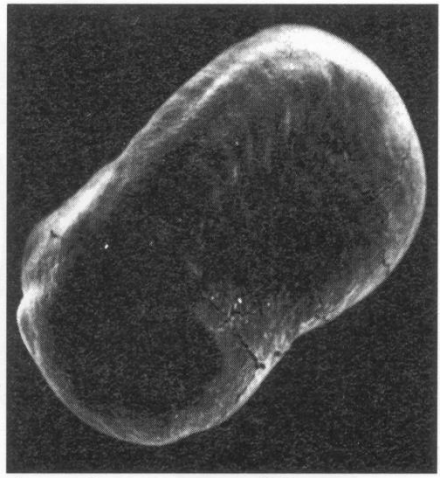
Jeune neurula au stade gouttière neurale



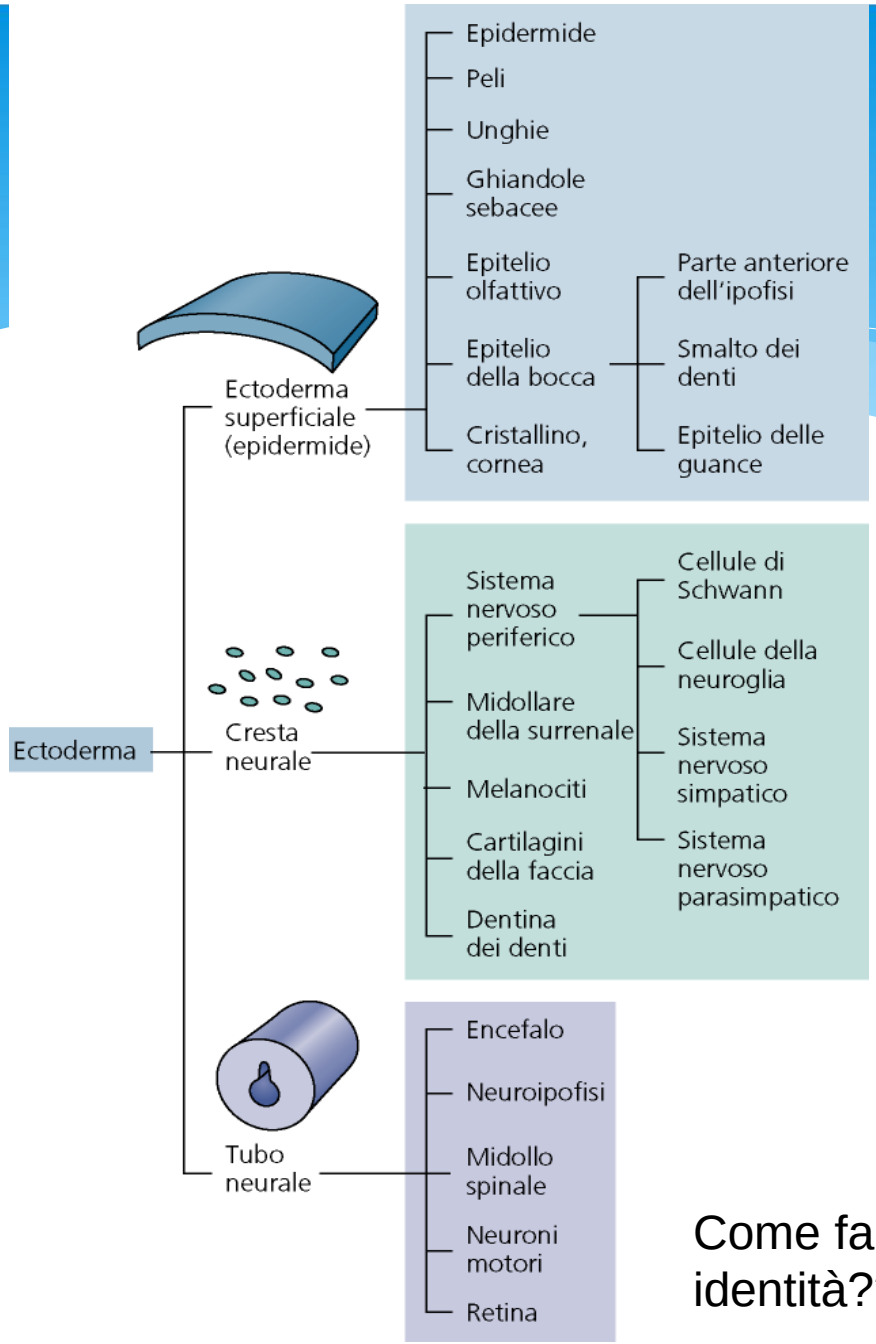
Mi-neurula, la gouttière neurale est fermée dans la région troncale

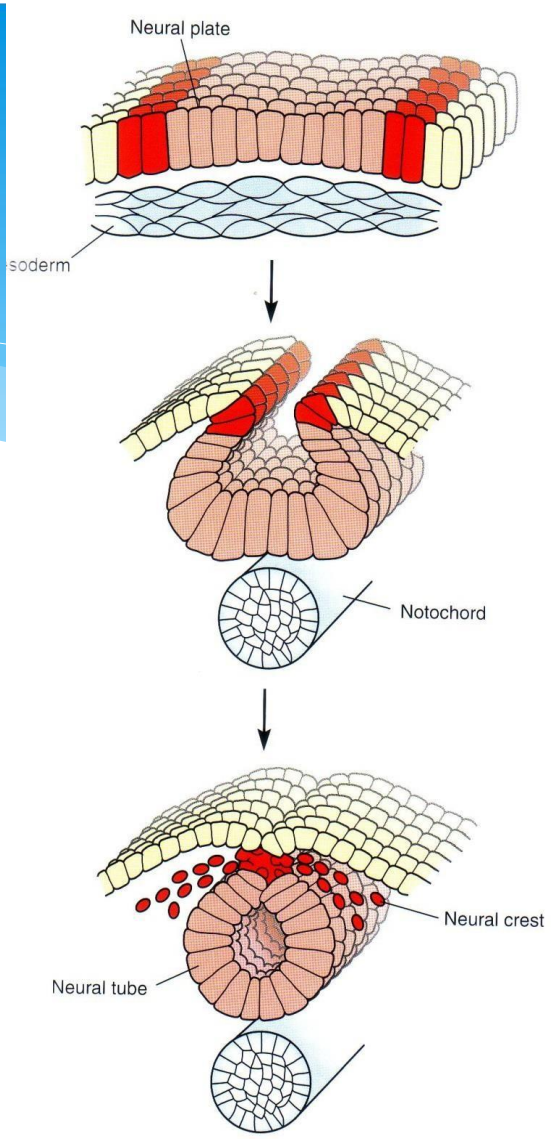


Neurula âgée



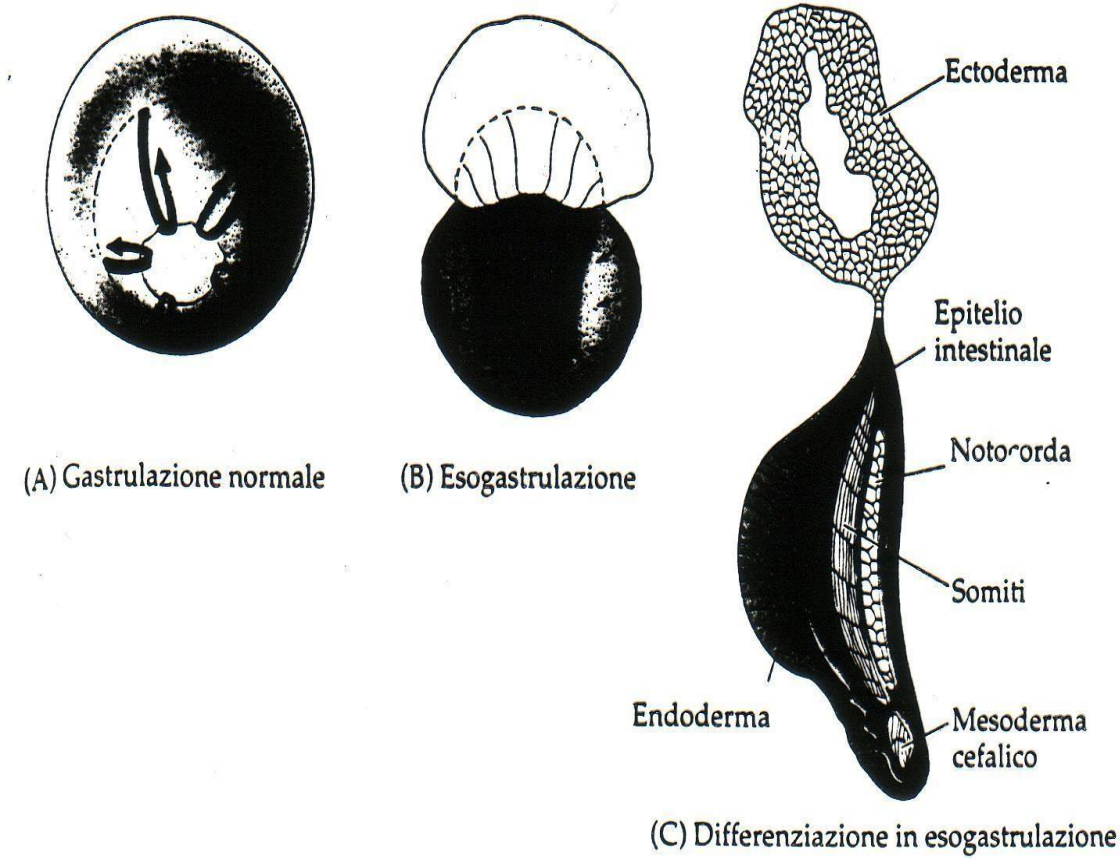
Jeune bourgeon caudal





Come fa il neuroectoderma ad acquisire questa identità???

Esogastrule di Holtfreter



(A) Gastrulazione normale

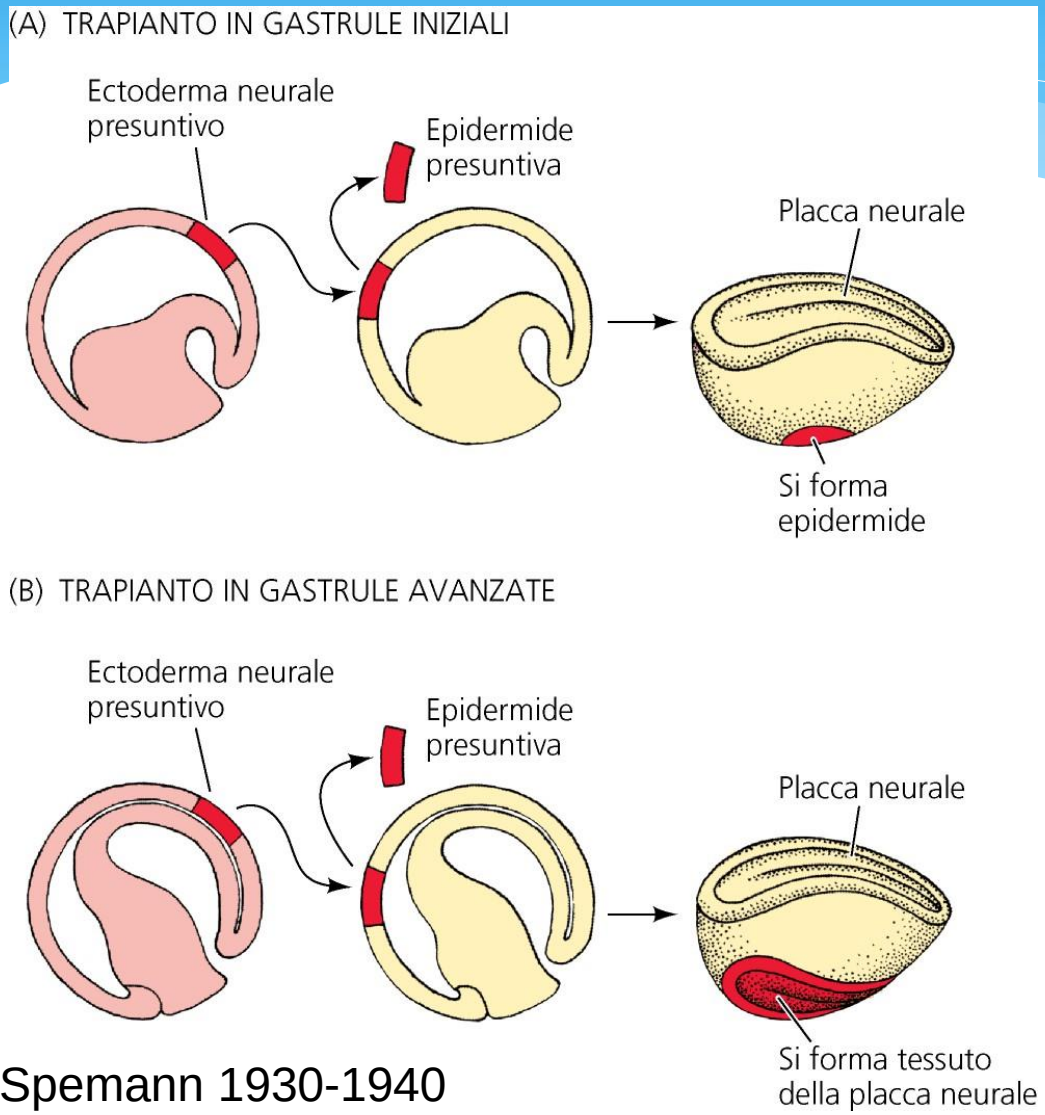
(B) Esogastrulazione

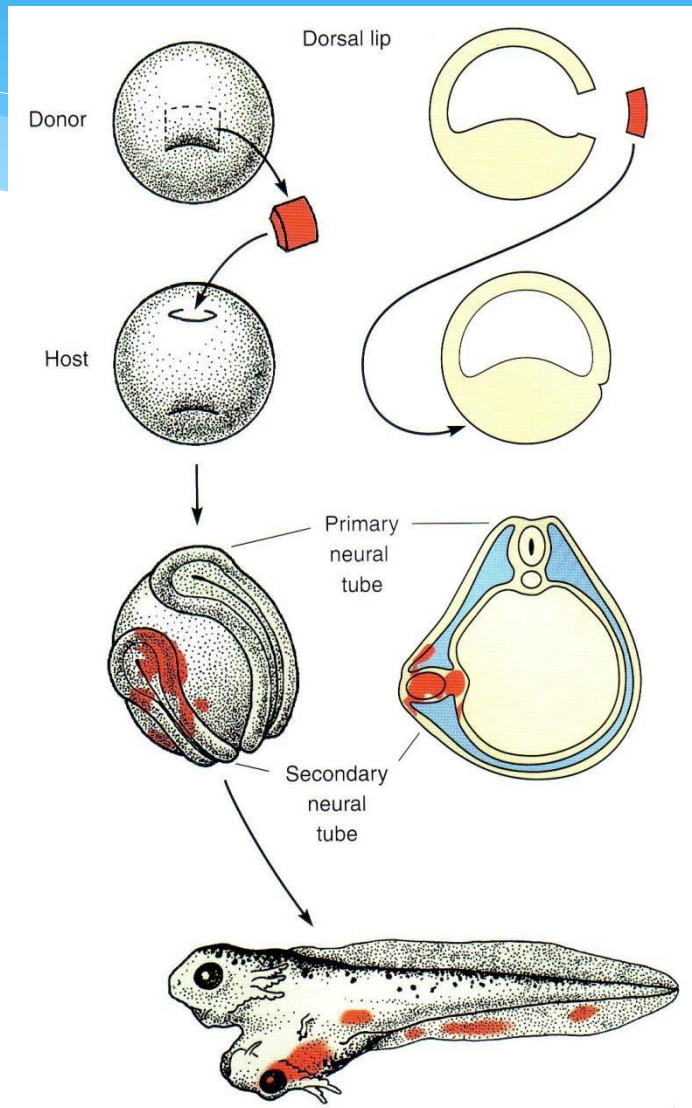
(C) Differenziazione in esogastrulazione

Figura 16.35
Esogastrulazione. (A) Nella gastrulazione normale, il mesoderma si involve sotto l'ectoderma. Tu[illegible]ia, quando l'embrione di anfibio viene posto in una soluzione salina ipertonica, il mesoderma subisce esogastrulazione (B), estroflettendendosi all'esterno dell'ectoderma, anziché involversi nell'embrione. (C) L'ectoderma in queste esogastrulazioni non forma tessuto neurale. (Da Holtfreter e Hamburger, 1955.)

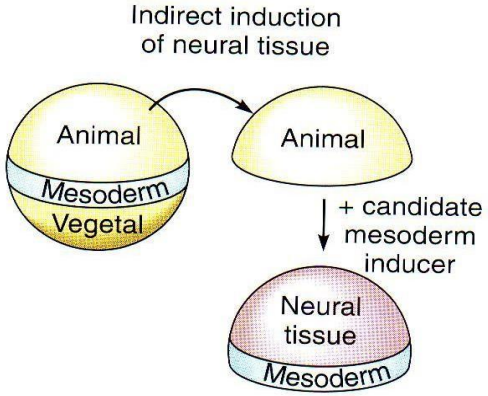
La mancata involuzione del mesoderma sotto il neuroectoderma determina l'assenza di sistema nervoso?

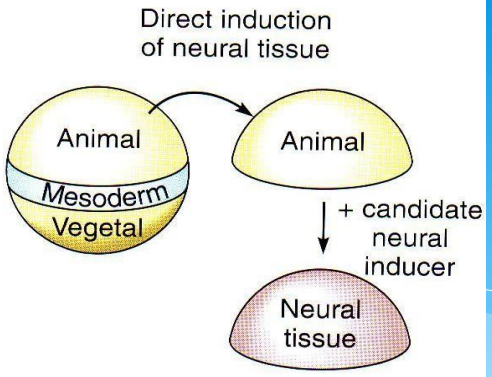
Quando viene specificato il neuroectoderma?





Spemann 1930-1940

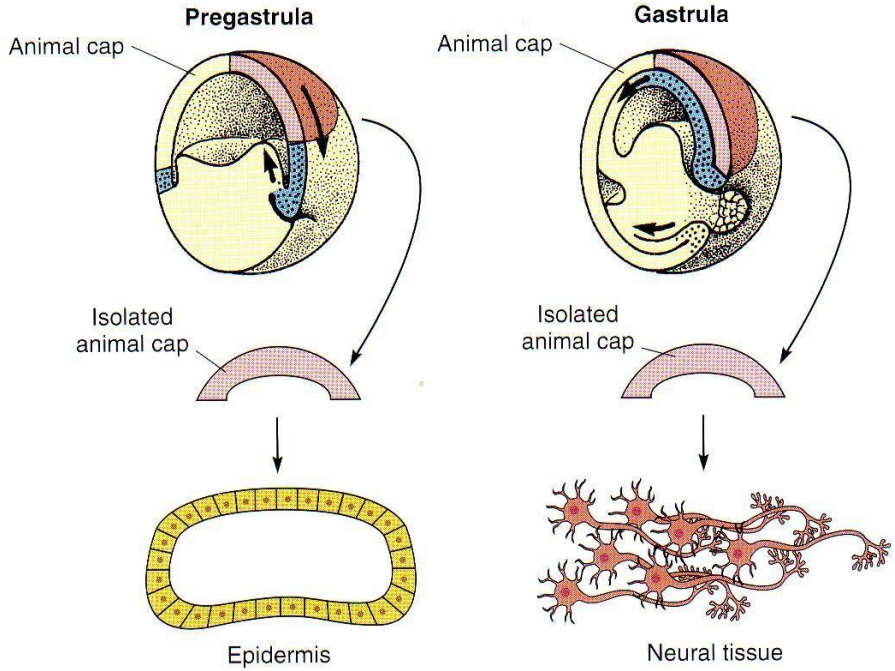




Fattori inducenti mesoderma

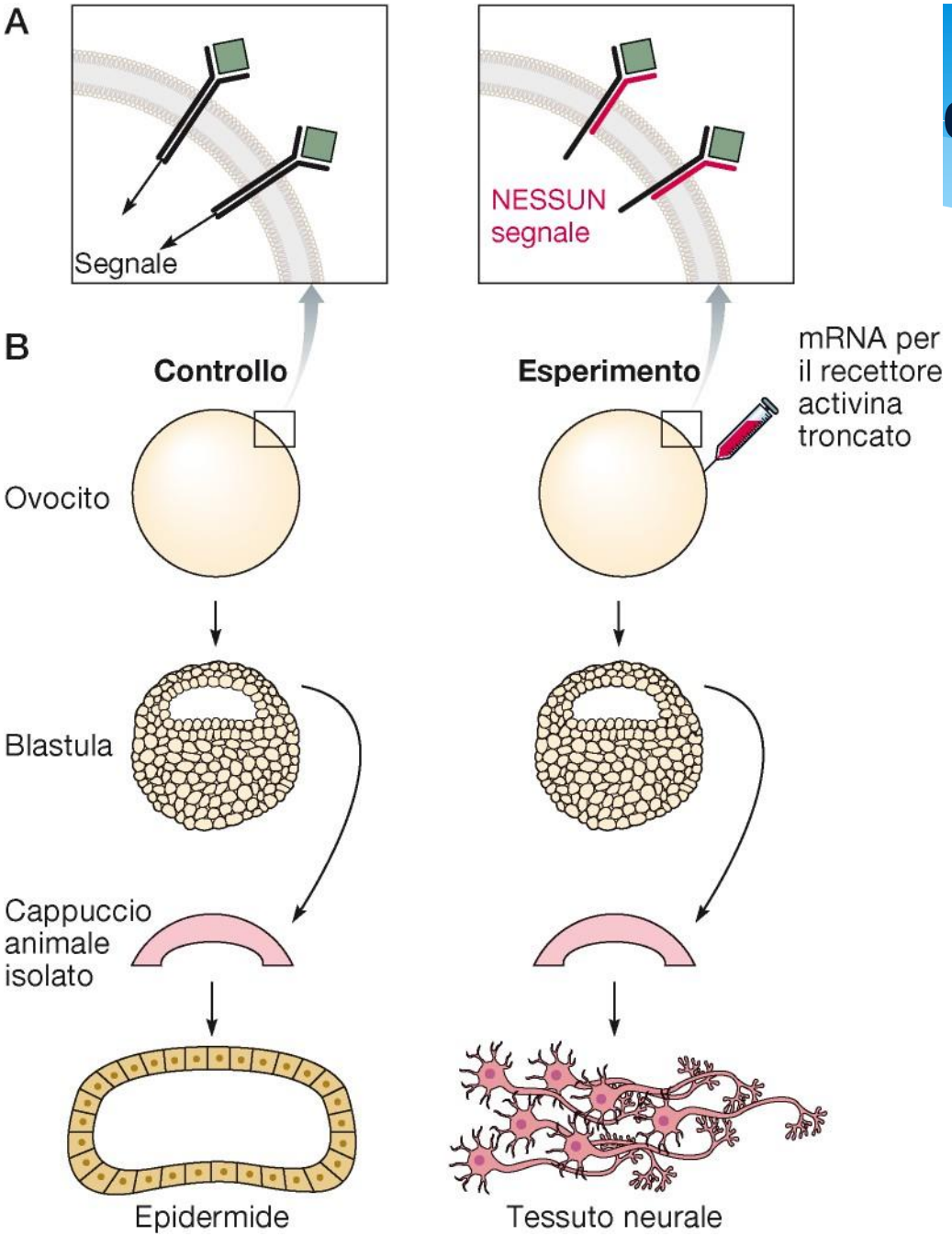
Fattori inducenti sistema nervoso

La specificazione del SN avviene durante la gastrulazione ???



Specificazione: iniziale acquisizione del destino maturativo. **Il processo è reversibile**

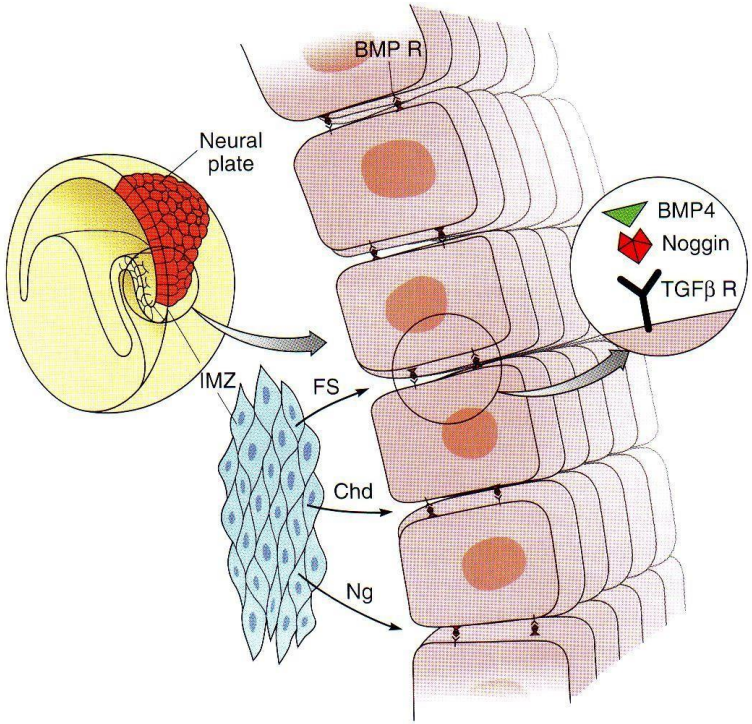
Determinazione del Neuroectoderma in Anfibi

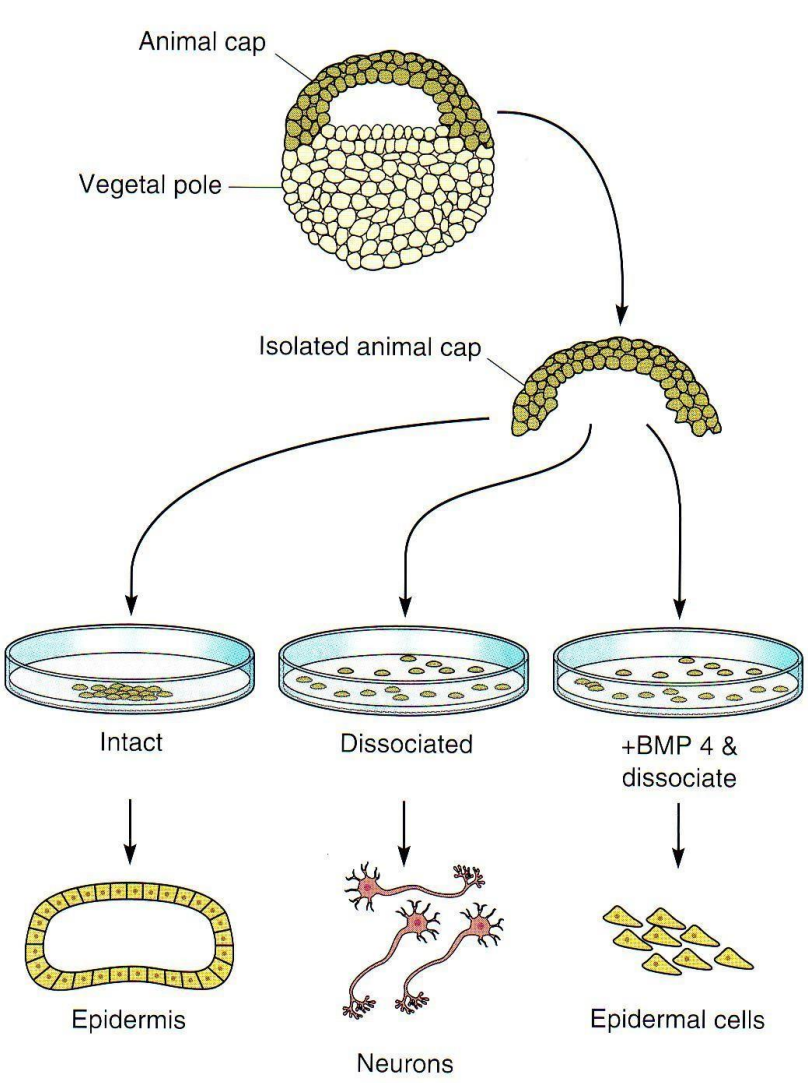


L'interferenza con la via di attivazione dell' activina, non consente la formazione del mesoderma, ma permette la formazione del sistema nervoso.

Fattori Tgf Beta hanno un effetto Inibitorio sulla formazione di SN

BMP 4 (TGF-beta factor)
Bone Morphogenetic Protein

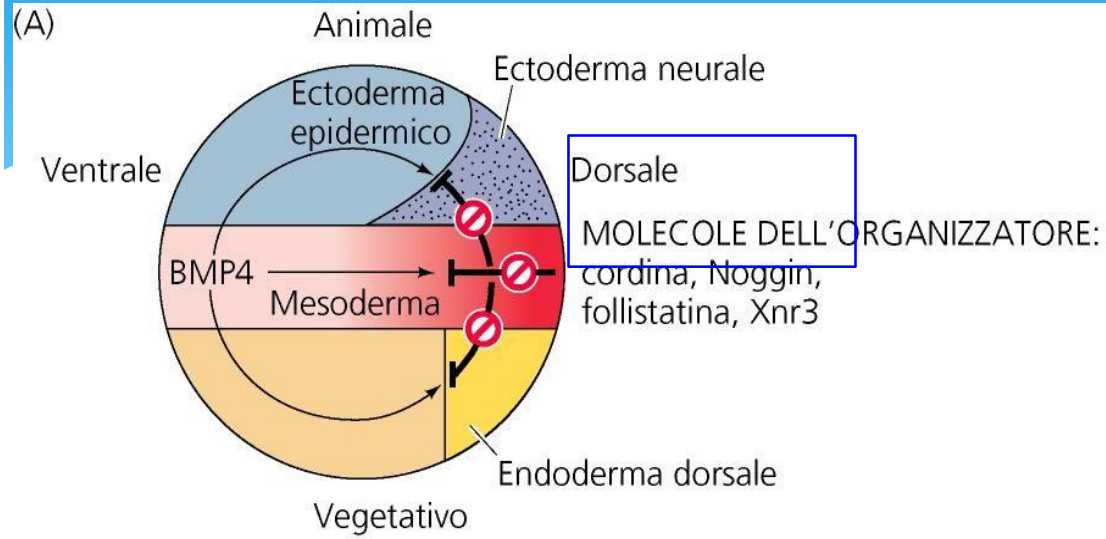


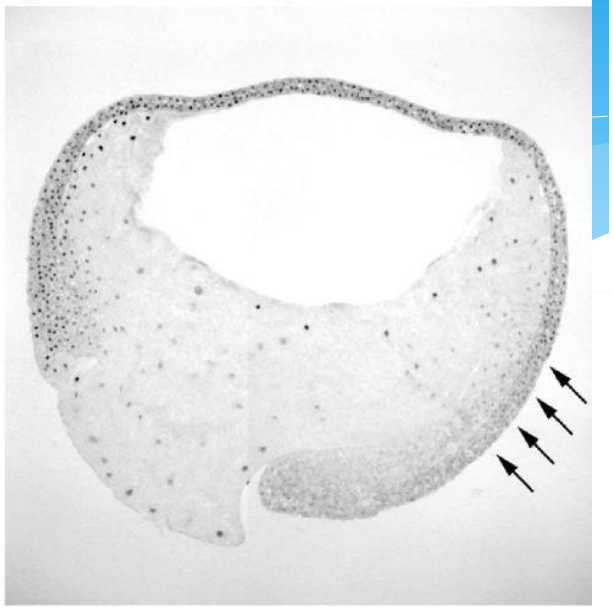


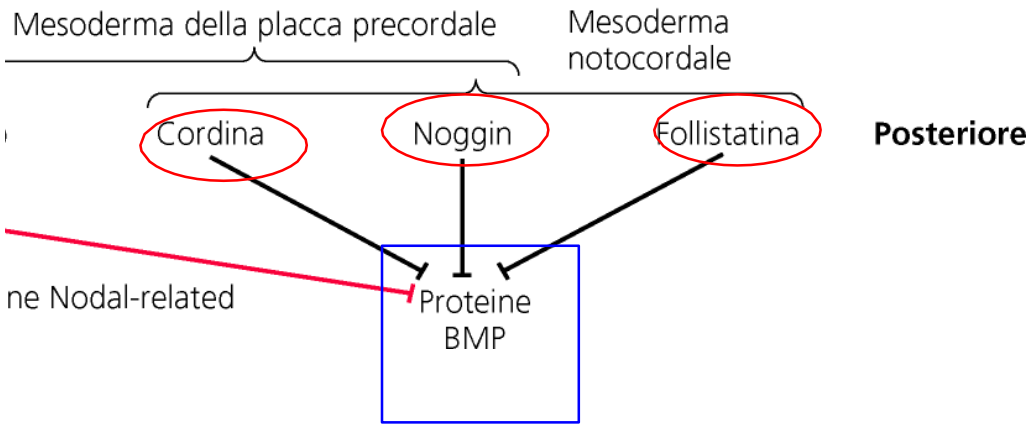
Il destino neurale è soppresso quando l'ectoderma è organizzato come tessuto in quanto produttore di BMP4

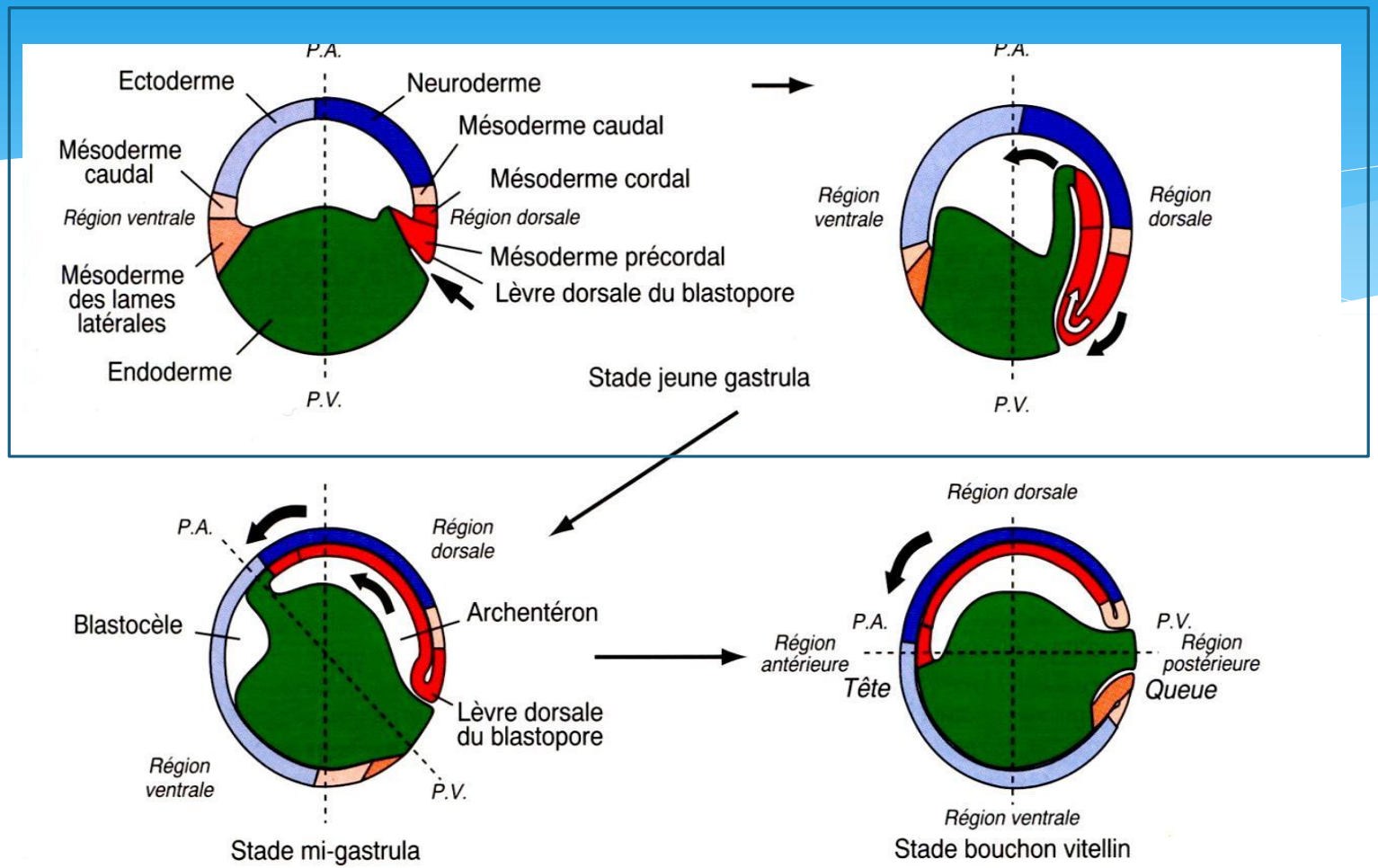
Gli inibitori della via BMP

(per avere sistema nervoso bisogna contrastare la via TGF B)



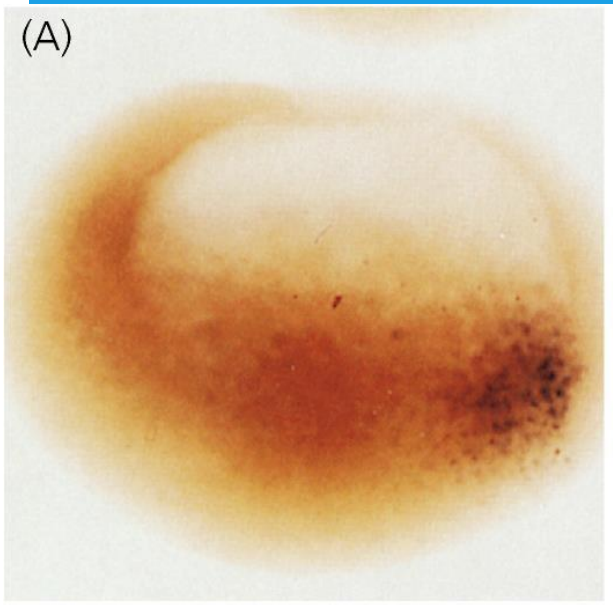


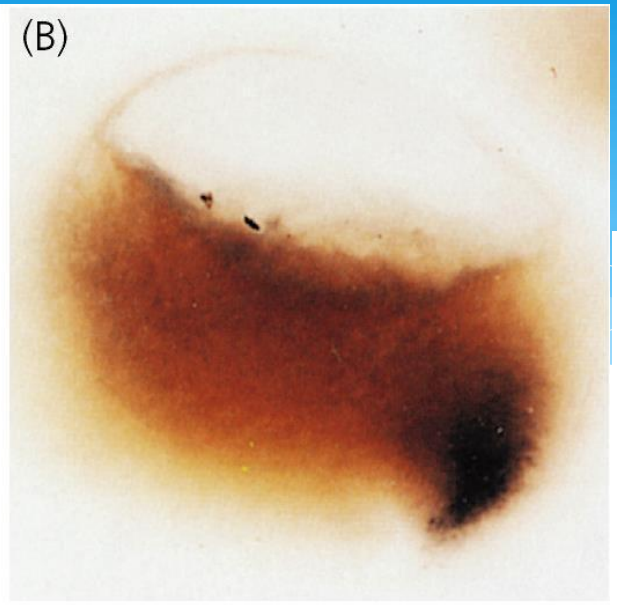


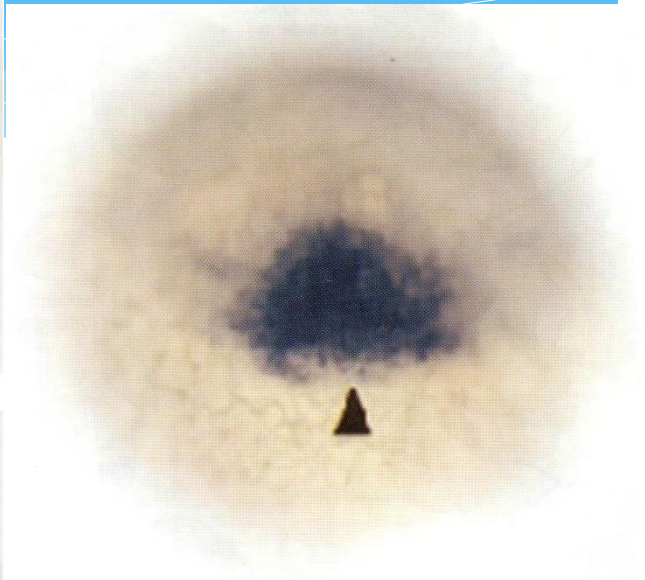


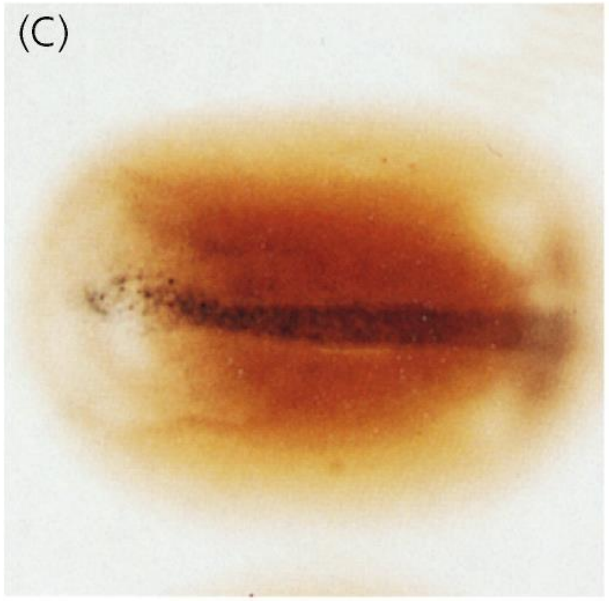
L’insieme dei segnali planari e verticali prodotti dal mesoderma , rilasciano inibitori della via TGFb)

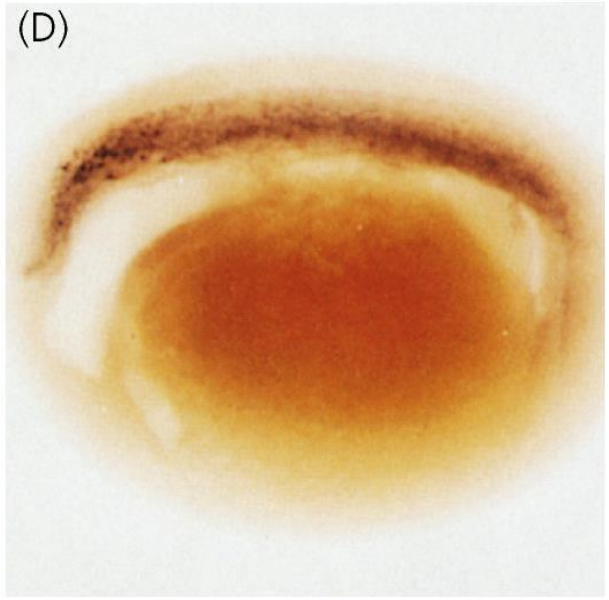
Espressione di Noggin e Cordina





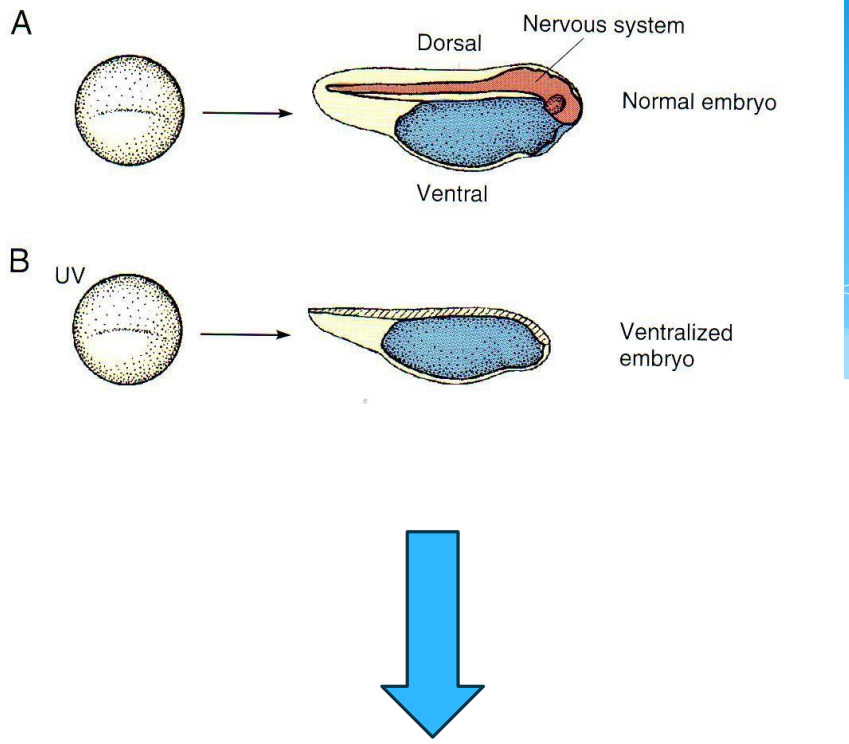






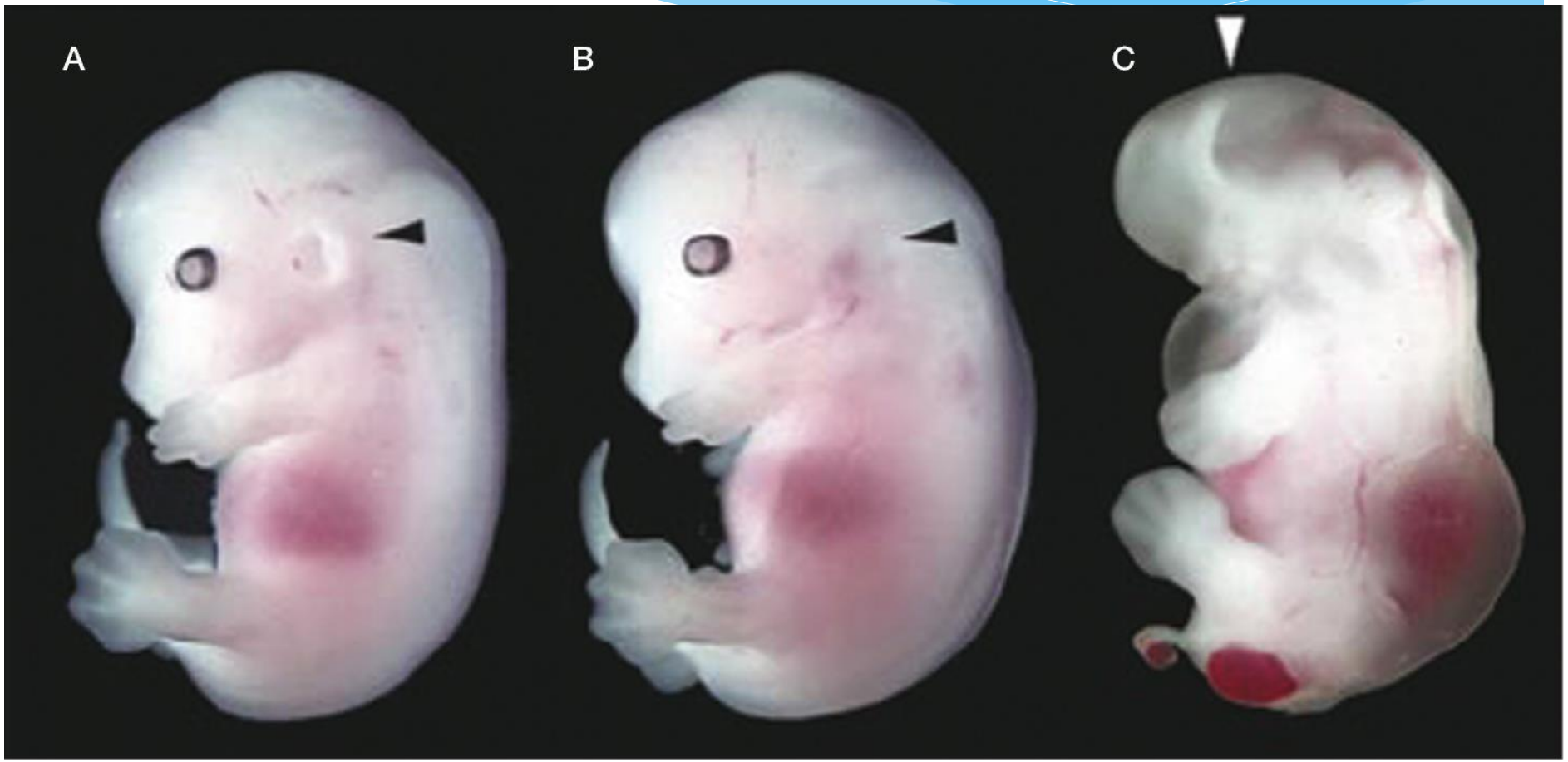
Noggin

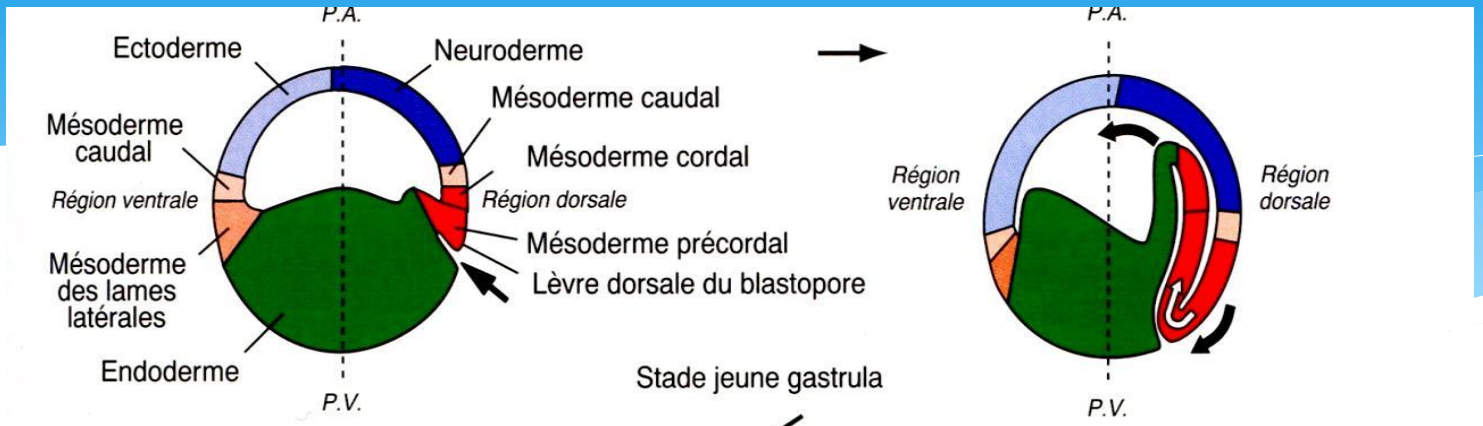
Noggin protegge l'area neuroectodermica dall'azione della BMP4



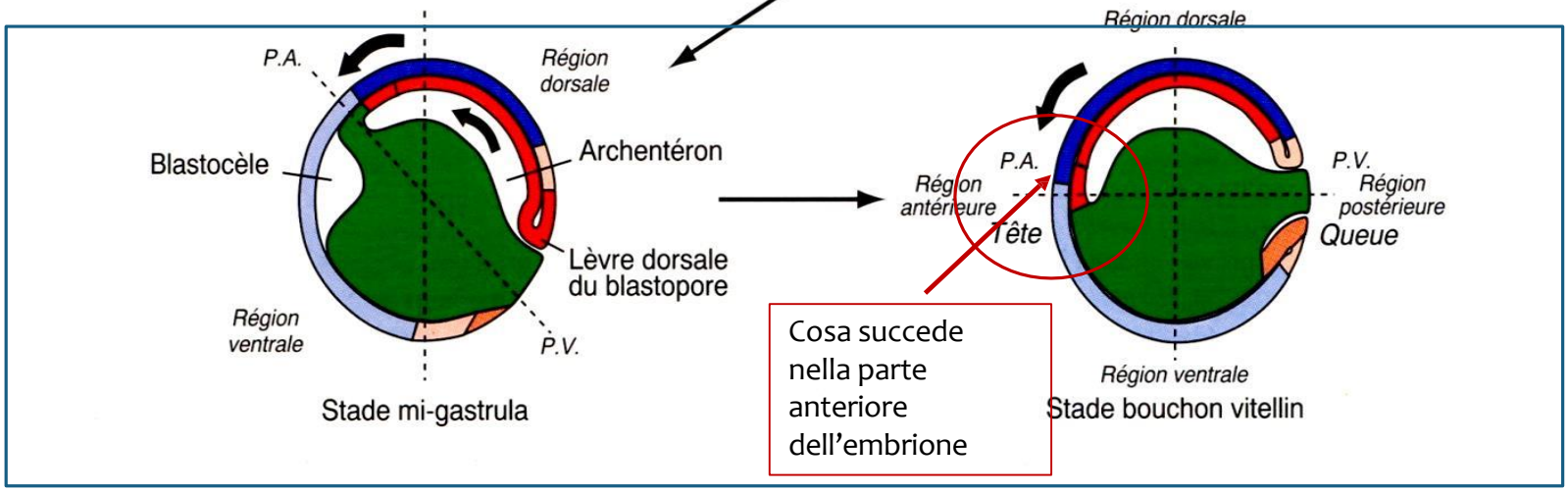
La calotta animale intatta sotto stimolo di Noggin forma neuroectoderma

WT nog-/- nog/chord-/-

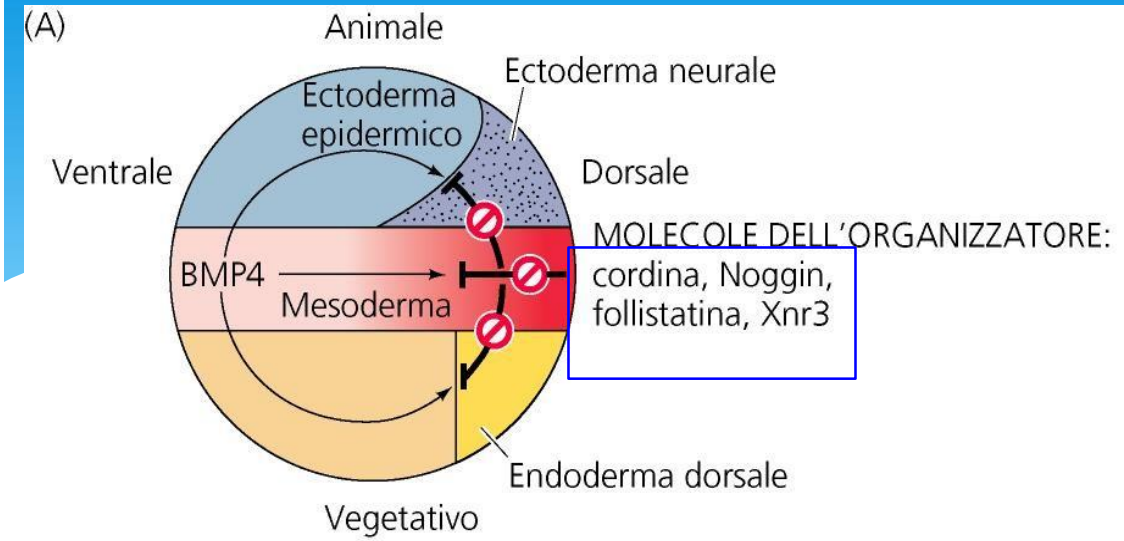


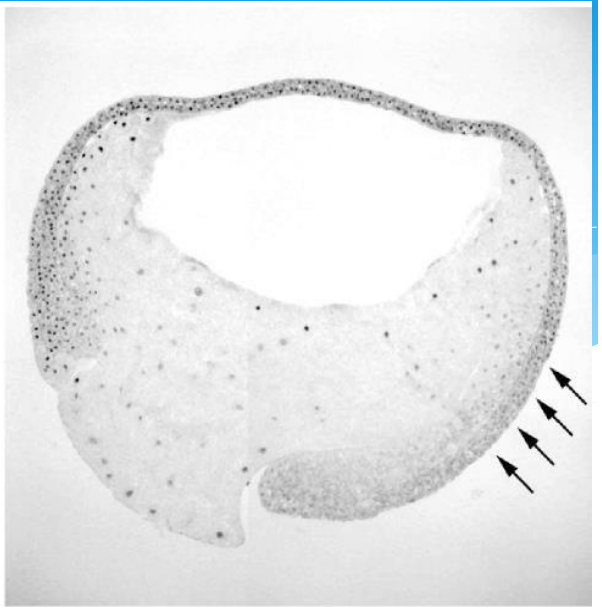


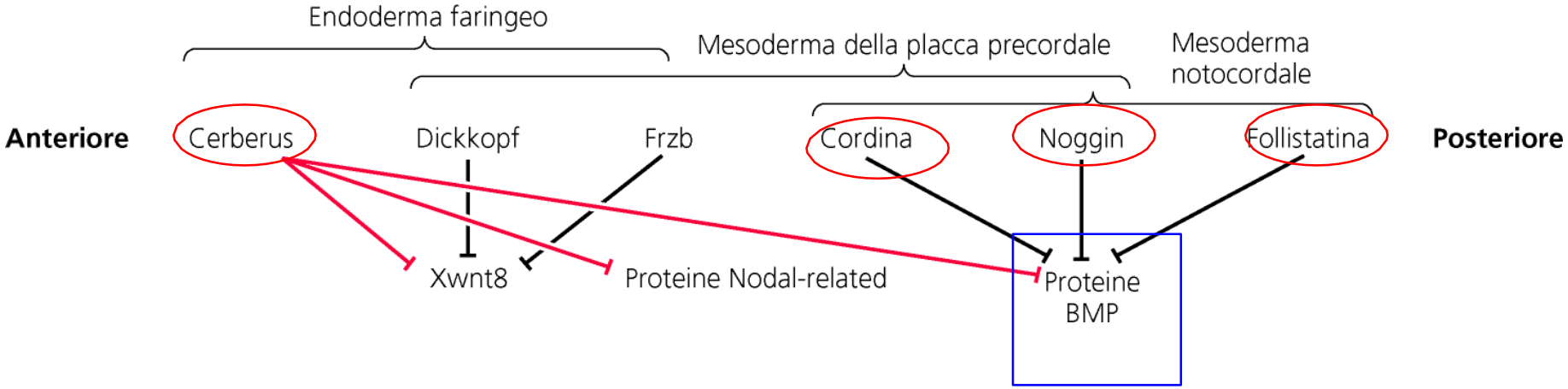
Stade jeune gastrula

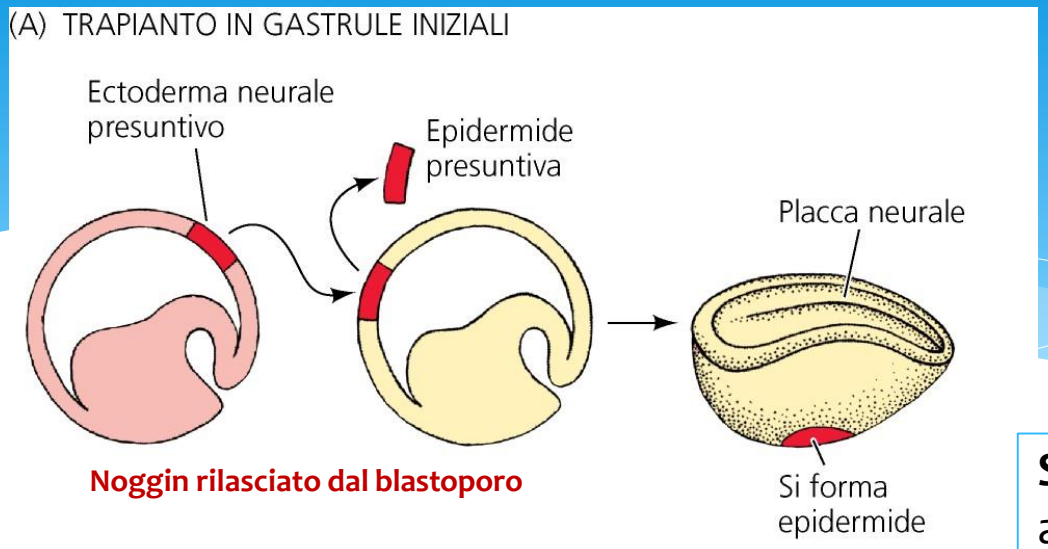


Cosa succede nella parte anteriore dell'embrione

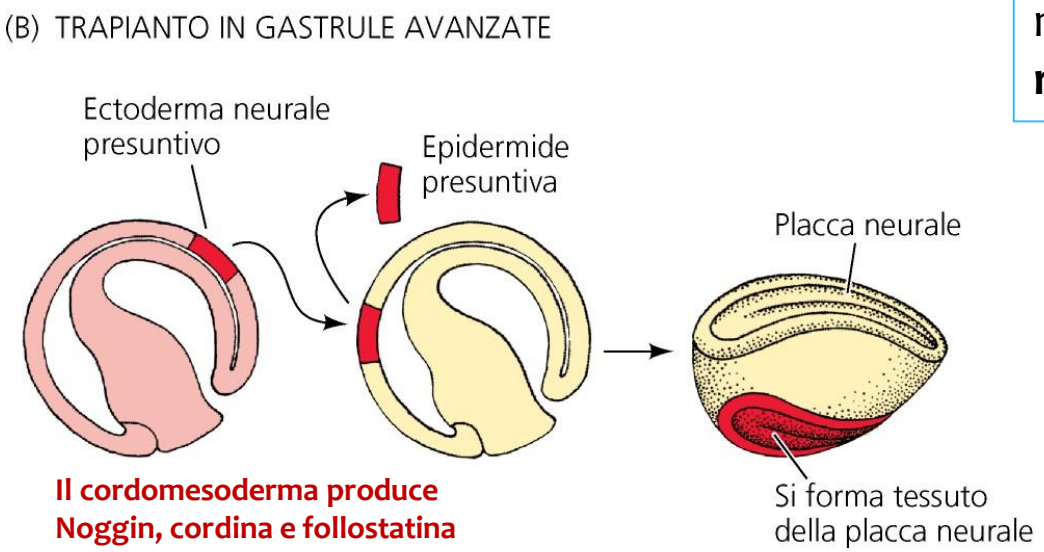

(A)
Animale
Ectoderma neurale
Ectoderma epidermico
Ventrale
Dorsale
BMP4
Mesoderma
MOLECOLE DELL'ORGANIZZATORE:
cordina, Noggin, follistatina, Xnr3
Endoderma dorsale
Vegetativo


(B)


Endoderma faringeo
Mesoderma della placca precordale
Mesoderma notocordale
Anteriore
Cerberus
Dickkopf
Frzb
Cordina
Noggin
Follistatina
Posteriore
Xwnt8
Proteine Nodal-related
Proteine BMP



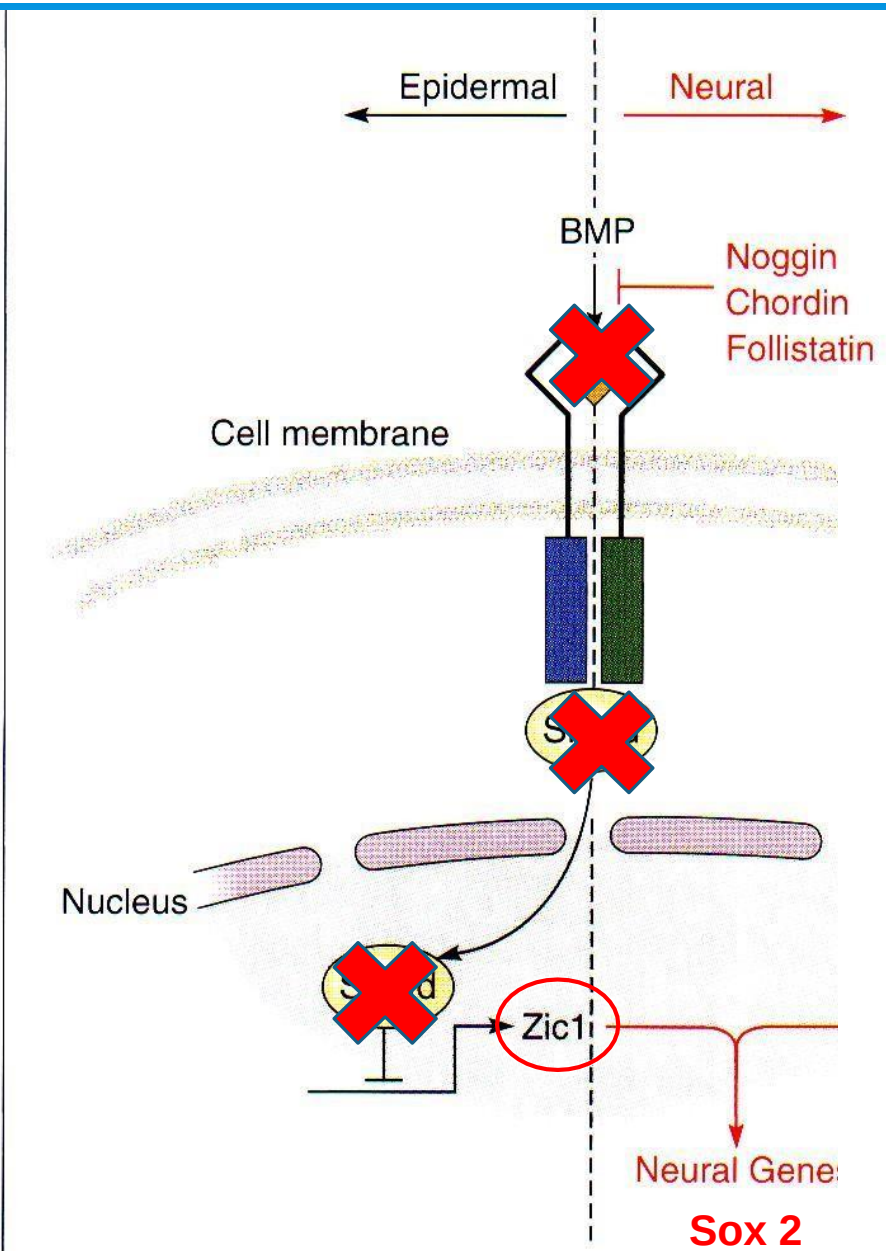
Noggin rilasciato dal blastoporo



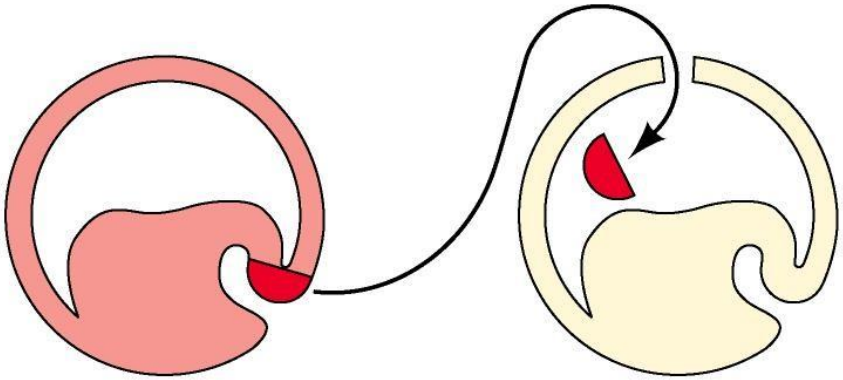
Il cordomesoderma produce Noggin, cordina e follostatina

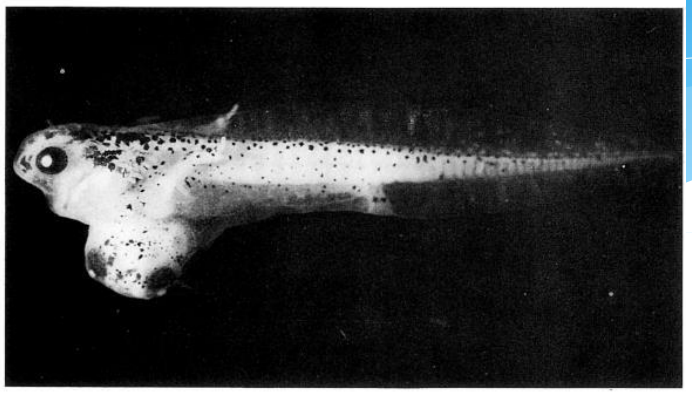
Specificazione: iniziale acquisizione del destino maturativo. **Il processo è reversibile**

Determinazione: acquisizione del destino maturativo. **Il processo è irreversibile**

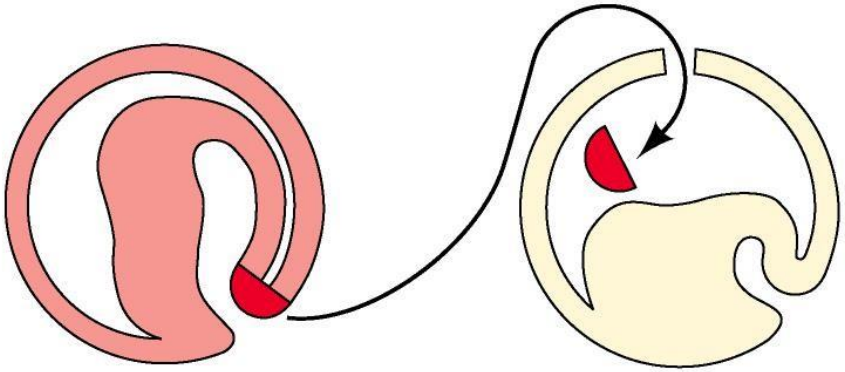

Epidermal
Neural
BMP
Noggin
Chordin
Follistatin
Cell membrane
Nucleus
Zic1
Neural Gene
Sox 2

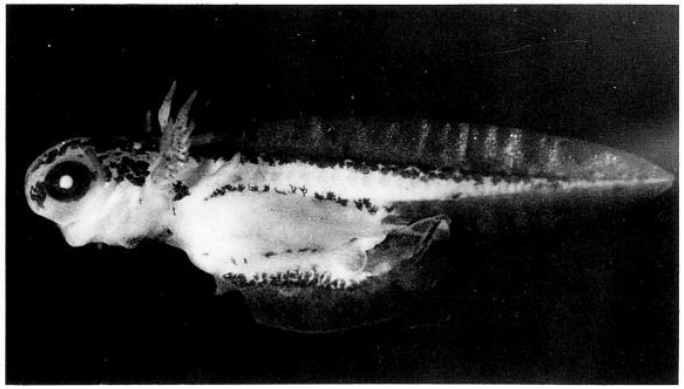
(A) Trapianto del labbro dorsale di gastrula in stadio iniziale



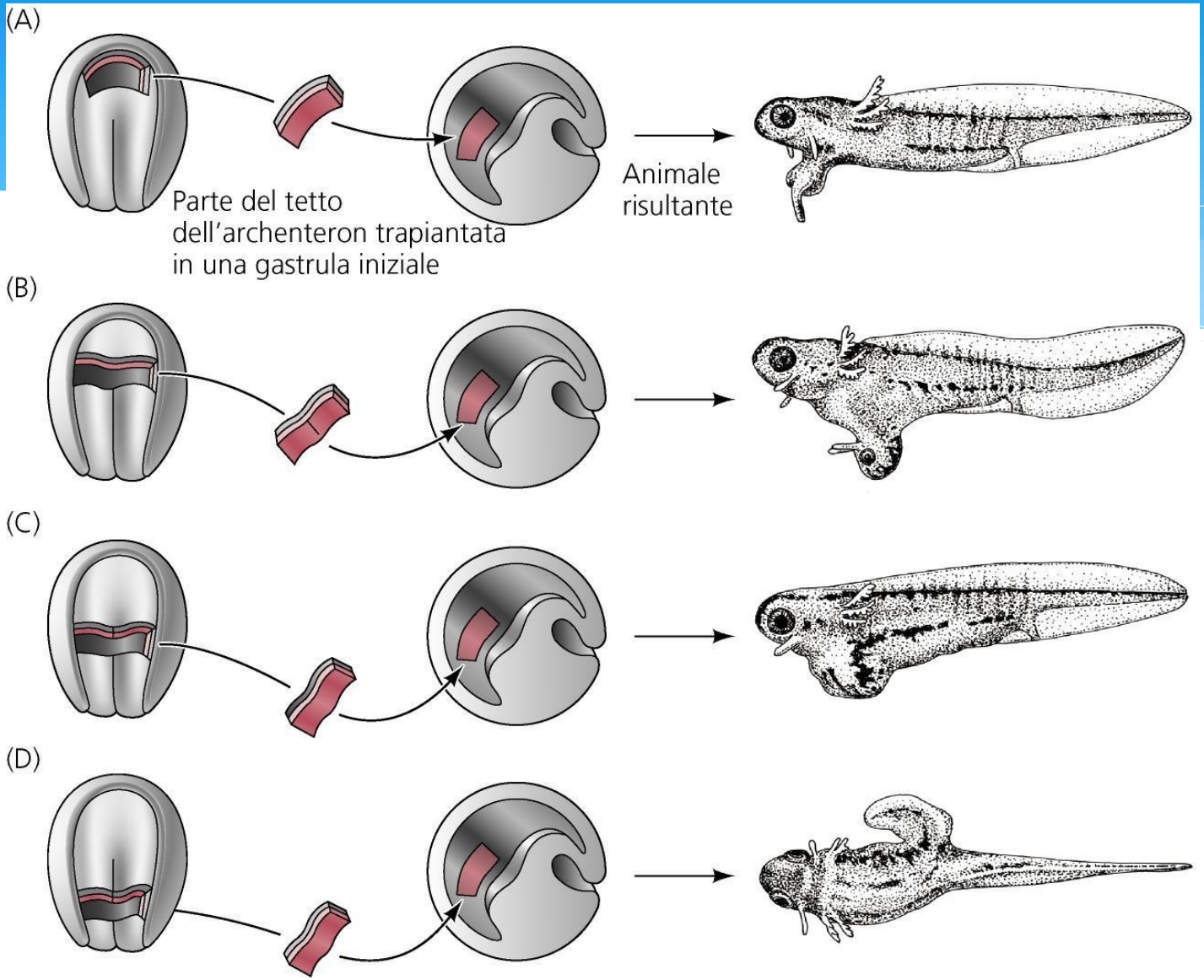


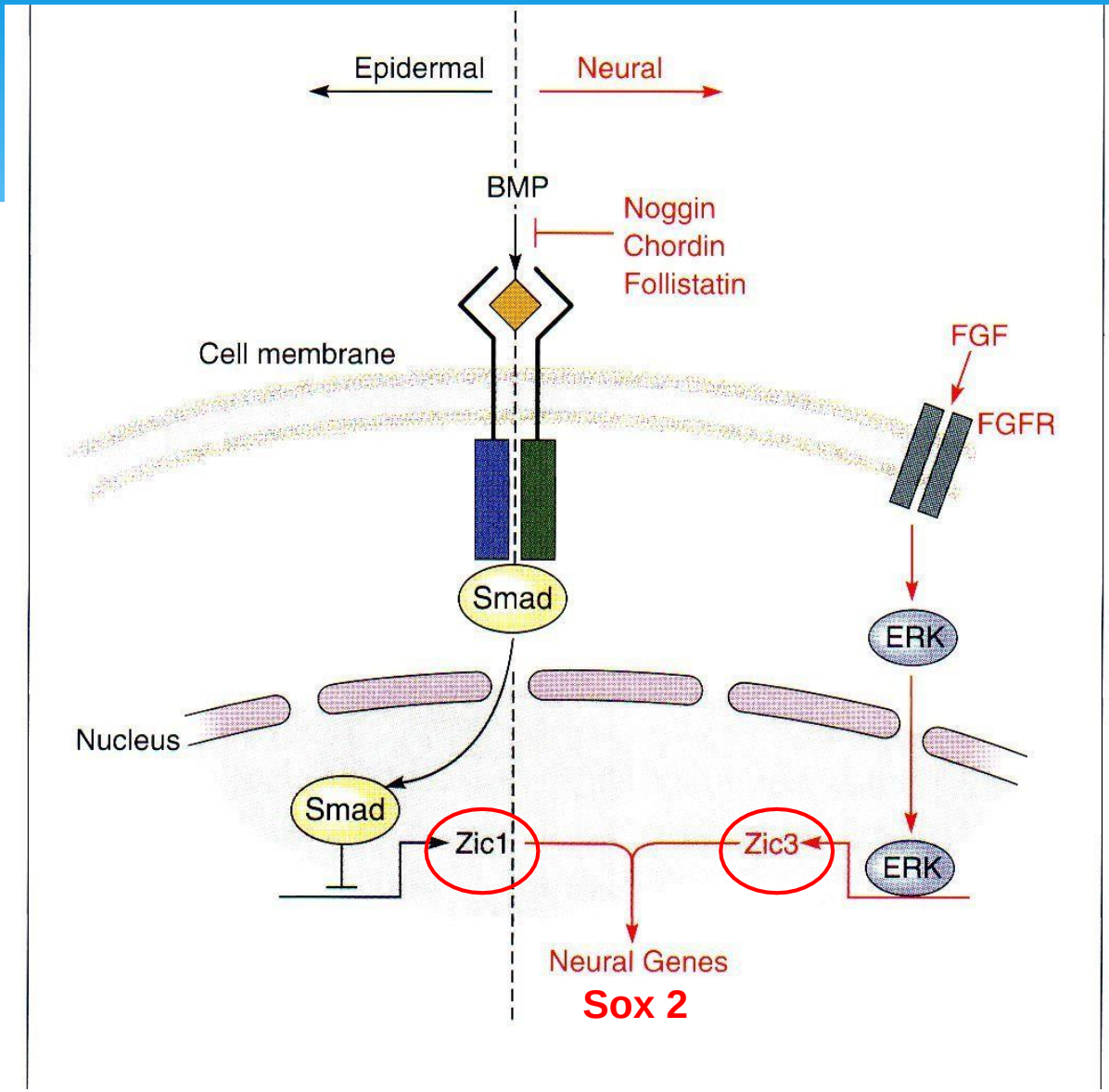
(B) Trapianto del labbro dorsale di gastrula in stadio avanzato





FGF posteriorizza il sistema nervoso


(A)
Parte del tetto
dell'archenteron trapiantata
in una gastrula iniziale
Animale
risultante
(B)
(C)
(D)


Epidermal
Neural
BMP
Noggin
Chordin
Follistatin
Cell membrane
FGF
FGFR
Smad
ERK
Nucleus
Smad
Zic1
Zic3
ERK
Neural Genes
Sox 2

Sviluppo del Sistema Nervoso

- Specificazione /Induzione
- Proliferazione
- Determinazione del fenotipo cellulare



Neuroni Glia

- Migrazione
- Differenziamento

Neurone Crescita assonale

Formazione sinapsi