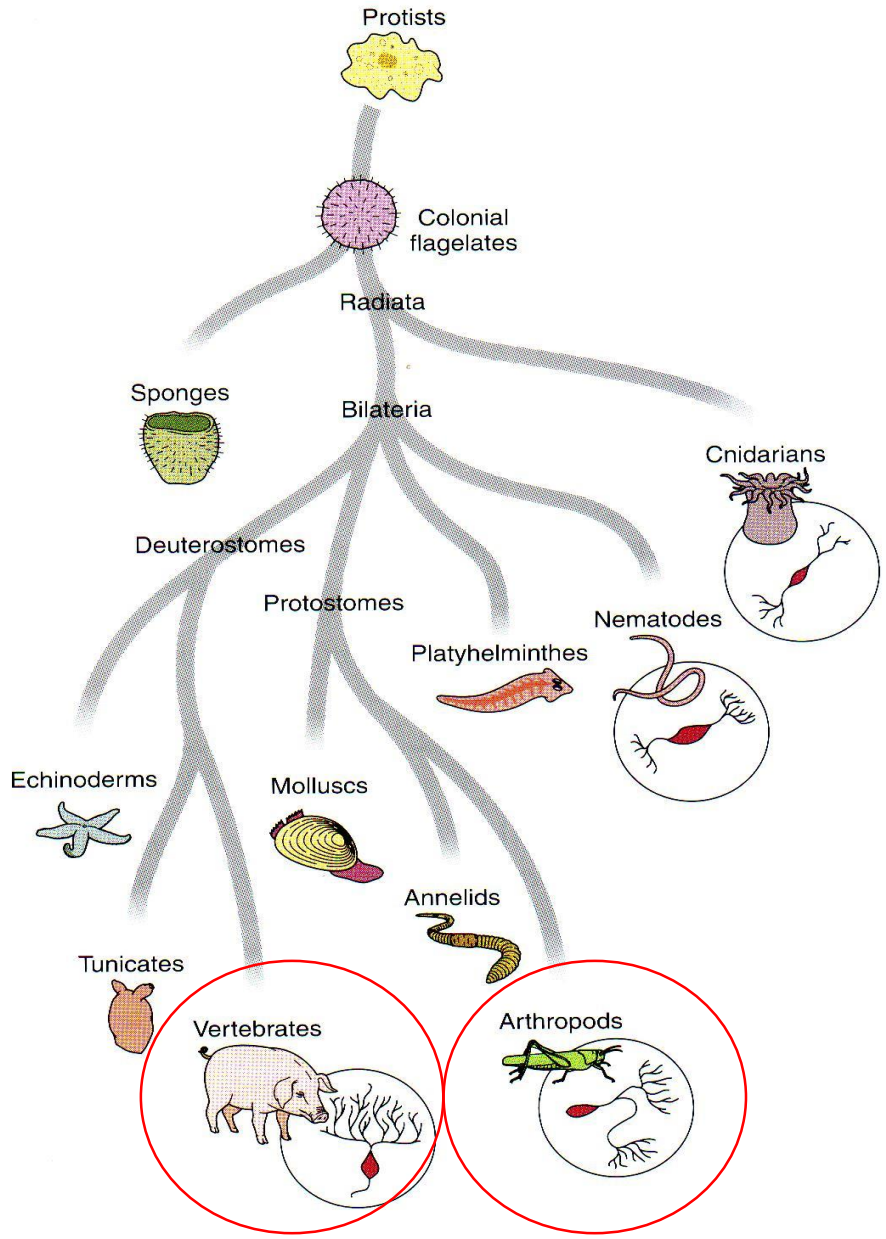
# Specificazione del sistema nervoso  nei Vertebrati



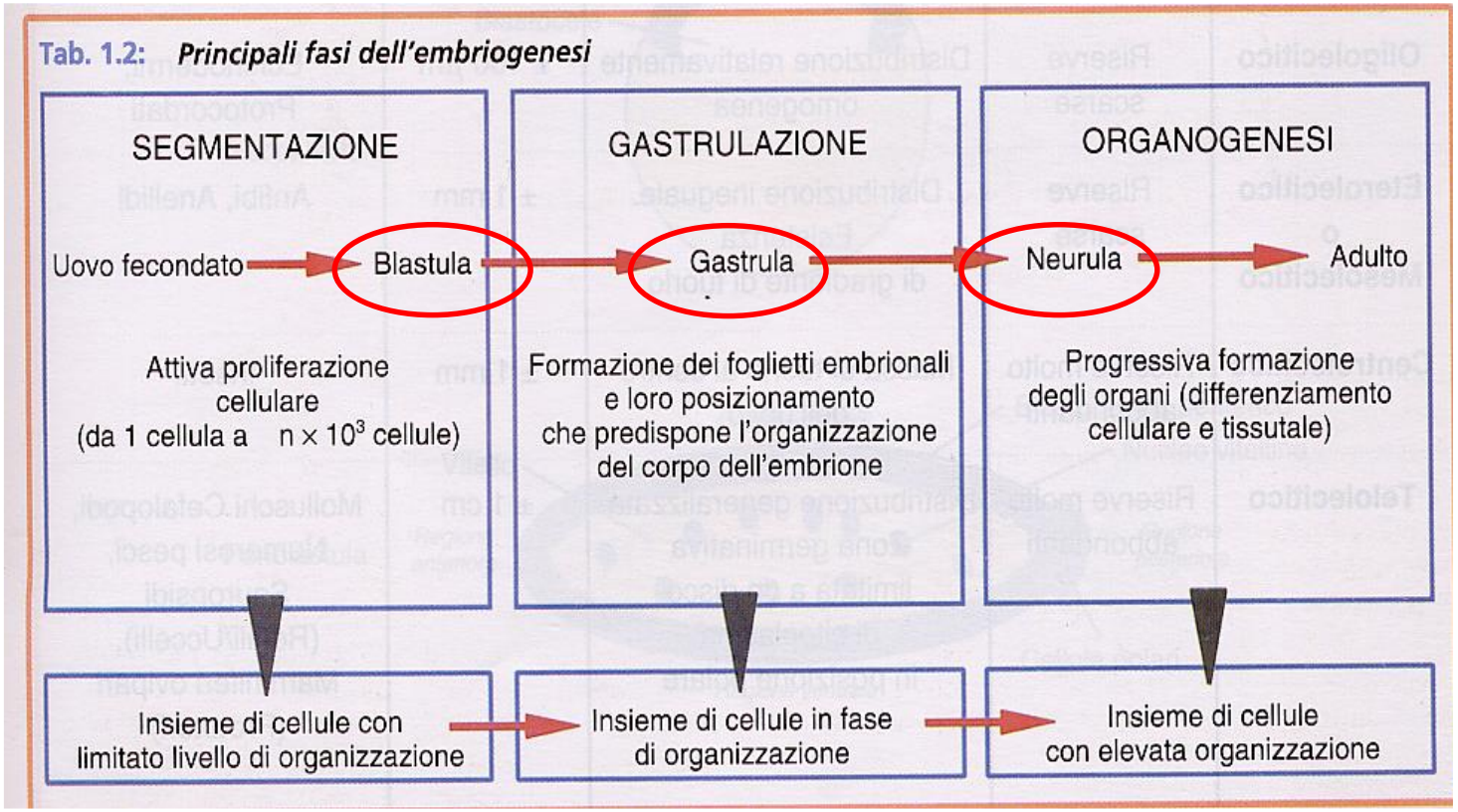

- Tutti gli organismi pluricellulari possiedono neuroni riconoscibili con lunghi processi e con attività elettrica simile

- 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.

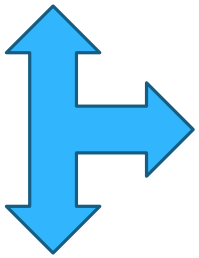
# Qualche breve cenno di embriologia

# Embriologia dei Vertebrati



# I Foglietti embrionali

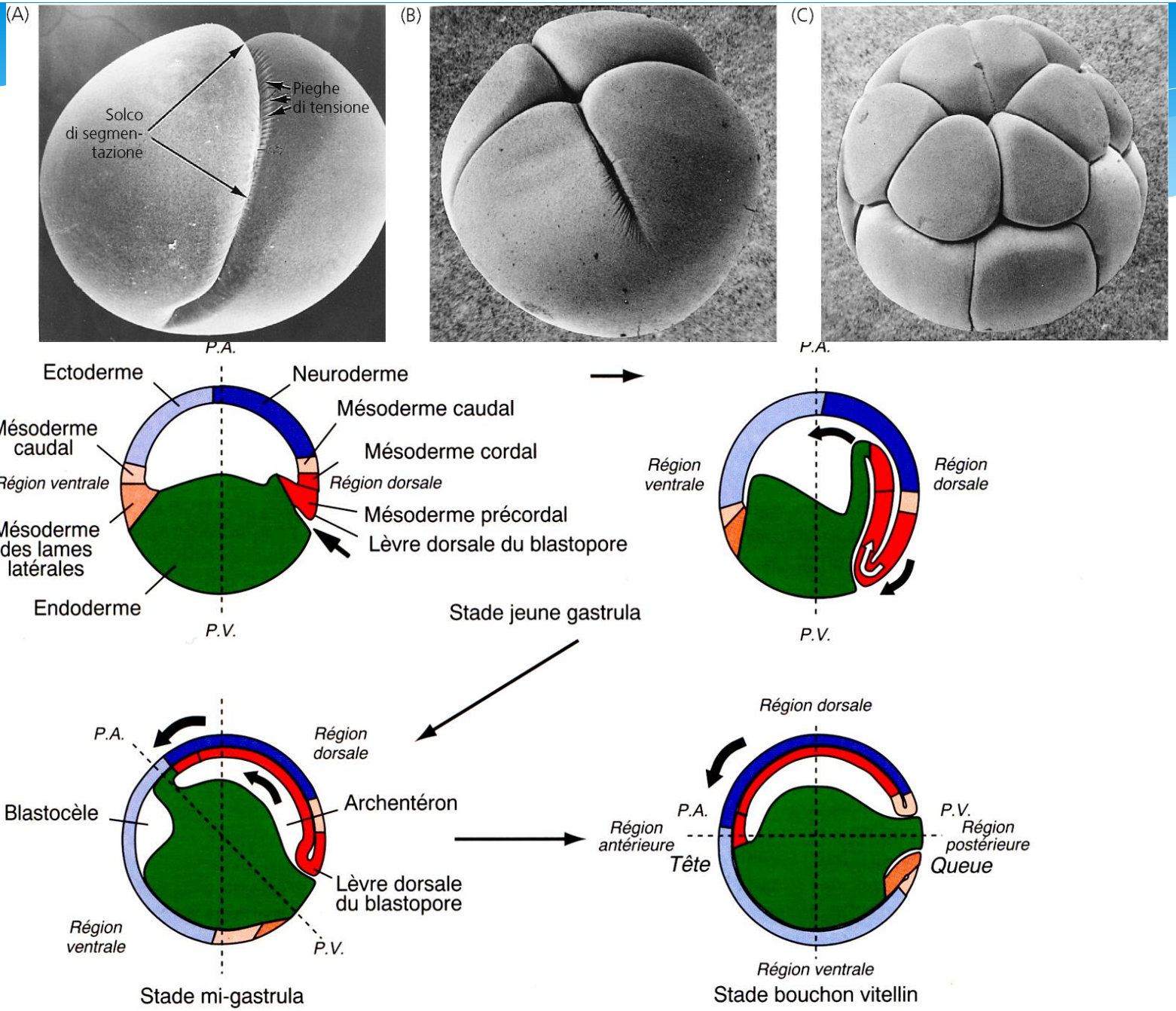
**ECTODERMA**

**Gastrulazione**  **MESODERMA**

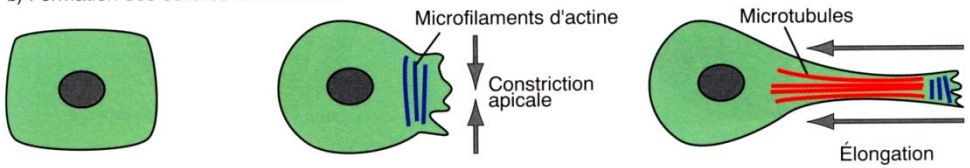
**ENDODERMA**

**Organogenesi**  **Sviluppo degli organi**

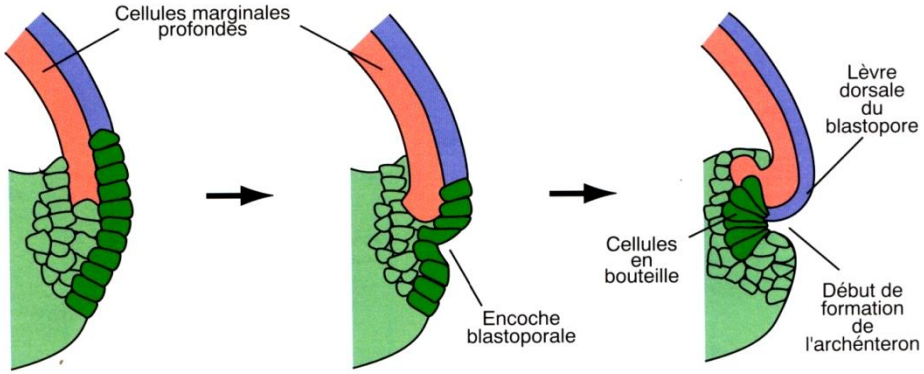
**Neurulazione:** Processo che caratterizza l'iniziale sviluppo del sistema nervoso nei vertebrati

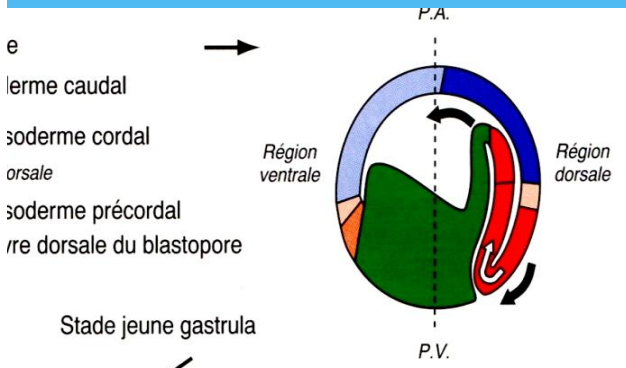

(A)
Solco di segmen-tazione
Pieghe di tensione
(B)
(C)
P.A.
Ectoderme
Neuroderme
Mésoderme caudal
Mésoderme caudal
Mésoderme cordal
Région ventrale
Région dorsale
Mésoderme précordal
Mésoderme des lames latérales
Lèvre dorsale du blastopore
Endoderme
P.V.
Stade jeune gastrula
Région ventrale
Région dorsale
P.V.
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

b) Formation des cellules en bouteille

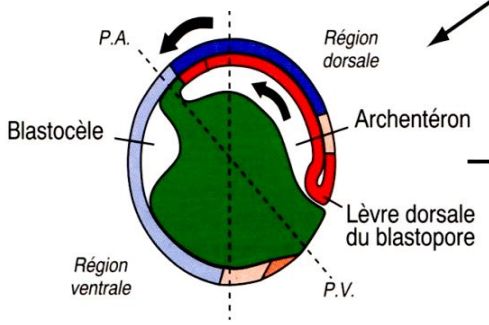



c) Schémas de la formation de l'archentéron

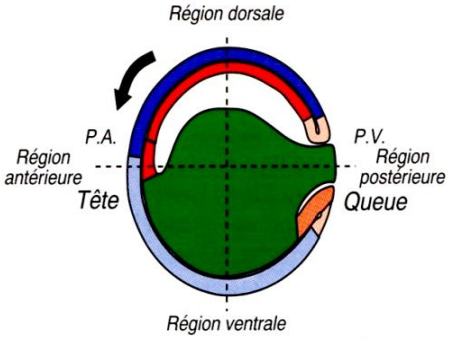


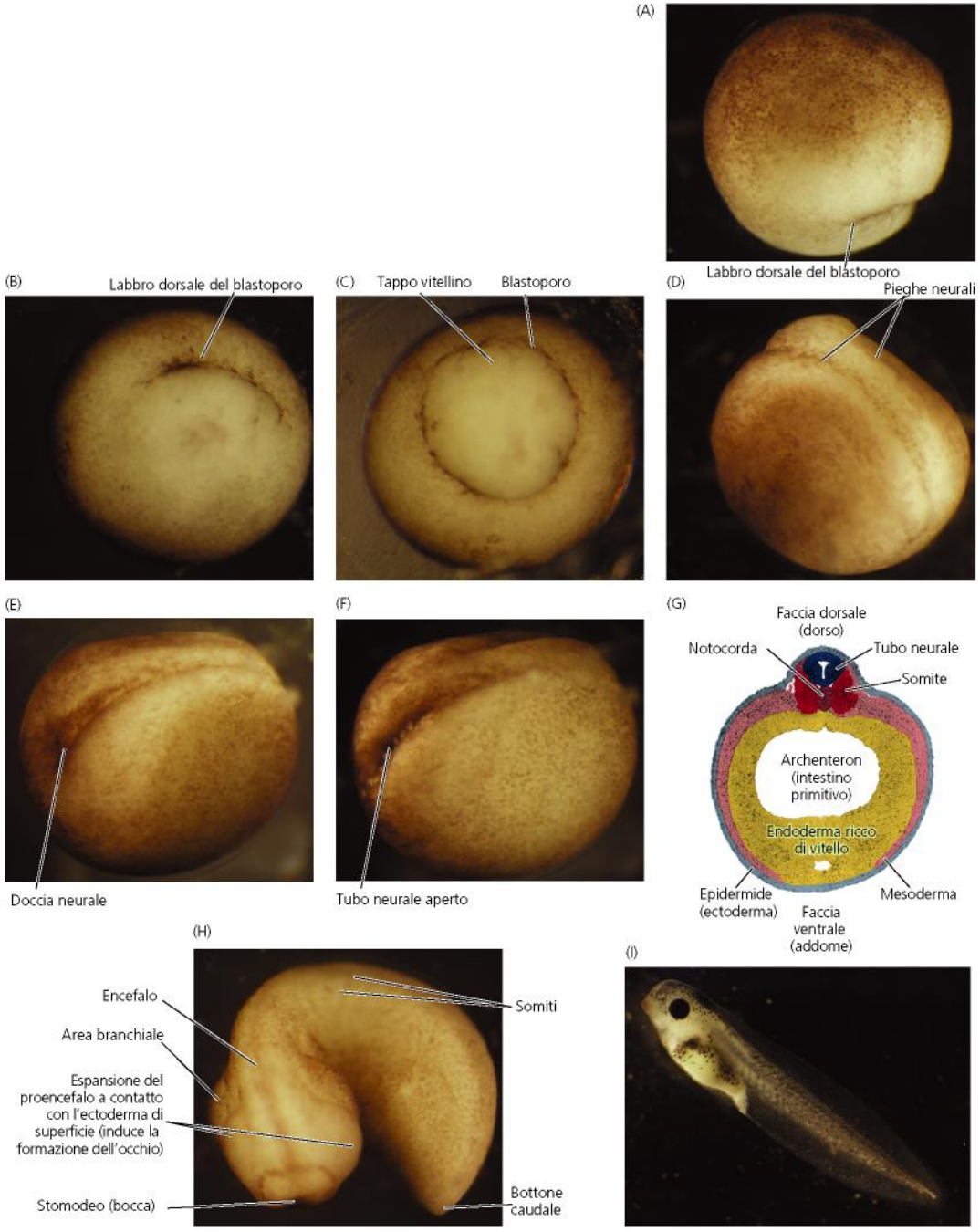

Stade jeune gastrula



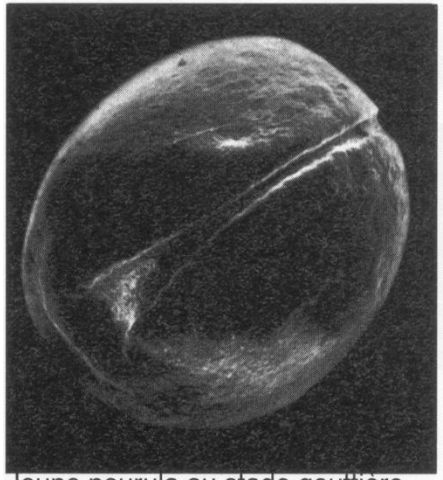

Stade mi-gastrula



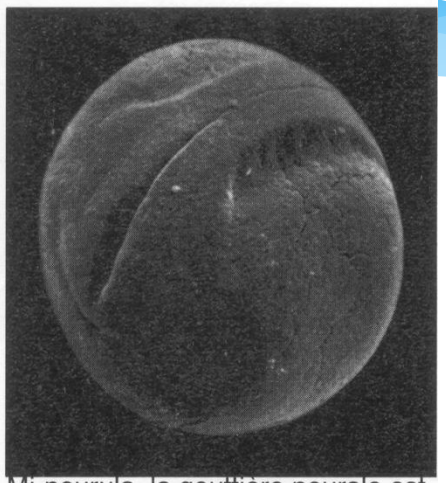

Stade bouchon vitellin


(A)
Labbro dorsale del blastoporo
(B)
Labbro dorsale del blastoporo
(C)
Tappo vitellino
Blastoporo
(D)
Pieghe neurali
(E)
Doccia neurale
(F)
Tubo neurale aperto
(G)
Faccia dorsale (dorso)
Notocorda
Tubo neurale
Somite
Archenteron (intestino primitivo)
Endoderma ricco di vitello
Epidermide (ectoderma)
Mesoderma
Faccia ventrale (addome)
(H)
Encefalo
Somiti
Area branchiale
Espansione del proencefalo a contatto con l'ectoderma di superficie (induce la formazione dell'occhio)
Stomodeo (bocca)
Bottone caudale
(I)

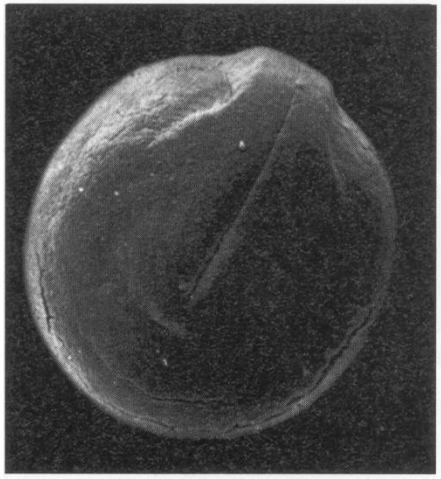
b) La neurulation, microphotographies d'embryons de xénope (les embryons sont dégangués et sans membrane de fécondation, x 50)



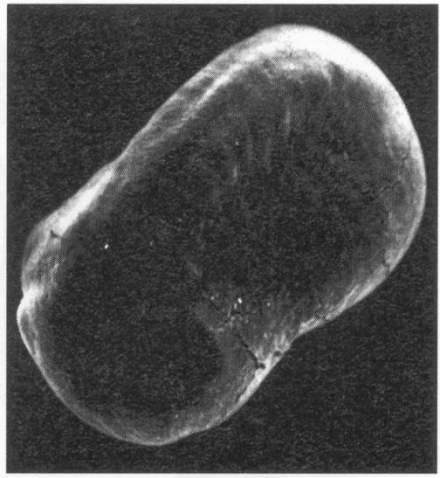
Jeune neurula au stade gouttière neurale



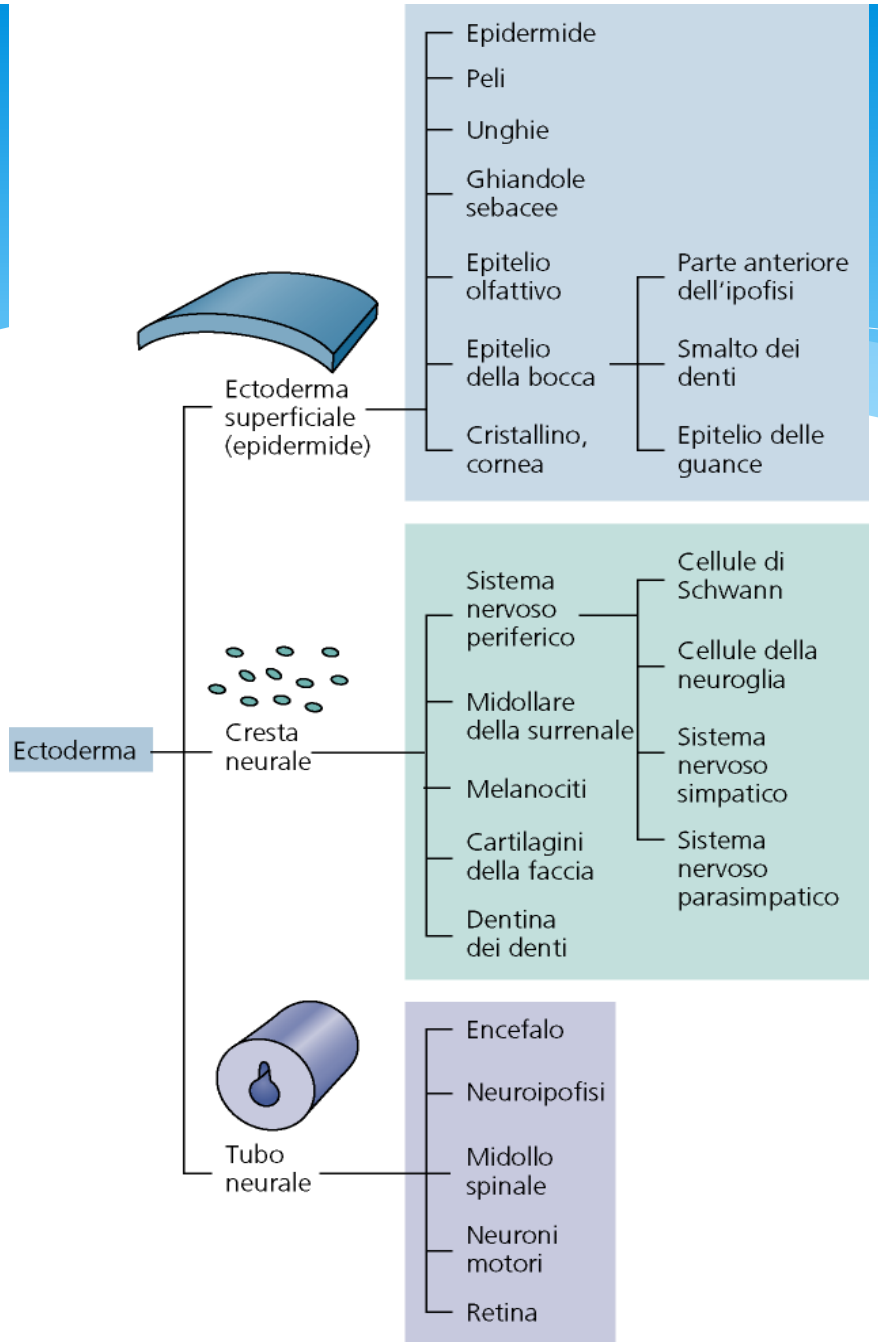
Mi-neurula, la gouttière neurale est fermée dans la région troncale

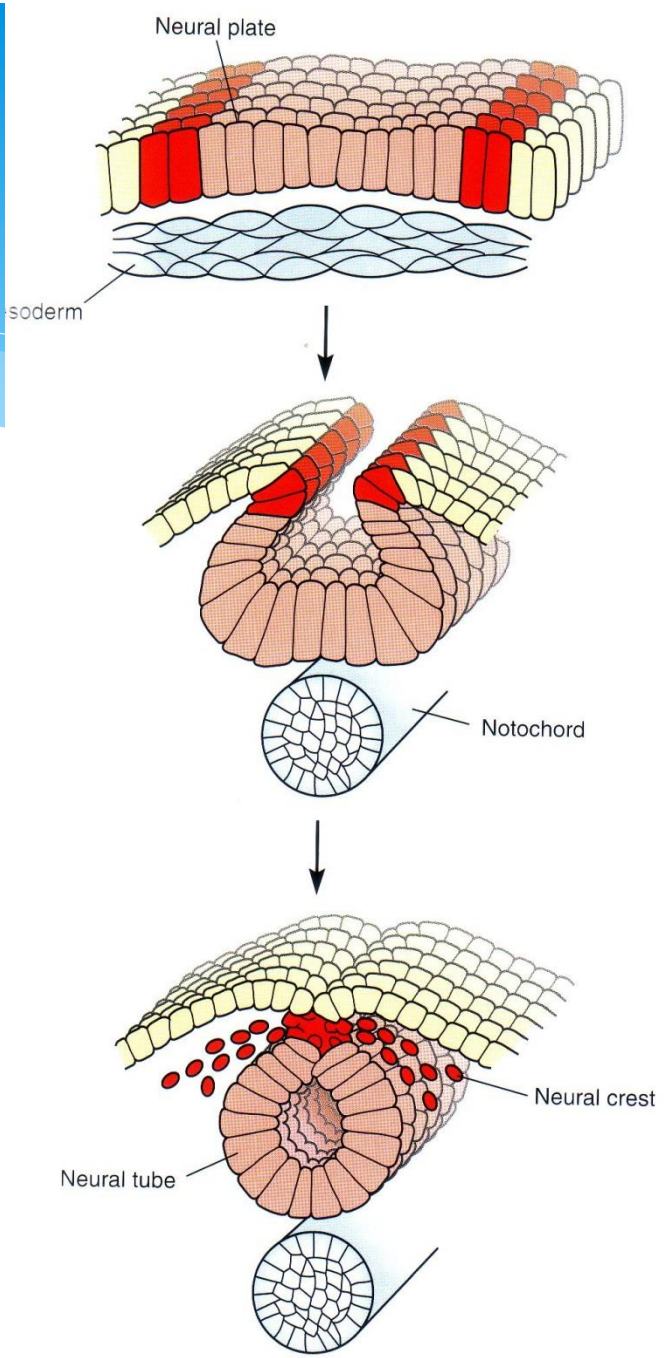


Neurula âgée

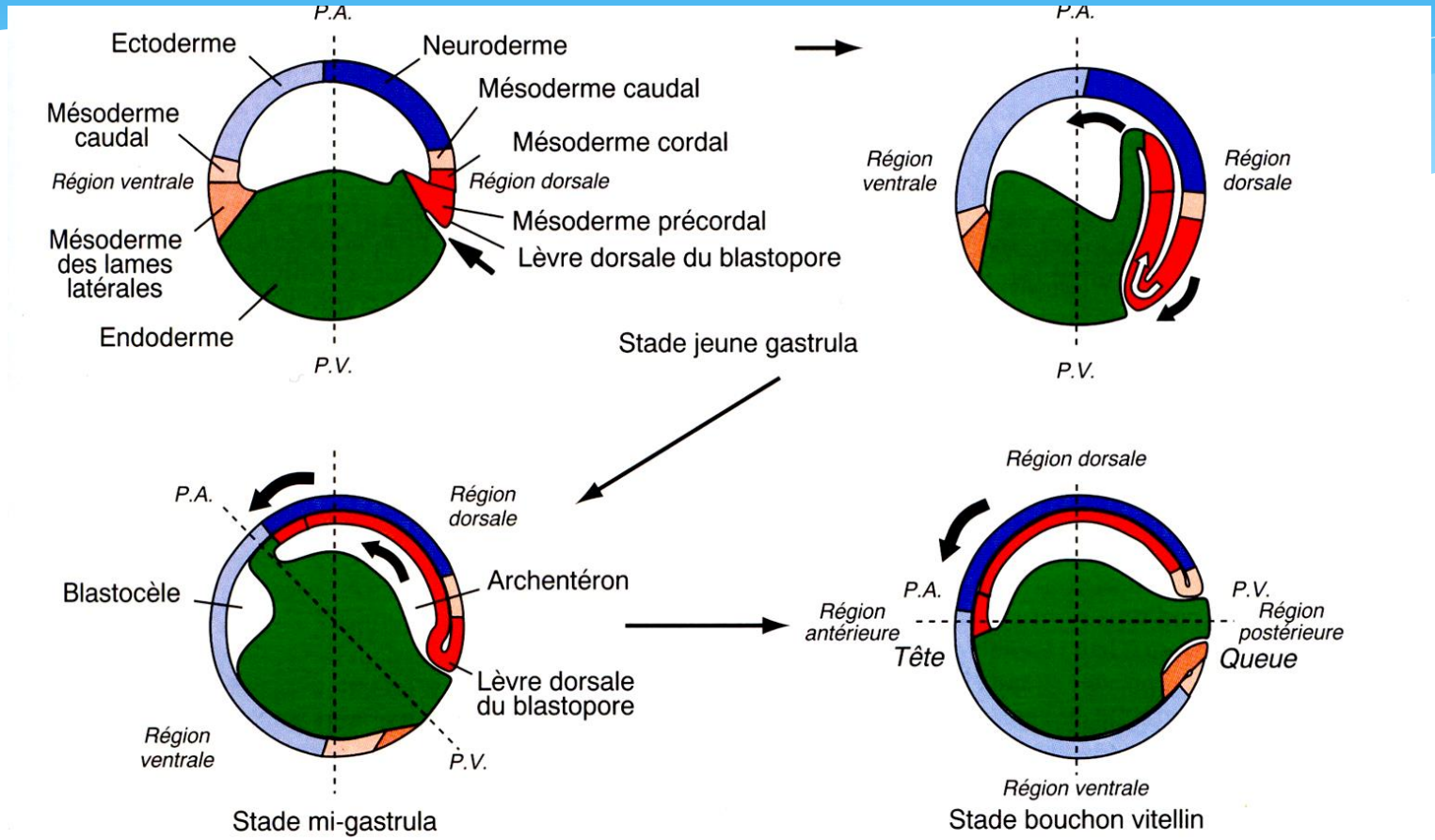


Jeune bourgeon caudal

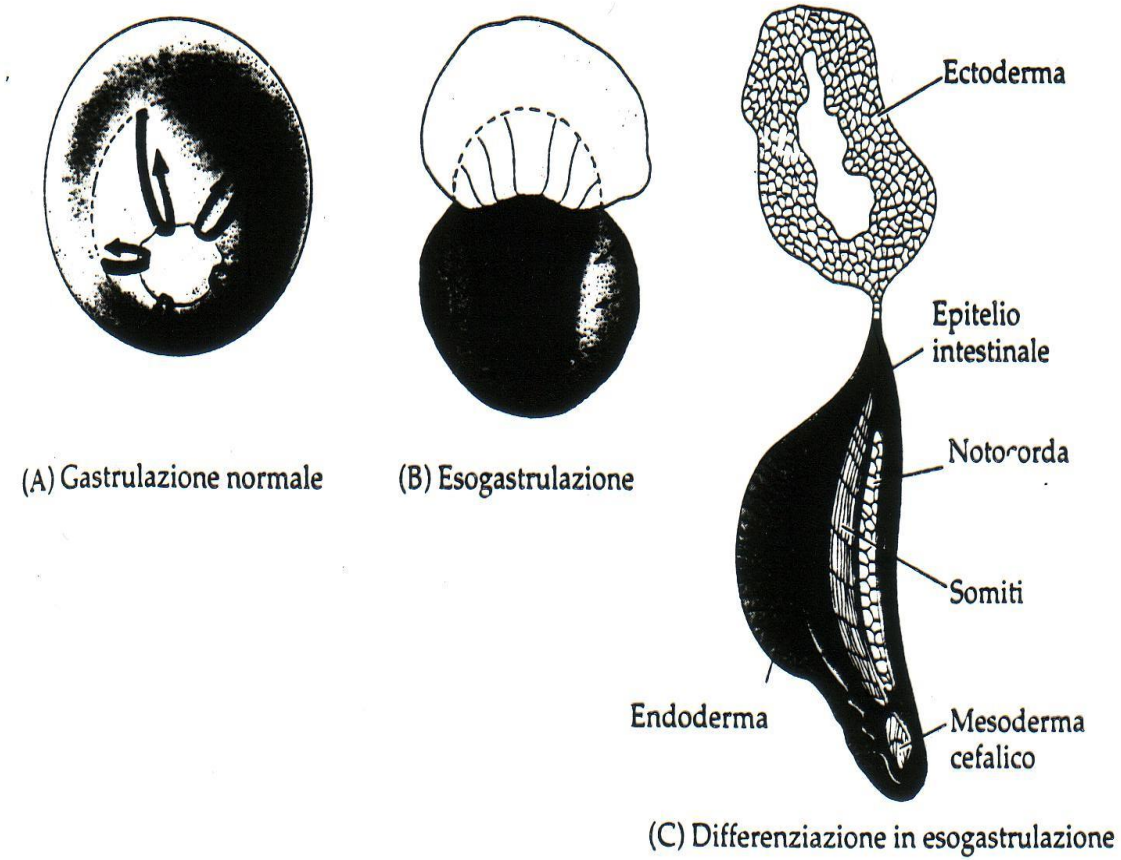

Ectoderma
Ectoderma superficiale (epidermide)
Epidermide
Peli
Unghie
Ghiandole sebacee
Epitelio olfattivo
Epitelio della bocca
Cristallino, cornea
Parte anteriore dell'ipofisi
Smalto dei denti
Epitelio delle guance
Cresta neurale
Sistema nervoso periferico
Midollare della surrenale
Melanociti
Cartilagini della faccia
Dentina dei denti
Cellule di Schwann
Cellule della neuroglia
Sistema nervoso simpatico
Sistema nervoso parasimpatico
Tubo neurale
Encefalo
Neuroipofisi
Midollo spinale
Neuroni motori
Retina


Neural plate
soderm
Notochord
Neural crest
Neural tube

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



# Esogastrule di Holtfreter



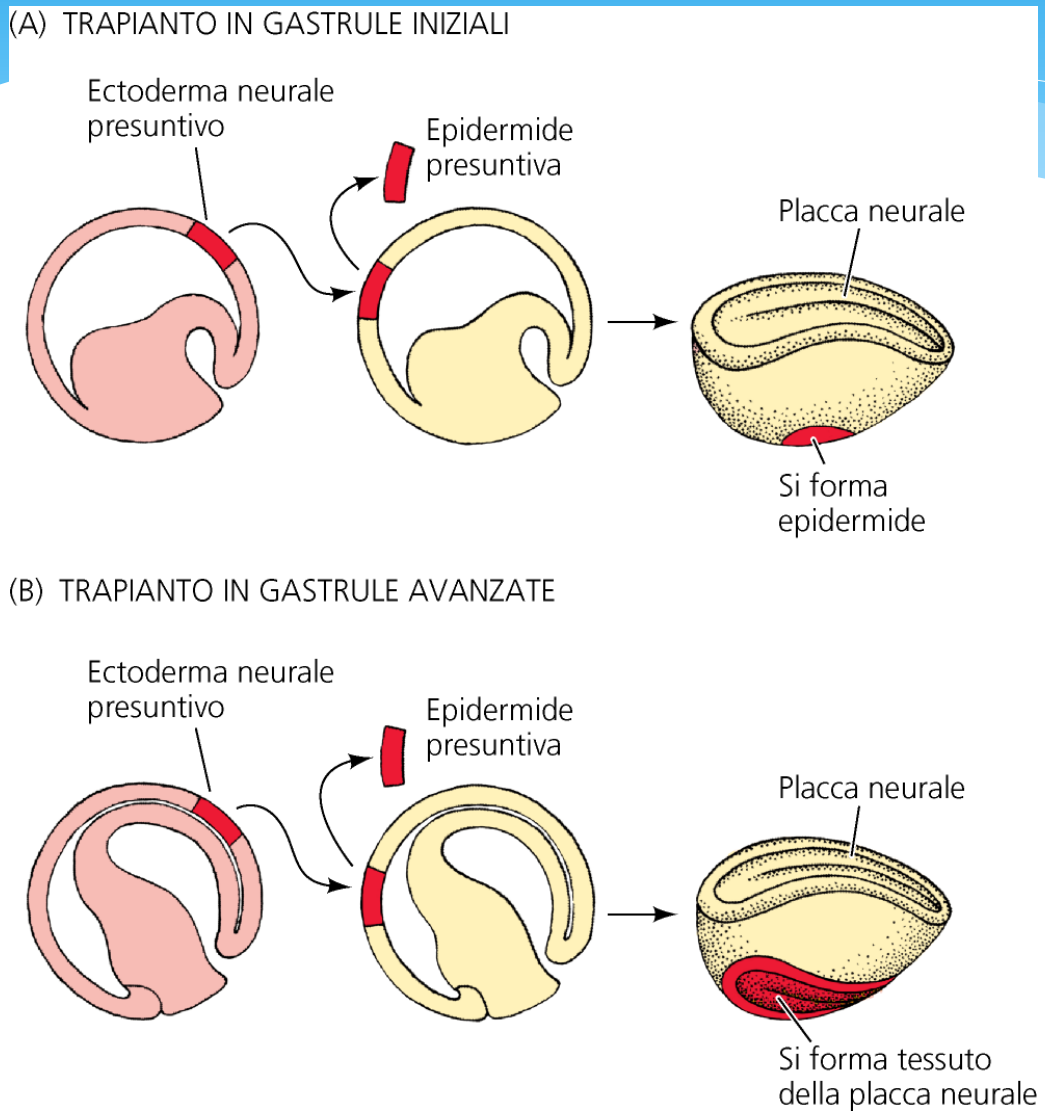

(A) Gastrulazione normale

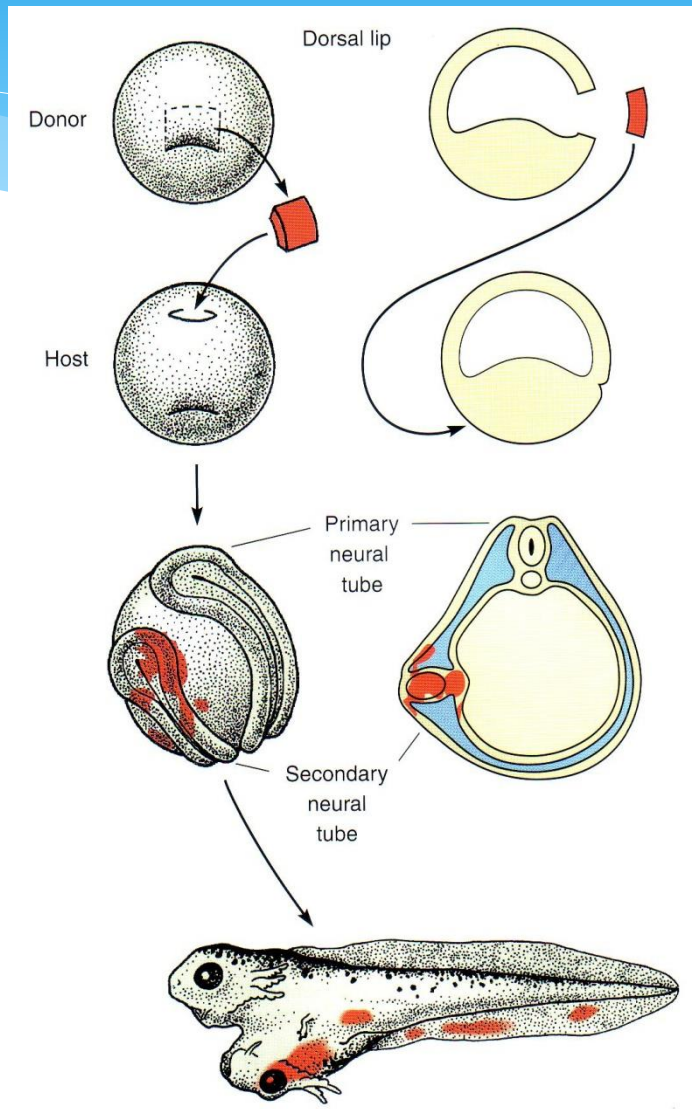
(B) Esogastrulazione

(C) Differenziazione in esogastrulazione

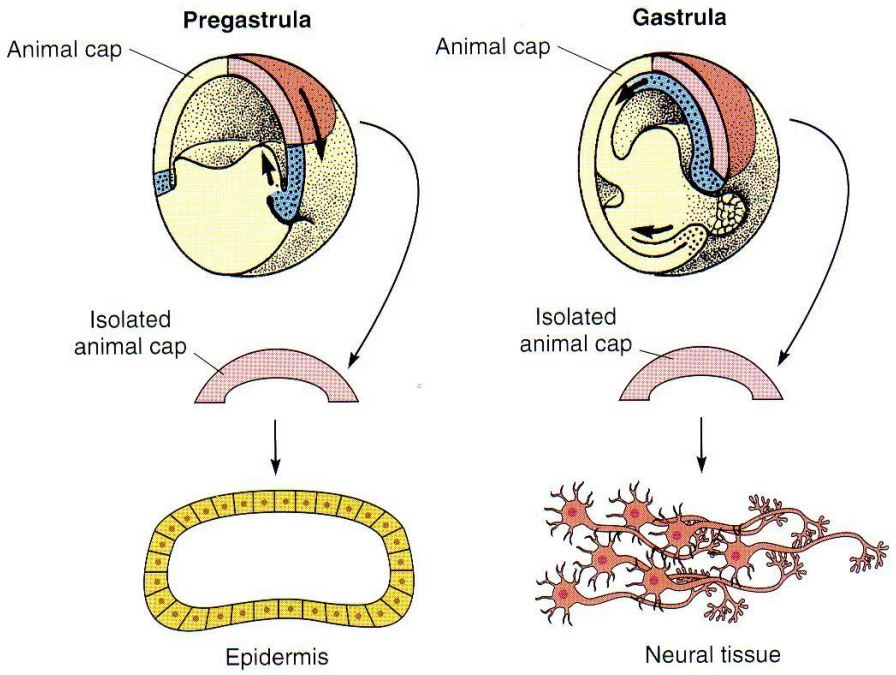
**Figura 16.35**
Esogastrulazione. (A) Nella gastrulazione normale, il mesoderma si involve sotto l'ectoderma. Tu[illegible]ia, quando l'embrione di anfibio viene posto in una soluzione salina ipertonica, il mesoderma subisce esogastrulazione (B), estroflettendendosi all'esterno dell'ectoderma, anziché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

# Quando viene specificato il neuroectoderma?

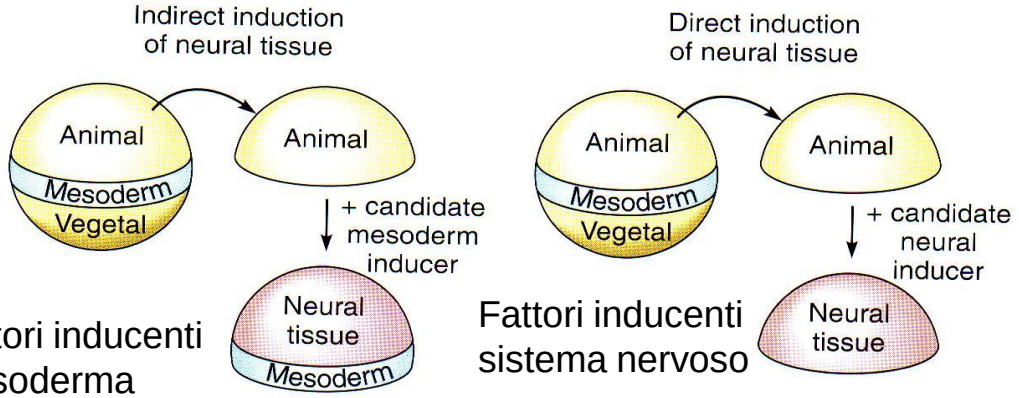


## La specificazione del SN avviene durante la gastrulazione ???



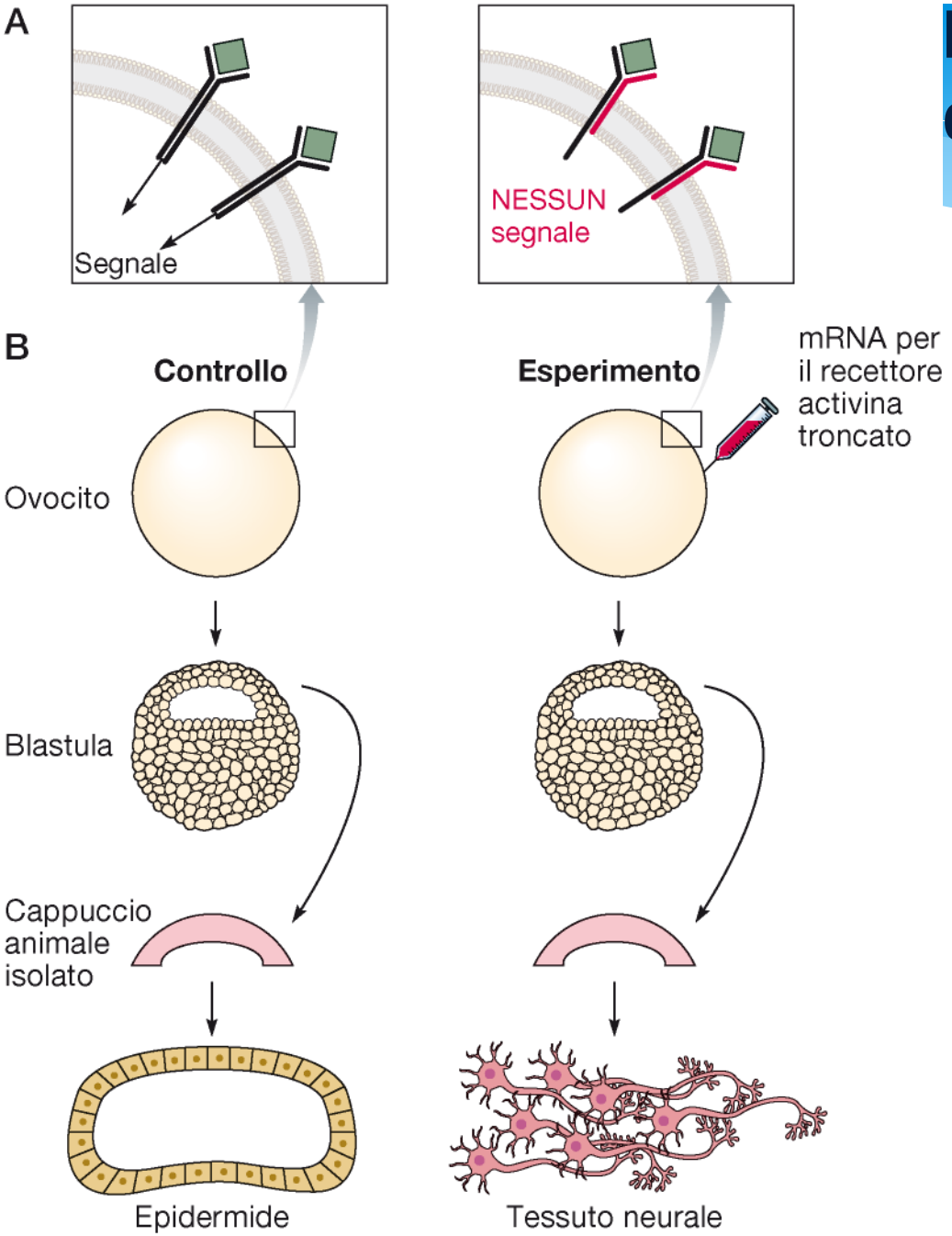

**Specificazione:** iniziale acquisizione del destino maturativo. **Il processo è reversibile**




Fattori inducenti mesoderma

Fattori inducenti sistema nervoso

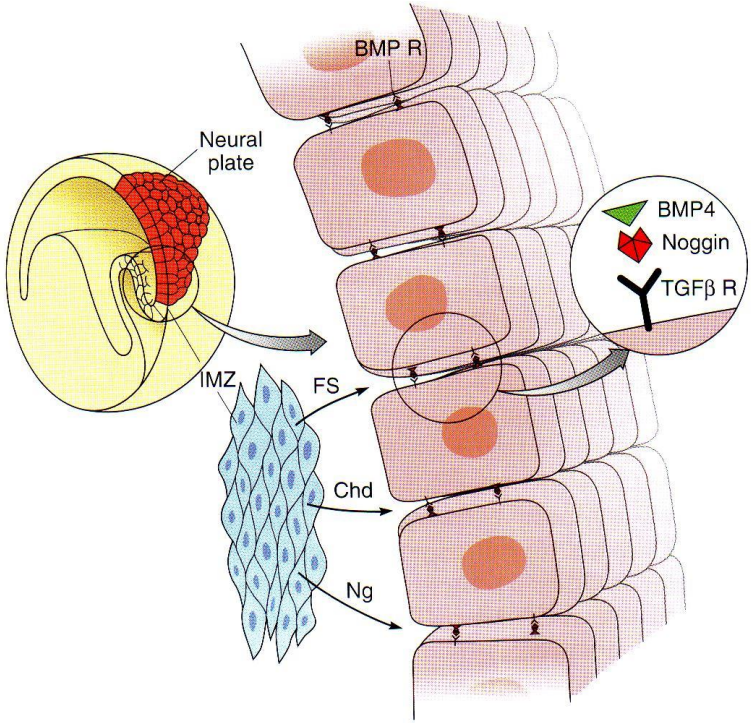
# Determinazione del Neuroectoderma in Anfibi

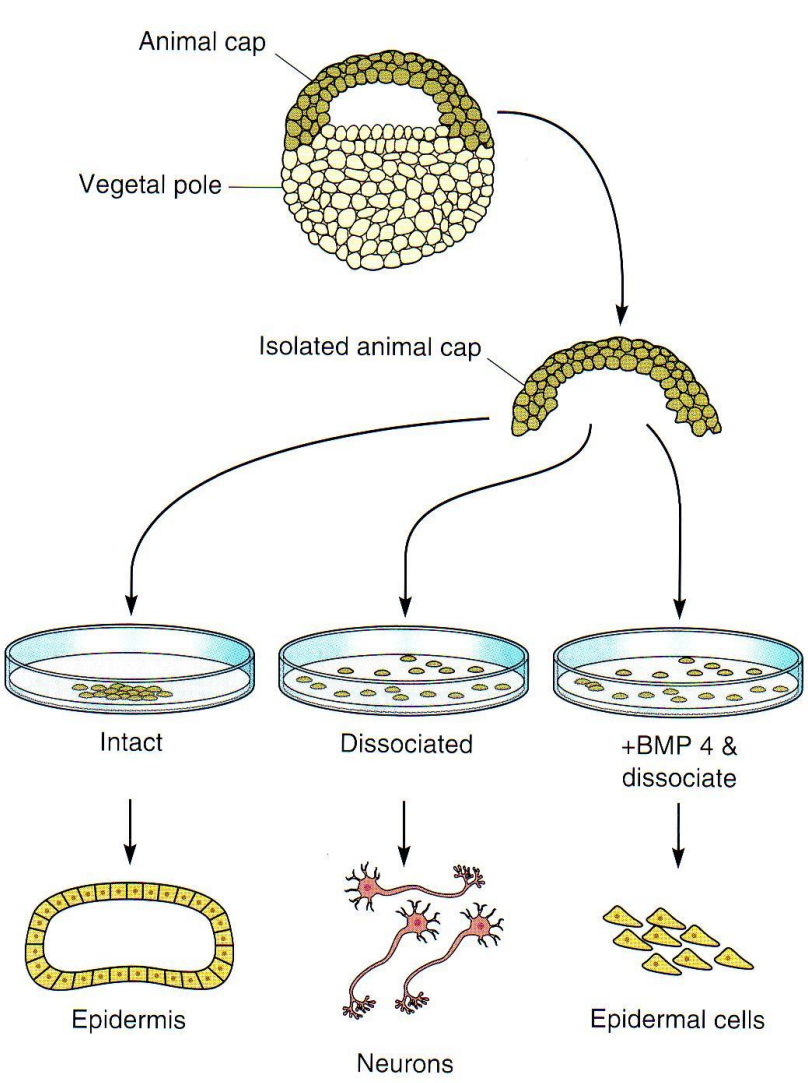



L'interferenza con la via di attivazione dell' activina, non consente la formazione del mesoderma, ma permette la formazione del sistema nervoso.

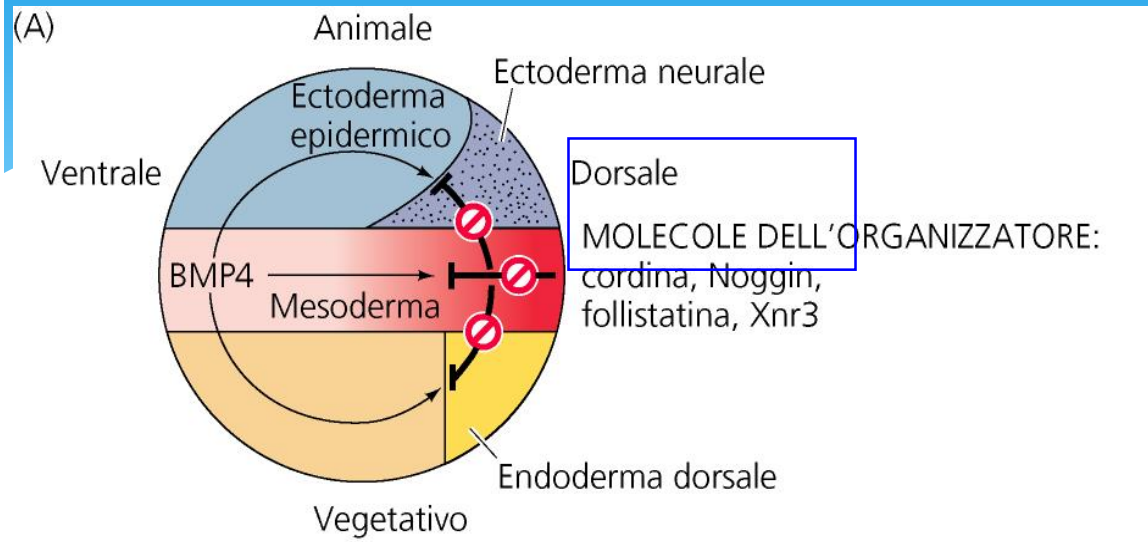
**Fattori Tgf Beta hanno un effetto Inibitorio sulla formazione di SN**

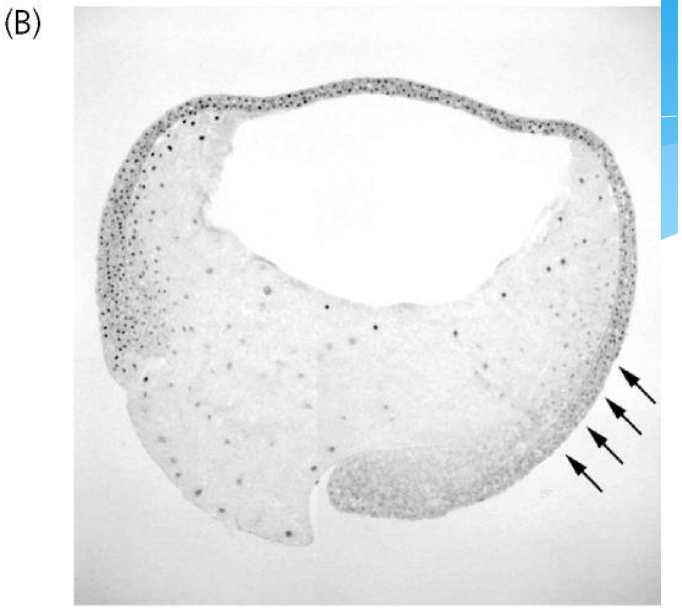
# BMP 4 (TGF-beta factor)
# Bone Morphogenetic Protein

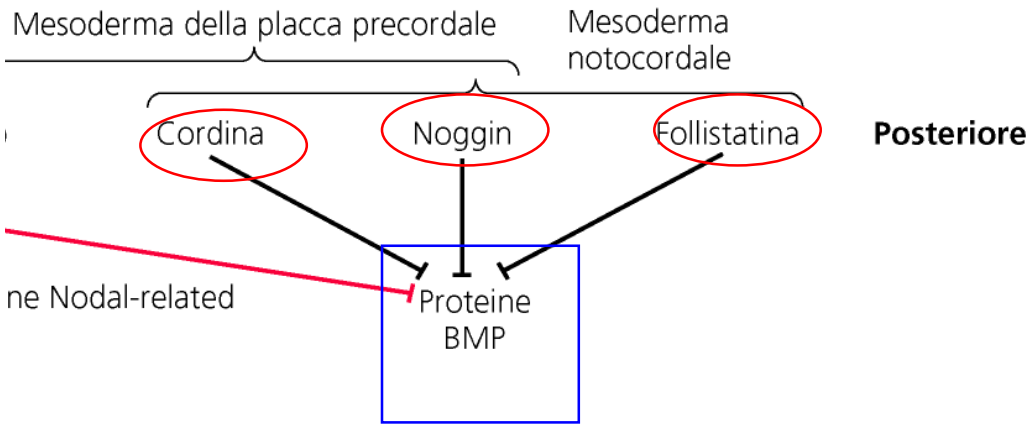


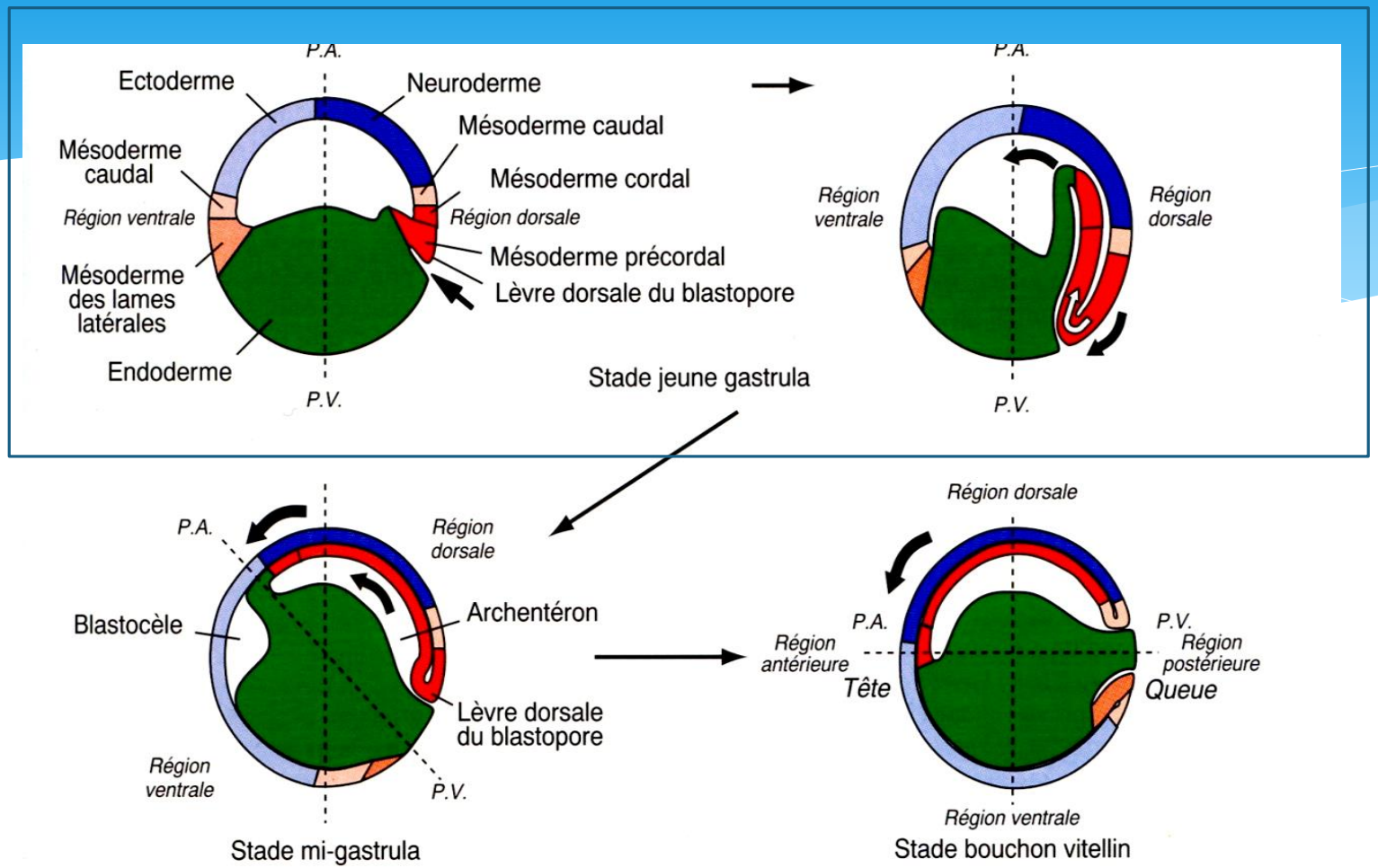



# Gli inibitori della via BMP4

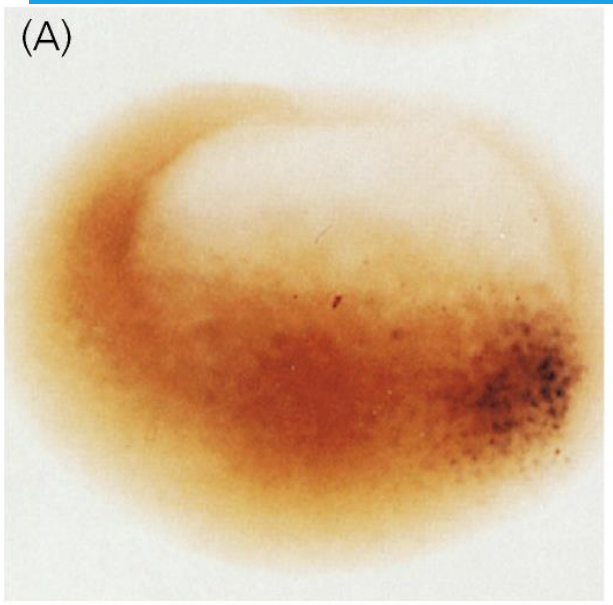


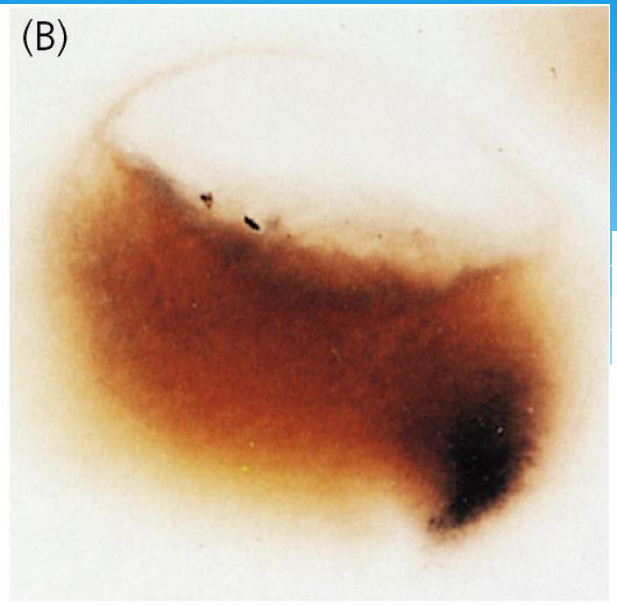



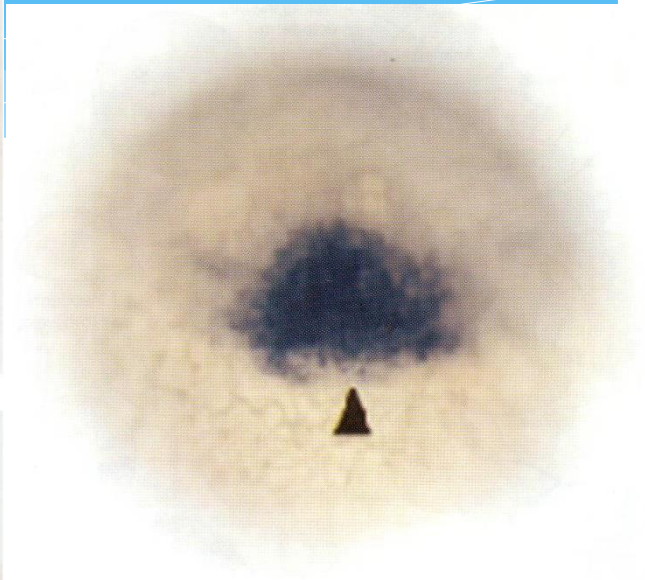



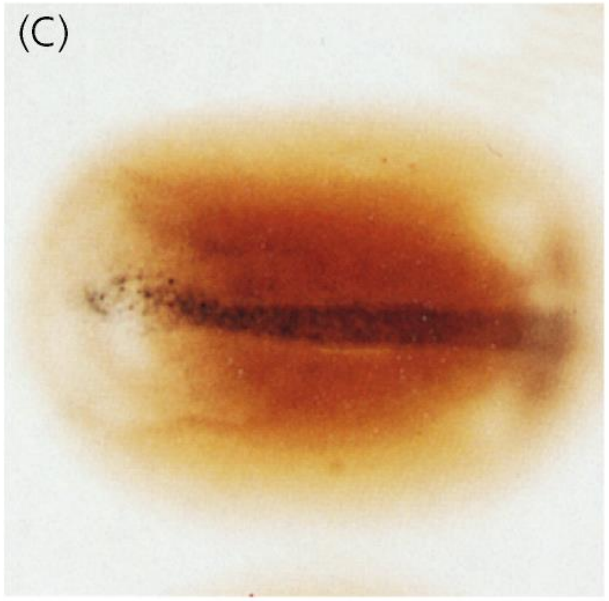

P.A.
Ectoderme
Neuroderme
Mésoderme caudal
Mésoderme caudal
Mésoderme cordal
Région ventrale
Région dorsale
Mésoderme précordal
Mésoderme des lames latérales
Lèvre dorsale du blastopore
Endoderme
P.V.
P.A.
Région ventrale
Région dorsale
P.V.
Stade jeune gastrula
P.A.
Région dorsale
Blastocèle
Archentéron
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

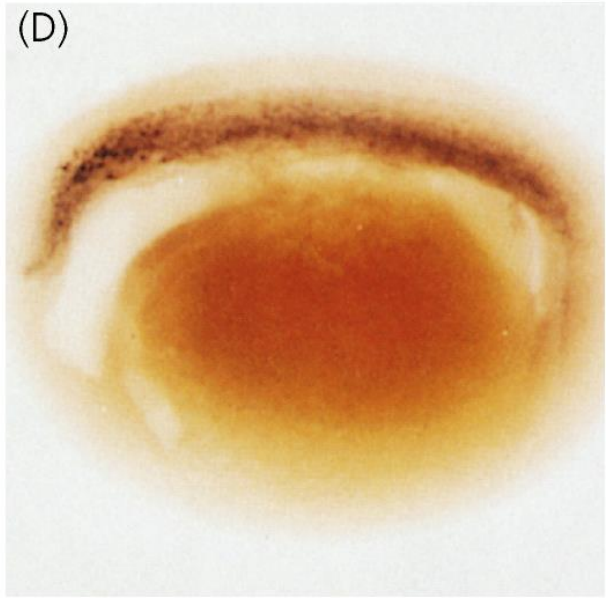
# Espressione di Noggin e Cordina



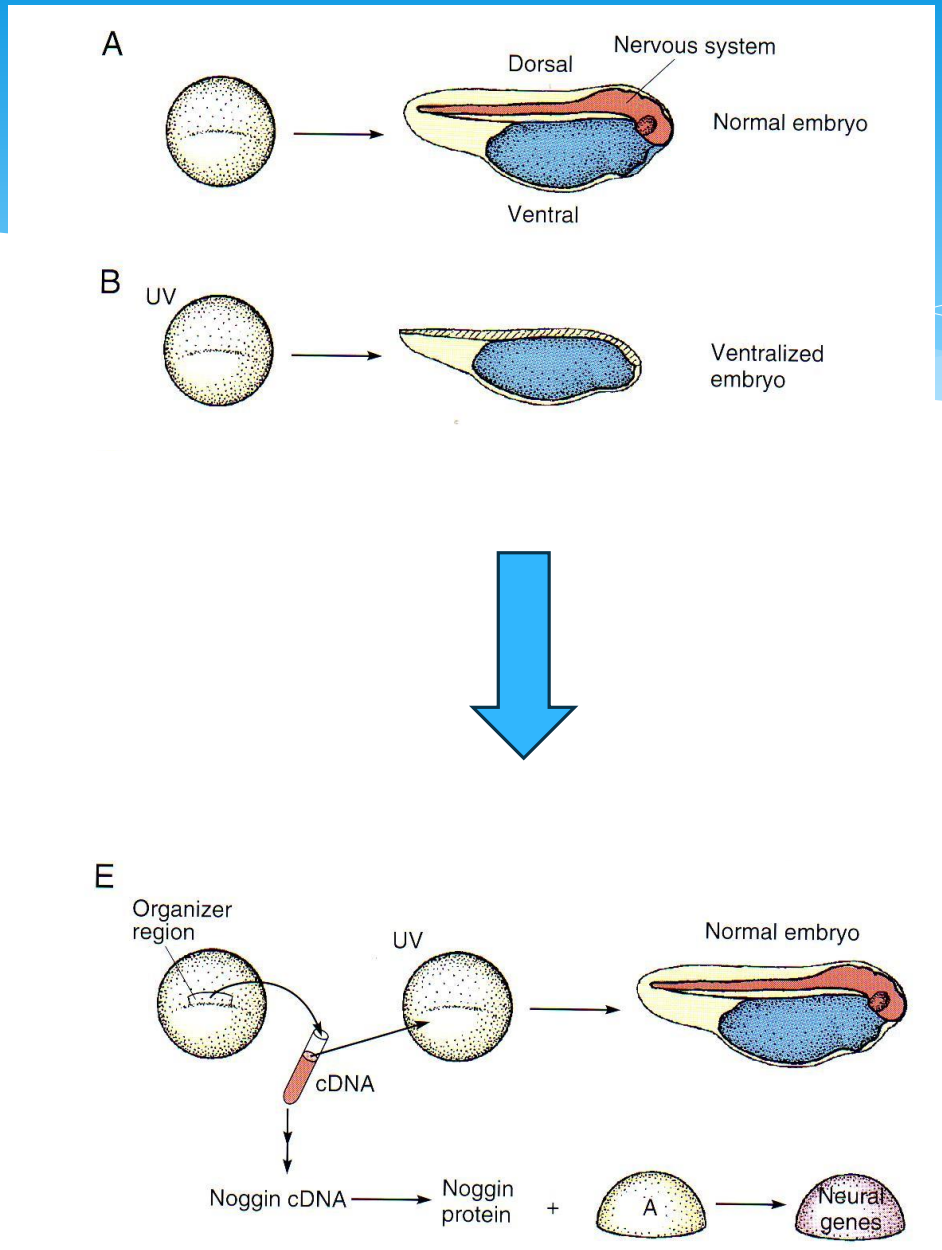





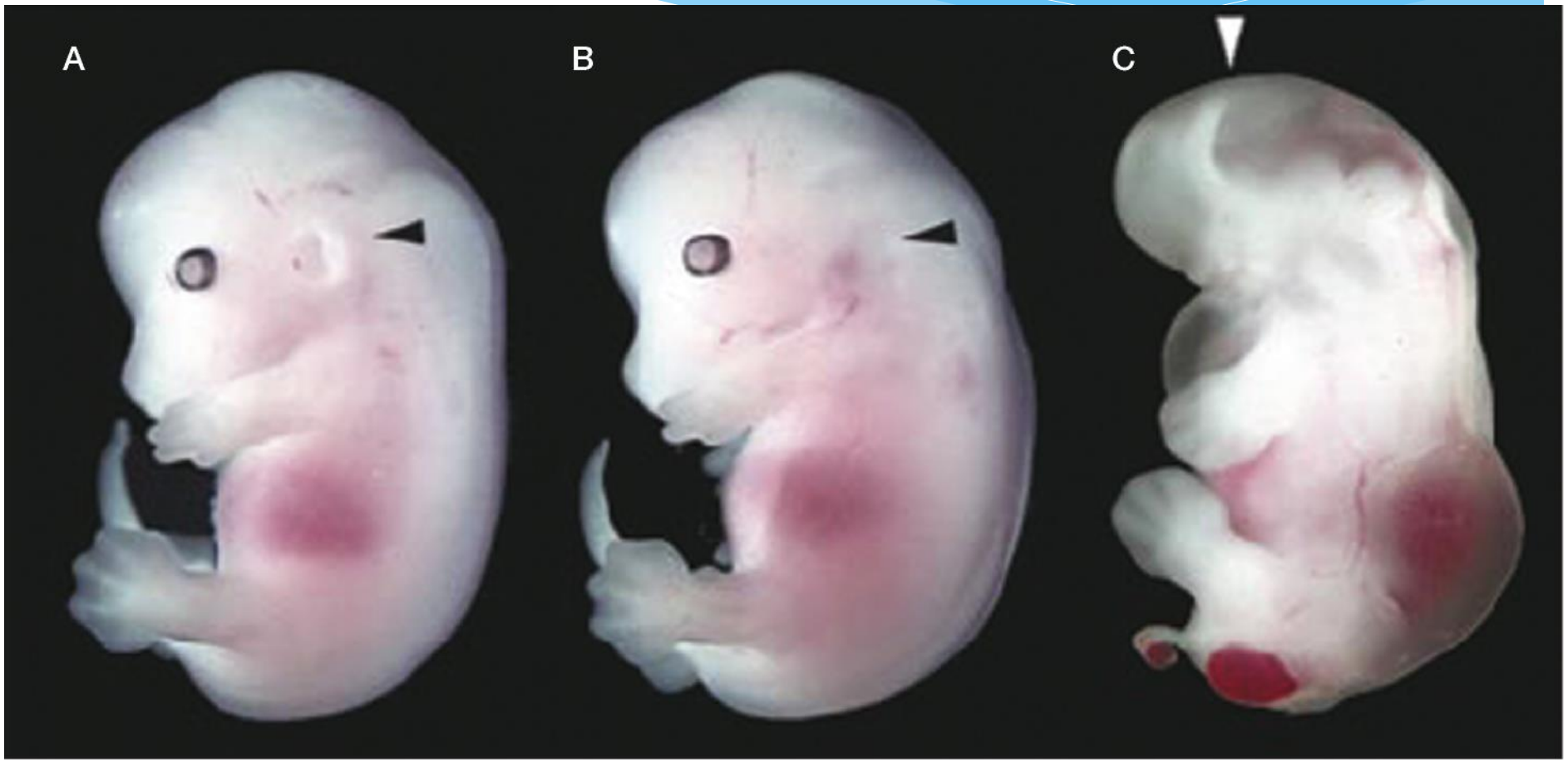



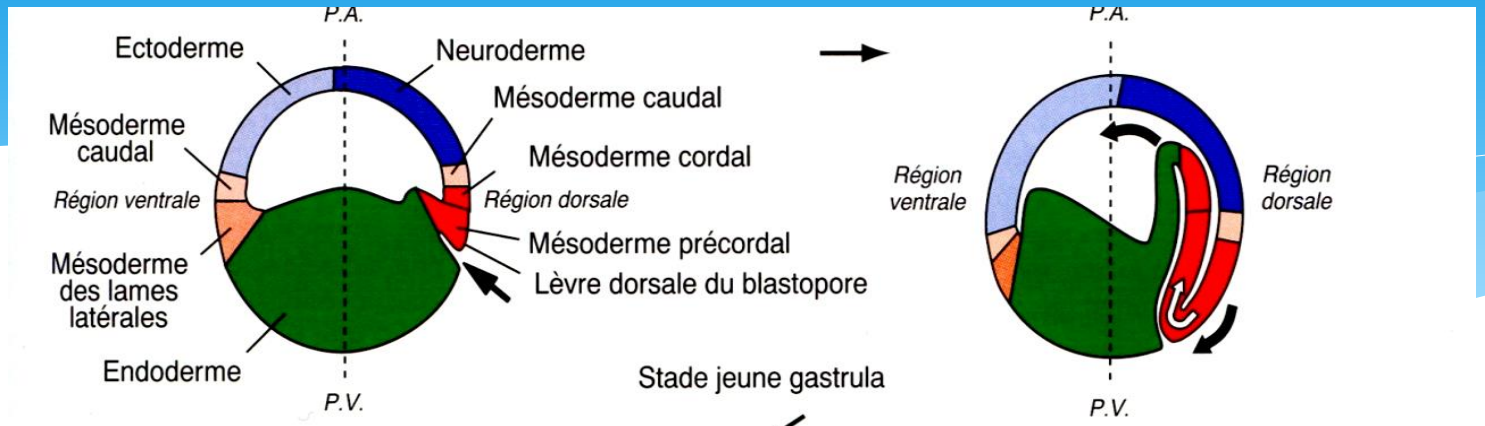
# Noggin

Noggin protegge l'area neuroectodermica dall'azione della BMP4

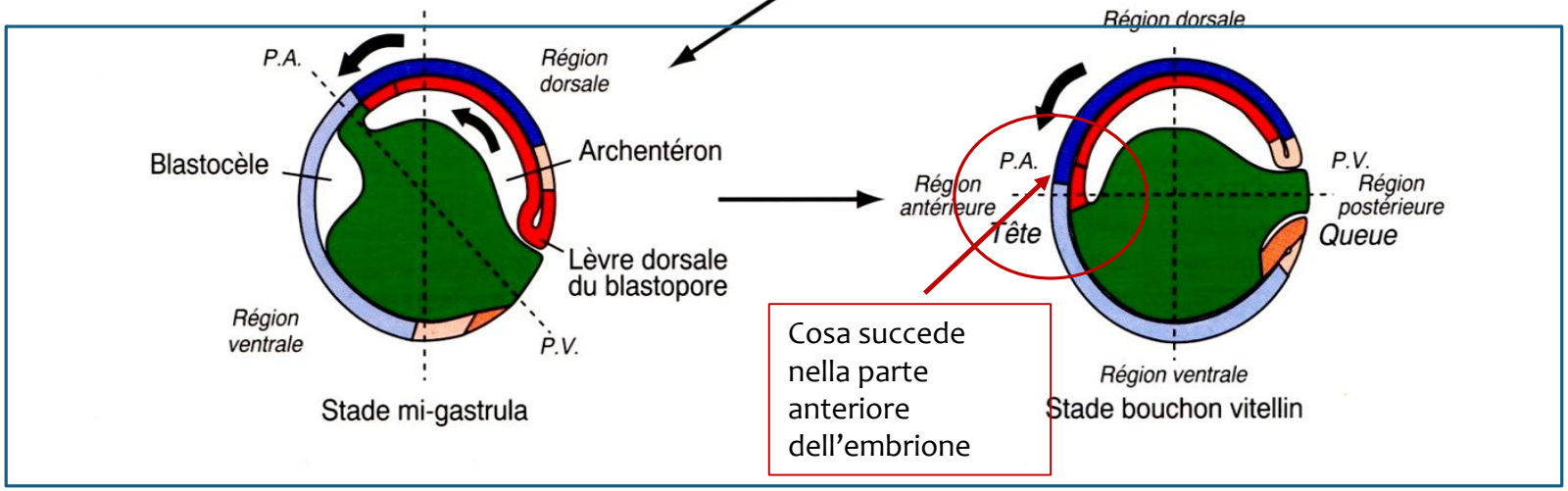


# WT nog-/- nog/chord-/-

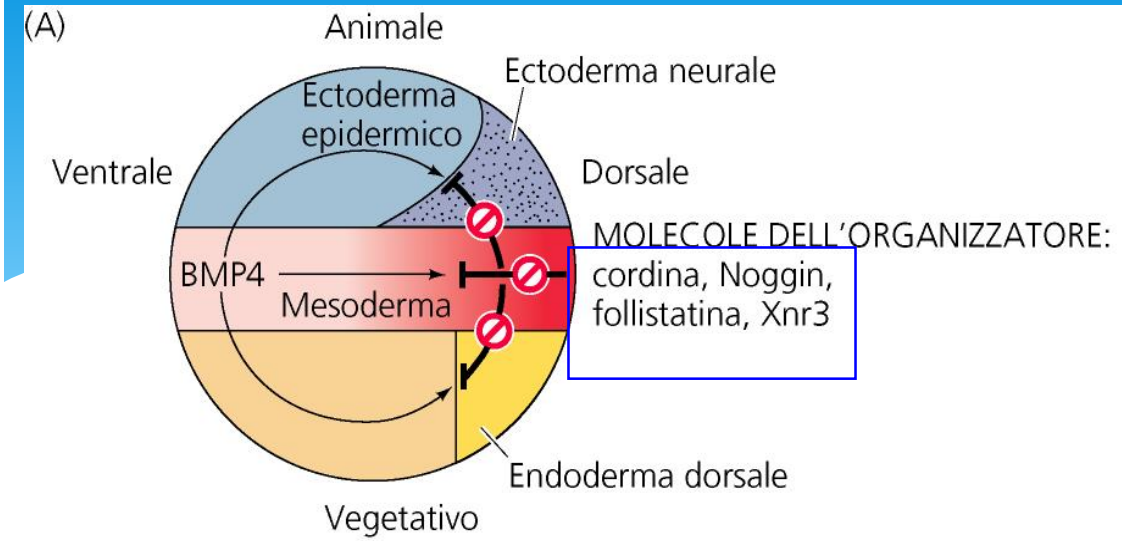


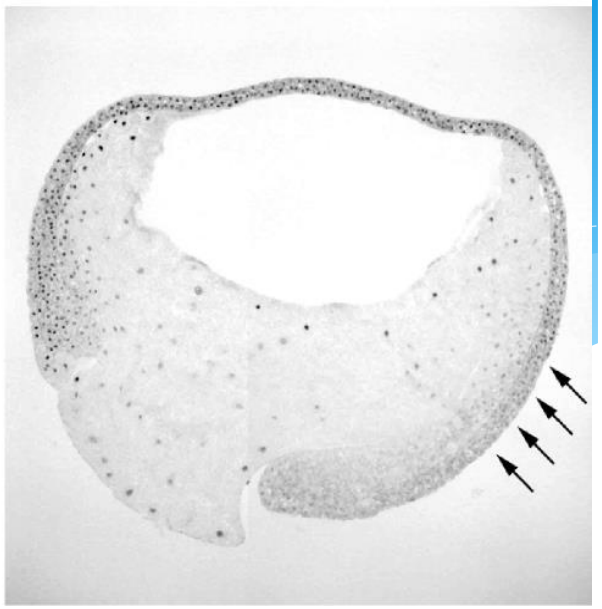


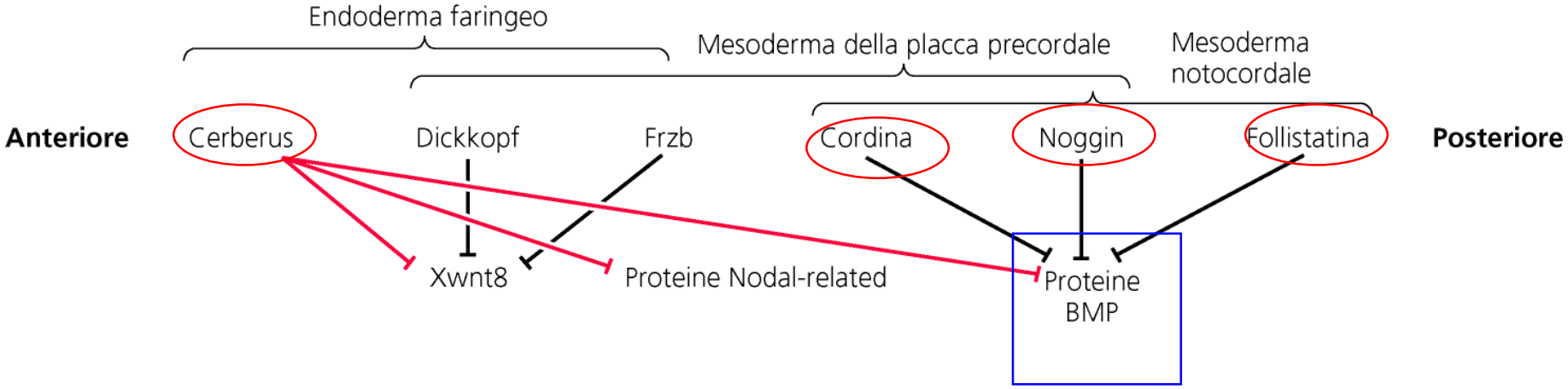

Stade jeune gastrula

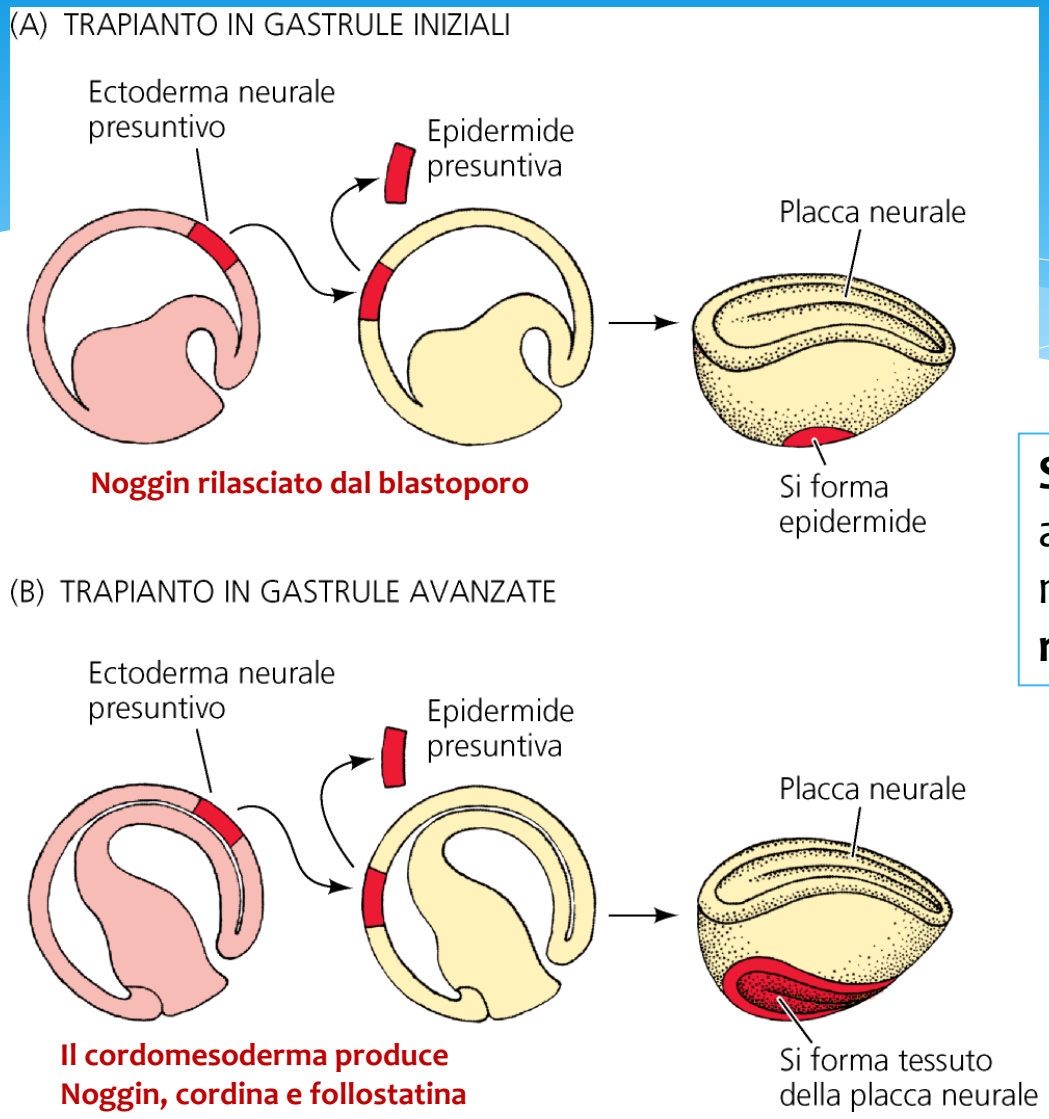



Cosa succede nella parte anteriore dell'embrione


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

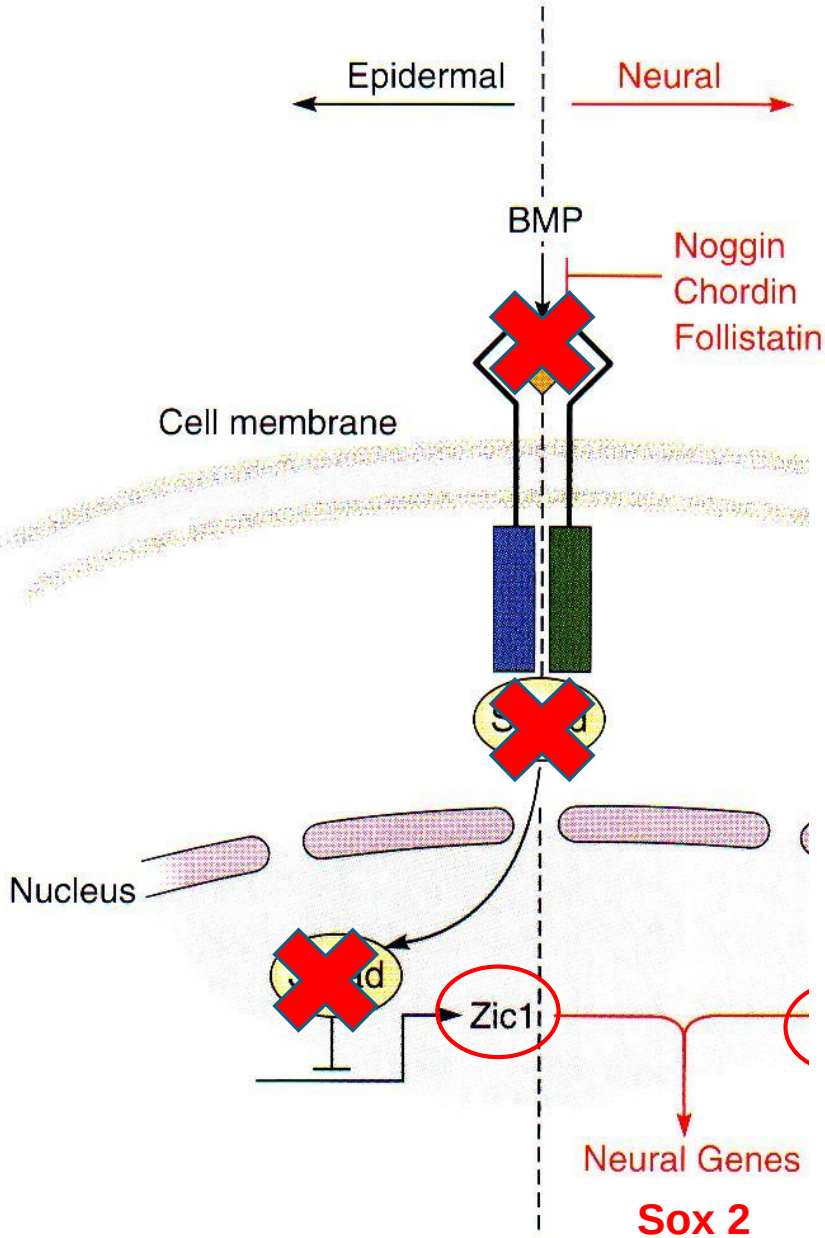

(B)


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

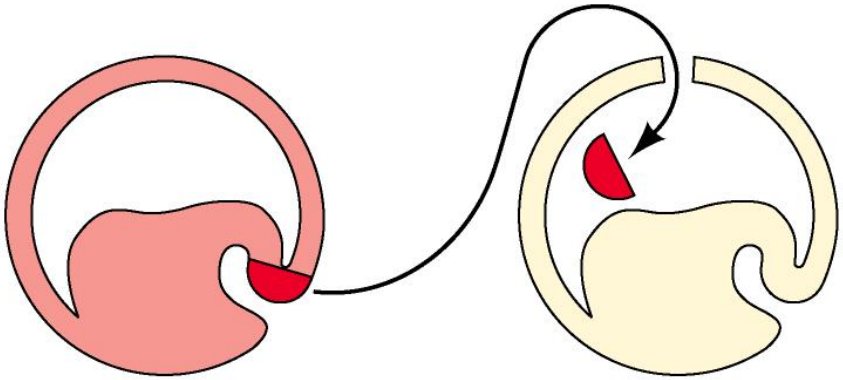


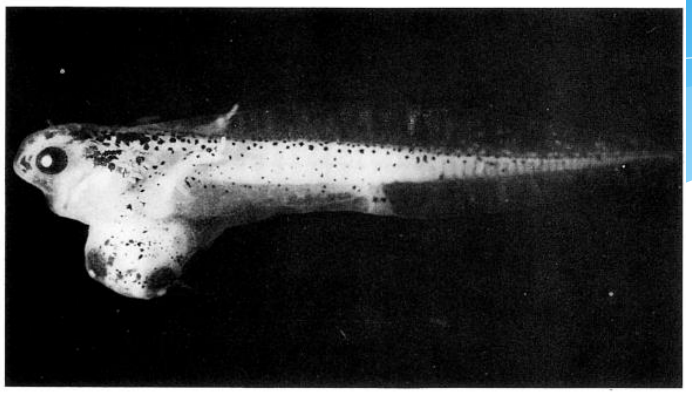

**Specificazione:** iniziale acquisizione del destino maturativo. **Il processo è reversibile**

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

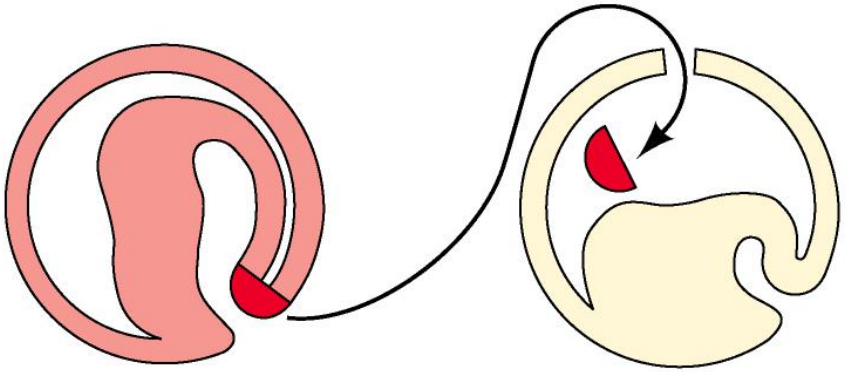

Epidermal
Neural
BMP
Noggin
Chordin
Follistatin
Cell membrane
Nucleus
Zic1
Neural Genes
Sox 2

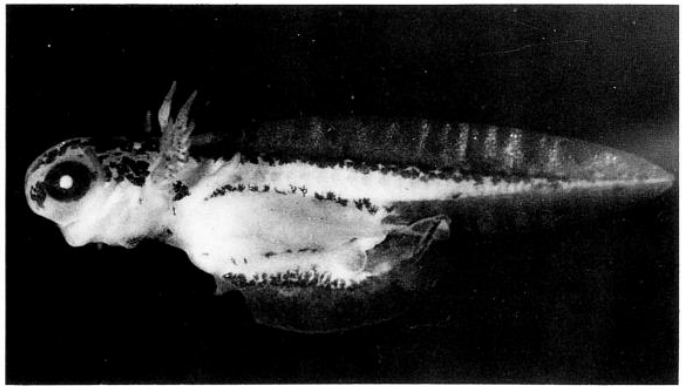
(A) Trapianto del labbro dorsale di gastrula in stadio iniziale



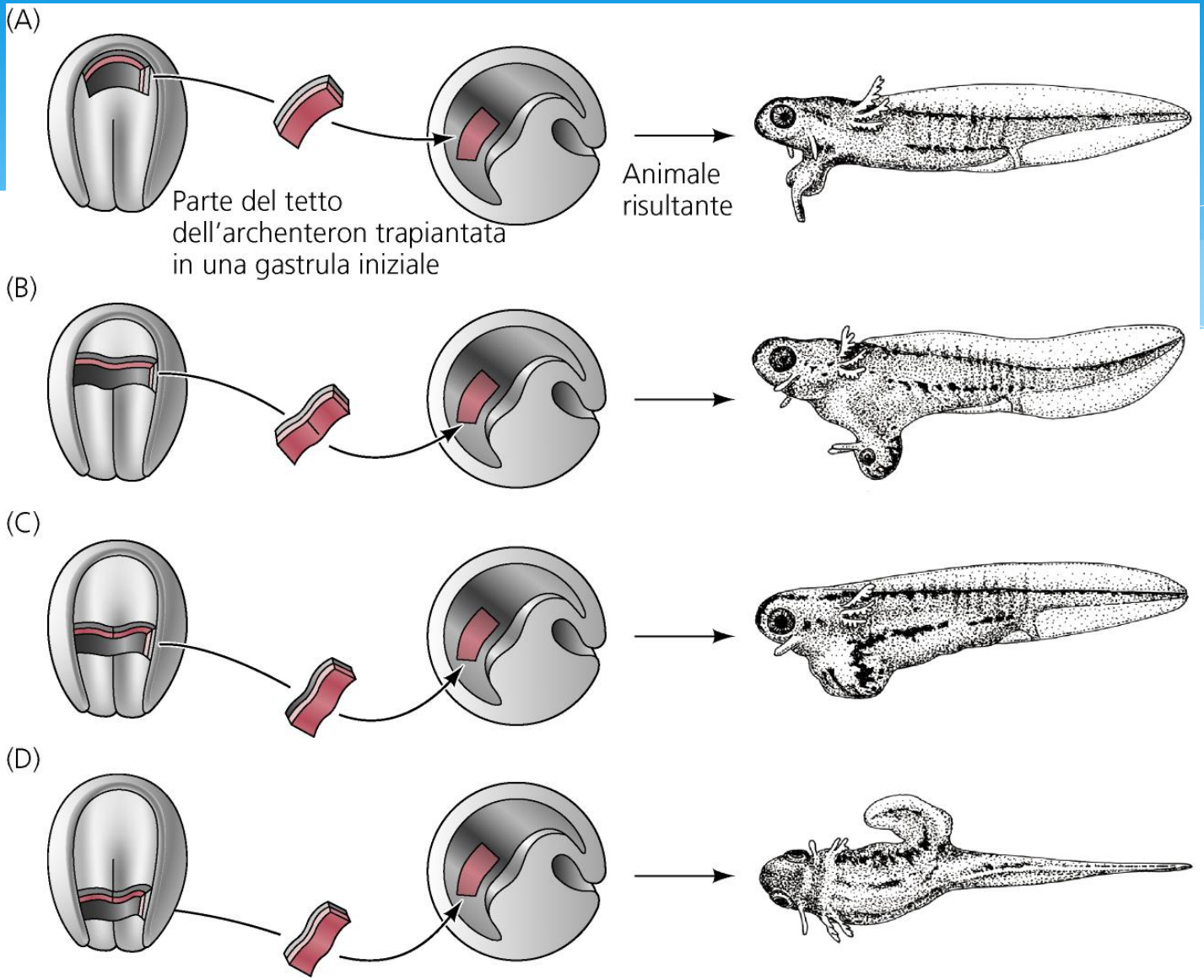


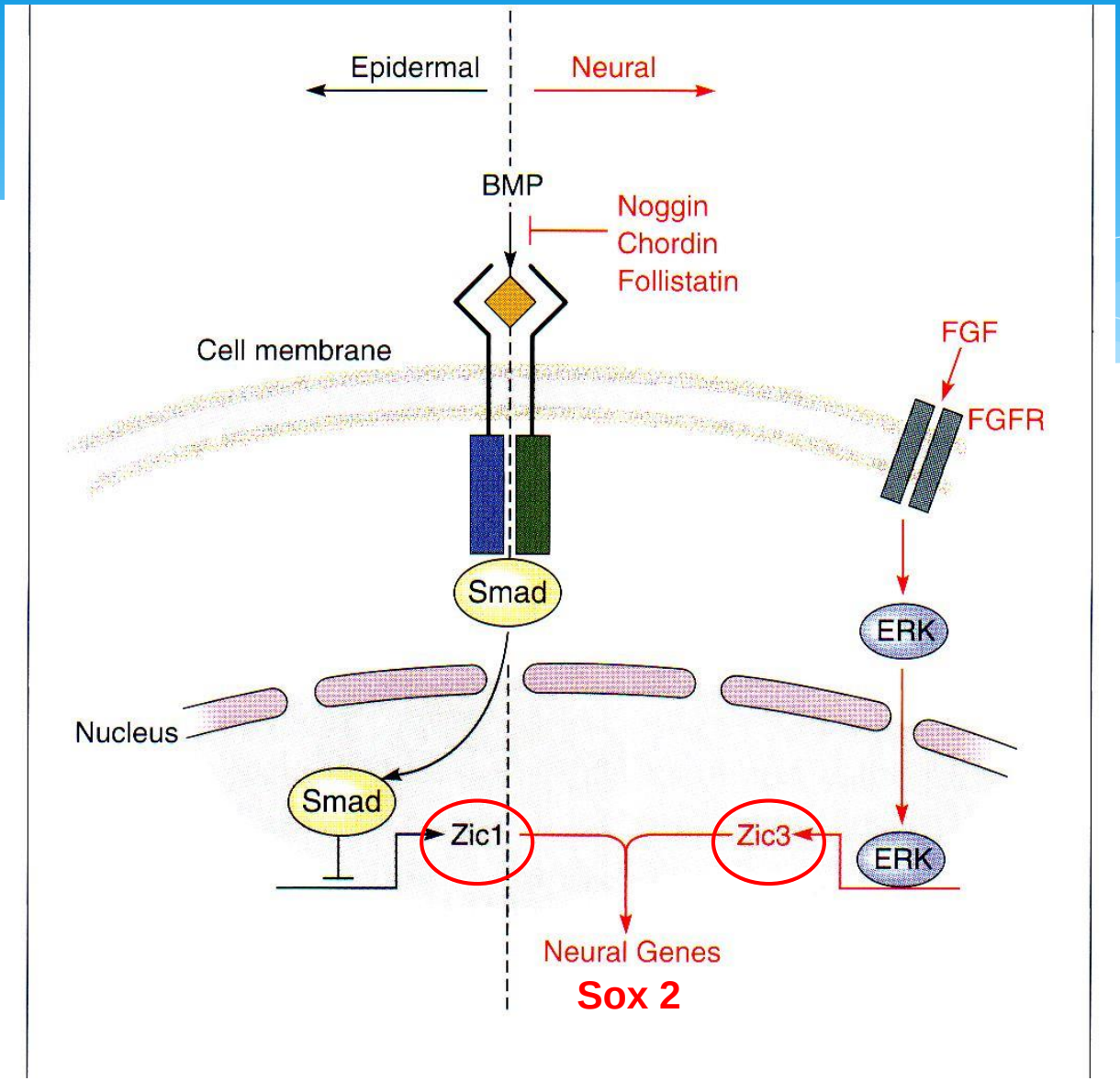
(B) Trapianto del labbro dorsale di gastrula in stadio avanzato





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