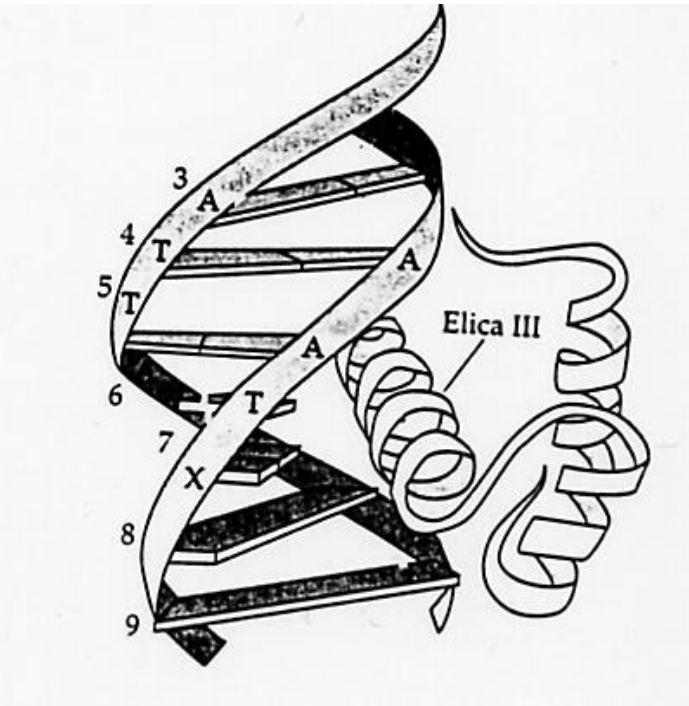
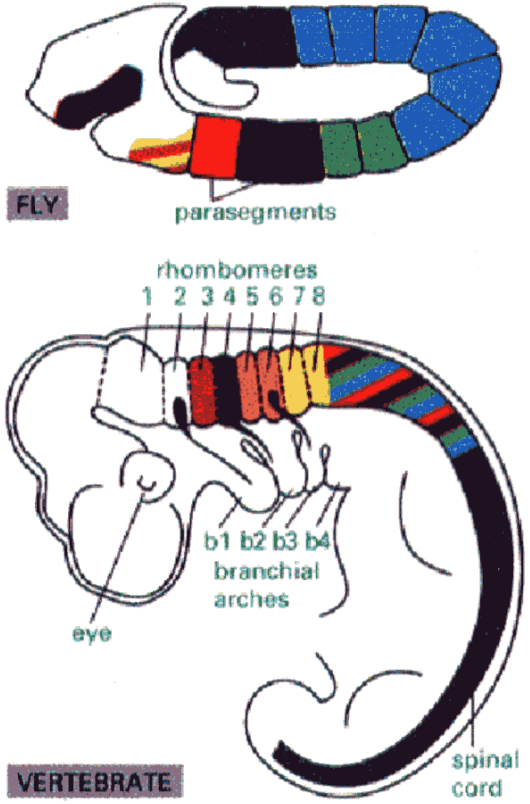
Geni HOX

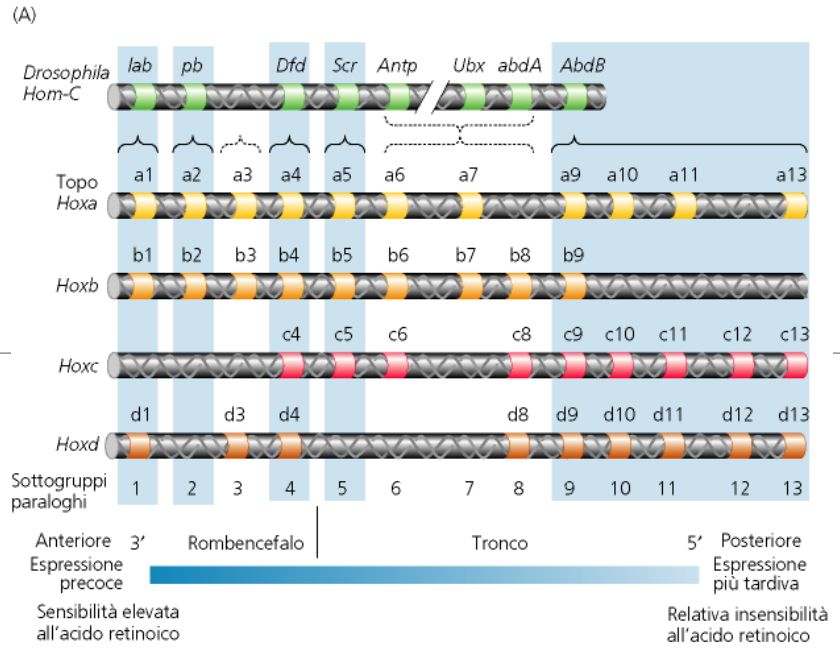


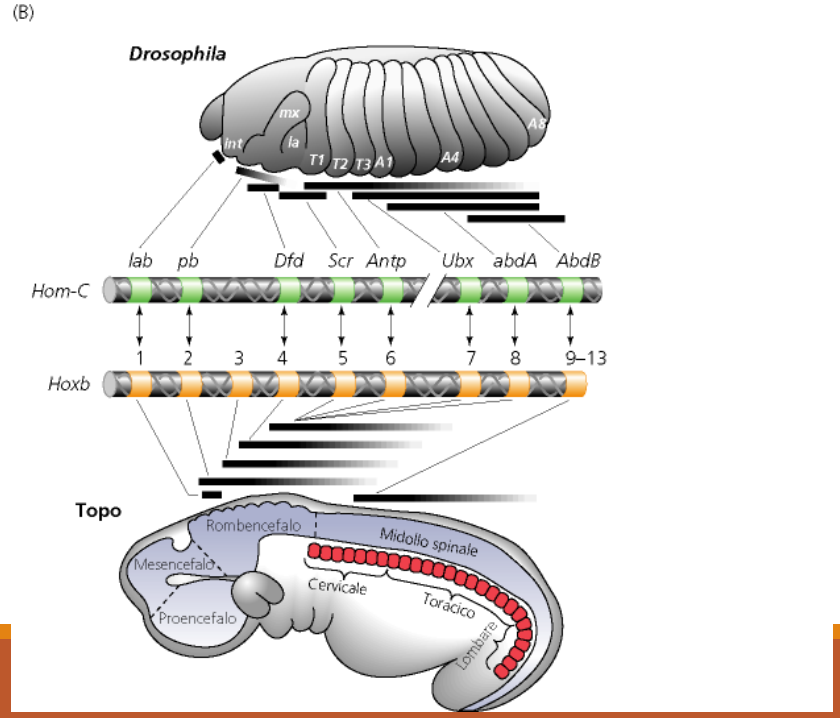
Geni omeotici nei mammiferi



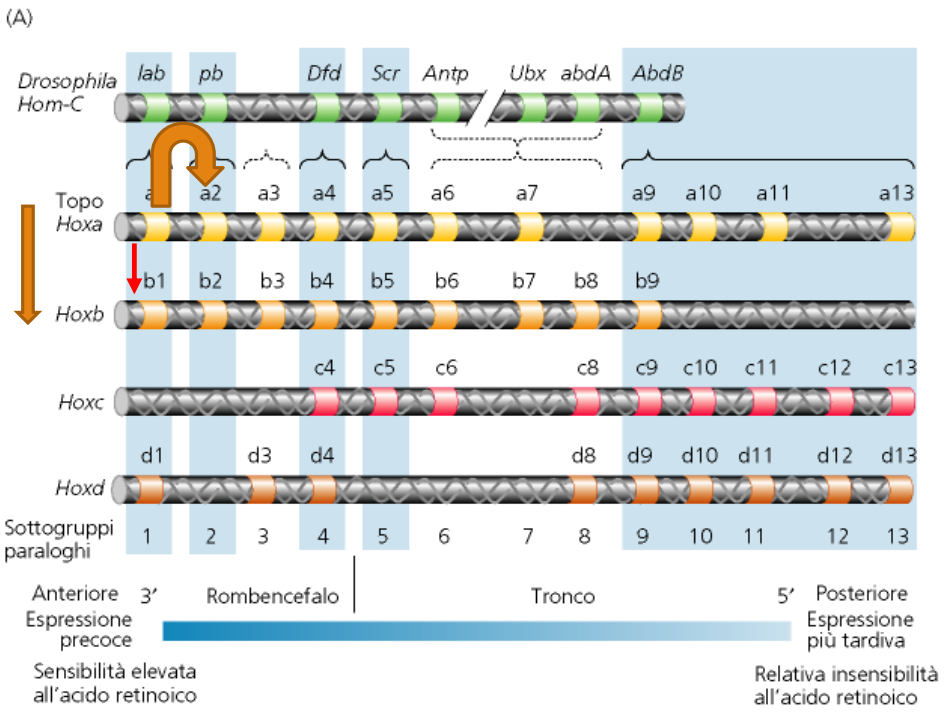
Geni Hox

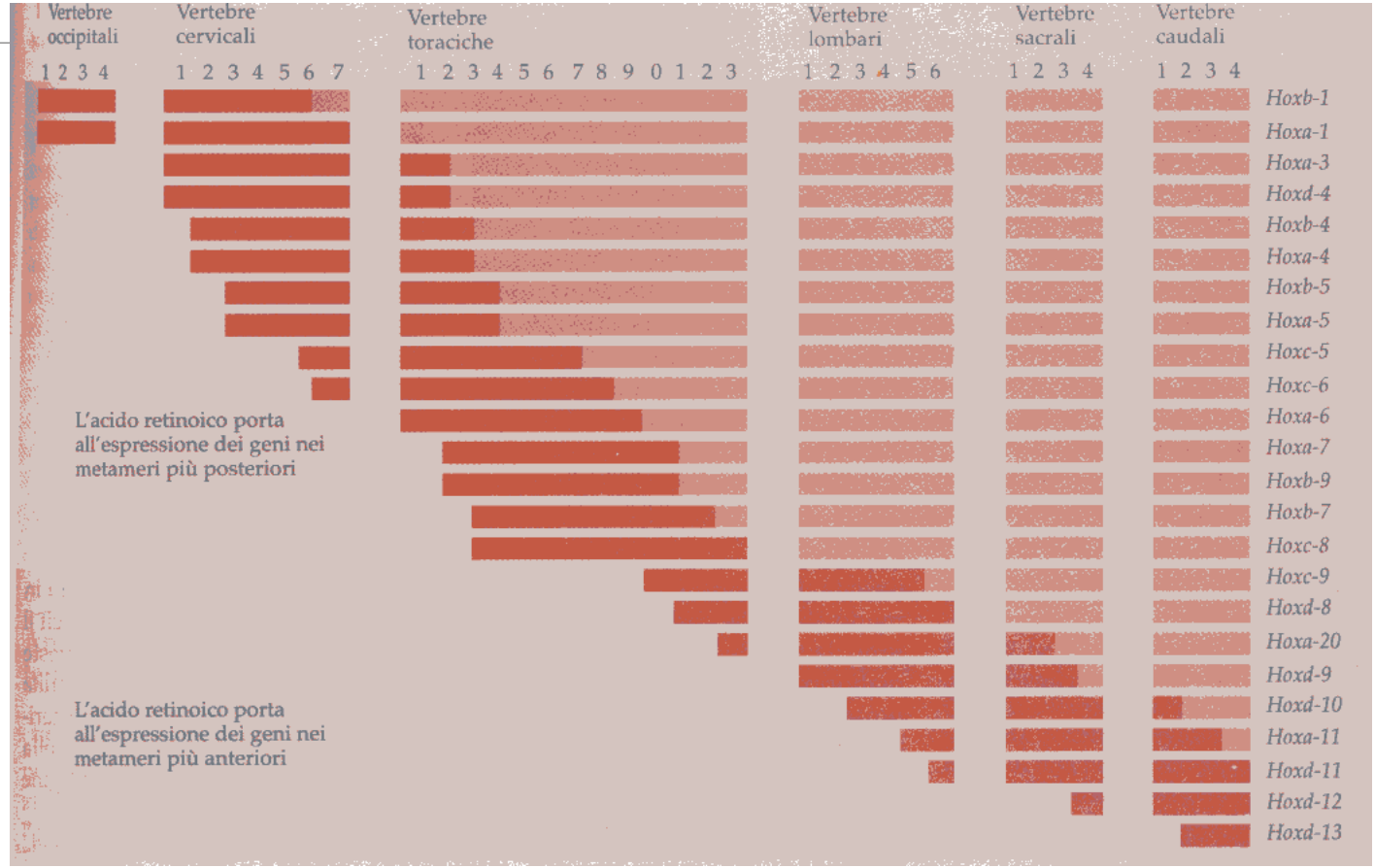
Amplificazione del cluster



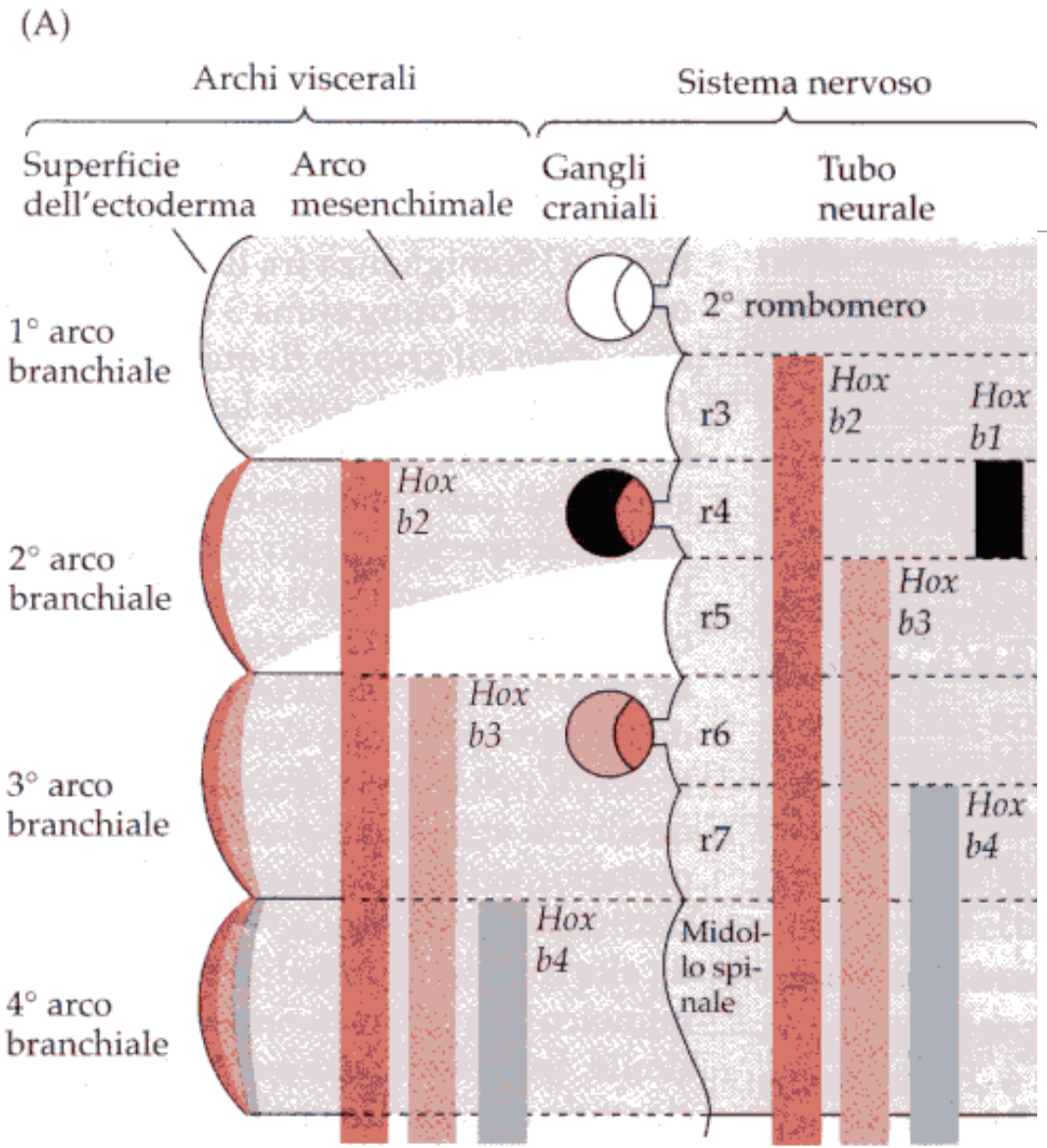


Come si esprimono i geni Hox





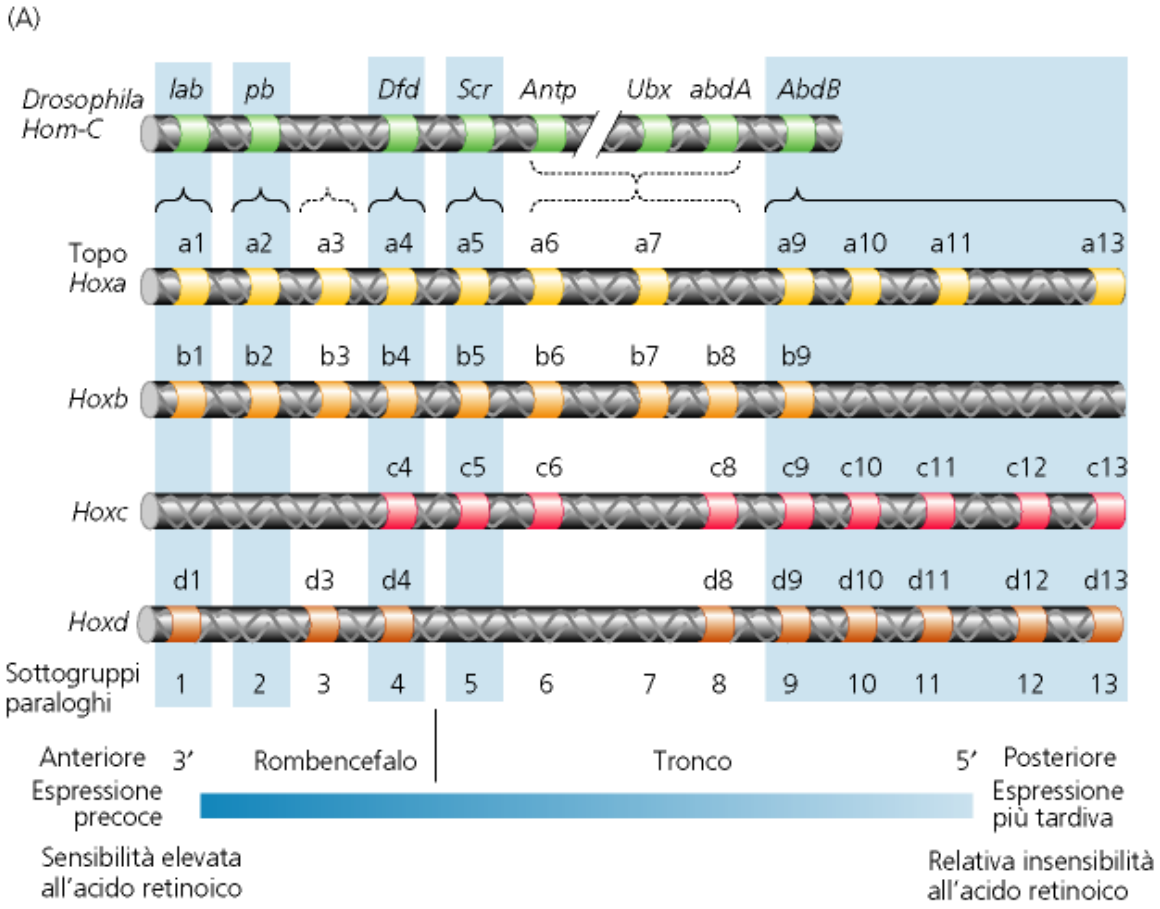
Regolazione positiva intra-cluster e inter-cluster (colinearità spazio –temporale)



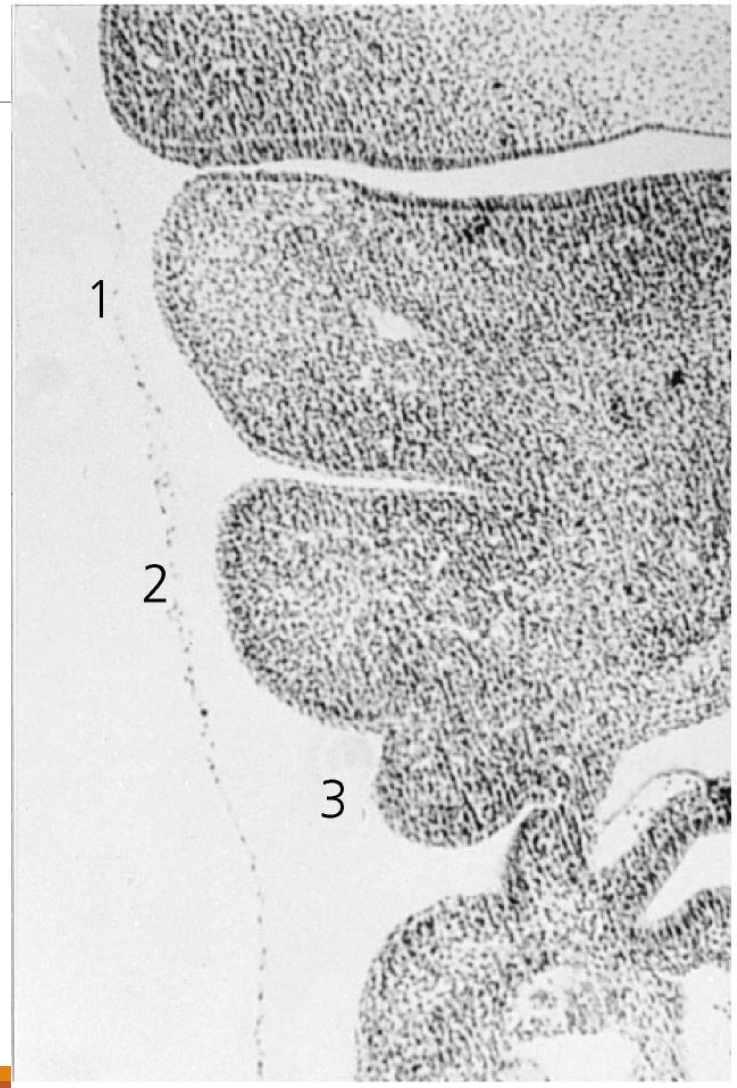
Dove sono espressi????

1. Notocorda
2. Somiti
3. Tubo neurale
4. Creste neurali

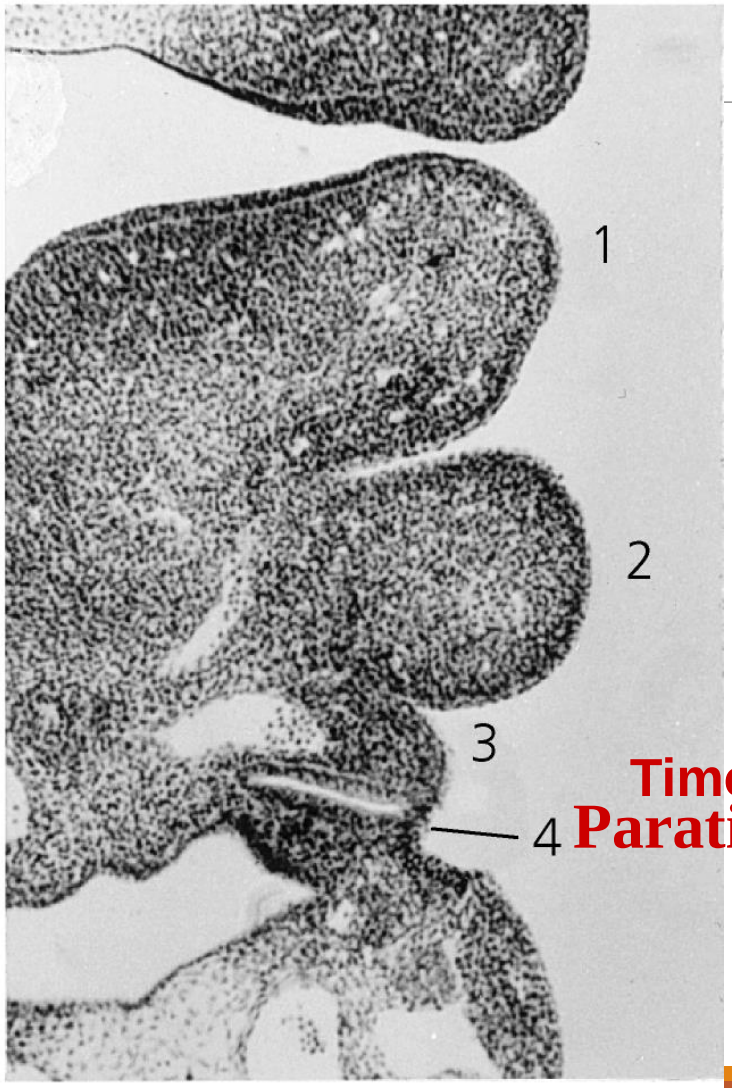
Perché cosi tanti geni omeotici nel vertebrato?????



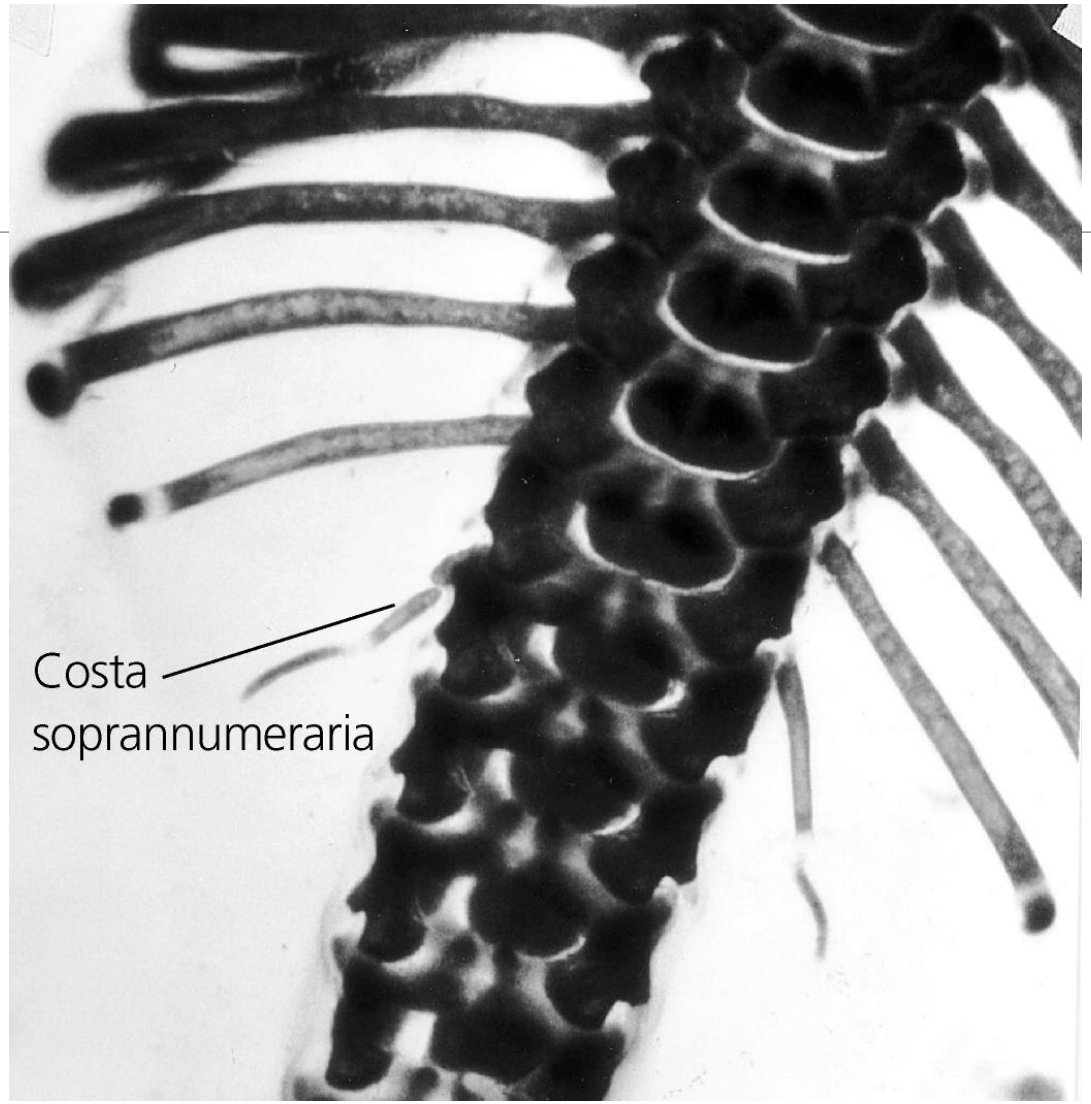
Mutazioni omeotiche



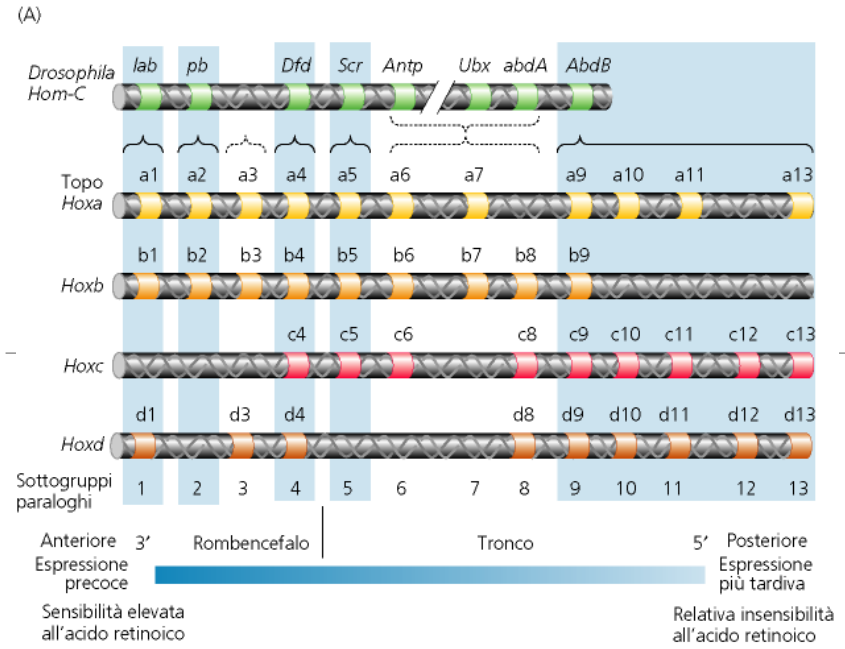
Hoxa-3$^{-/-}$



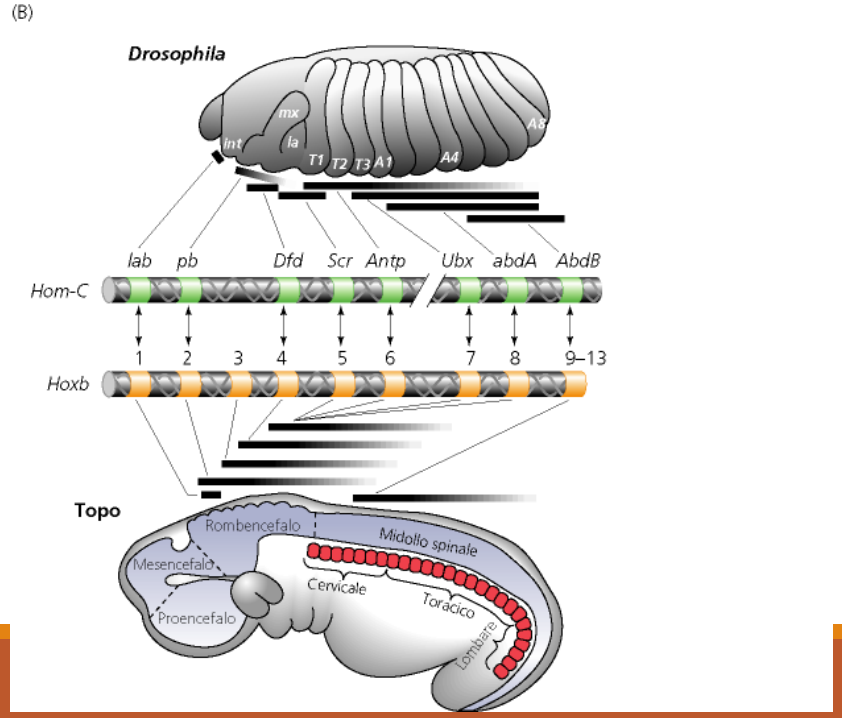
Hoxa-3$^{+/-}$



Espressione di Hox C8. La prima vertebra lombare forma costole

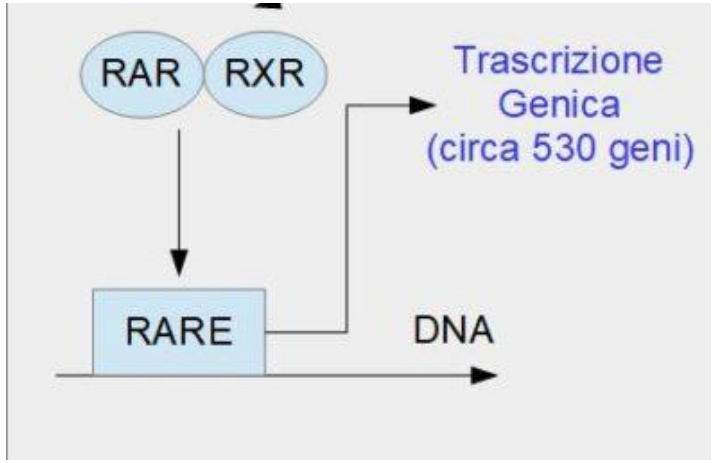


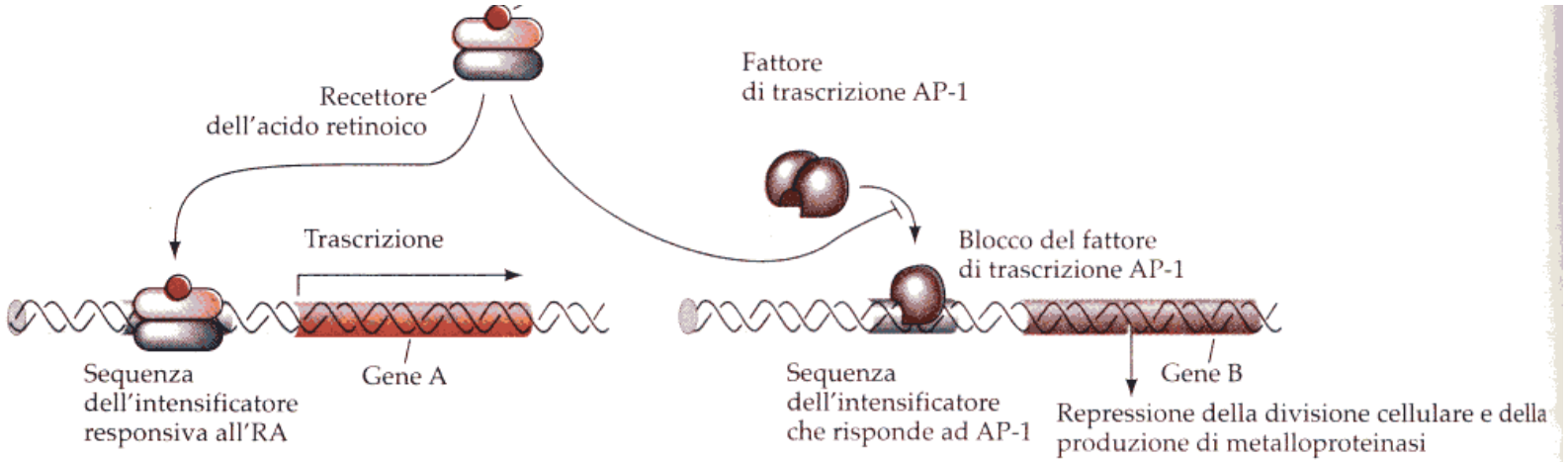
Come viene regolata l'espressione dei geni HOX?



E' sufficiente le regolazione intra-cluster ed inter-cluster?

Acido retinoico regola l'espressione dei geni HOX



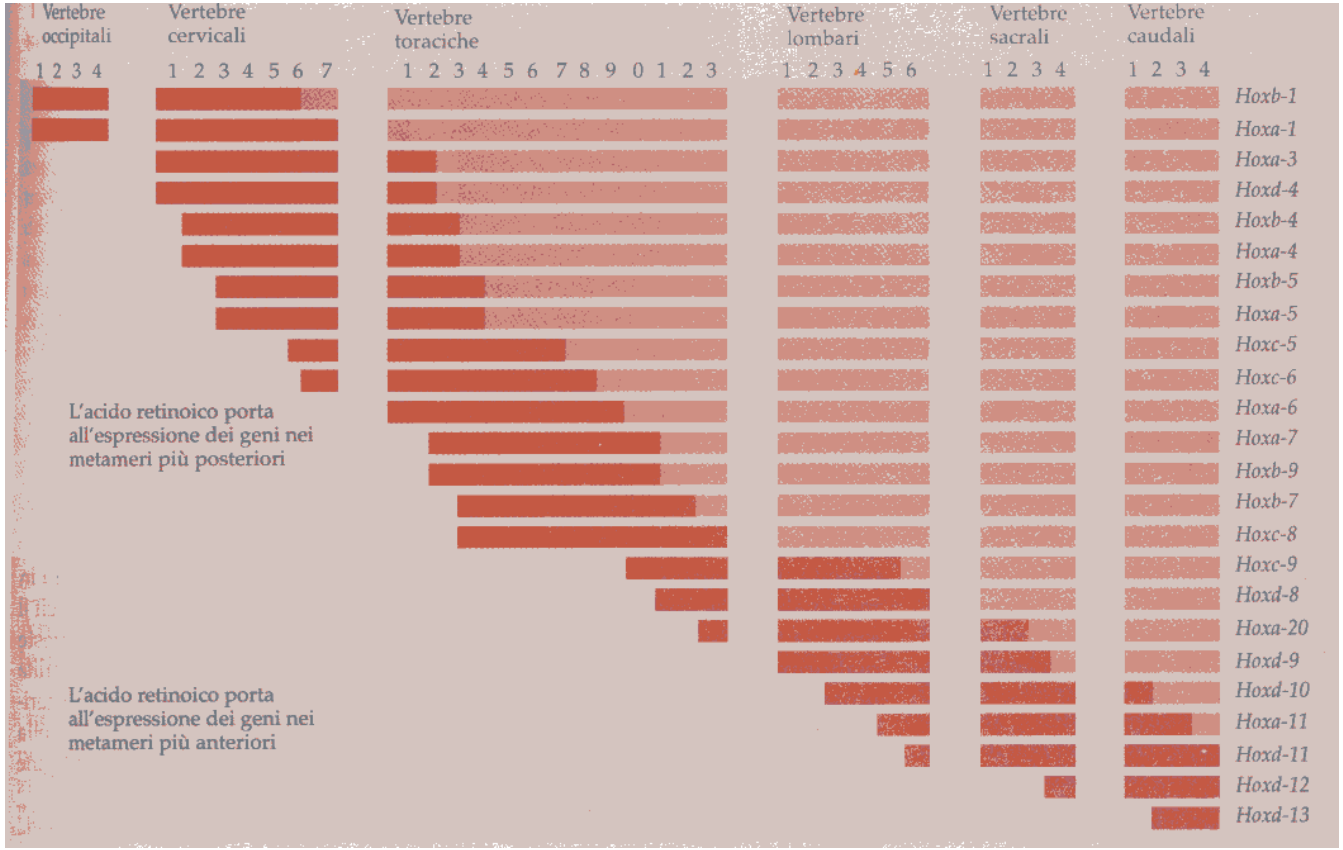


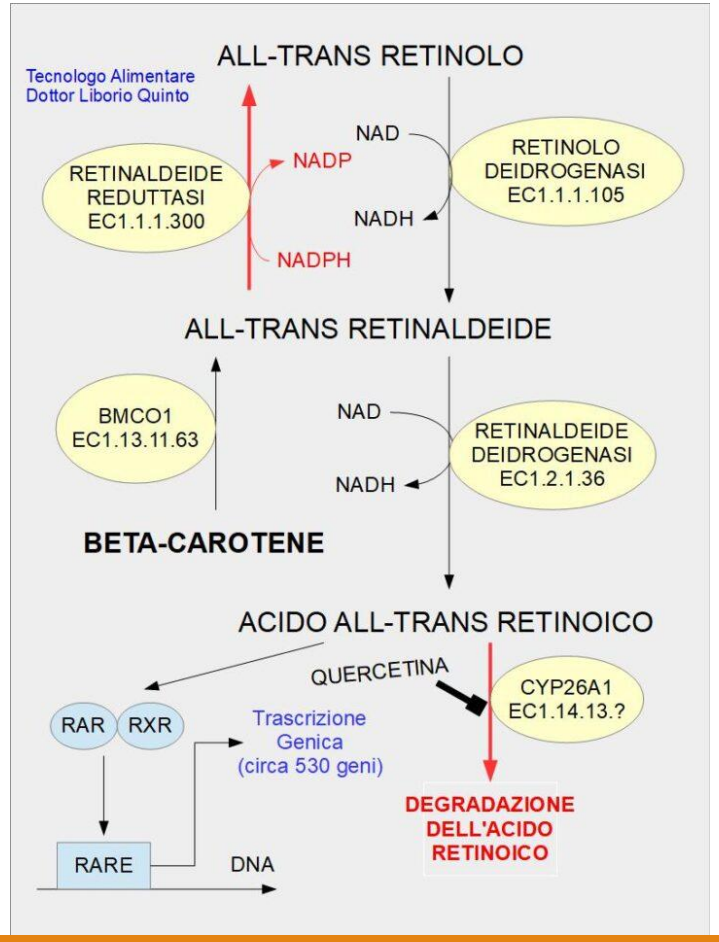
1. **Prodotto dal nodo di Hensen**
2. **Si forma un gradiente molecolare lungo l'asse A-P**

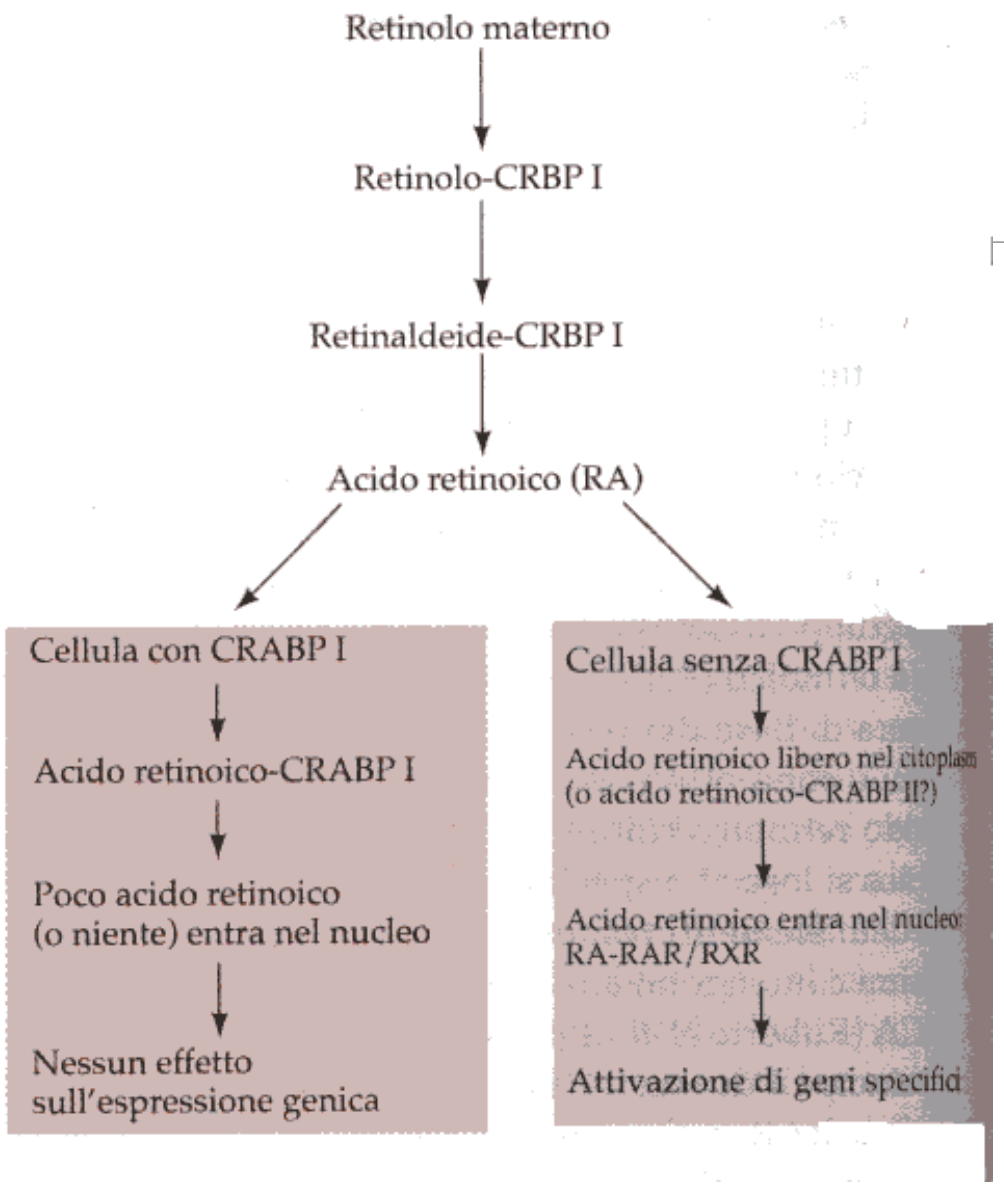
Gradiente Antero-posteriore di acido retinoico

Retinoic Acid

La regolazione dei livelli di acido retinoico lungo l'asse antero-posteriore avviene attraverso un equilibrio tra la sintesi da parte delle retinoide deidrogenasi e la degradazione da parte delle CYP26A, creando gradienti di concentrazione che guidano lo sviluppo corretto delle strutture embrionali.







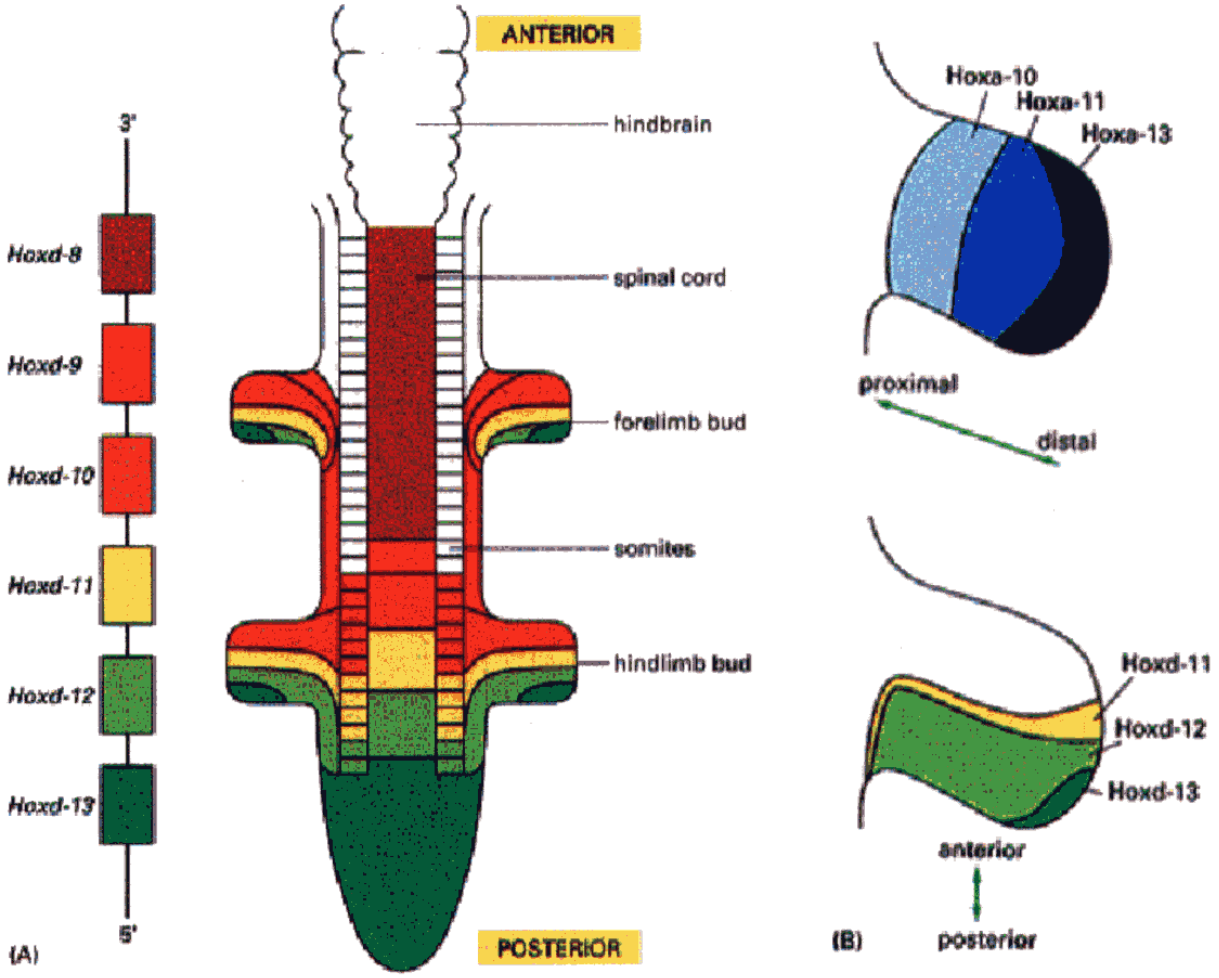
La concentrazione dell'acido retinoico che agisce nella cellule è finemente regolata dal livello di espressione intracellulare di RAR/RXR e CRABP

Agenti Teratogeni

Tabella 17.1 Alcuni agenti ritenuti responsabili di disorganizzazione nello sviluppo fetale umano[a]

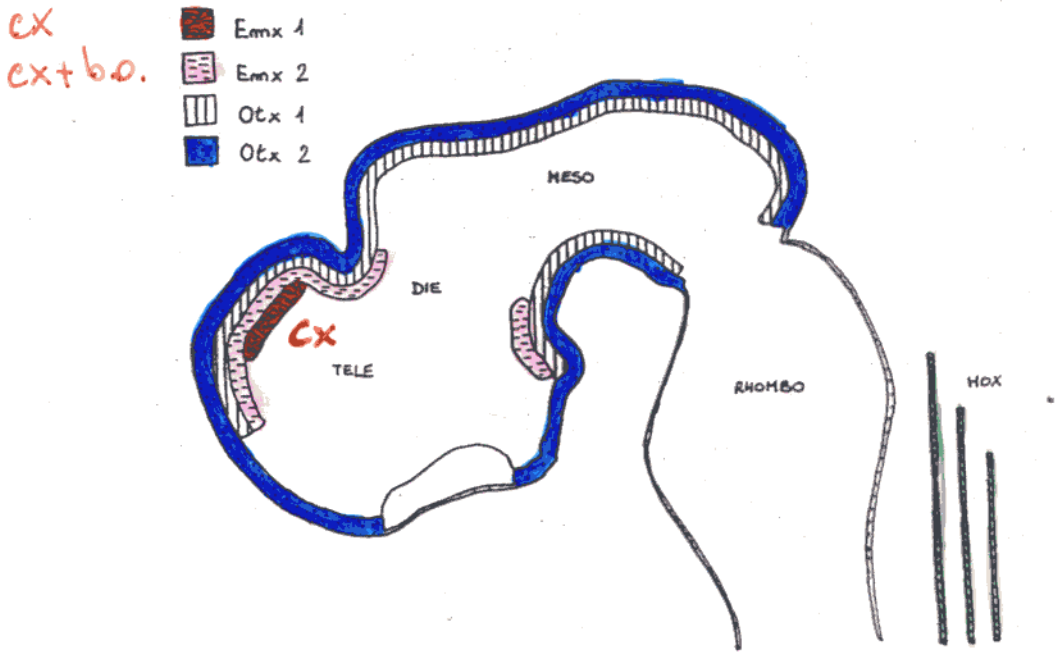
FARMACI E SOSTANZE CHIMICHE
Acido retinoico (Isotretionina, Accutane)
Acido valproico
Alcol
Aminoglicosidi (Gentamicina)
Aminopterina
Agenti antitiroidei (PTU)
Bromuro
Fumo di sigaretta
Cocaina
Cortisone
Dietilstilbestrolo
Difenilidantoina
Eroina
Piombo
Metilmercurio
Penicillamina
Streptomicina
Tetraciclina
Talidomide
Trimetadione
Varfarina
RADIAZIONI IONIZZANTI (RAGGI X)
IPOTERMIA
AGENTI INFETTIVI
Citomegalovirus
Herpes simplex
Parvovirus
Rosolia
Toxoplasma gondii (toxoplasmosi)
Treponema pallidum (sifilide)
Virus coxsackie
PATOLOGIE METABOLICHE DELLA MADRE
Diabete
Deficit dietetici, malnutrizione
Fenilchetonuria
Patologie autoimmuni (inclusa incompatibilità Rh)

Geni Hox nella formazione dell’arto



La regione della testa non esprime geni HOX, ma esprime altri omeotici omologhi di geni di Drosophila

FIGURA 6.10
I geni EMX e OTX nella regionalizzazione del cervello embrionale



Empty spiracles: Emx
Orthodendicle: Otx