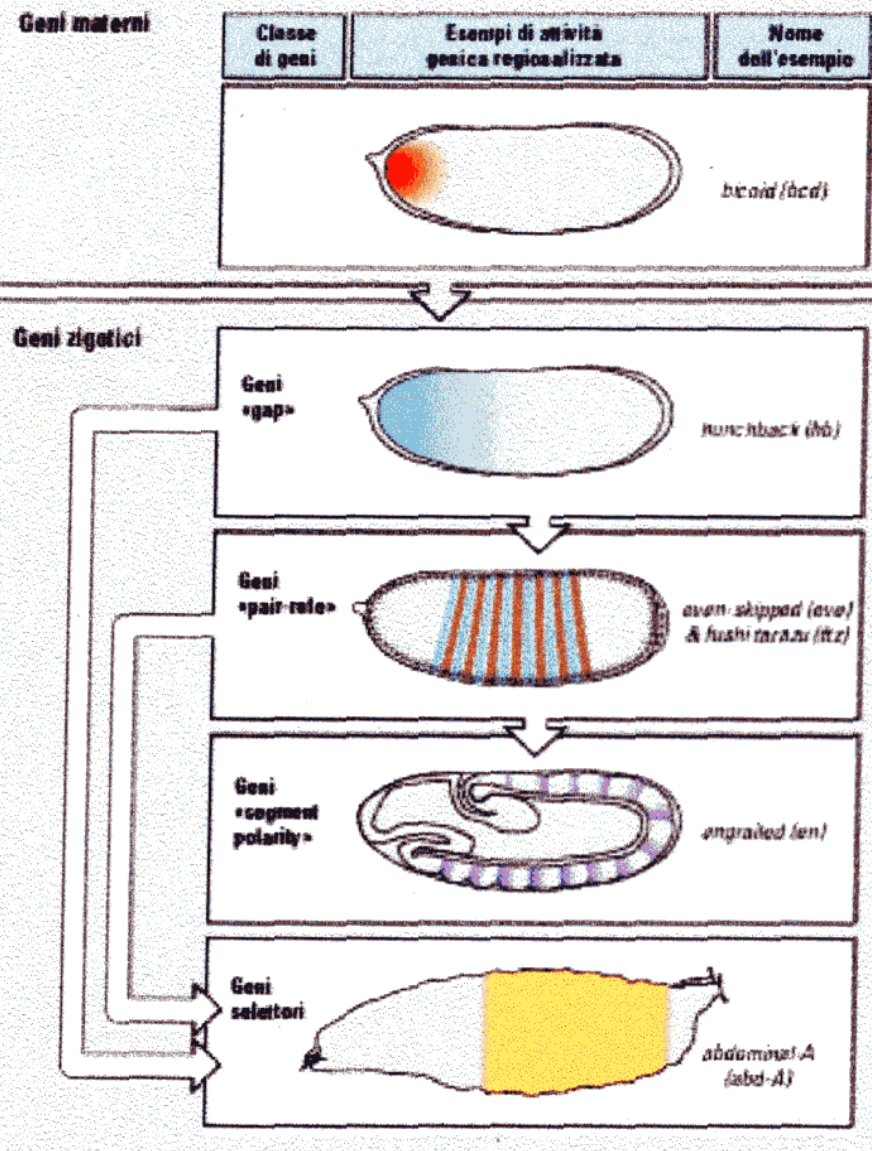
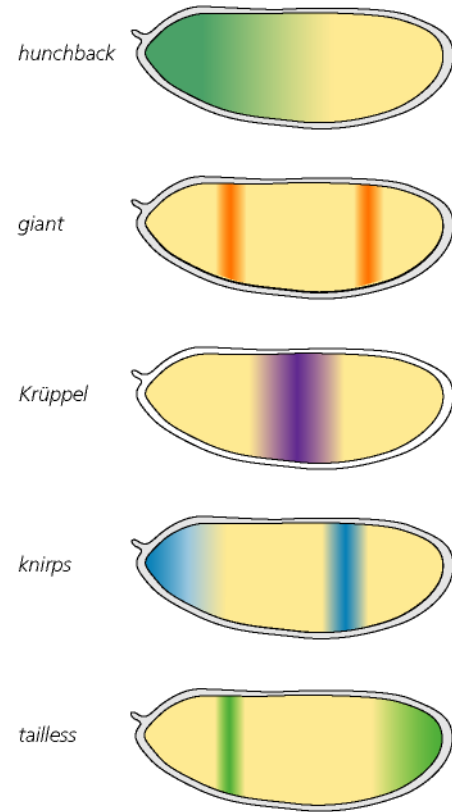


Determinazione Asse A-P

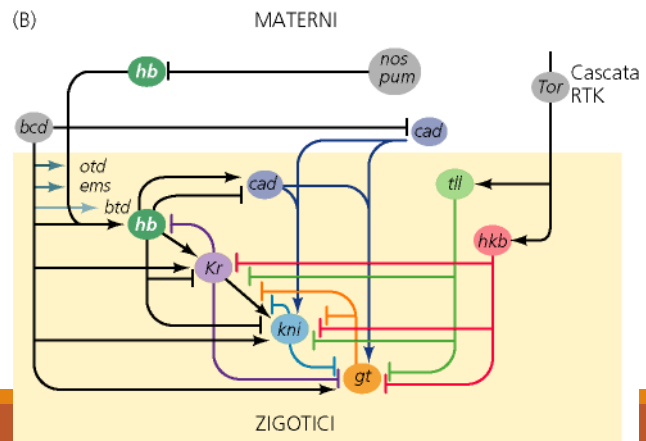
DROSOPHILA M.

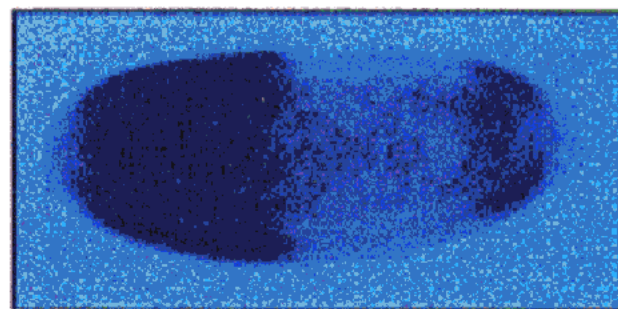
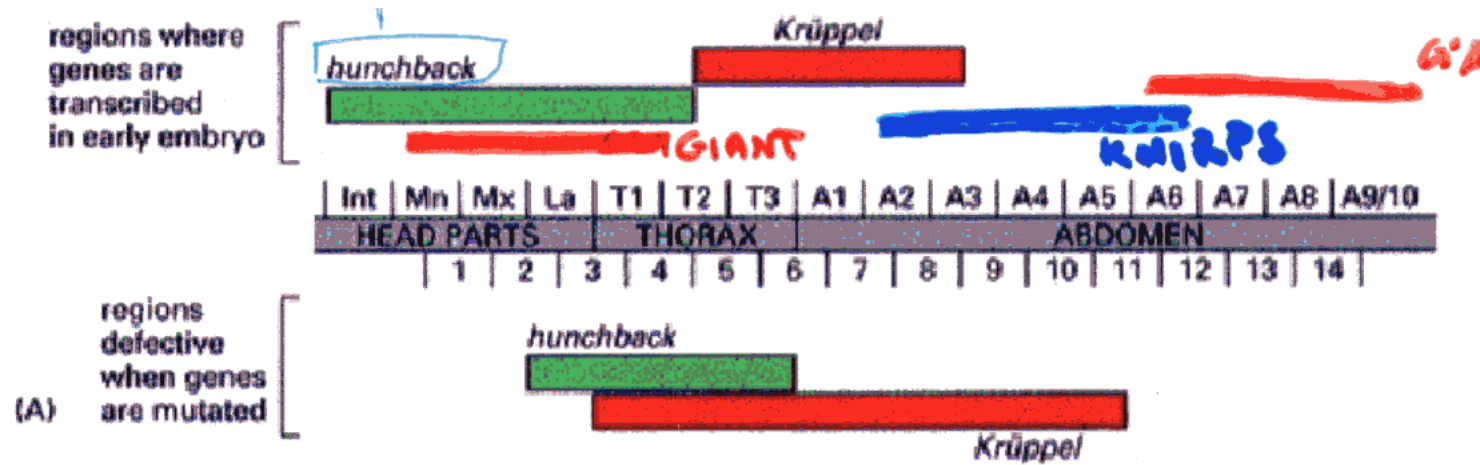


(A) Espressione dei geni gap

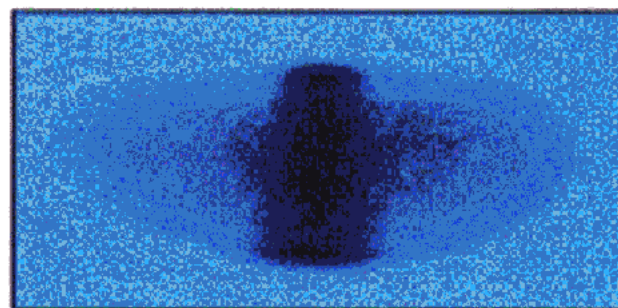


Geni GAP



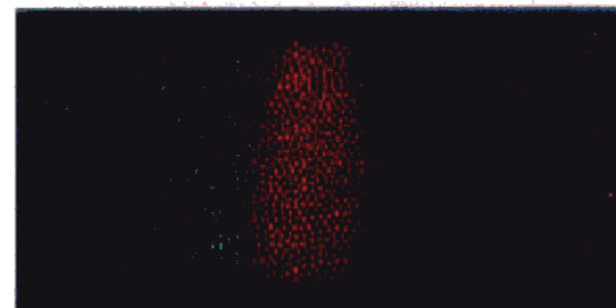


hunchback



(B)

Krüppel



(C)

Geni pair-rule

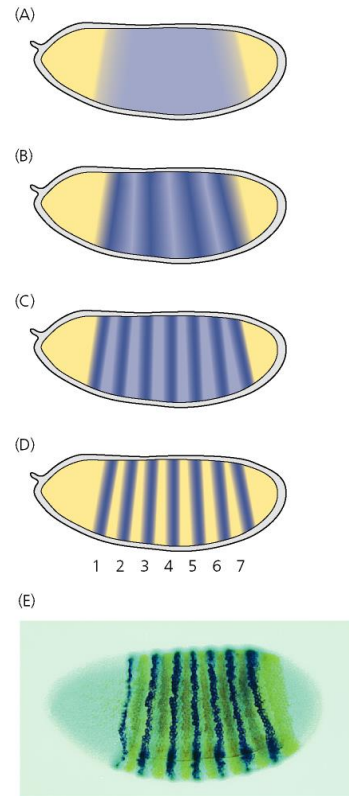
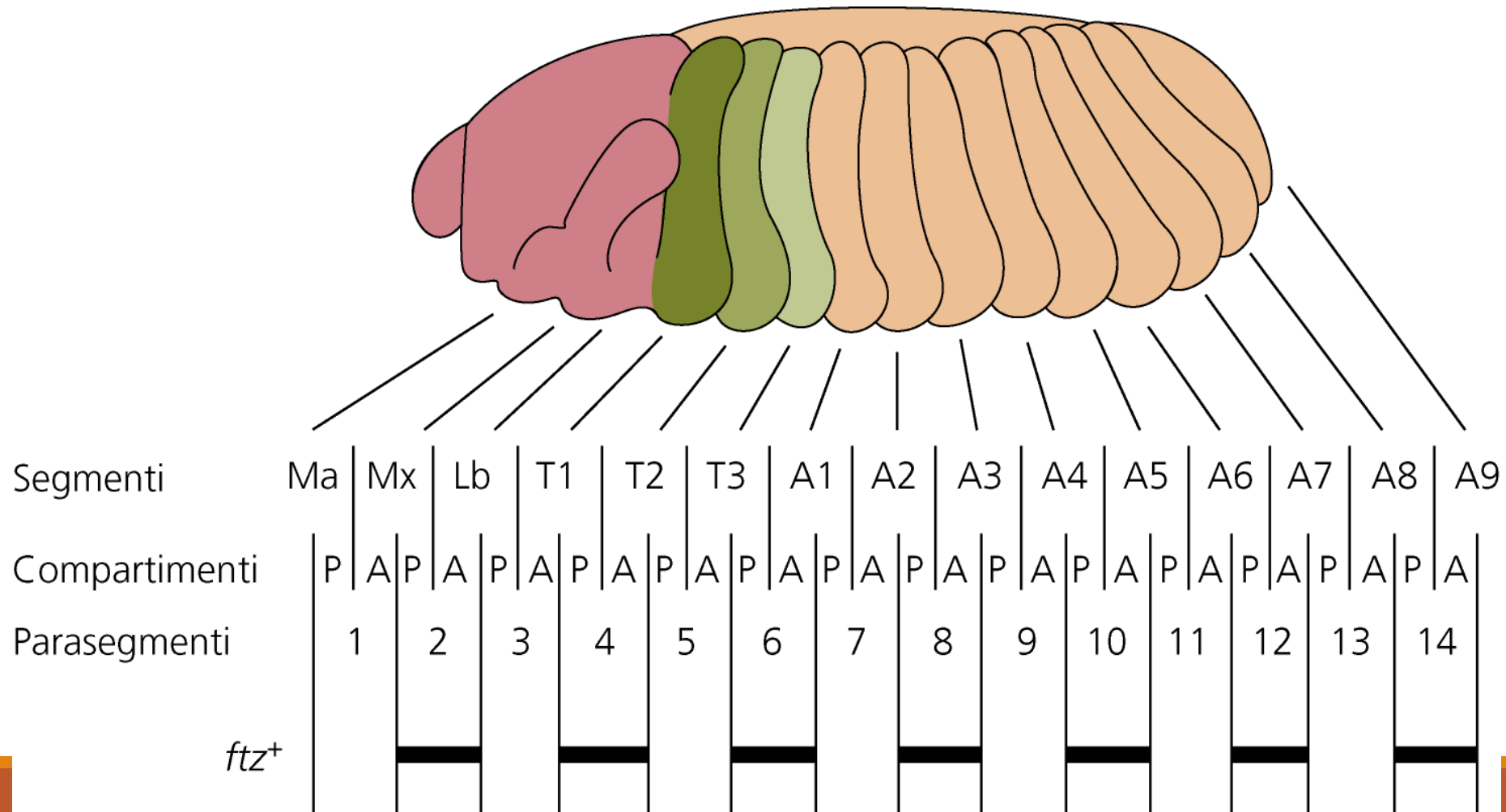


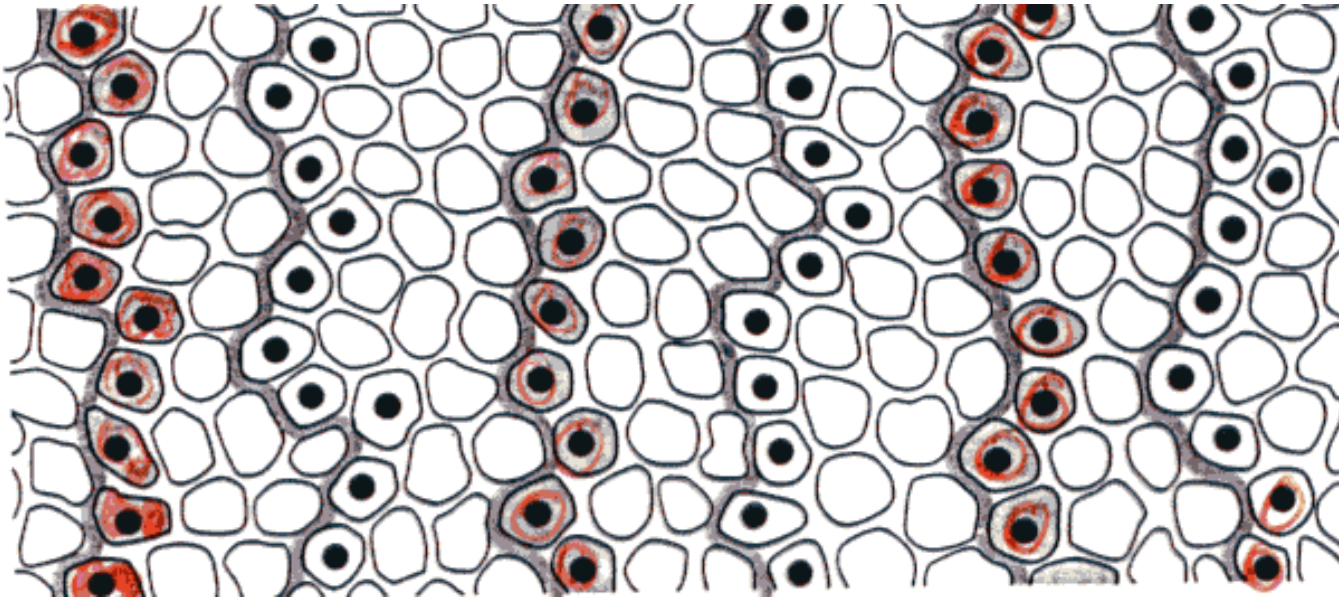
Tabella 9.2 Principali geni che regolano il piano di formazione dei segmenti in *Drosophila*

Categoria	Nome del gene
Geni gap	<i>Krüppel (Kr)</i> <i>knirps (kni)</i> <i>hunchback (hb)</i> <i>giant (gt)</i> <i>tailless (tll)</i> <i>huckebein (hkb)</i> <i>buttonhead (btd)</i> <i>empty spiracles (ems)</i> <i>orthodenticle (otd)</i>
Geni pair-rule primari	<i>hairy (h)</i> <i>even-skipped (eve)</i> <i>runt (run)</i>
Geni pair-rule secondari	<i>fushi tarazu (ftz)</i> <i>odd-paired (opa)</i> <i>odd-skipped (odd)</i> <i>sloppy-paired (slp)</i> <i>paired (prd)</i>
Geni segment polarity	<i>engrailed (en)</i> <i>wingless (wg)</i> <i>cubitus interruptusD (ciD)</i> <i>hedgehog (hh)</i> <i>fused (fu)</i> <i>armadillo (arm)</i> <i>patched (ptc)</i> <i>gooseberry (gsb)</i> <i>pangolin (pan)</i>

Geni pair-rule e i parasegmenti



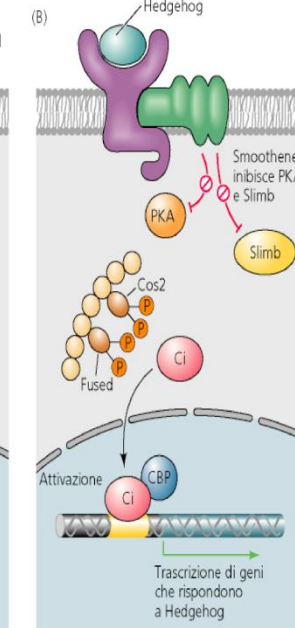
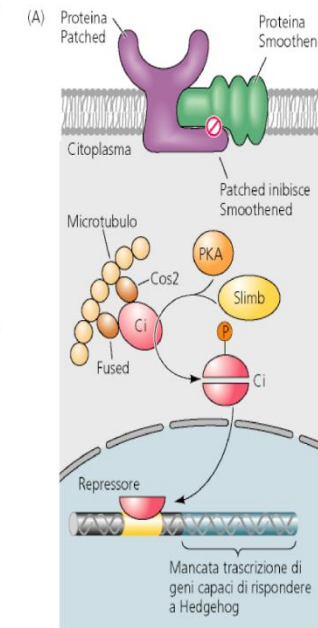
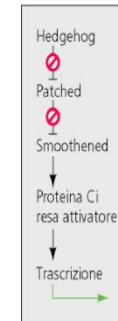
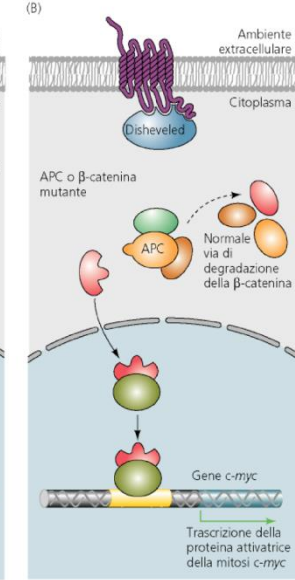
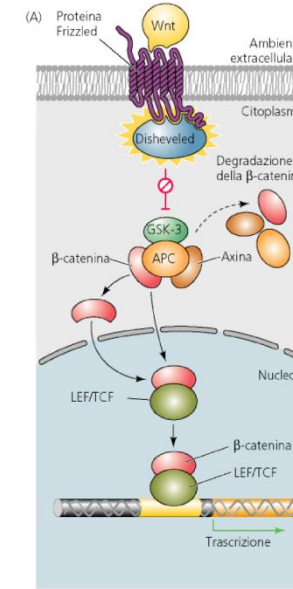
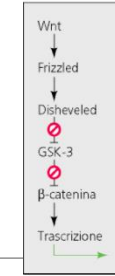
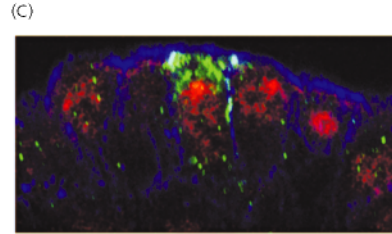
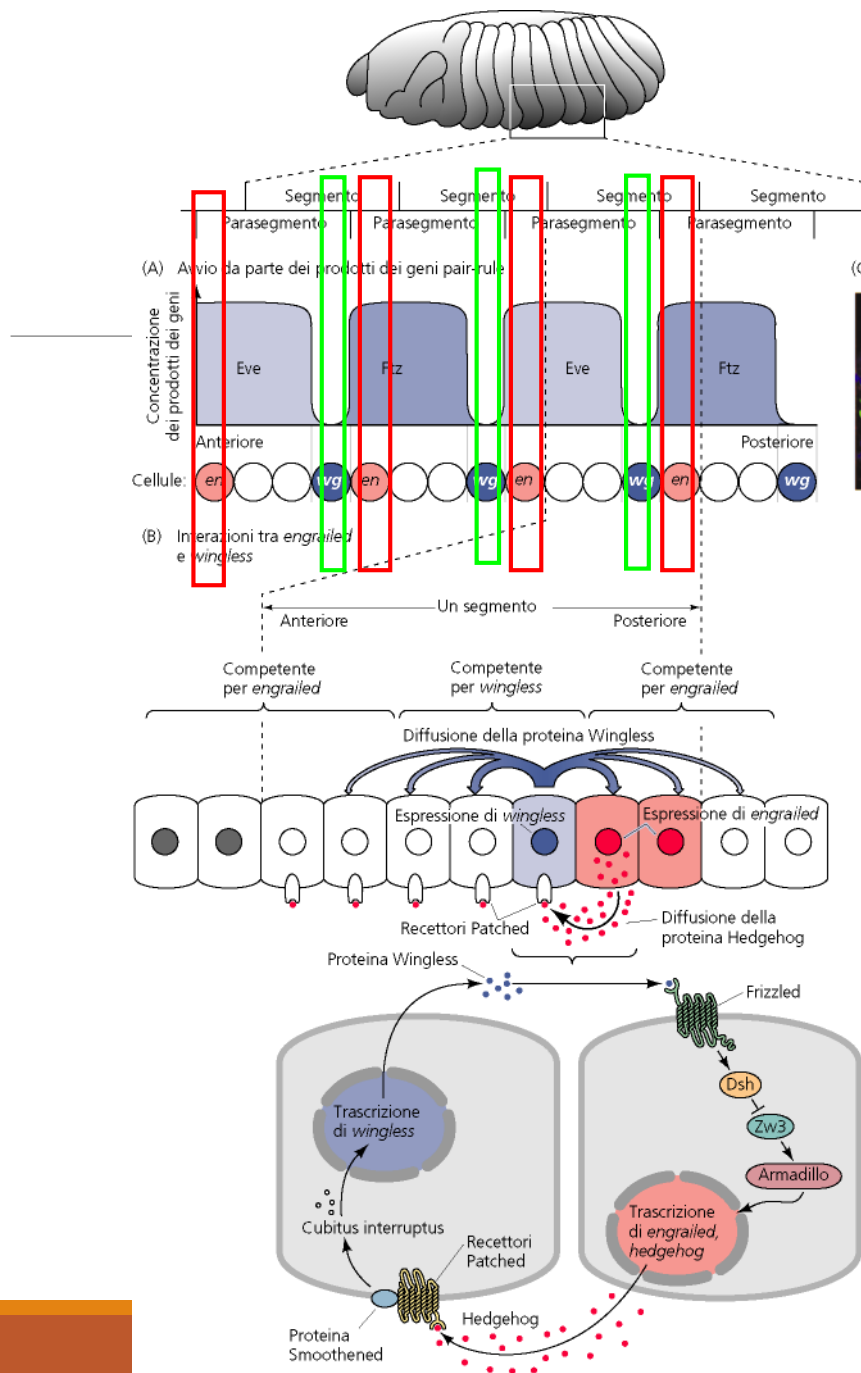
Geni segment polarity

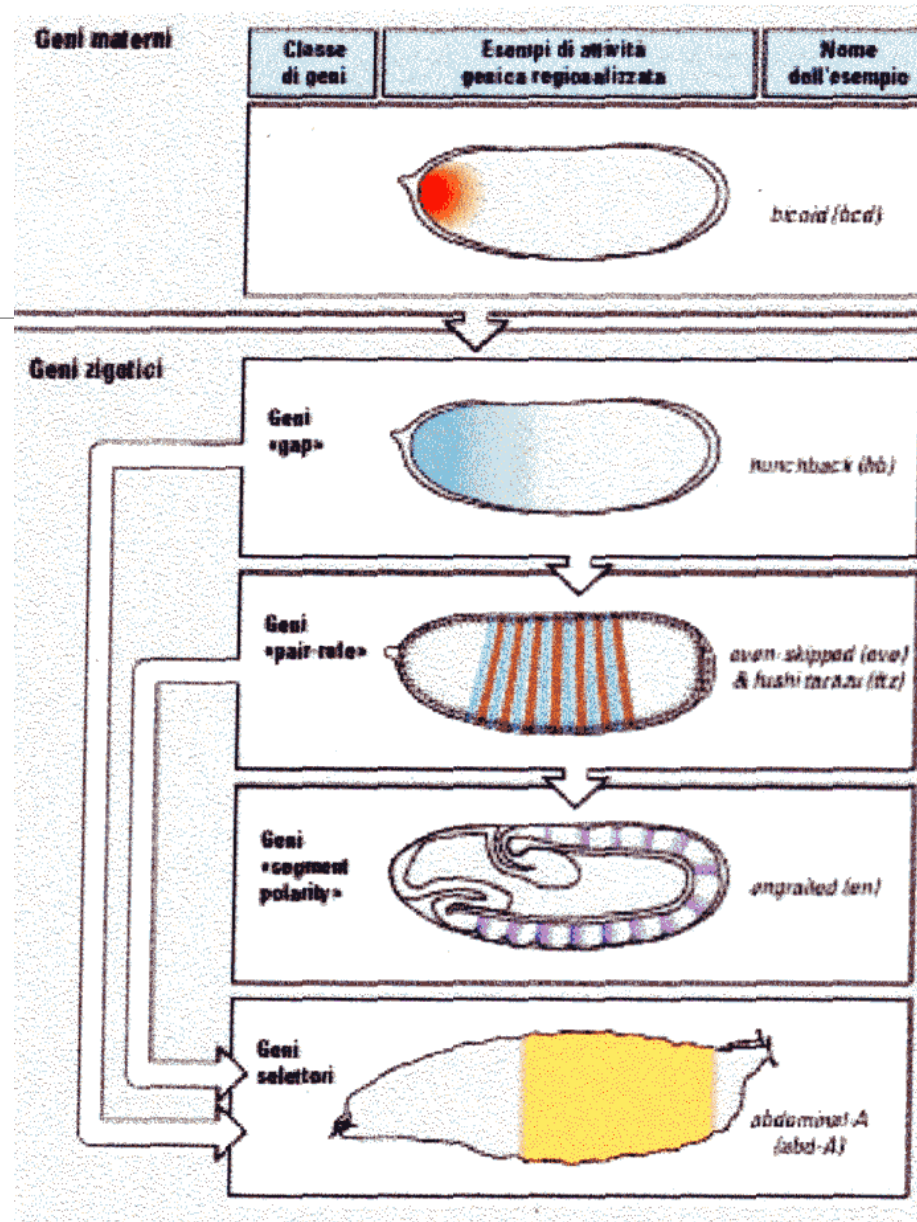


*Even skipped e
fushi tarazu*
controllano
l'espressione di
engrailed

I geni della pol segm.
definiscono il confine
tra i parasegmenti

Engrailed Wingless

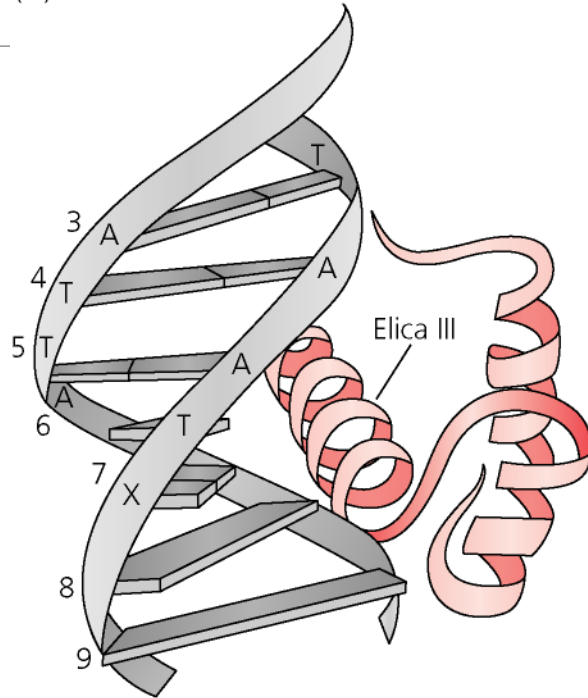




Geni selettori omeotici

Fattori di trascrizione omeodominio

(A)

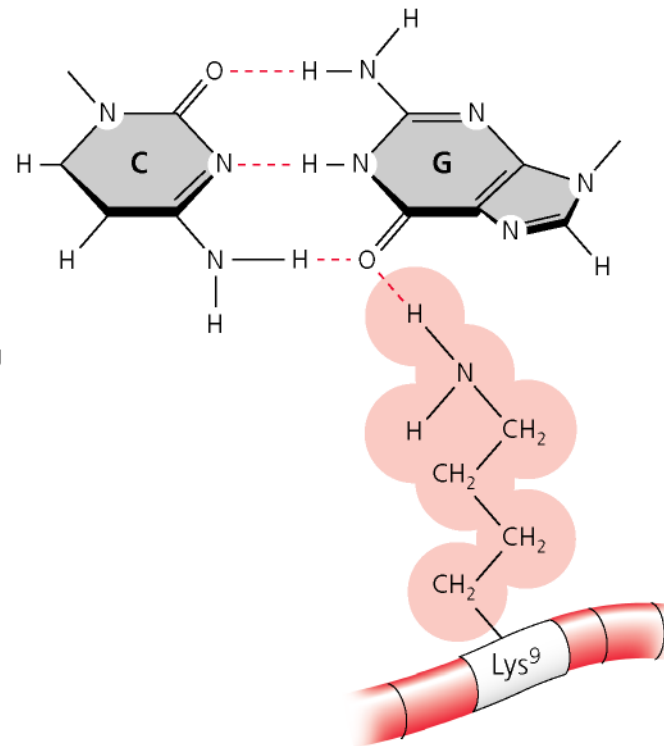


(B)

Sito Bicoid, coppia di basi 7

Citosina

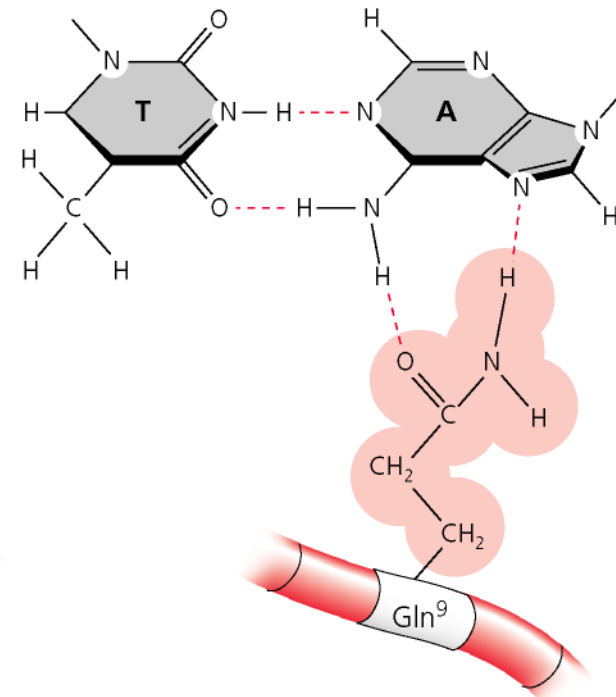
Guanina



Sito Antp, coppia di basi 7

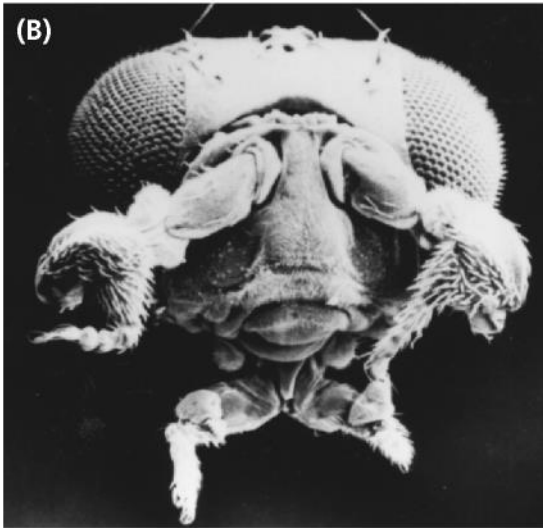
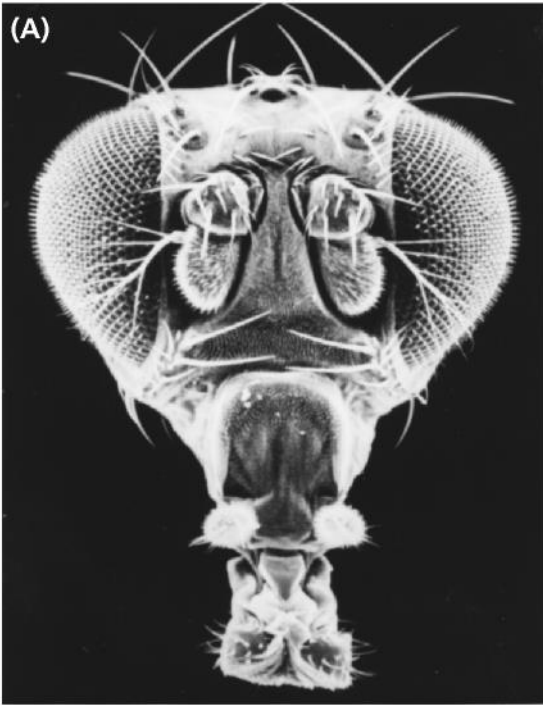
Timina

Adenina



Omeodominio di 60 aa

HtH

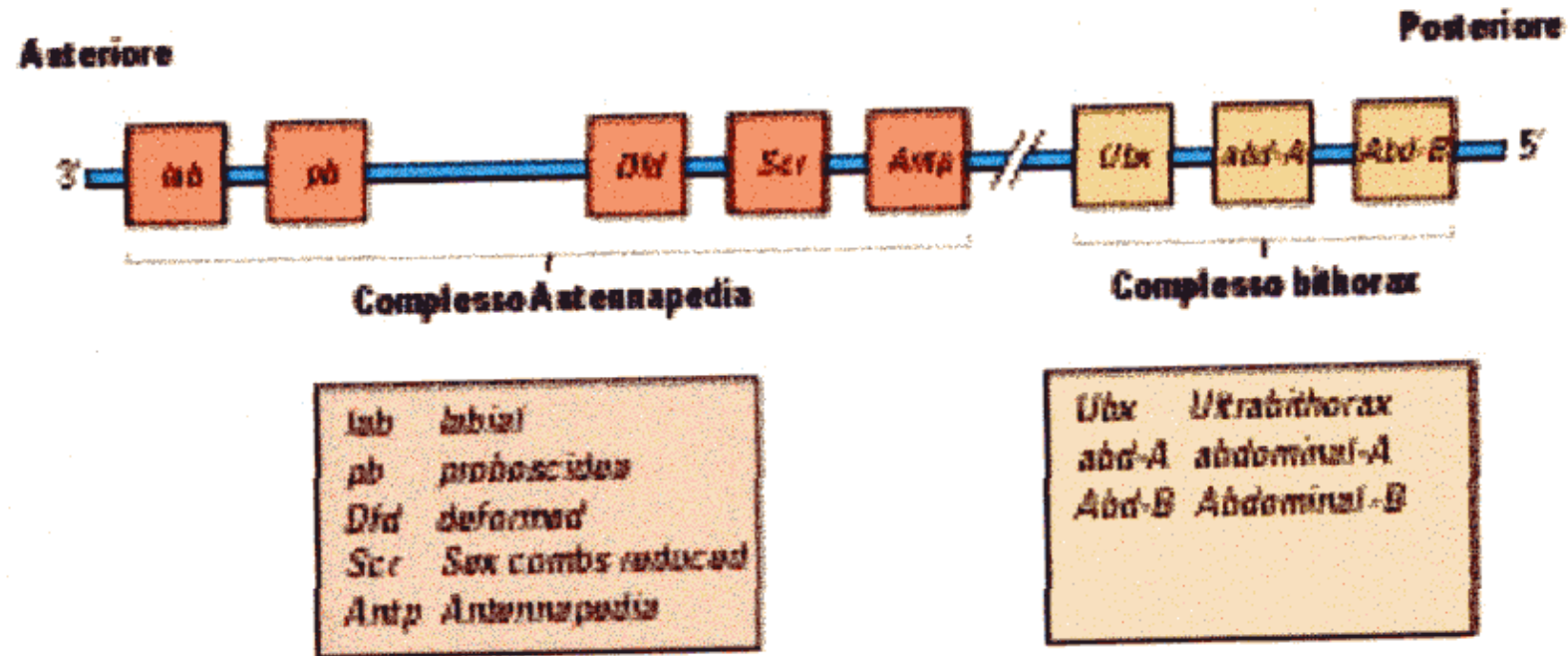


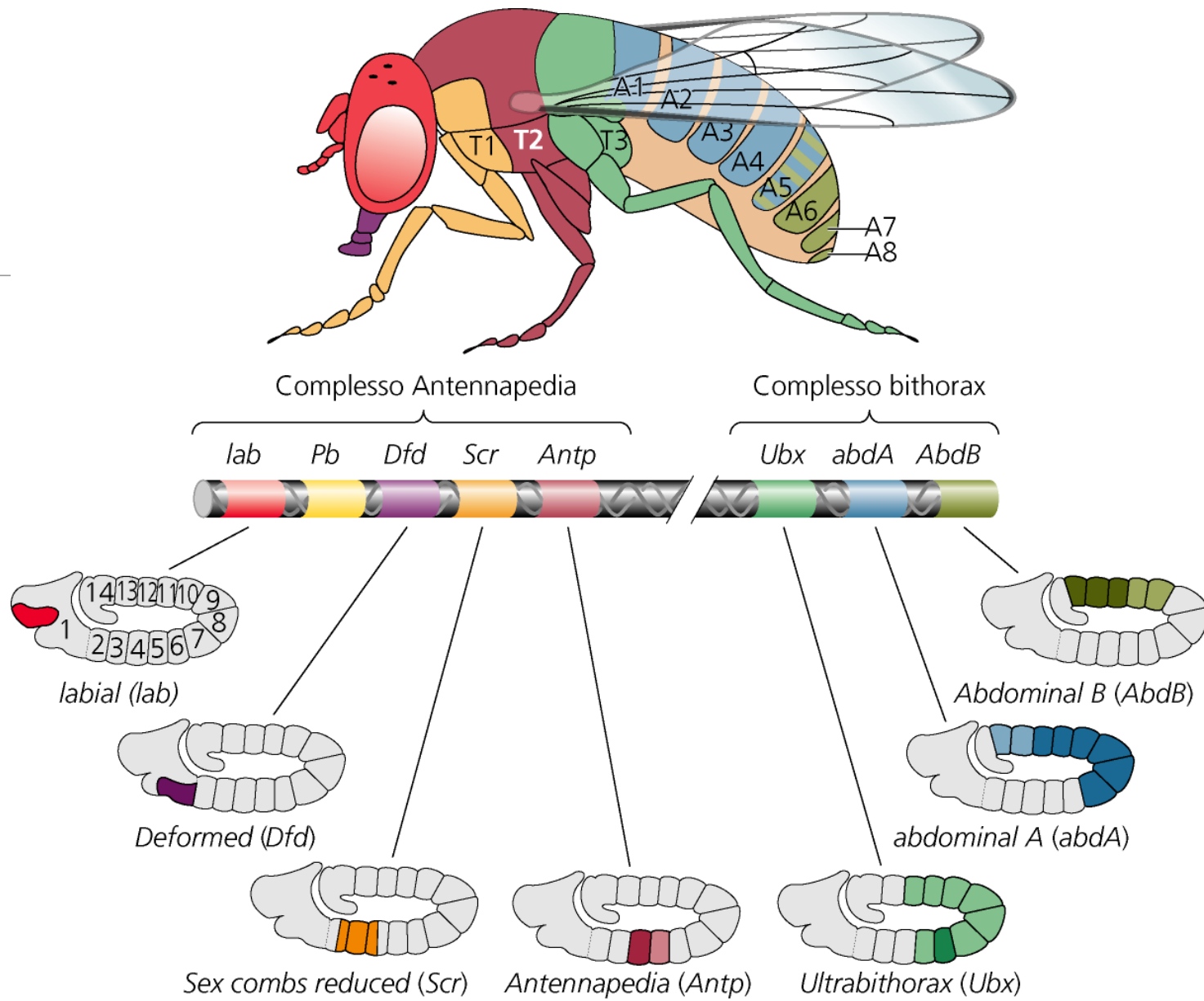
Mutazioni omeotiche



Omeotici propriamente detti

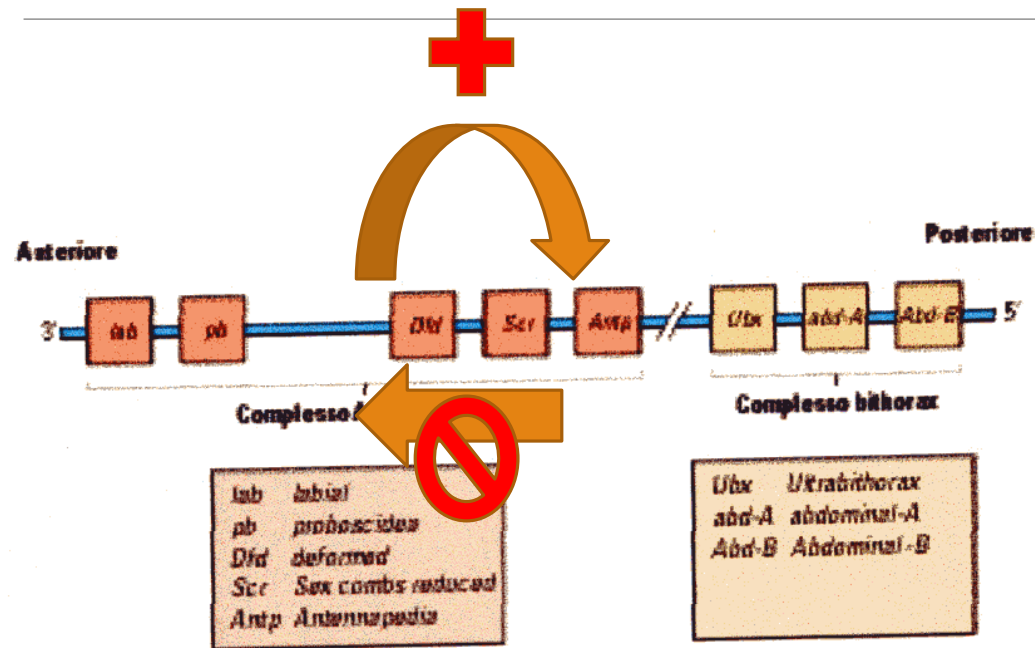
Complesso HOM-C



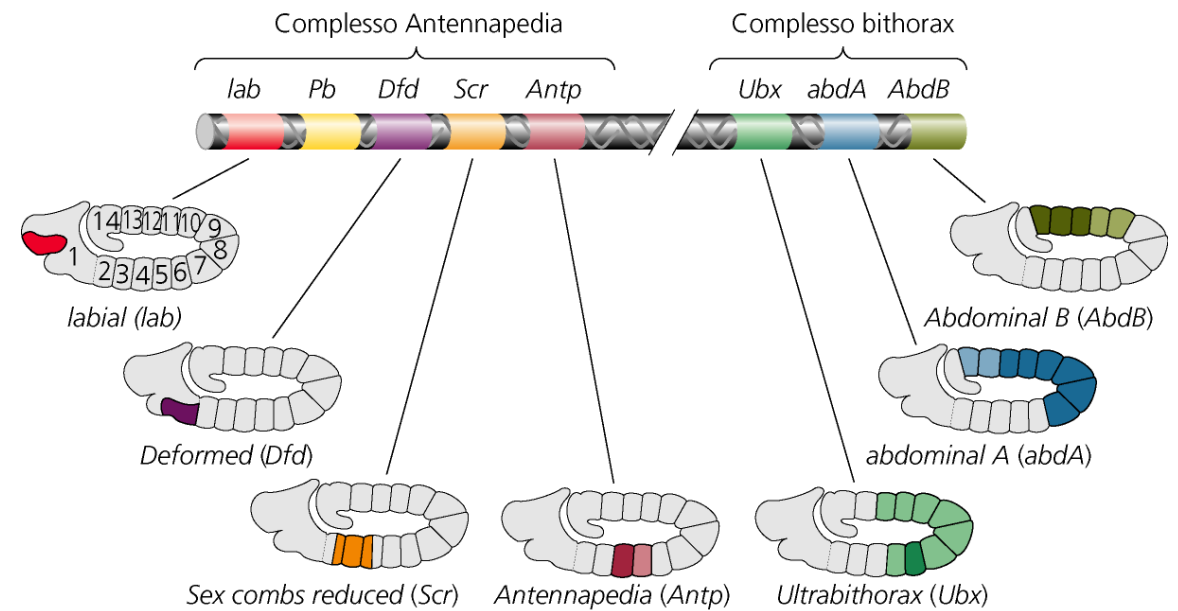


1. Co-linearità spazio-temporale; 2. identità del segmento

Omeotici propriamente detti

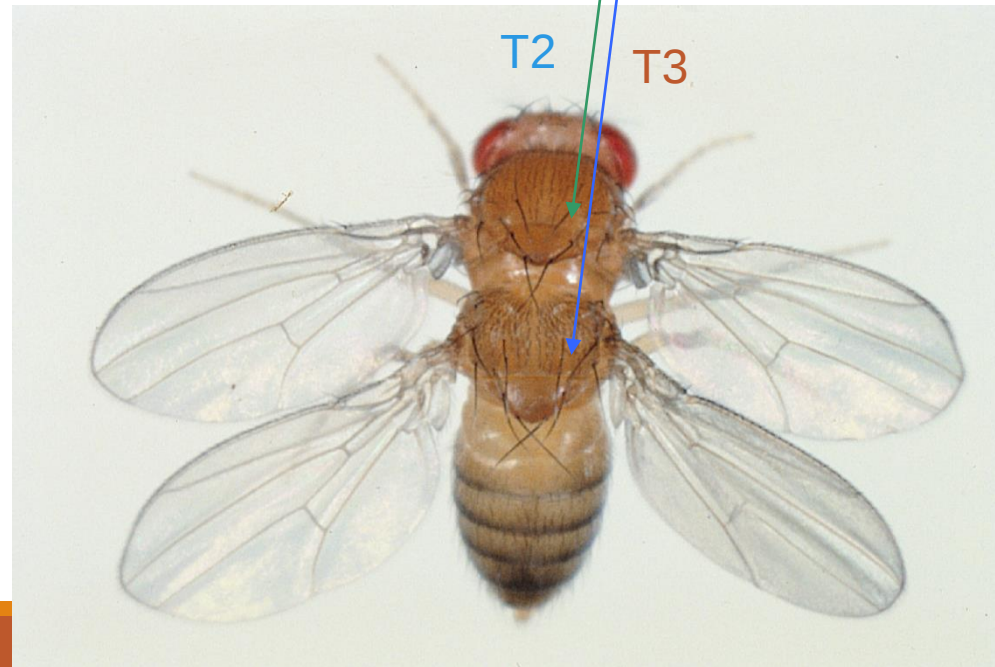
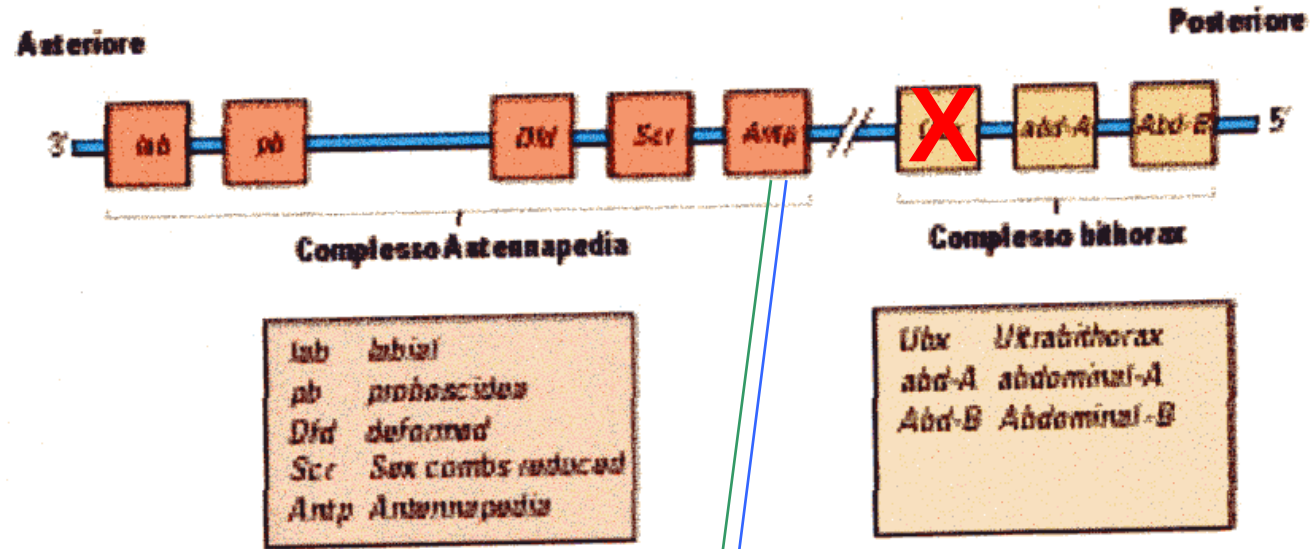


Complesso Hom-C



1. Co-linearità spazio-temporale; 2. identità del segmento

Mutazione Bithorax



Geni omeotici



Proteine omeotiche



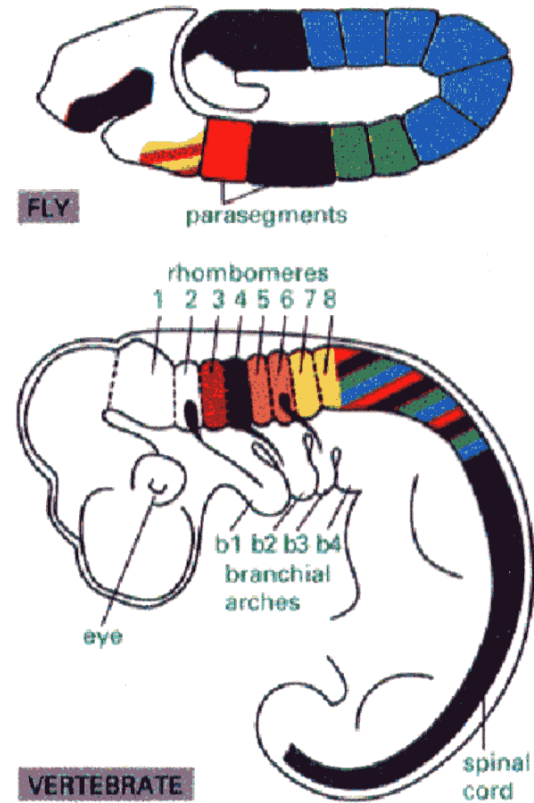
Geni realizzatori

I principali geni coinvolti nella specificazione del «pattern» nell'embrione precoce di *Drosophila*

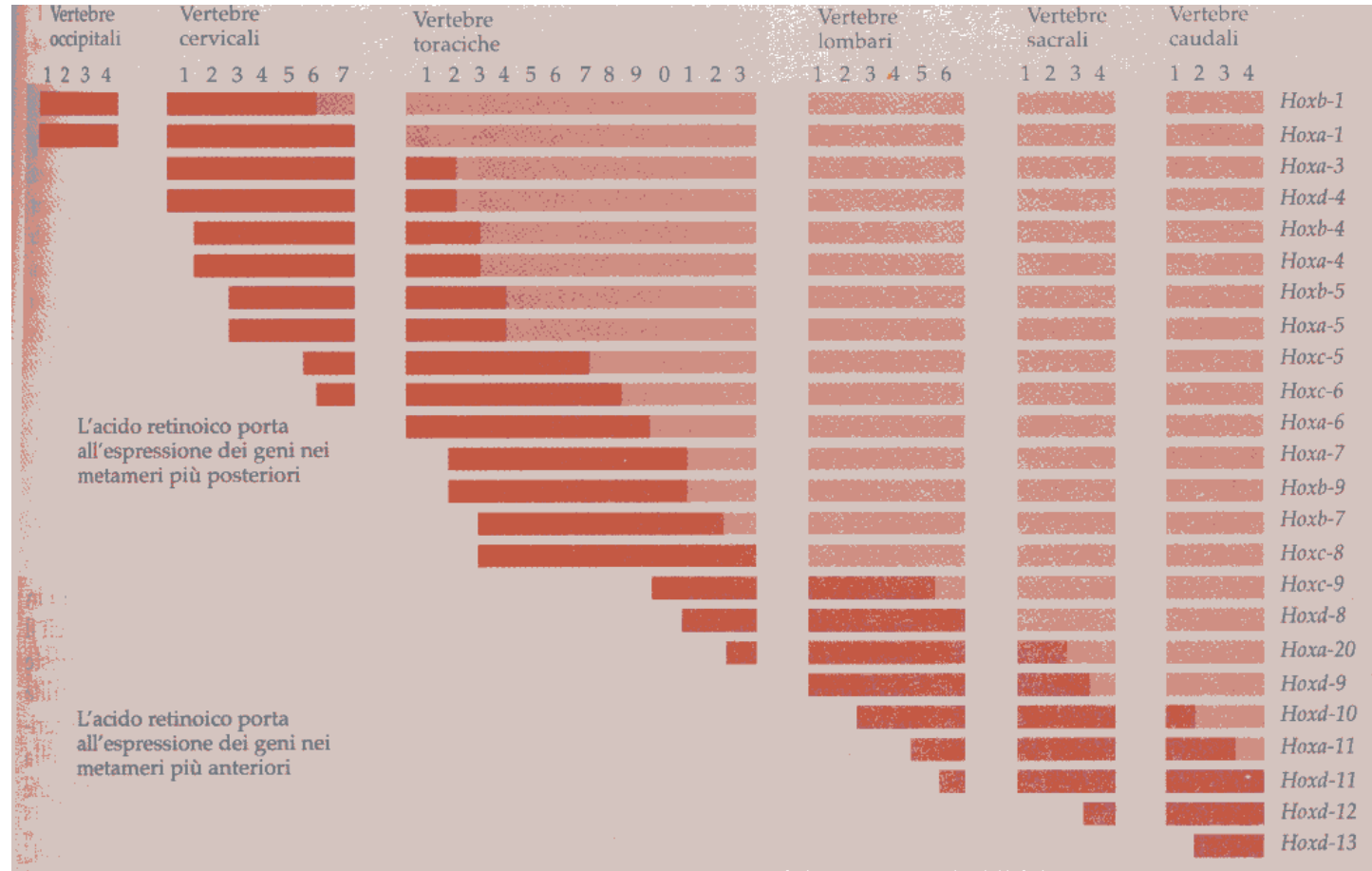
	Gene	Materno/ zigotico	Natura della proteina	Fattore di trascrizione (T), recettore (R), proteina segnale (S)	Funzione (dove nota)
Sistema antero-posteriore	<i>bicoid</i>	M	Omeodominio	T	Morfogeno, attiva <i>hunchback</i> zigotica altri geni «gap»
	<i>hunchback</i>	M	Dita di zinco	T	Morfogeno, attiva i geni «gap»
	<i>nanos</i>	M			Inattiva mRNA/proteina di <i>hunchback</i> materno; coinvolto nella formazione d gradiente della proteina hunchback materna
	<i>gurken</i>	M	Proteina secreta della famiglia TGF- α	S	Specifica l'asse dell'oocita
	<i>exuperantia</i>	M			Localizzazione di mRNA materni (ad esempio <i>bicoid</i>)
	<i>oskar</i>	M			Specificazione del plasma germinale
Sistema terminale	<i>torso</i>	M	Recettore tirosina chinasi	R	L'attivazione specifica le regioni term
	<i>torso-like</i>	M		S	Ligando della proteina torso
Geni «gap»	<i>hunchback</i>	Z	Dita di zinco	T	Localizzano l'espressione dei geni «p rule»
	<i>Krüppel</i>	Z	Dita di zinco	T	
	<i>knirps</i>	Z	Dita di zinco	T	
	<i>giant</i>	Z	Cerniera di leucine	T	
	<i>tailless</i>	Z	Dita di zinco	T	
Geni «pair-rule»	<i>even-skipped</i>	Z	Omeodominio	T	Delimita i parasegmenti dispari
	<i>fushi tarazu</i>	Z	Omeodominio	T	Delimita i parasegmenti pari
	<i>hairy</i>	Z	«Helix-loop-helix»	T	
Geni della polarità segmentale	<i>engrailed</i>	Z	Omeodominio	T	Definisce la regione anteriore del parasegmento e la posteriore del segmento
	<i>hedgehog</i>	Z	Secreta o di membrana	S	
	<i>wingless</i>	Z	Secreta	S	
	<i>gooseberry</i>	Z	Omeodominio	T	
	<i>patched</i>	Z	Di membrana	R	
	<i>smoothened</i>	Z	Di membrana	R	
Geni selettori Complesso bithorax	<i>Ultrabithorax</i>	Z	Omeodominio	T	L'attività combinatoria dà identità ai parasegmenti 5÷13
	<i>abdominal-A</i>	Z	Omeodominio	T	
	<i>Abdominal-B</i>	Z	Omeodominio	T	

[illegible]

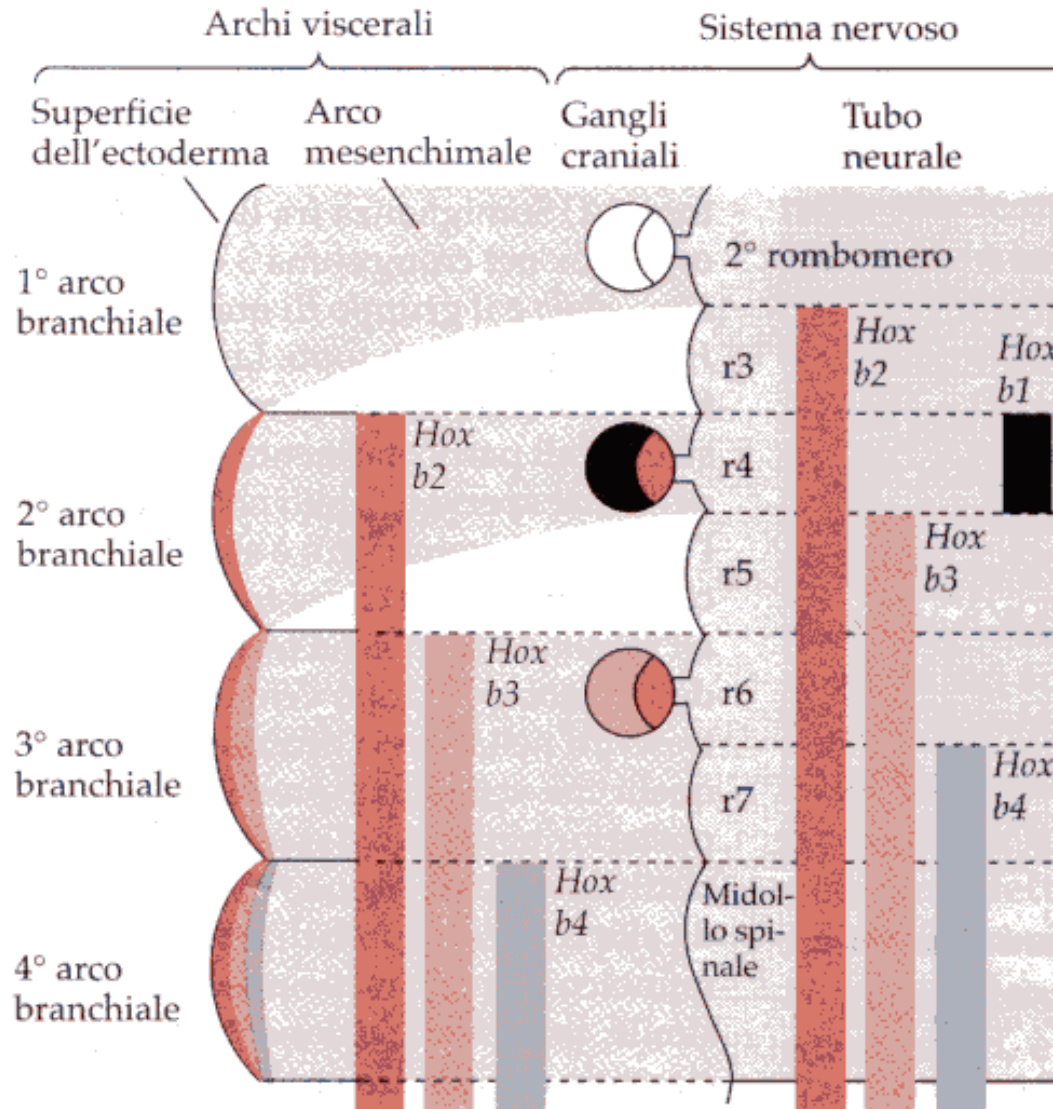
Geni omeotici nei mammiferi



Territori di espressione dei geni Hox



(A)

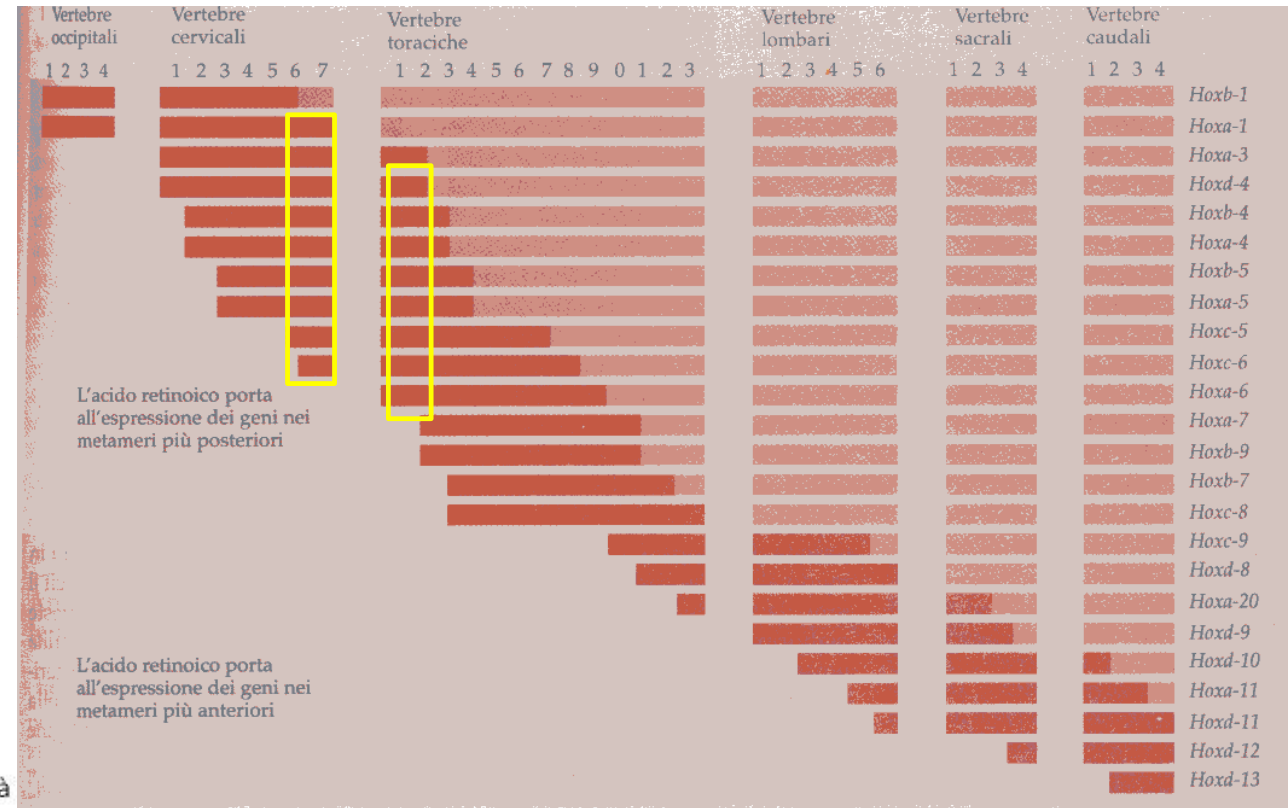
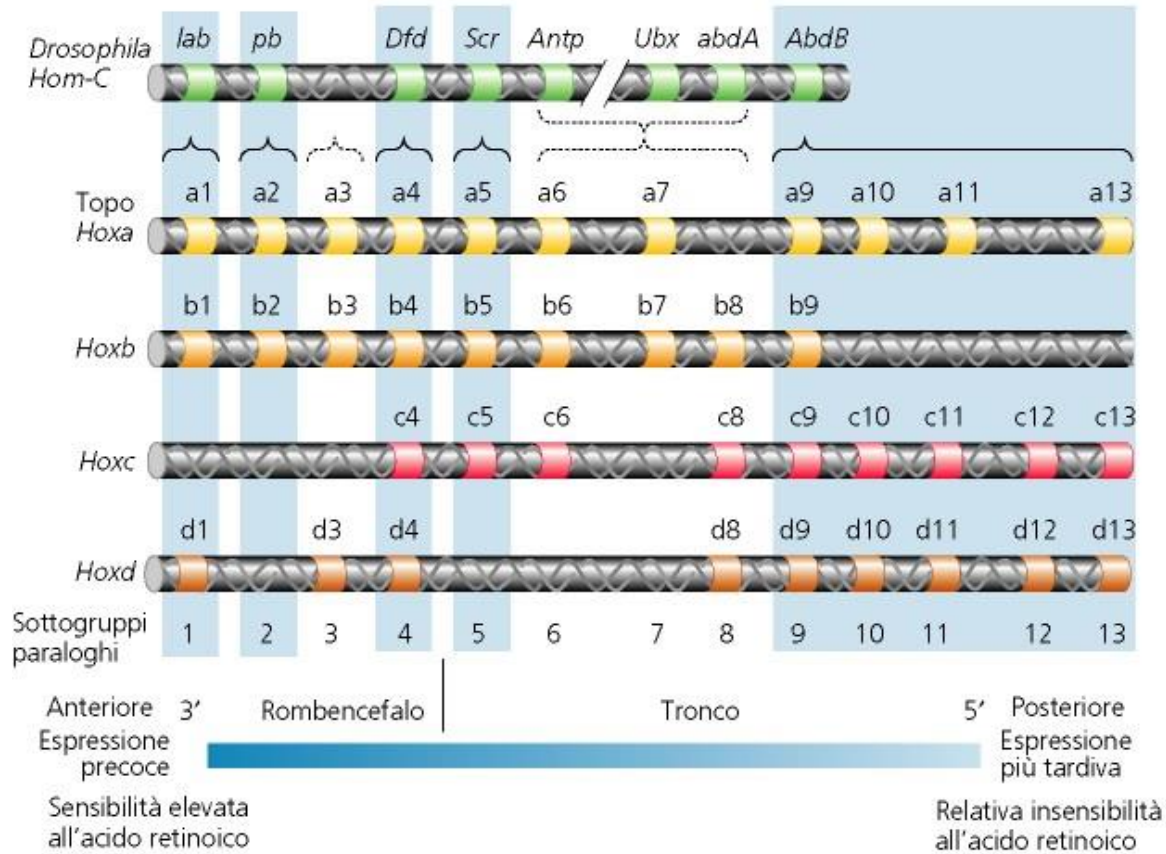


Dove sono espressi???

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

Territori di espressione dei geni Hox

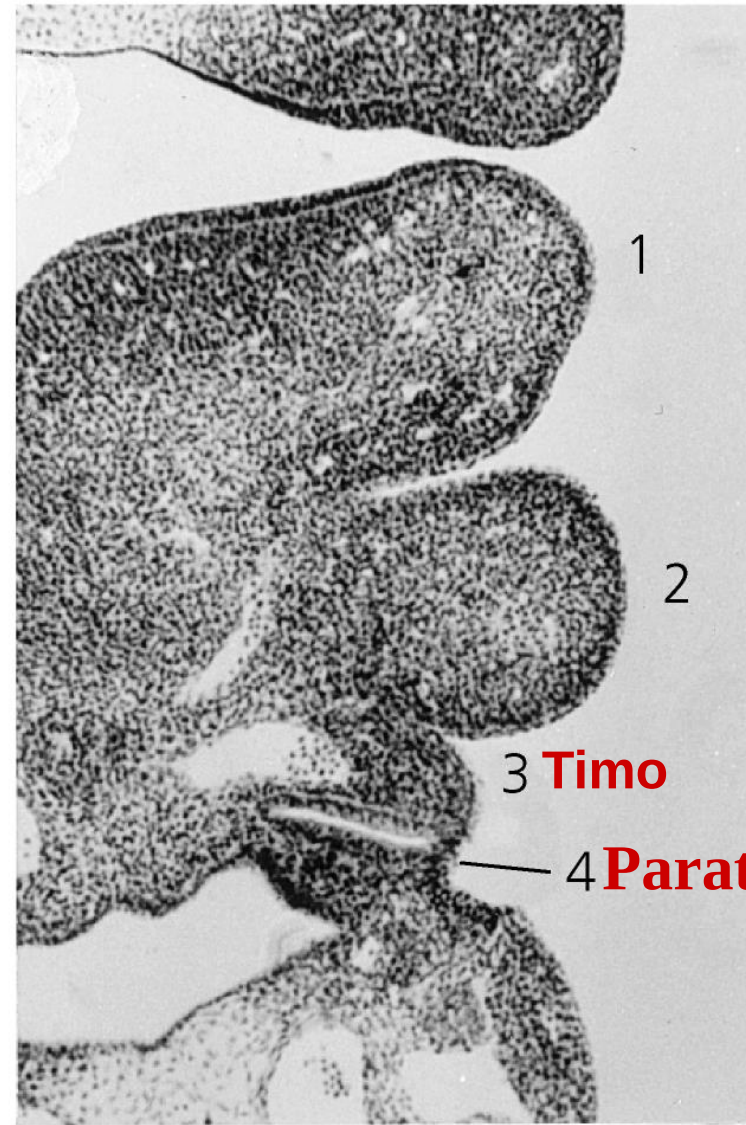
(A)



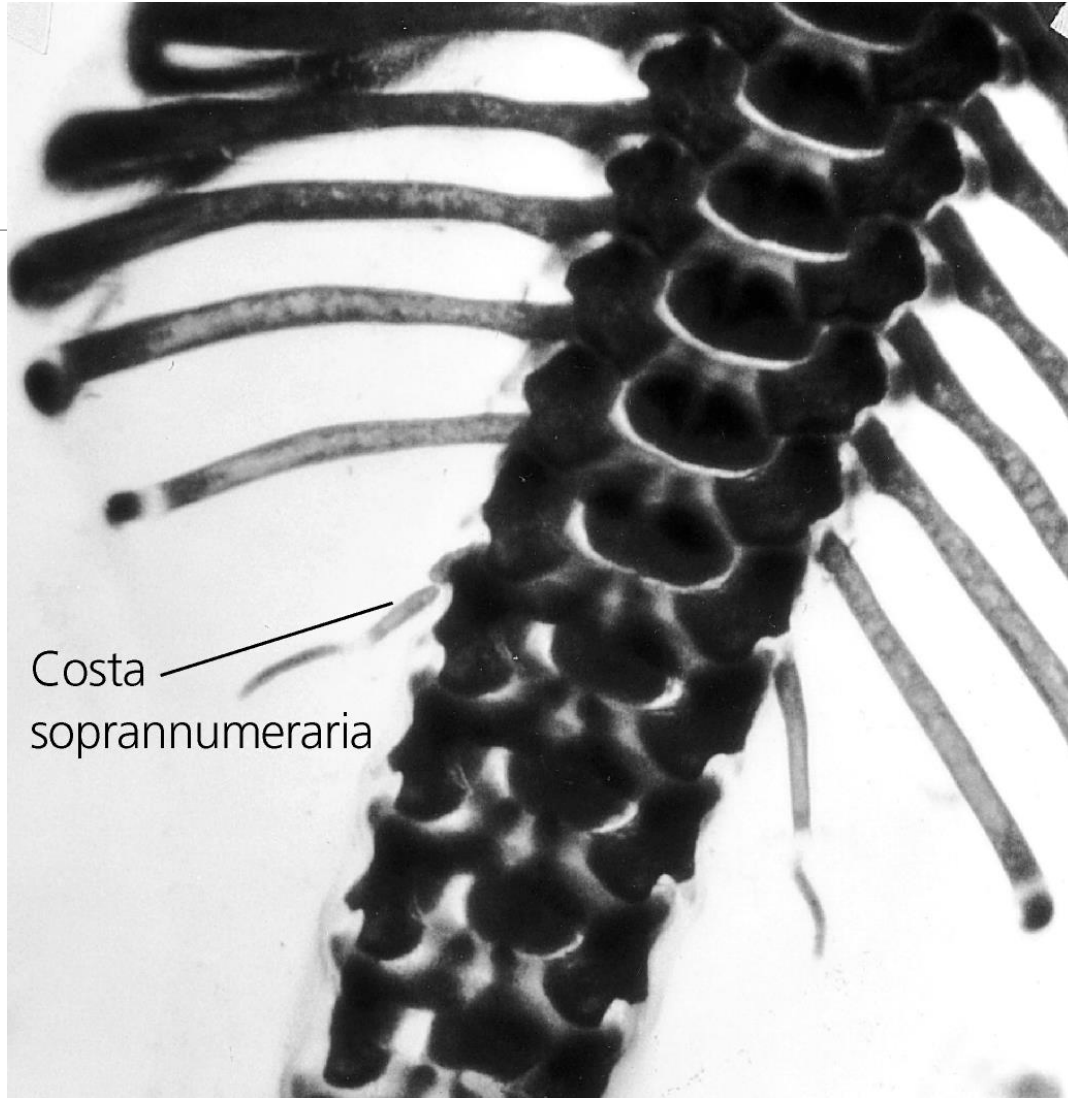
Mutazioni omeotiche



Hoxa-3^{-/-}

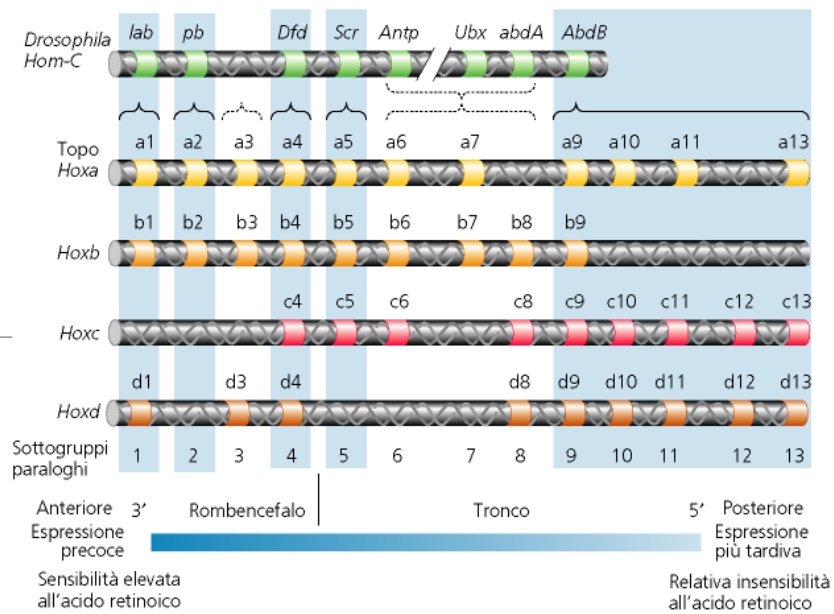


Hoxa-3^{+/-}



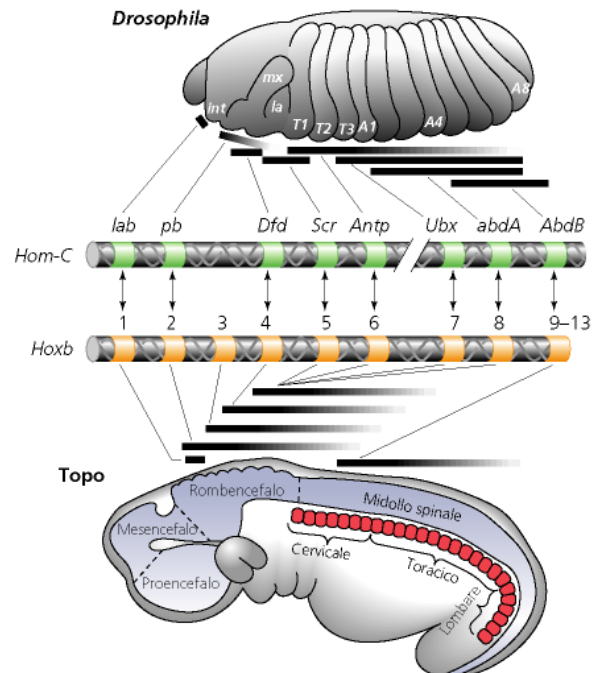
**Espressione di Hox C8 nella
1a vertebra lombare forma
costole**

(A)



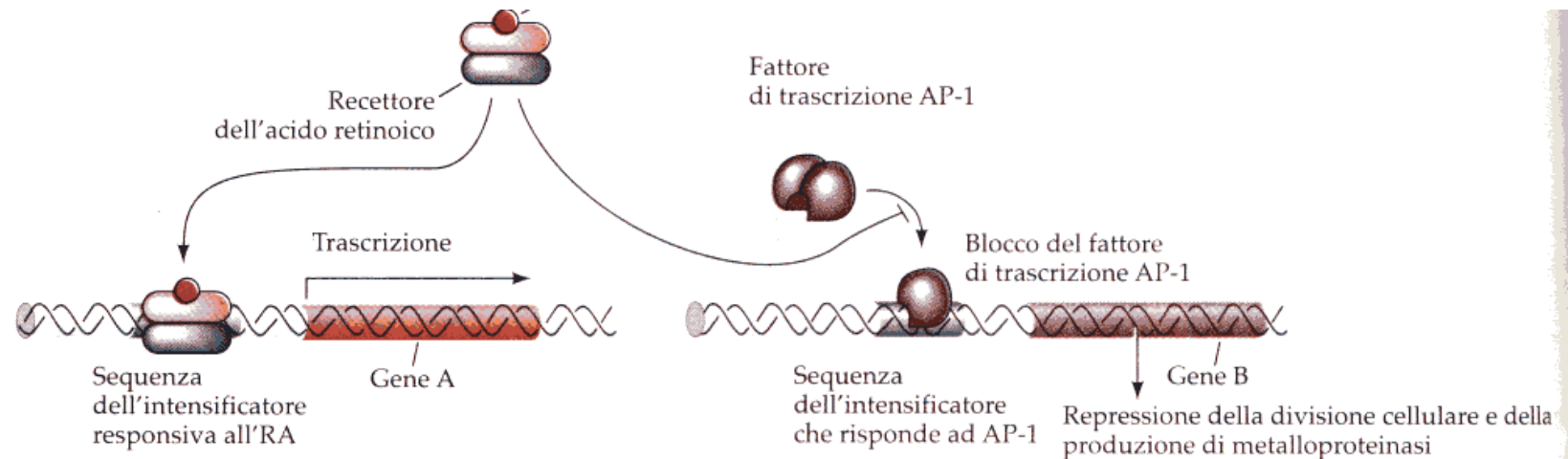
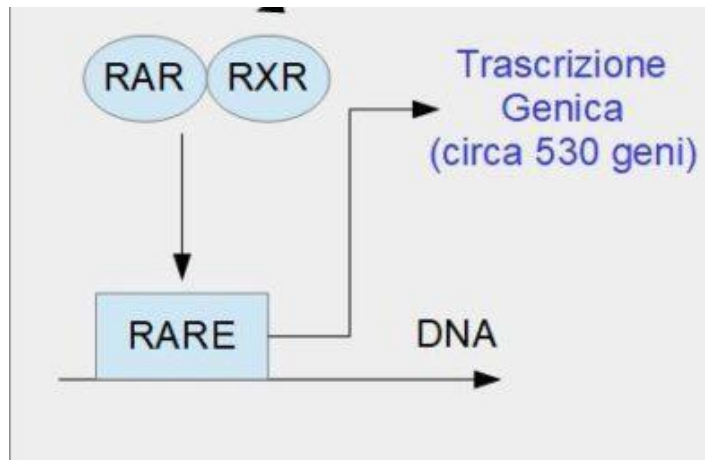
Come viene regolata l'espressione dei geni HOX?

(B)



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

Acido retinoico regola l'espressione dei geni HOX

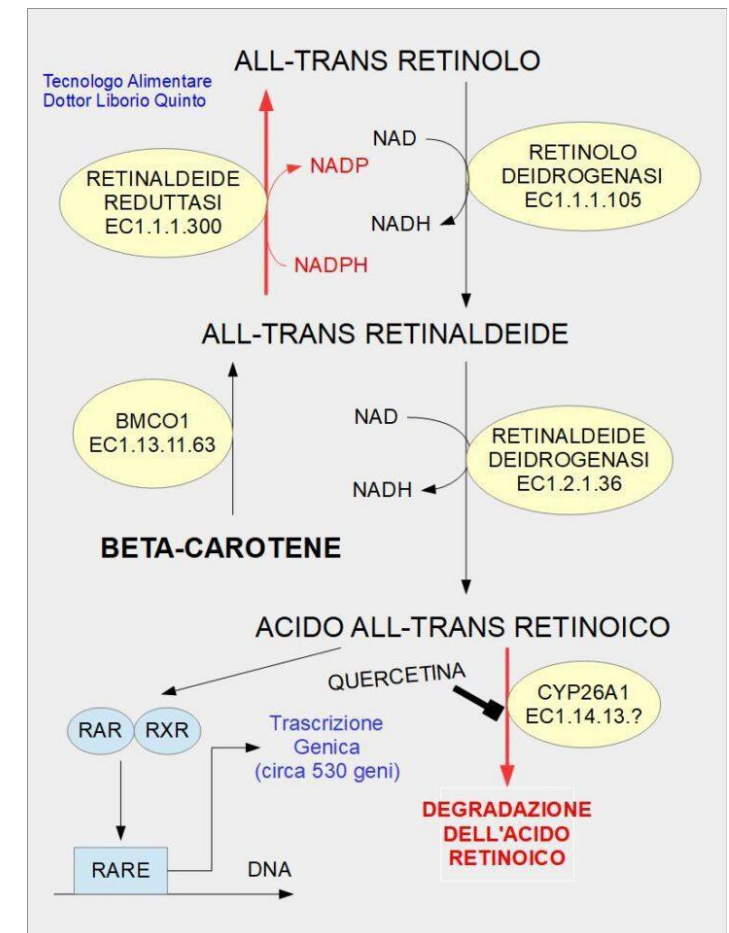
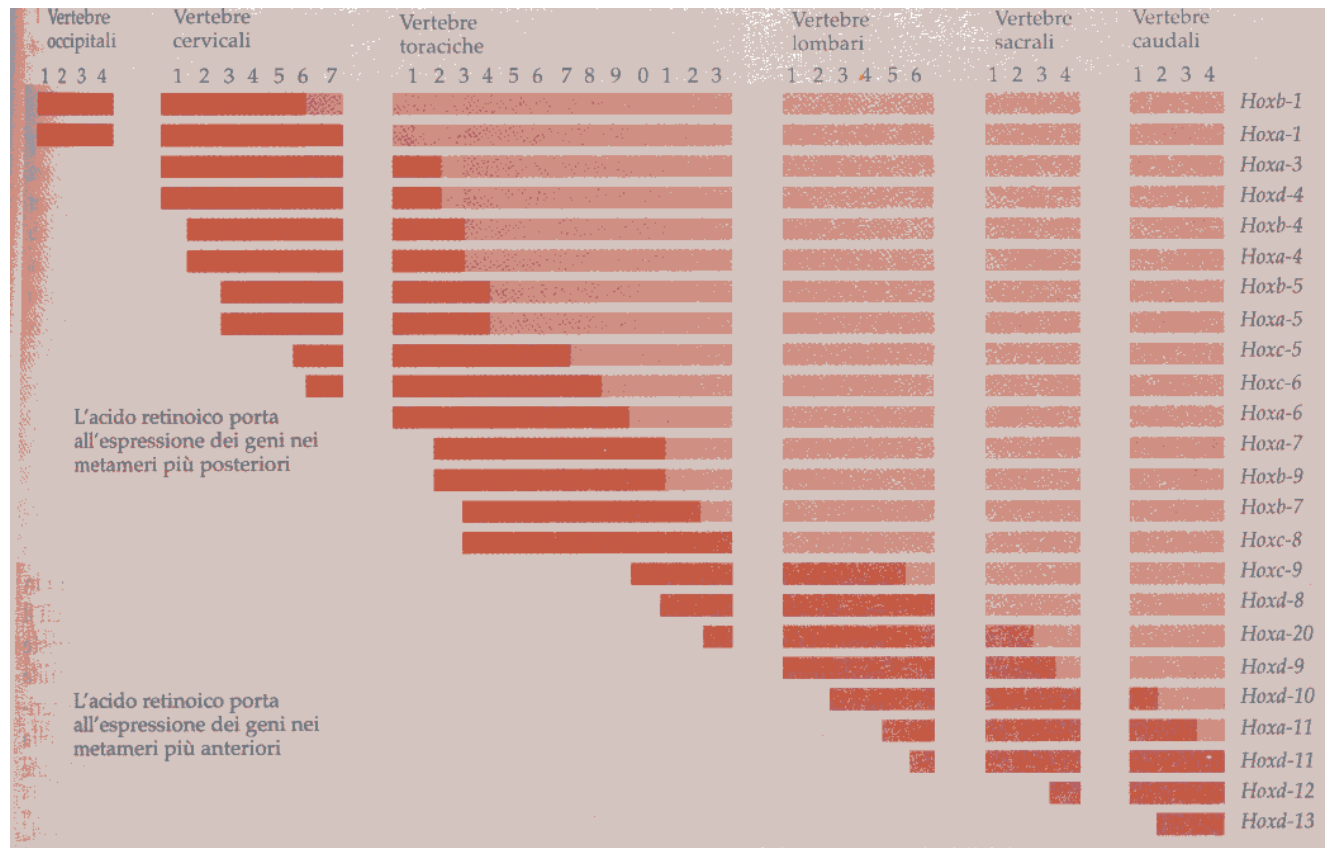


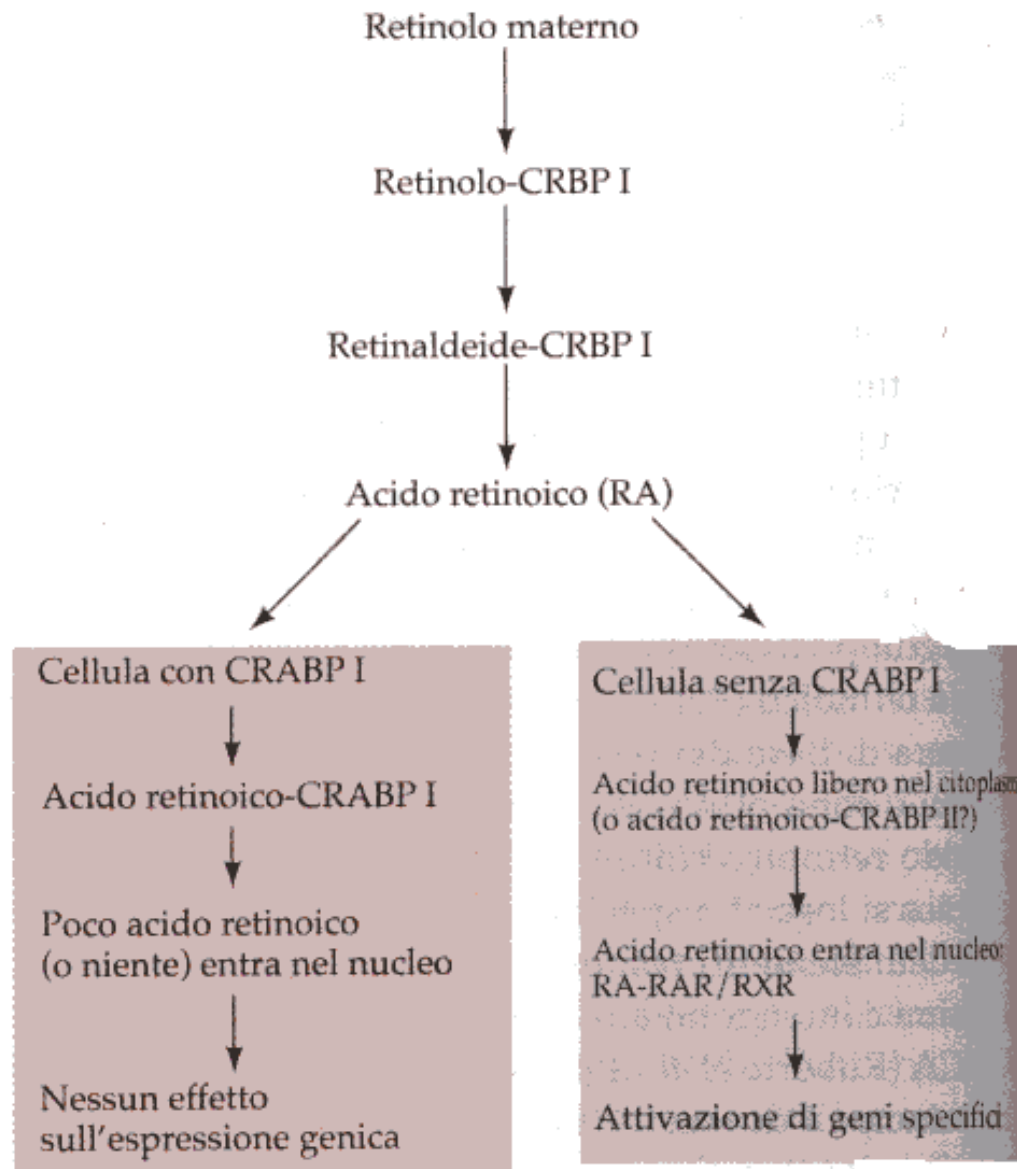
1. Prodotto dal nodo di Hensen
2. Si forma un gradiente molecolare lungo l'asse A-P

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





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

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

FARMACI E SOSTANZE CHIMICHE

Acido retinoico (Isotretinoina, Accutane)

Acido valproico

Alcol

Aminoglicosidi (Gentamicina)

Aminopterina

Agenti antitiroidei (PTU)

Bromuro

Fumo di sigaretta

Cocaina

Cortisone

Dietilstilbestrolo

Difenilidantoina

Eroina

Piombo

Metilmercurio

Penicillamina

Streptomina

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

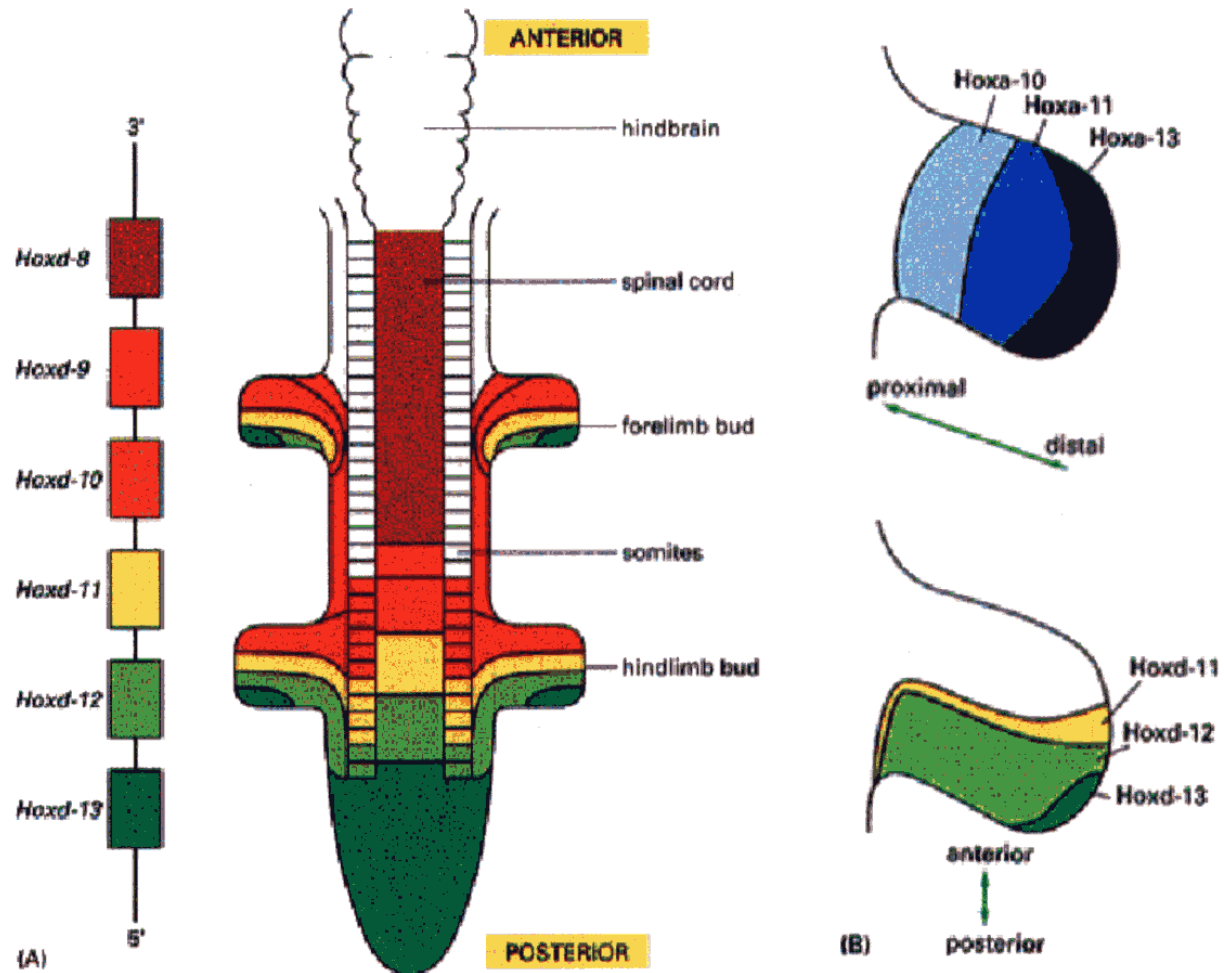
Deficit dietetici, malnutrizione

Fenilchetonuria

Patologie autoimmuni (inclusa incompatibilità Rh)

Agenti Teratogeni

Geni Hox nella formazione dell'arto



La regione della testa non esprime geni HOX

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

