

A proteína nuclear Snail é expressa do lado direito apenas
 Snail: fator de transcrição

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DETERMINAÇÃO DO EIXO LEVO-DEXTRO EM Gallus

Esquerda Direita

Pitx2 Snail

HH 10

Antes de Pitx-2, o Nodal é expresso exclusivamente no lado ESQUERDO
 Nodal: proteína secretada

HH8-

Schlange et al 2002

A assimetria de expressão de Nodal (=Xnr-1 em Xenopus) é conservada evolutivamente

Direita Esquerda

Xenopus

Direita Esquerda

Anfióxo

Intestino primitivo
 Edodermo
 Neuroporo
 Placa neural
 Notocorda

ALTERAÇÕES DO EIXO LEVO-DEXTRO AFETAM A EXPRESSÃO DE NODAL

Nodal (Xnr-1) regula a expressão de Pitx-2

A injection of CMV-LacZ

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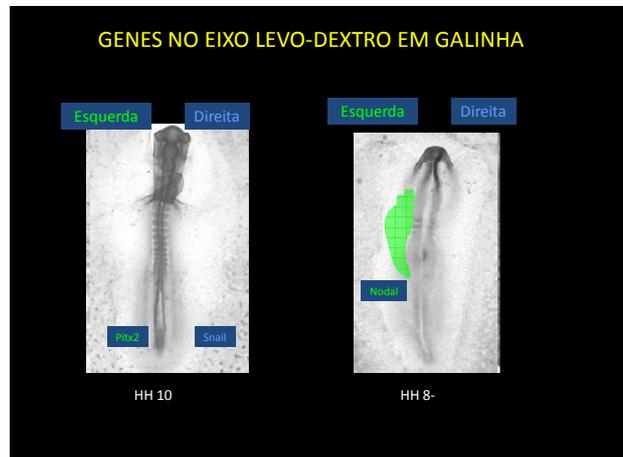
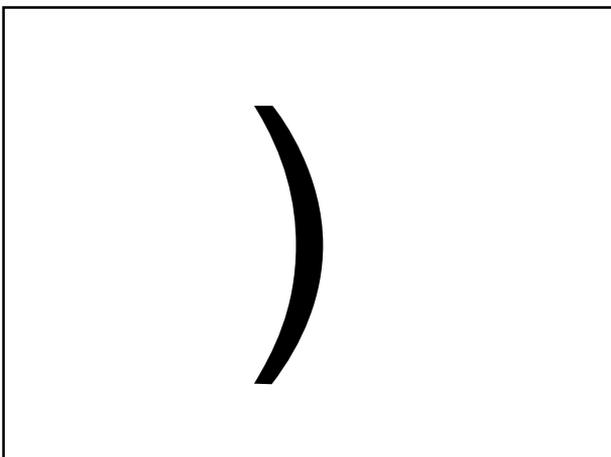
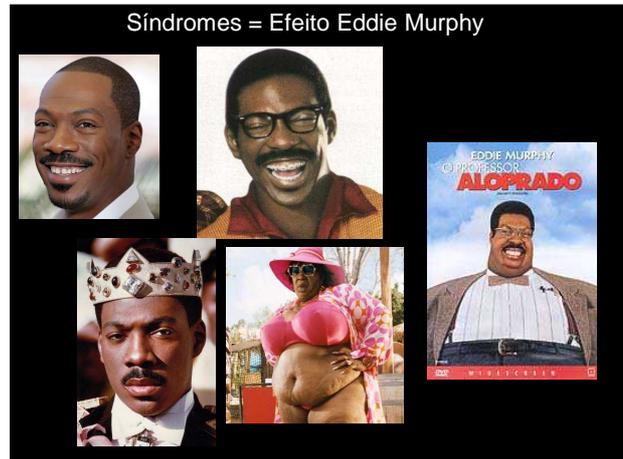
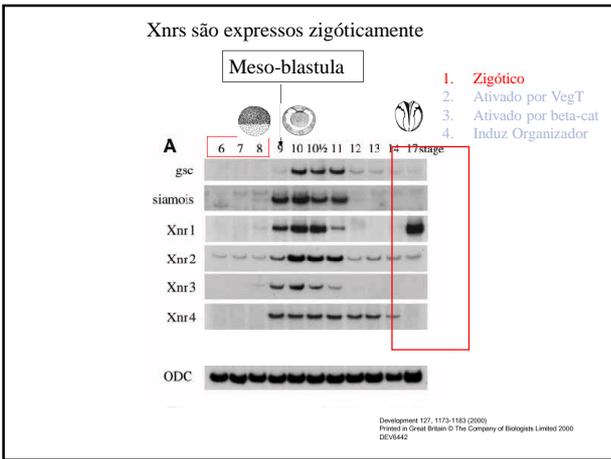
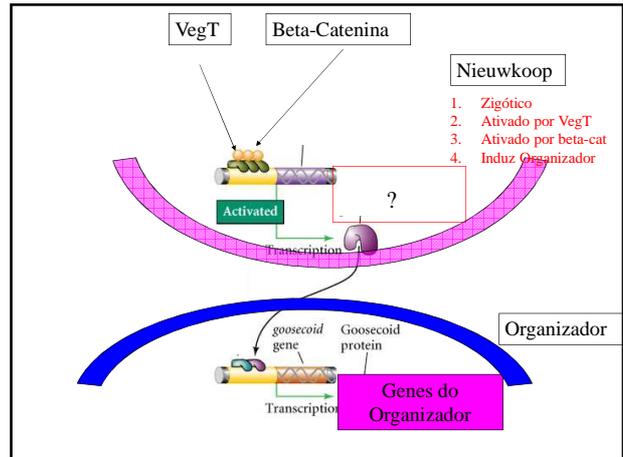
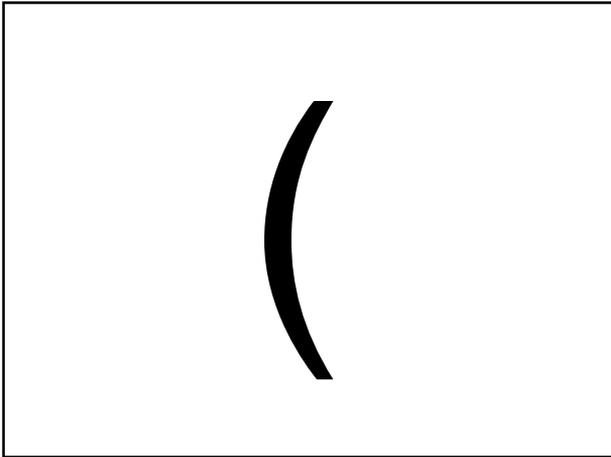
A' Pitx2

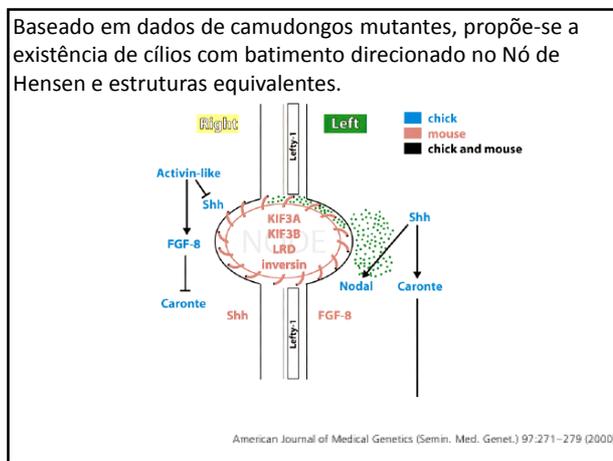
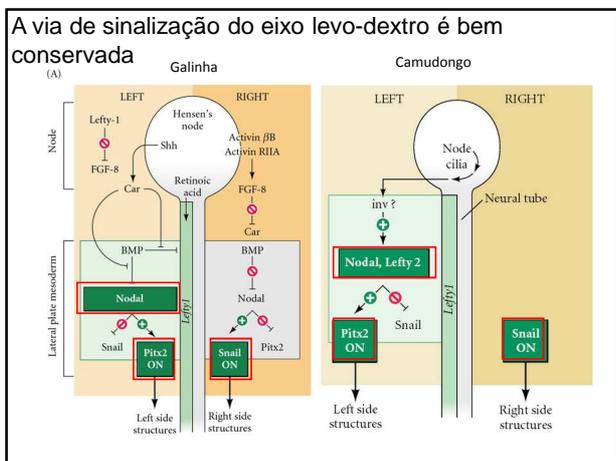
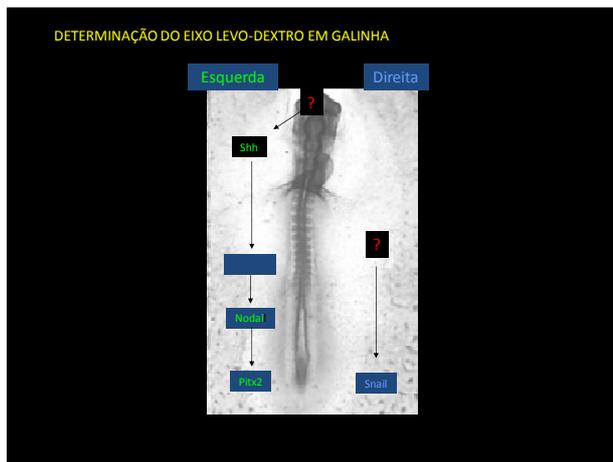
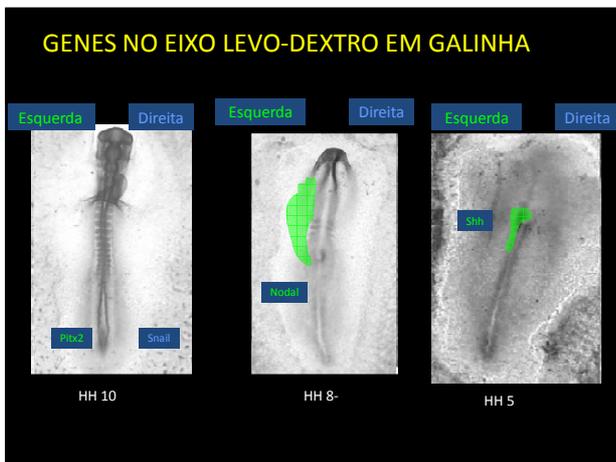
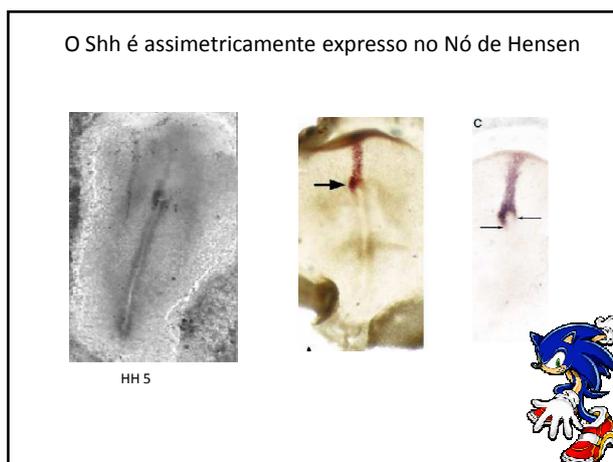
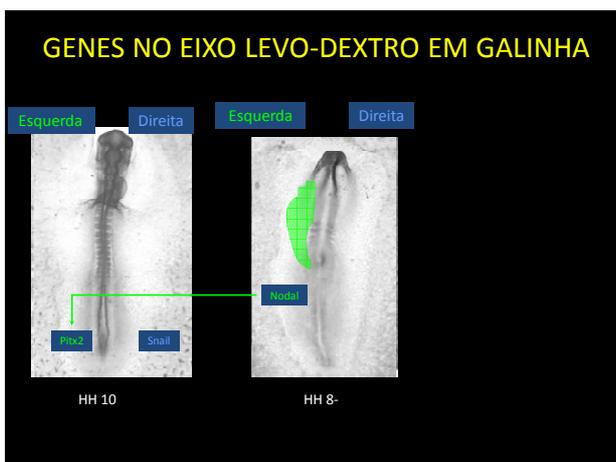
B injection of Xnr1 RNA

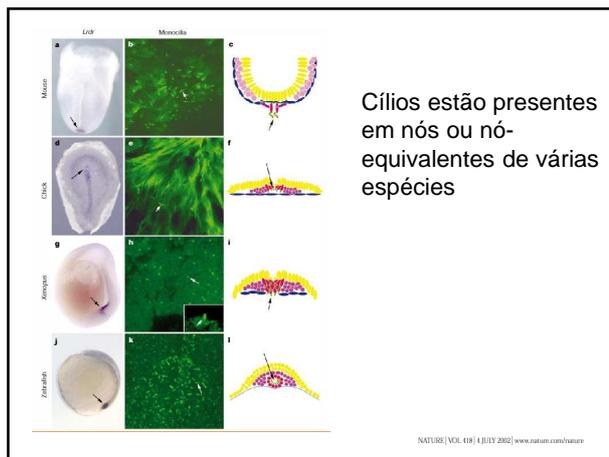
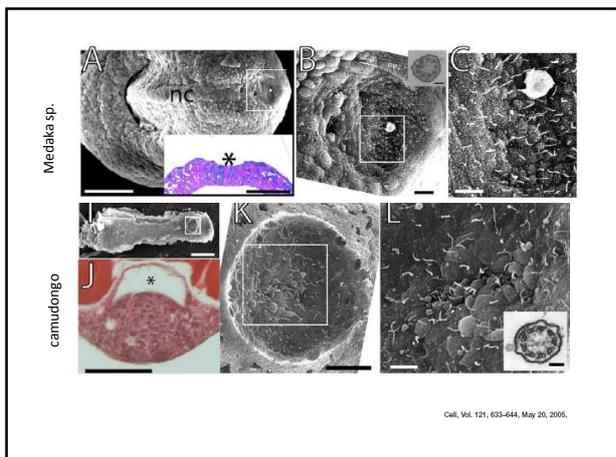
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B' Pitx2

Development 128, 1225-1234 (1999)
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 DEV2373



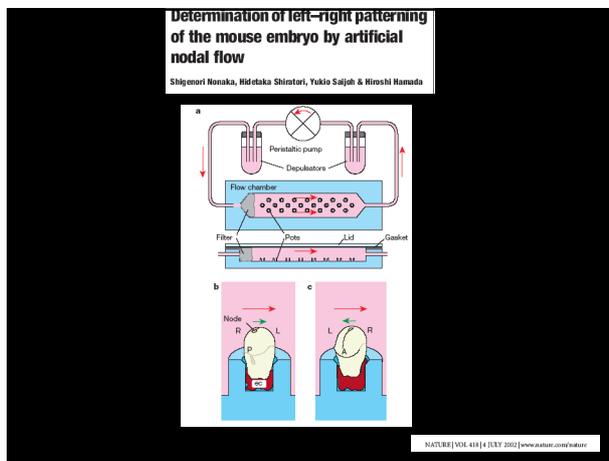
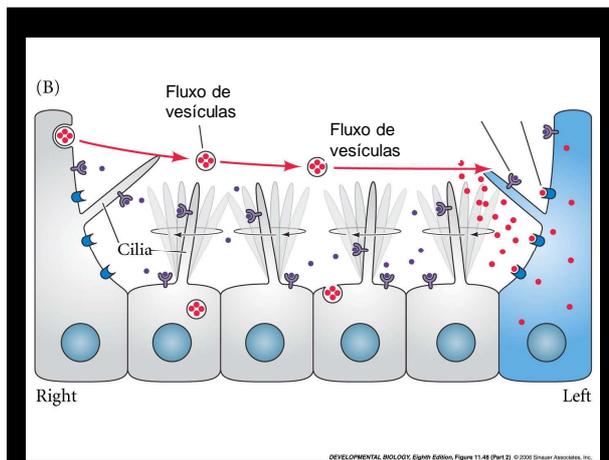




A presença dos cílios precede o aparecimento do primeiro gene assimétrico

	Onset of <i>Lcfr</i> mRNA expression	Appearance of nodal cilia	Earliest conserved asymmetric gene expression
Mouse	Gastrula, 7.5 d.p.f.	Gastrula, 7.5 d.p.f.	<i>Nodal</i> , 8.25 d.p.f., 3–5 somites
Chick	Gastrula, HH4	Gastrula, HH4	<i>Nodal</i> , HH7, 0–2 somites
Xenopus	Stage-11 gastrula	Stage-14 neurula	<i>Xnr-7</i> (<i>Nodal</i>), stage-17 neurula
Zebrafish	80% epiboly gastrula	Four somites	<i>Cyclops</i> (<i>Nodal</i>), 20 somites

*Asymmetric gene expression of *Sonic hedgehog* at the node occurs at HH5 (gastrulation) before *Nodal* expression, but seems to be unique to the chick embryo. d.p.f., days post-fertilization.



O que determina a direcionalidade dos cílios?

Desenvolvimento neural

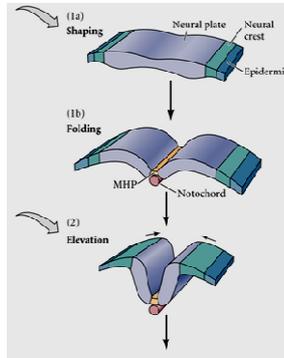
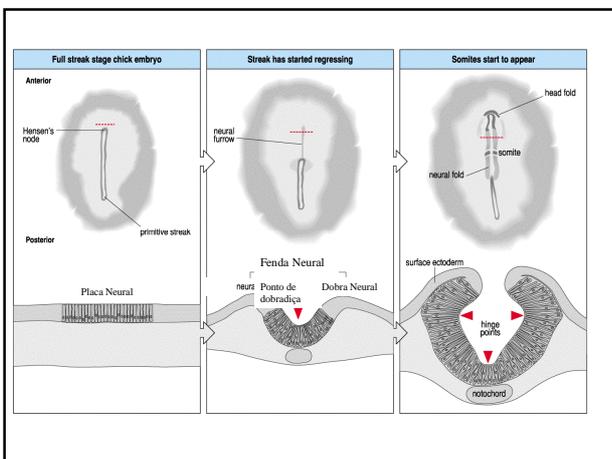
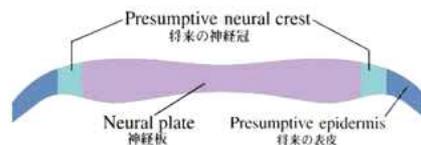


Gilbert 8a Ed

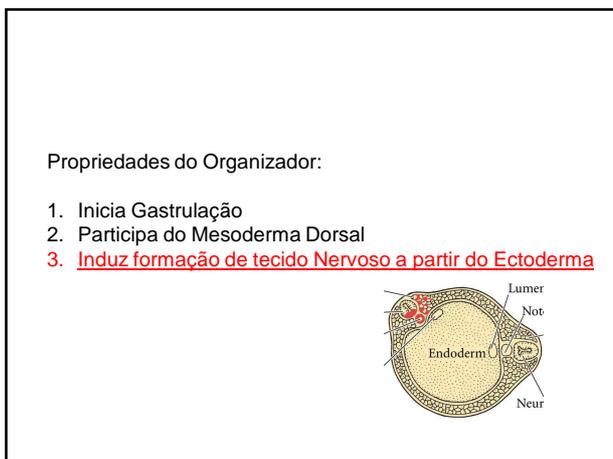
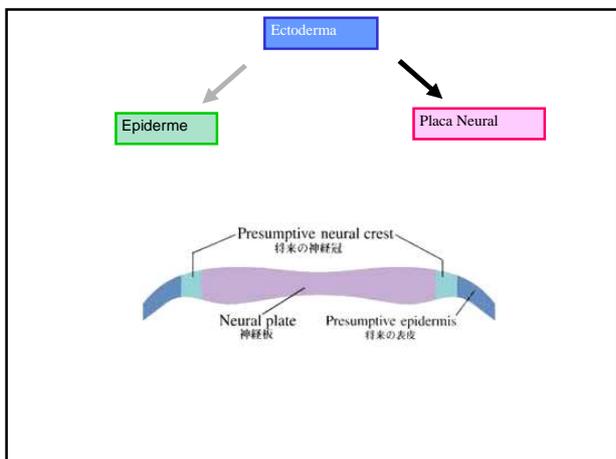
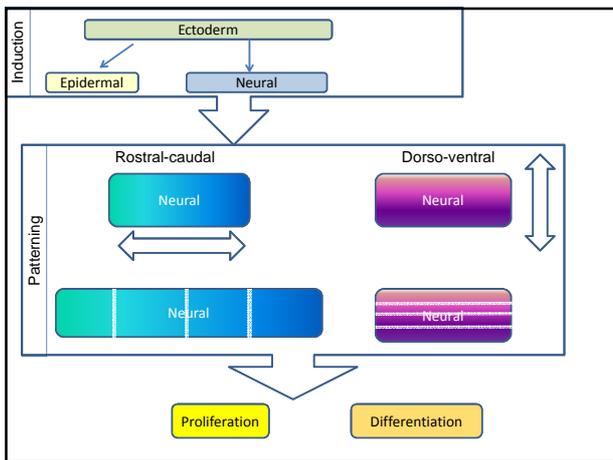
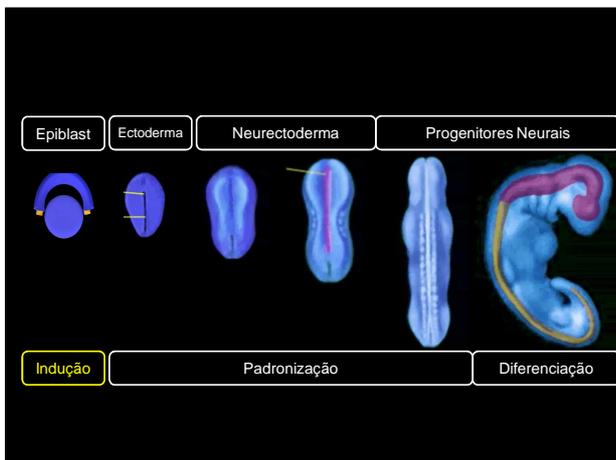
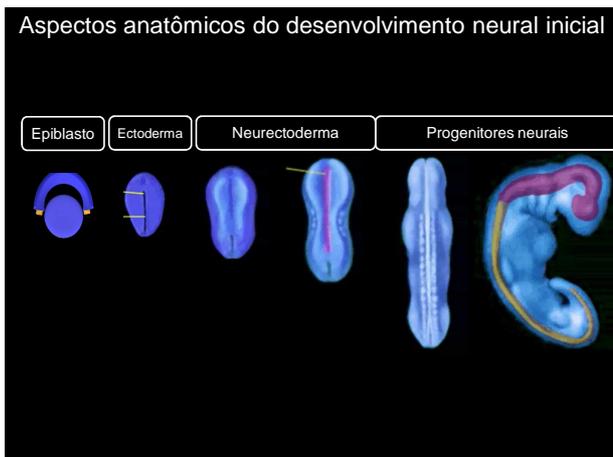
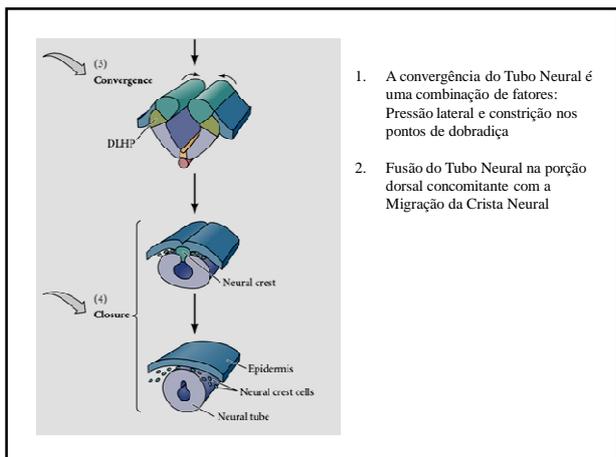
Anatomical aspects of early neural development



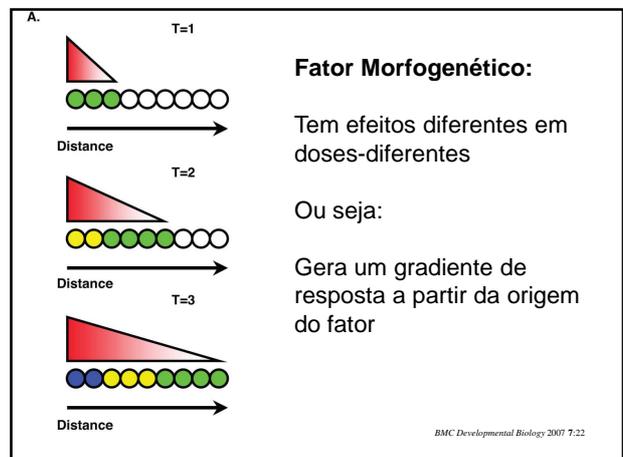
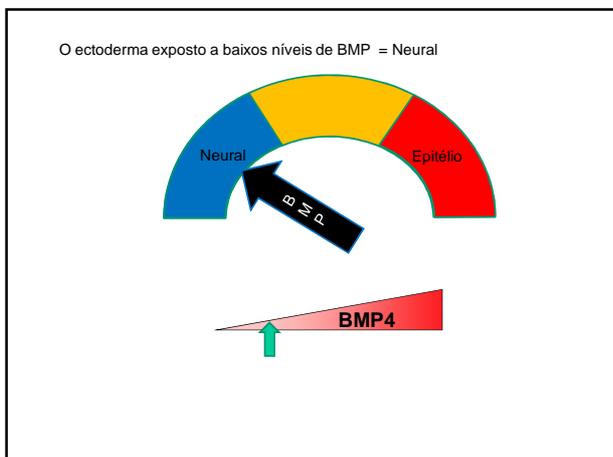
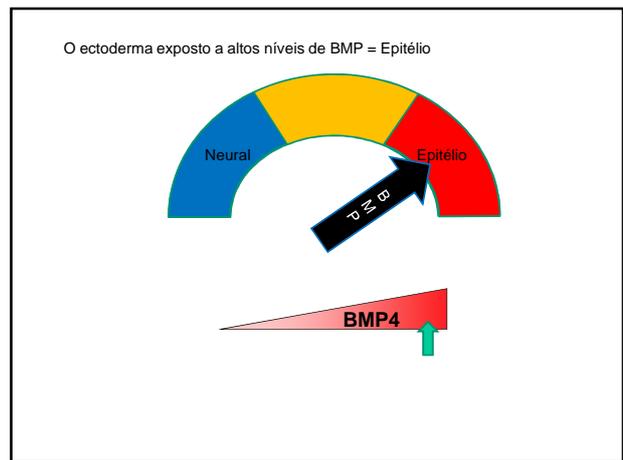
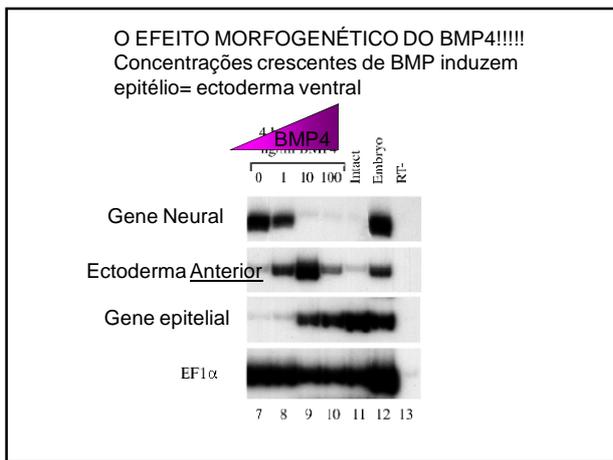
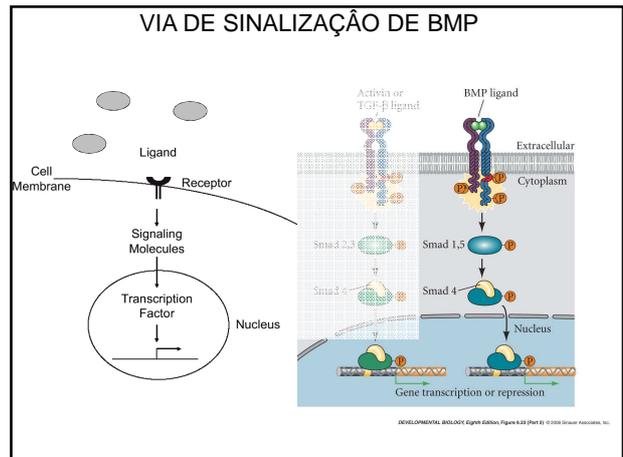
Crump Institute for Biological Imaging



1. Indução da formação da PLACA NEURAL pelo Mesoderma (Mudança na forma celular, expressão de marcadores gênicos)
2. Associação da Placa Neural com a Notochorda subjacente; constricção apical nas células da borda da Placa Neural
3. Dobramento da Placa Neural



Signals in early <i>Xenopus</i> development		
Factor	Protein family	Effects
Mesoderm induction		
Xnr-1	TGF- β family	
Xnr-2	TGF- β family	
Xnr-3	TGF- β family	
Derriere	TGF- β family	
Vg-1	TGF- β family	
Activin	TGF- β family	
Mesoderm patterning		
Bone morphogenetic protein (e.g. BMP-4)	TGF- β family	ventral mesoderm patterning
Xwnt-8	Wnt family	ventralizes mesoderm
Fibroblast growth factor (FGF)	FGF	ventral mesoderm induction
Noggin		dorsalizes—binds BMP-4
Chordin		dorsalizes—binds BMP-4
Frizbee		dorsalizes—binds BMP-4

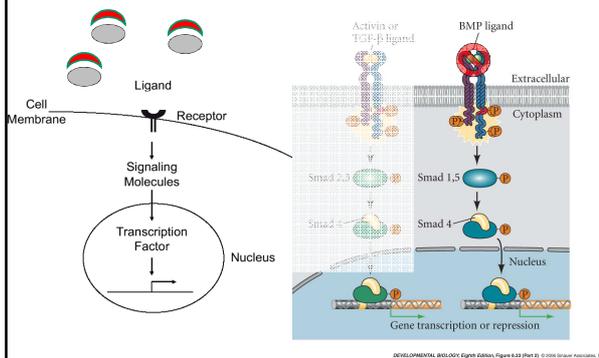


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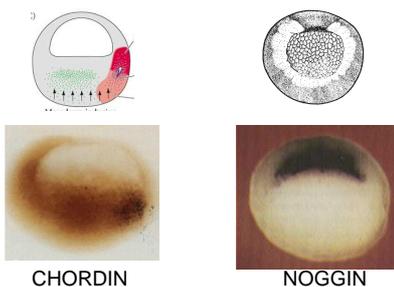
A INIBIÇÃO DE BMP determina a formação de NEURAL



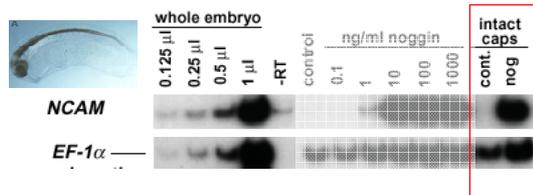
Existem proteínas extracelulares que são inibidores de BMP e atuam evitando a ligação de BMP com o seu Receptor



Existem INIBIDORES de BMP4 no ORGANIZADOR

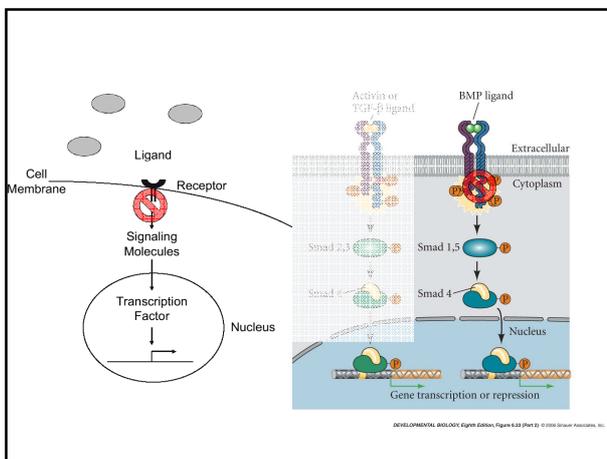


Noggin em explantes de ectoderma induz expressão de genes neurais



Development 124, 2477-2488 (1997)

Isto prova que BMP4 comanda a decisão de epitélio e placa neural a partir do ectoderma?

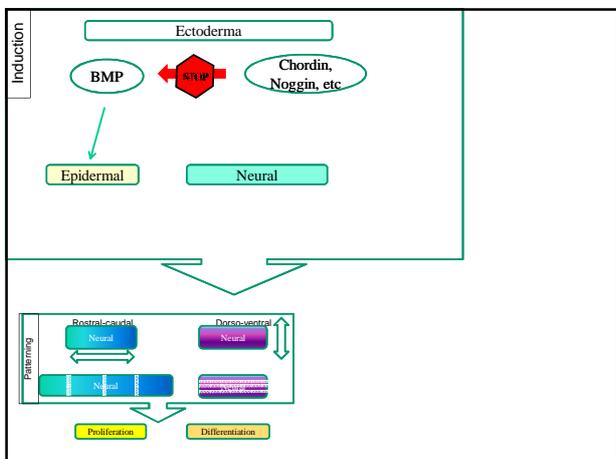
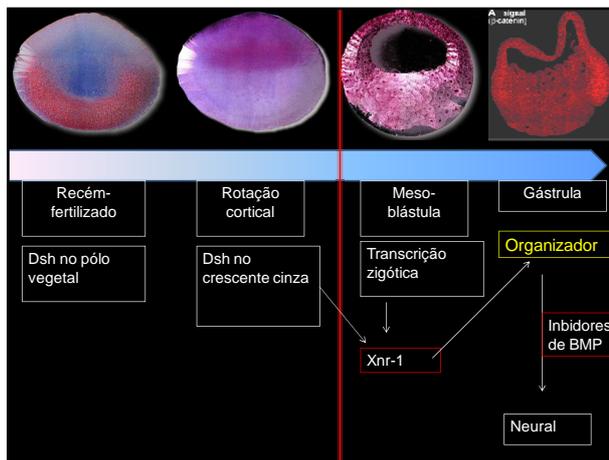
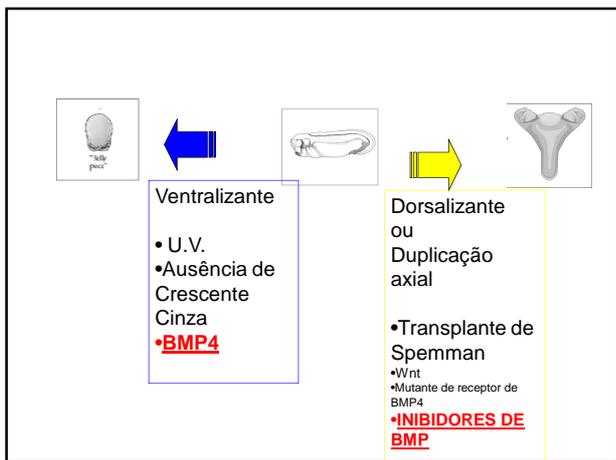


mRNA de Receptor de BMP4 não-sinalizante	Normal	Eixo Duplo
0	88%	0
20		
200		

Suzuki et al. 1994

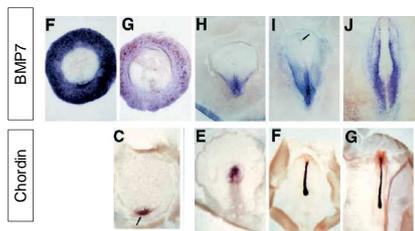
mRNA de Receptor de BMP4 não-sinalizante	Normal	Eixo Duplo
0	88%	0
20	52%	27%
200	7%	76%

Suzuki et al. 1994



A indução neural em aves também ocorre através da inibição do BMP?

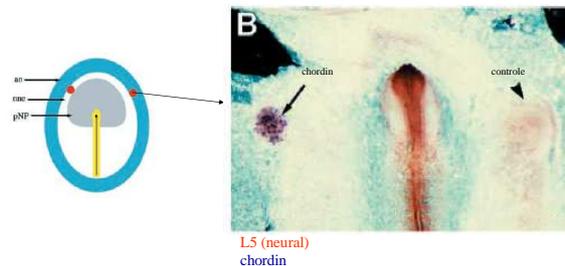
BMP7 e o inibidor Chordin no embrião de galinha têm expressões complementares



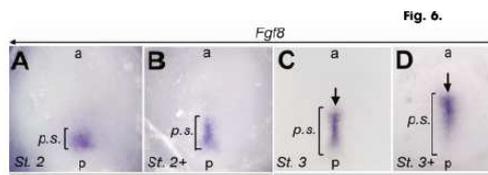
Development 125, 507-519 (1998)

MAS, em aves chordin ~~não~~ induz genes neurais no ectoderma

Development 125, 507-519 (1998)



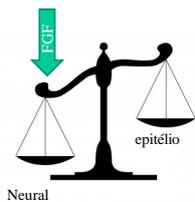
FGF é expresso na linha média do embrião de galinha



DEVELOPMENTAL DYNAMICS 229:422-432, 2004
Chapman et al Dev Dyn 2004 Mar;229(3):668-76.

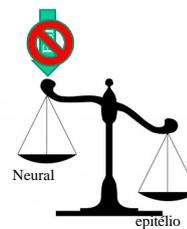
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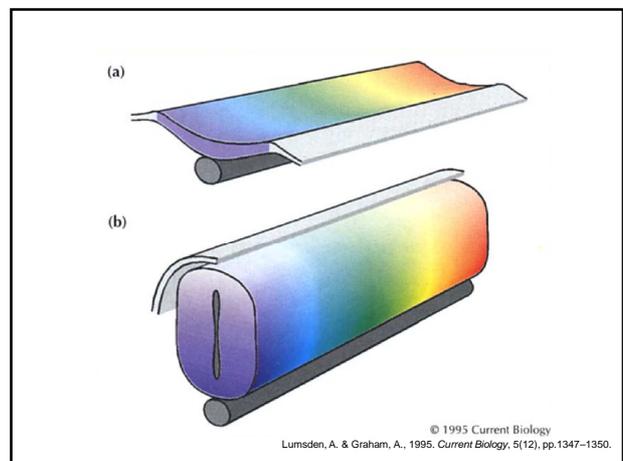
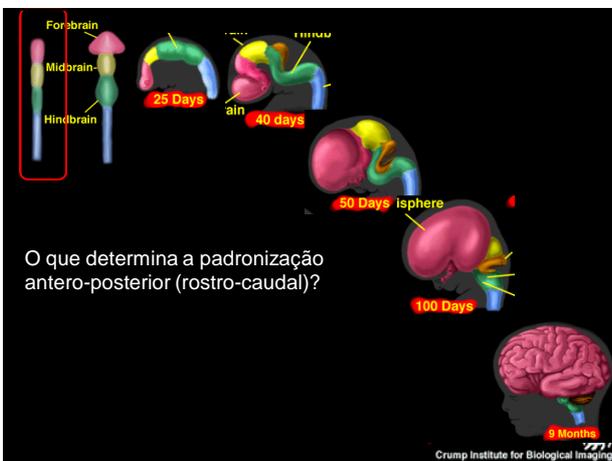
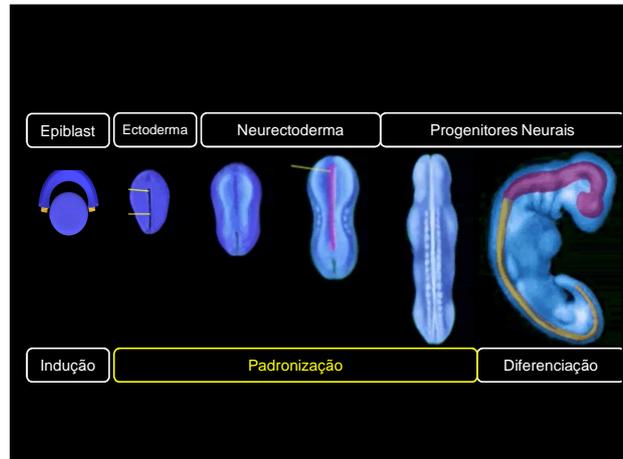
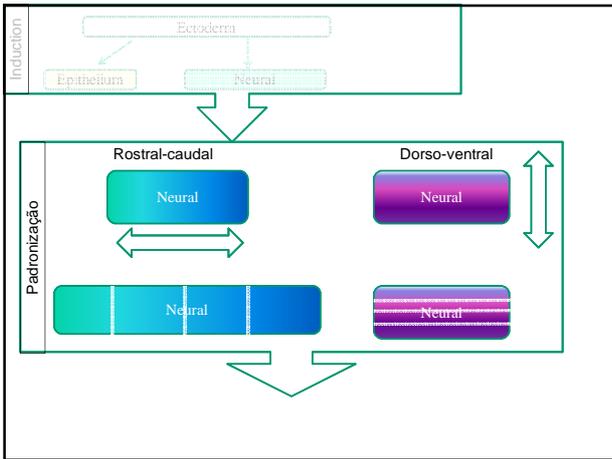
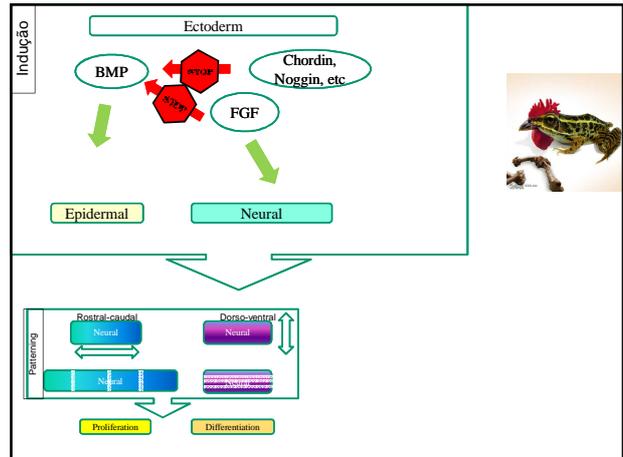
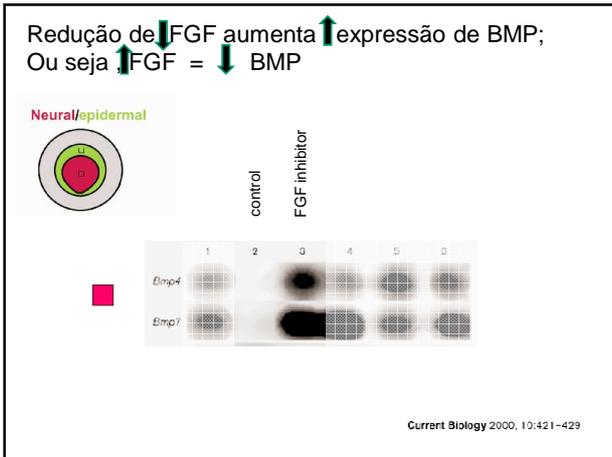
O FGF determina a formação de Neural

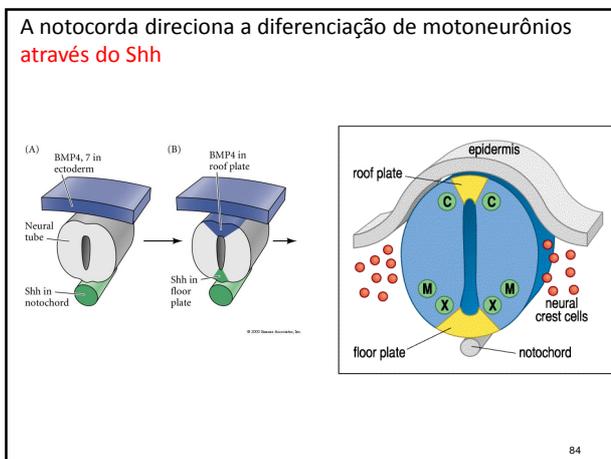
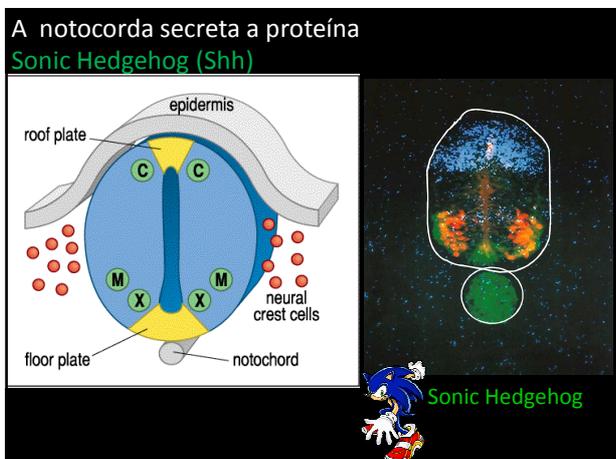
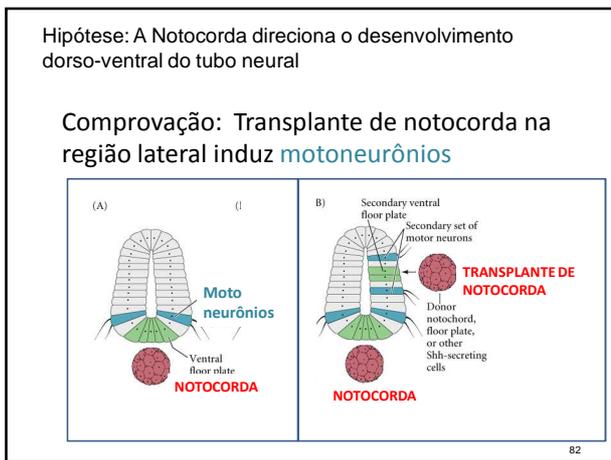
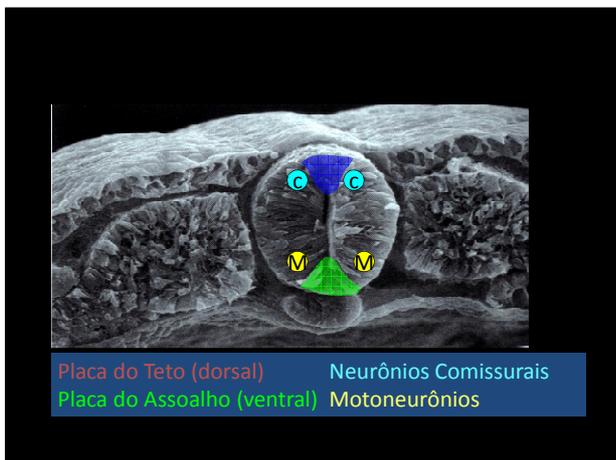
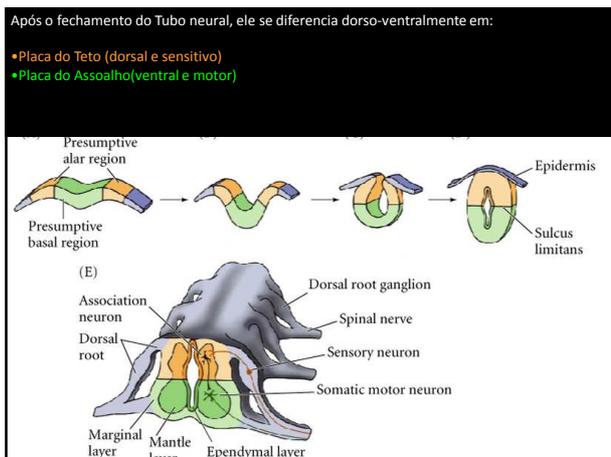
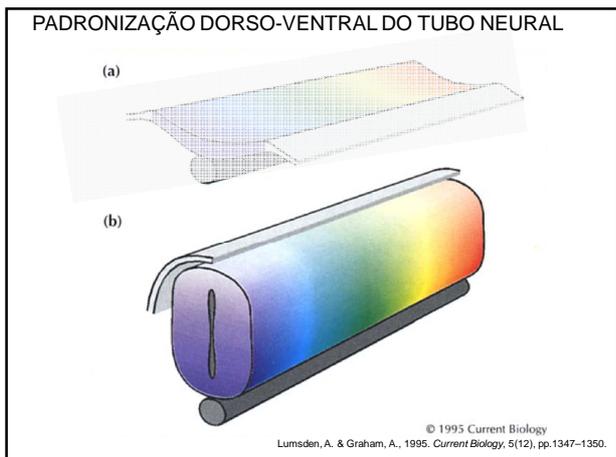


Hipótese:

A INIBIÇÃO DE FGF determina a formação de Epitélio







O padrão dorso-ventral do tubo neural provém de assimetria molecular:
 Dorsal: Epiderme > Família BMP
 Ventral: **Notocorda** > **Sonic Hedgehog** > inibidores BMP

J., 2000. *Development* 127(22), pp.4855-66.
 Gilbert *Developmental Biology* 8th ed. 85

