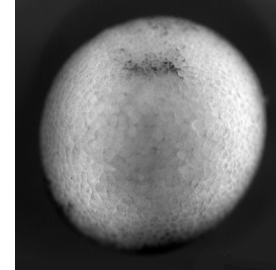


Human Development: *Fertilization through gastrulation*

Michael M. Shen, Ph.D.

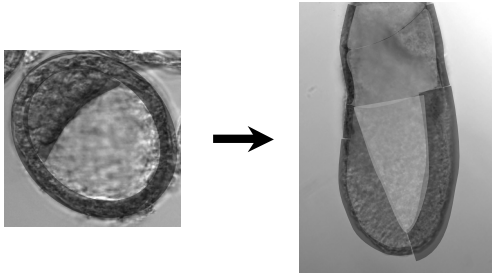
Departments of Medicine and Genetics & Development
Columbia University Medical Center

Gastrulation movements in the frog embryo

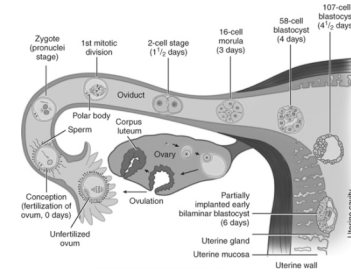


Vegetal view

From blastula to gastrula

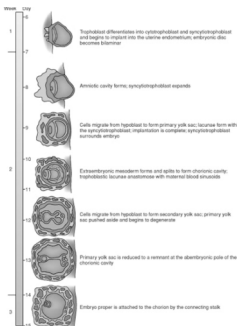


The first week of development



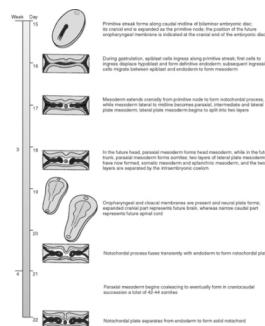
- Fertilization
- Cleavage stages
- Blastocyst formation
- Early lineage specification
- Implantation

The second week of development



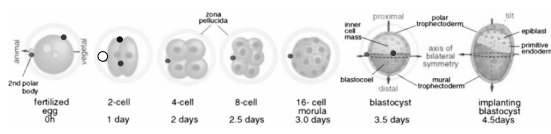
- Trophoblast differentiation
- Yolk sac formation
- Anterior-posterior axis patterning
- Initiation of gastrulation

The third week of development



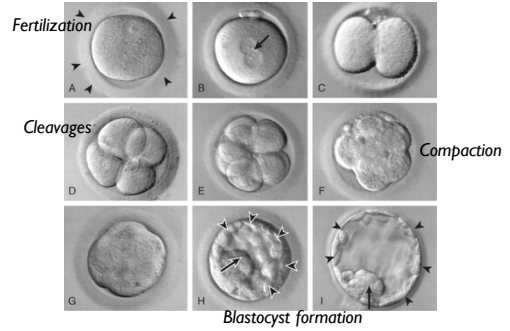
- Endoderm and mesoderm ingression
- Mesoderm lineage specification
- Left-right patterning
- Neural plate formation
- Axial midline formation

Pre-implantation mouse development

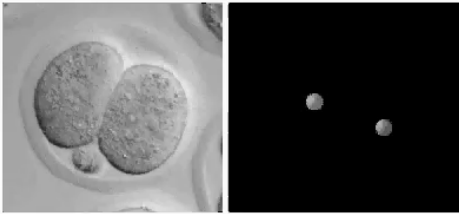


- Reductive cleavage
- Blastomere potency
- Inside-outside allocation of lineage progenitors
- Compaction
- Blastocyst formation
- Emerging morphological asymmetry

Human embryo development in culture



Early cleavages of the mouse embryo

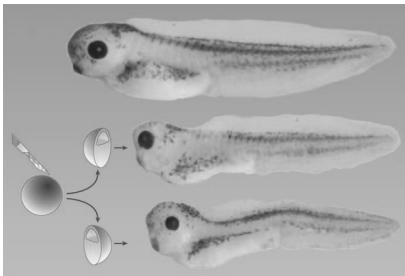


(Bischoff et al. (2008))

Key properties of vertebrate embryogenesis

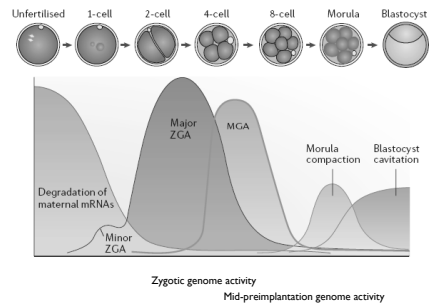
- Regulative development
- Early blastomeres are totipotent*

Regulative development of the vertebrate embryo

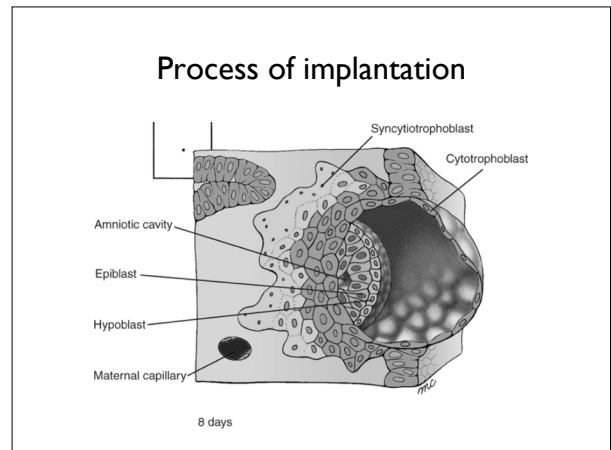
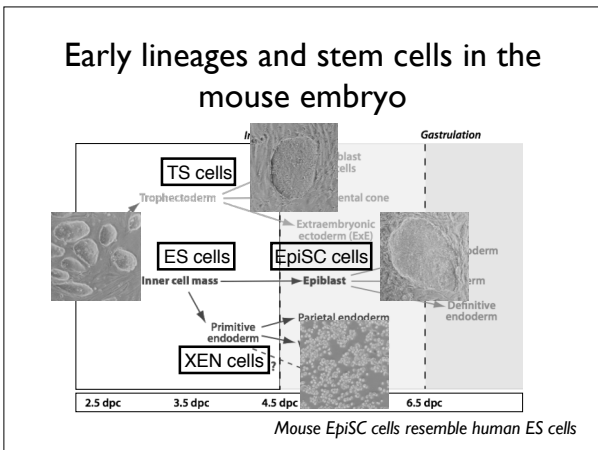
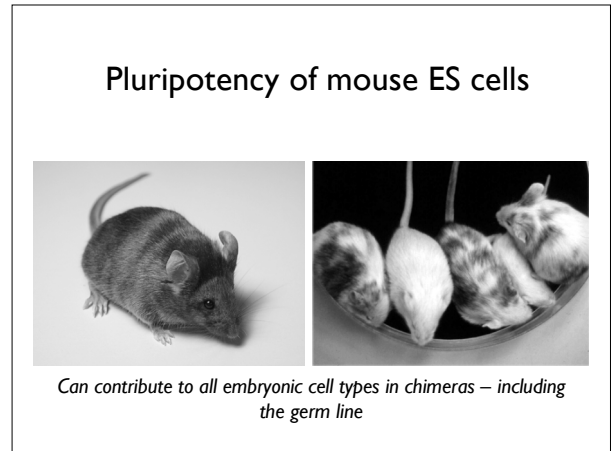
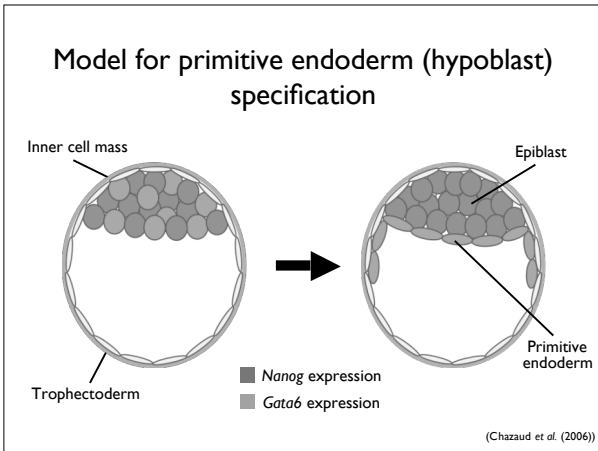
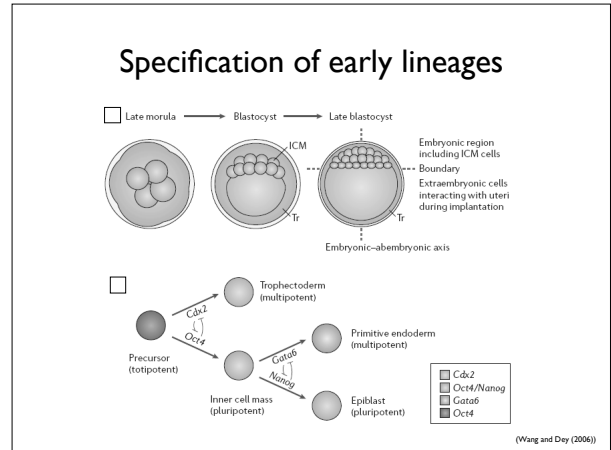
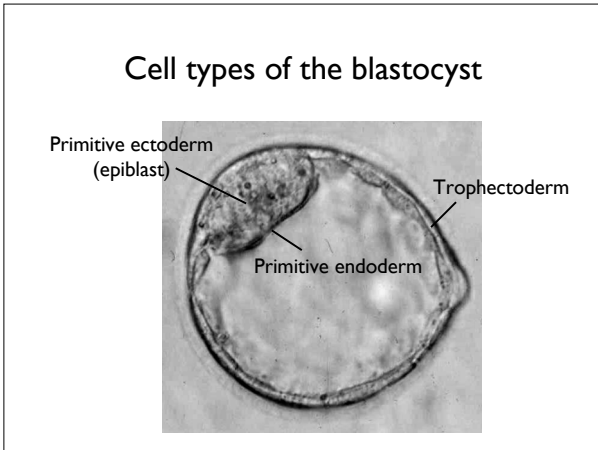


(DeRobertis (2006))

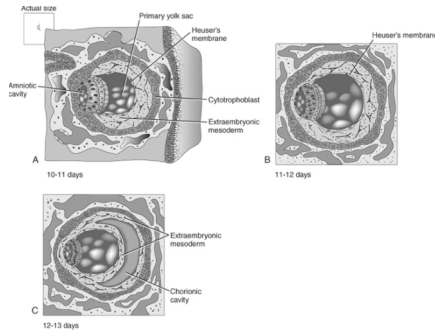
Gene expression at pre-implantation stages in the mouse



(Wang and Day (2006))



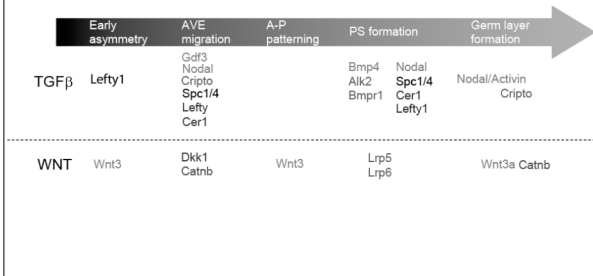
Formation of extraembryonic tissues



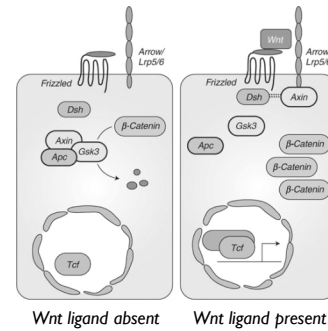
Key properties of vertebrate embryogenesis

- Regulative development
- Patterning at a distance by soluble morphogens

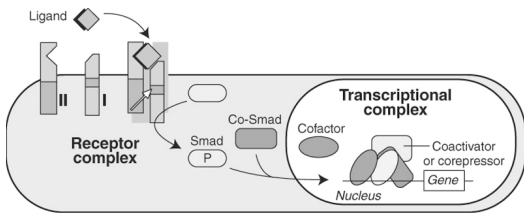
Two major signaling pathways regulate early patterning and differentiation



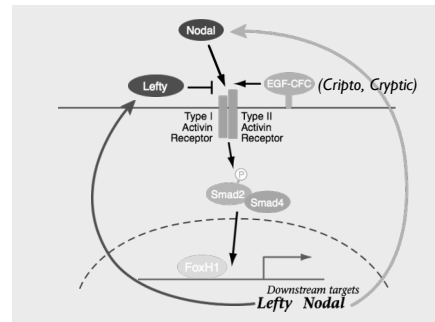
Schematic pathway for canonical Wnt/beta-catenin signaling



Schematic pathway for TGF-beta signaling



The Nodal signaling pathway



Key properties of vertebrate embryogenesis

- Regulative development
- Patterning at a distance by soluble morphogens
- Common patterning mechanisms underlie distinct embryo morphologies

Schematic of early mouse development

(Adapted from Hogan et al. (1994))

Morphological relationship between mouse and human embryos

Cup-shaped vs discoid
mouse human

(Eakin and Behringer)

Key properties of vertebrate embryogenesis

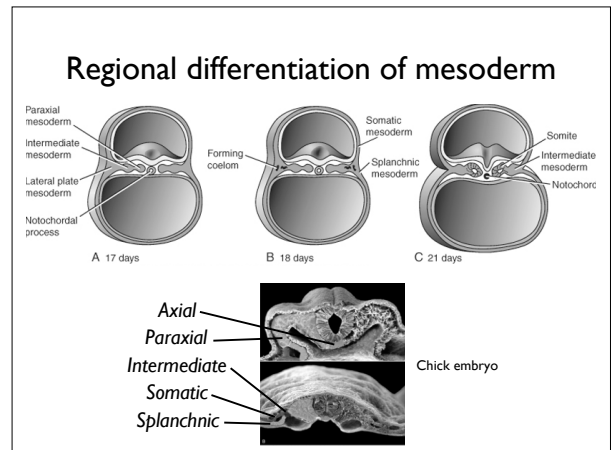
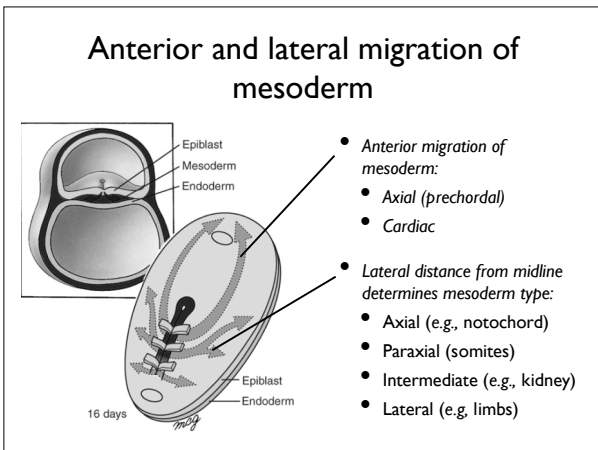
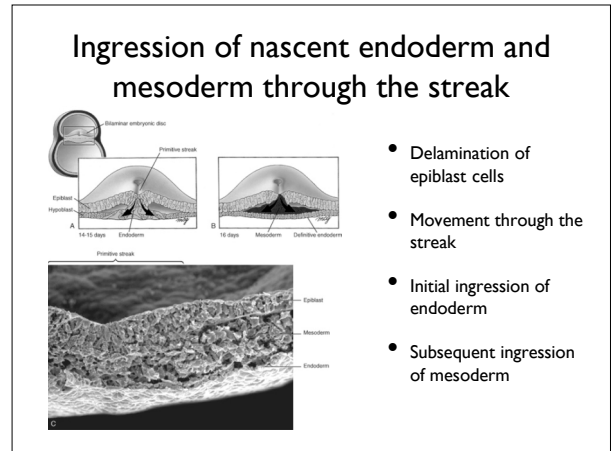
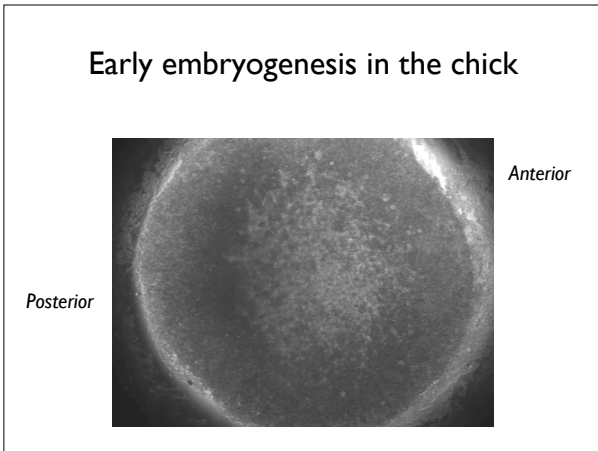
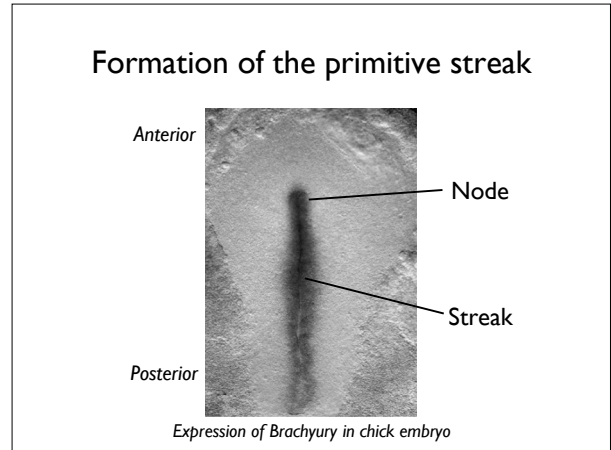
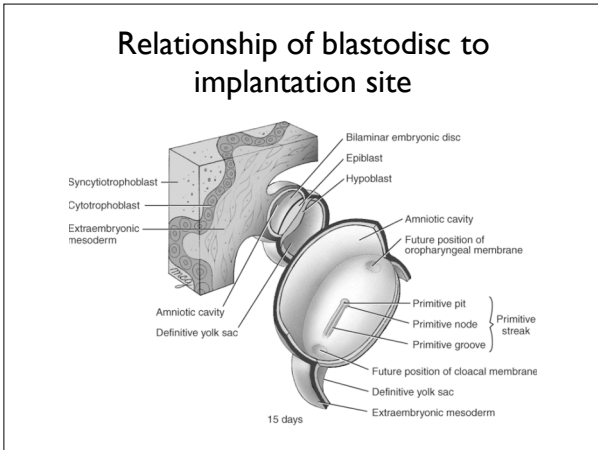
- Regulative development
- Patterning at a distance by soluble morphogens
- Common patterning mechanisms underlie distinct embryo morphologies
- Antagonism of secreted ligands and inhibitors

Specification of the anterior-posterior axis in the mouse

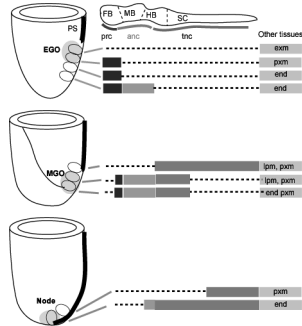
■ Nodal and Cripto activity ■ Nodal inhibitor activity (Lefty, Cerberus)

Movement of the anterior visceral endoderm

View from anterior side



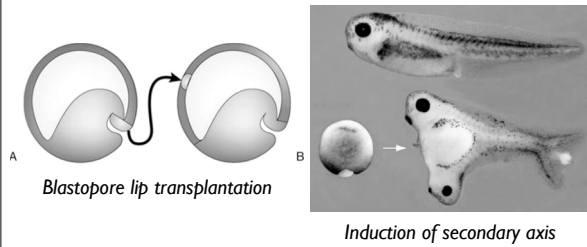
Anterior-posterior patterning of axial mesoderm



Key properties of vertebrate embryogenesis

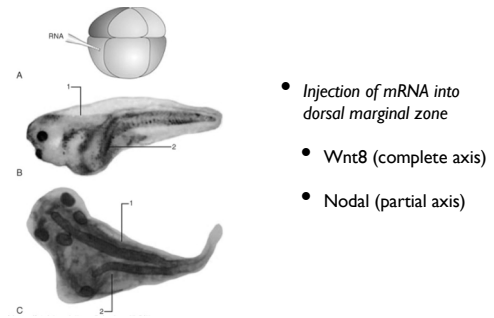
- Regulative development
- Patterning at a distance by soluble morphogens
- Common patterning mechanisms underlie distinct embryo morphologies
- Antagonism of secreted ligands and inhibitors
- Instructive inductive interactions

Spemann-Mangold organizer experiment

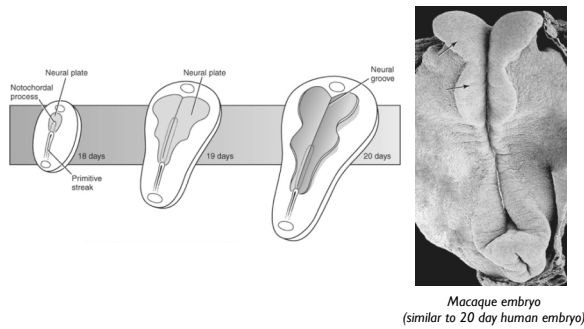


(DeRobertis and Kurrod (2004))

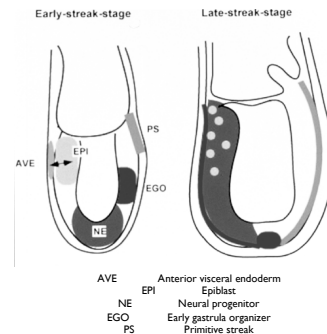
Injection of Wnts or Nodal can induce a secondary axis

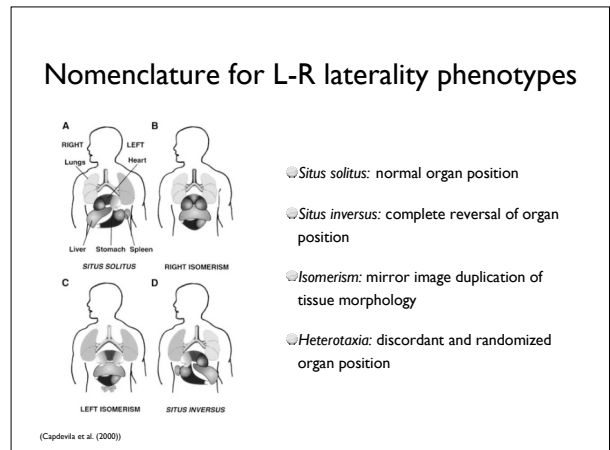
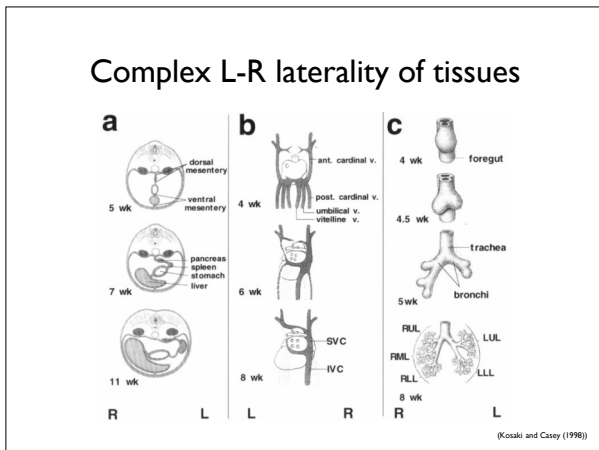
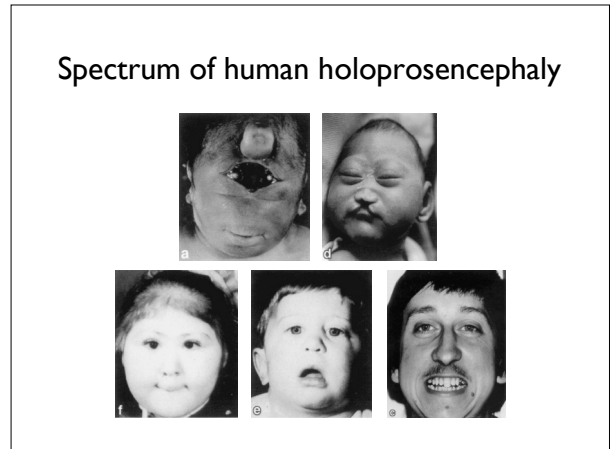
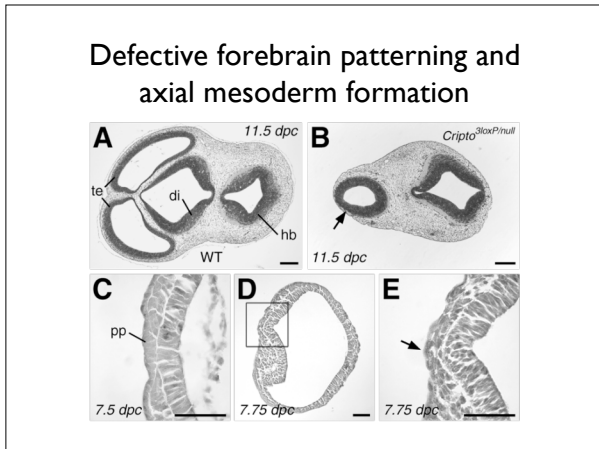
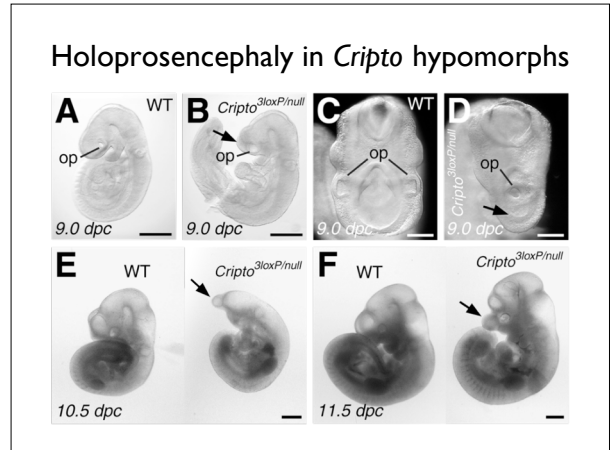
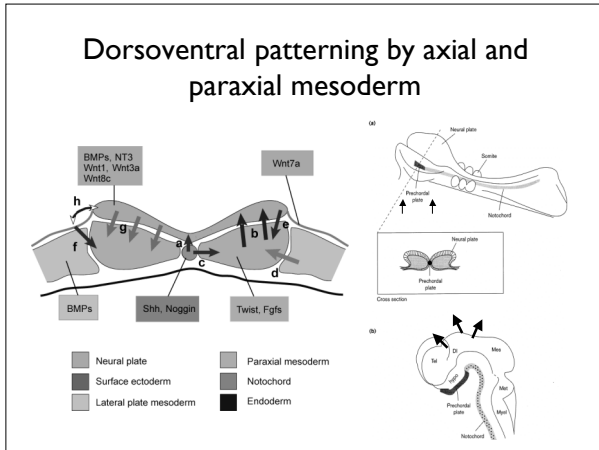


Formation of the neural plate



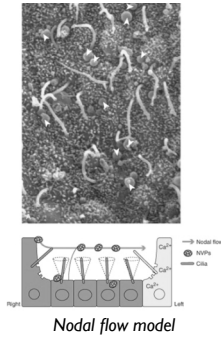
Inductive interactions and head formation





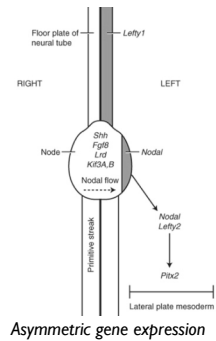
Stages of L-R laterality determination

- Initial symmetry breaking

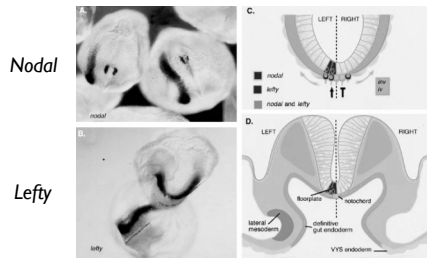


Stages of L-R laterality determination

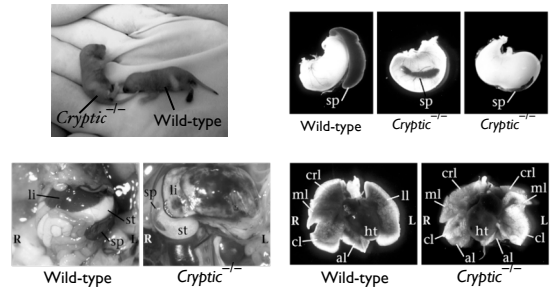
- Initial symmetry breaking
- Propagation and maintenance of an asymmetric signal
- Specification of tissue-specific laterality



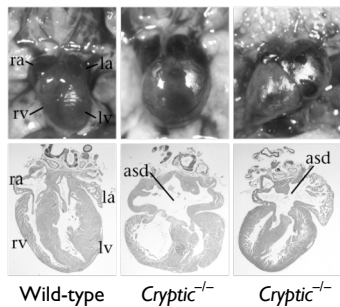
Asymmetric expression of *Nodal* and *Lefty*



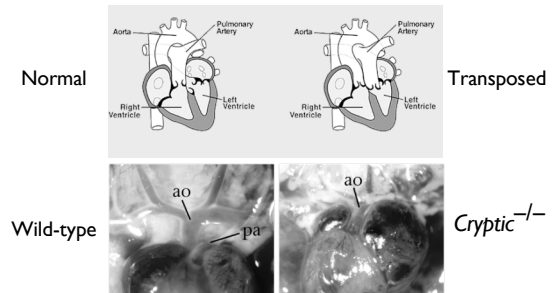
Left-right laterality defects in *Cryptic* mutants



Cardiac defects in *Cryptic* mutants



Transposition of the great arteries



HD2 - Gastrulation

