Morphogenesis: generation of tissue types

Neurulation: ~5 hours after gastrulation in xenopus

- Formation of the neural plate: elevation of the neural fold
    - Convergence and extension of the epithelium allow elevation of the neural fold
    - Lateromedial movement of the cells promote intercalation, allow anterior-posterior extension
- Bending of the neural fold
    - Medial hinge point and lateral hinge points bend to close the neural tube
    - At medial hinge point, apical constriction via actomyosin contractility bends the neural plate. (F-actin and MyoIIb)
- Closure of neural tube
    - Protrusion of neuroectoderm cells form cell-cell junction - close the neural tube
    - Rostral neuropore close on Day25, Causal neuropore close on Day27
    - Failure of closure lead to craniaorachischisis (entire), spina bfida(partial) and anencephaly(head)

- Closure points modelled in mice
    - Closure 1: from hindbrain towards caudal side
    - Closure 2: along the forebrain
    - Closure 3: Rostral-most point closes posteriorly
    - Closure 5: Caudal-most point closes rostrally

PCP/Wnt pathway: **mutant** celsr1 lead to severe neural tube defects

- **Fluorescence imaging** shows medialateral arrangement of actomyosin filaments in medial hinge point
- **siRNA knockdown of celsr1** lead to decreased apical constriction, lack of orientation biased actomyosin
- **siRNA knockdown of vangl2** lead to lack of convergence and extension, short and wide neural plate, shorter notochord.

Shh signalling: generation of hinge points

- Speculation: BMP need to be inhibited to generate lateral hinge point
- Shh is released from the notochord, induce medial hinge point formation
- Shh inhibit noggin, which inhibits BMP2, Shh have positive effect on BMP2
- Shh expression at ventral levels prevent the formation of lateral hinge points
- Lower Shh concentration dorsaly lead to generation of lateral hinge point, Shh aberrant expression lead to NTD

Fusion of the dorsal neural tube:

- Surface ectoderm form protrusions, result in zippering of the neural tube
    - **Phalloidin staining of F-actin** shows the extensive network and involvement of actomyosin fibres
    - **Vangl2** abrogation in surface ectoderm only, leads to failure to close the neural tube

Neural crest migration

- Neural fold ectoderm becomes mesenchymal cells, become delaminated and migratory
    - Loss of E-cadherin, loss of apicobasal polarity, migratory.
- Induction of neural crest: BMP4
    - **Experiment culturing** ectodermal cells with non-neural ectoderm or BMP4 produce neural crest cells.
- Neural crest cells establishment and maintainence by mesoderm population:

    - **Culturing experiment shows**: culturing ectodermal tissue with dorsolateral marginal mesoderm lead to expression of NCC marker snail2
    - **Culturing experiment shows:** culturing NCC cells with intermdiate mesoderm lead to maintainence of snail2 expression, without intermediate mesoderm lead to disappearance of snail2 marker
- Mesoderm regulate NCC formation with Wnt signalling, and BMP signalling from the ectoderm.