Neural Development

• How does a single cell make a brain???
• How are different brain regions specified???

Neural Development

• How do cells become neurons?
  – Environmental factors
  – Positional cues
  – Genetic factors
  • Competence
    Cell lineage
    Timing

Neural Development depends on genes and environment

Keywords in Development

Induction: Cells are instructed to adopt a fate by signals in the environment.

Competence: the ability of a cell to respond to a signal. It depends on the receptors, transcription factors, etc expressed by the cell.

Differentiation: Cell elaborates a specific developmental program.

Determination: A cell is restricted in its developmental potential.
Major Processes in Development

1. Mitosis
   - cell division
2. Patterning
   - cells are arranged in proper positions
   - the body plan is established
3. Differentiation
   - cells become different from each other
   - they acquire specific functions

Initial Steps in the Development of the Nervous System:

- Fertilization
- Cleavage
- Gastrulation
- Neurulation

Looking at early development of the nervous system: Xenopus Frog
Gastrulation is the process by which the embryo acquires 3 germ layers. There is intense cell movement and rearrangement.
Neurulation: Formation of the Neural Tube

After Gastrulation comes Neurulation. During Neurulation, the neural plate invaginates, and the neural folds close to form the neural tube.

Long After Neurulation:

- How do cells become neurons?
Classic experiment showing the induction of the nervous system

Hans Spemann discovered the organizer—Nobel 1935

Expt: Transplant different parts of the developing embryo (donor) into another embryo (host)

Result: 1) If the dorsal lip is transplanted, a second embryonic axis forms
2) The second embryo has both host and donor tissue
The organizer region is responsible for converting ectoderm into neural cells.

Model: Inductive signal in dorsal lip instructs ectoderm

How does the organizer instruct epidermal cells?

Experiment: Dissociate animal cap, grow in culture
Result: Neurons can form in the absence of the organizer

Model: Epidermis makes local signal that inhibits neural fate

How does the organizer instruct epidermal cells?

Experiment: Inject blastula with genes of interest. Do any cause animal cap to become neural?
Result: Expression of a dominant negative mutant of a BMP receptor results in neural fate.

Model: BMP signal instructs cells not to become neural
Activation of BMP signaling inhibits the neural fate

How does the organizer instruct epidermal cells?
Experiment:
Inject blastocyst with genes from the organizer and see if any cause the animal cap to become neural

Noggin is a secreted protein, expressed in the organizer and later in the notocord.
Noggin inhibits BMP signaling.
Follistatin and chordin have similar functions.

Inhibition of BMP signaling makes cells adopt neural fate
Current Model for how cells become neural

1) Default state is neural
2) Local secretion of BMPs by epidermis inhibits neural fate
3) Local secretion of noggin, chordin by dorsal lip or mesoderm inhibits BMP signaling
4) Inhibition of BMP signaling give rise to neural fate

Double Inhibition Model for Neural fate

Model: The ‘double inhibition model’ for neural fate

A cell’s fate will depend on the signals to which it is exposed as well as the developmental history of the cell (which genes they express)