Induction and Competence

Induction—one cell or group of cells changes the behavior (fate, differentiation, shape, mitotic activity, etc.) of another cell or group of cells.

Two main types of interactions:

Instructive—tissue A provides information to cause a response in tissue B:

- if remove tissue A, or place B in another environment --> no response
- if place tissue C with A, C responds (if competent—see below)
- e.g. notochord induces neural tube cells to form floor plate (fig 12.14)
  - if remove notochord-->no floor plate differentiation
  - if transplant notochord to lateral position-->lateral neural tube cells differentiate as floor plate cells
  - Sonic hedgehog (Shh) is expressed in notochord
  - can induce floor plate differentiation with Shh

Permissive—cells contain the information but require specific environment to express fate. (e.g. may require fibronectin substrate)

Competence—ability of cells to respond to inductive signal.

- e.g. amphibian optic vesicle can induce head ectoderm to form a lens. If transplant optic vesicle to ectopic sites in the head, get the formation of ectopic lens. If transplant optic vesicle to the trunk, get no lens formation. Only head ectoderm is competent to respond to induction.
  1. Receptor must be present
  2. Signal transduction pathway must be present and active
  3. may need to remove an inhibitor to respond
  4. cell fate may already be determined (gene expression profile “locked in”)

Often a temporal component—responding tissue may only be competent during a specific “developmental window”; earlier or later and the responding tissue is not competent.

Mesenchyme-epithelium interactions:

- mesenchyme--masses of loosely associated cells
- epithelium--sheets of tightly associated cells that form linings etc.

Generally mesenchyme induces epithelium (but not always).

Specificity of induction controlled by mesenchyme—for example, the position of tadpole appendages.

Response is controlled by the epithelium—for example, whether frog or newt appendages form.

Induction events often form cascades.

Lens formation: 1st, Neural plate induces competence and bias to form lens. Then optic lobe and optic cup specify lens fate and direct the exact location for lens formation.

Reciprocal Inductions. Following an initial inductive event, the induced cells in turn induce the original inducing cells. This is important for coordinating the proper sequence
of events and relative spatial relationships within complex organs developing from multiple tissues.

Eg. lens induction:
1. optic vesicle induces lens ectoderm to form lens placode
2. lens placode induces optic vesicle to form optic cup
3. lens placode later induces optic cup to form neural retina

Single cell inductions.
1. Ommatidia of Drosophila eye each contain 8 photoreceptor cells, R1-R8. R8 is first to form, R7 last. 2 mutants block the formation of R7 cells, *sevenless* (*sev*) and *bride of sevenless* (*boss*). **Genetic mosaics** (individuals containing both mutant and normal cells) show that SEV functions in the R7 cell. The gene is therefore said to function cell-autonomously. BOSS is required in the R8 cell for R7 formation and functions non-cell-autonomously.

![Diagram](image1)

*sevenless* genetic mosaics: if the R7 cell is mutant, it will not differentiate as R7, if it is wild type, it will differentiate normally. The phenotype of the R7 cell depends on the genotype of the R7 cell. Therefore, wild type *Sevenless* functions **cell autonomously**.

![Diagram](image2)

*boss* genetic mosaics: if the R8 cell is mutant, the R7 cell will not differentiate. If the R7 cell is mutant but the R8 cell is wild type, R7 will differentiate. The phenotype of the R7 cell depends on the genotype of the R8 cell. *Boss* functions **non-autonomously**.

SEV is a receptor tyrosine kinase. Activation initiates a signal transduction cascade leading to R7 cell fate.

BOSS is the ligand for SEV. BOSS is a 7 transmembrane G-protein coupled receptor. The interaction is juxtacrine.

2. C. elegans vulval induction
6 vulval precursor cells (VPCs) form an equivalence group (cells have equal
potencies).
Anchor cell (AC) from gonad signals VPCs to induce vulva formation. AC produces LIN-
3 (EGF) and LET-23 receptor on VPCs gets activated. Cell closest to AC gets induced
first and becomes central vulval cell (CVC). CVC then makes LAG-2 (Delta like) signal
which activates LIN-12 and inhibits neighboring VPCs from forming CVC. They then
form lateral vulval cells. Such negative induction of neighboring cells is called lateral
inhibition.

Randomness
Sometimes specific cell types differentiate from an equivalence group by stochastic
processes. An example is the formation of the peripheral nervous system of flies. The
neurogenic ectoderm is an equivalence group that forms epidermal cells and
neuroblasts. The neuroblasts develop in a regularly spaced pattern beginning with a
random process. Initially, all the cells are expressing Delta and Notch. Activation of
Notch inhibits expression of Delta. By chance, one cell expresses more Delta than it’s
neighbors. It’s neighbors will then have more Notch activation, leading to reduced Delta
expression. The first cell will then have less Notch activation and thus express more
Delta. This feedback loop leads to a situation where one cell is producing high levels of
signal while it’s neighbors are not. The high Delta expressing cell becomes a neuroblast
while the low expressers differentiate as epidermis. Mutations in the notch or delta
genes lead to all cells of the neurogenic ectoderm differentiating as neuroblasts. Thus in
the normal situation, the Delta signal blocks neuroblast fate and is another example of
lateral inhibition.