

LECTURE 28

(From CHAPTER 21: DEVELOPMENT OF MULTICELLULAR ORGANISMS)

Generation of positional information in the embryo (p. 1163-1175)

Figures covered: Fig. 21-7 through 21-21

Cells make developmental decisions long before they show visible changes

- Cell fate determination: cells are “determined” when they are irreversibly committed to a fate but haven’t yet manifested the fate.
- Cell differentiation: establishment of physical changes in cell associated with specialized/terminal cell fate
- Cell determination can be tested in transplantation expt’s (experimental embryology) (Fig. 21-7)
- Group of cells may be determined while single isolated cells from group may not (e.g., “autocrine/community effects” [Fig. 15-6] may modulate determination,)

Cells in the embryo can be regionally determined in stepwise manner

- express genes that define location-specific “positional values”; progressively more refined (evidence for this: Fig. 21-8, 21-9, more in later lectures)
- Fig. 21-8: Prospective thigh tissue grafted onto wing bud tip; exp’t shows early limb bud cells determined to be leg NOT wing, but not yet determined as to what PART of leg. Local signals in distal wing bud induce these cells to make distal leg parts (toe claws, NOT thigh).
- Fig. 21-9: two related T-box TFs, Tbx4 and Tbx5 expressed in hindlimb (leg) bud and forelimb (wing) bud, respectively

Two ways of making sister cells adopt different fates (Fig. 21-10)

- Asymmetric division: unequal partitioning of cell fate-determining factors
- Symmetric division, but cleavage plane oriented so daughters differ in proximity to inductive signals for cell fate change

Mechanisms by which fields of cells make cell fate decisions

- Fig. 21-11: Lateral inhibition (e.g., Delta/Notch signaling)
- Fig. 21-12: Inductive signaling
- Fig. 21-15: Sequential inductive signaling

Signaling proteins used repeatedly as inducers during animal development:

Table 21-1

- Ligands for receptor tyrosine kinases (e.g., EGF, FGF, ephrins)
- TGFbeta superfamily (e.g., TGFbeta, BMPs, Nodal)
- Wnt (ligand for receptor Frizzled)
- Hedgehog (ligand for Patched)
- Notch (receptor for Delta; both are transmembrane proteins)

Morphogens

- secreted signaling proteins that exert “graded effects” on cell fate induction in developing tissue (induce different fates at different concentrations)
- form concentration gradient that depends on source, rate of diffusion, degradation, inhibitors, etc.
- example: Sonic hedgehog (Shh) protein (Fig. 21-13): secreted from cells in posterior limb bud, forms gradient across limb bud; transplant’n of

polarizing region (or Shh-soaked bead) to anterior limb bud causes mirror-image duplic'n of distal limb parts

- Fig. 21-14: Two ways to create a morphogen gradient
 - Gradient of morphogen itself
 - Gradient of inhibitor of morphogen (e.g., gradient of Chordin, an inhibitor of BMPs)

Essential features of *C. elegans* development

- Simple body plan (Fig. 21-16); 2 sexes: males & hermaphrodite
- Genome sequenced
- Essentially invariant cell lineages (Fig. 21-17, 21-19)
- Sperm entry point defines future posterior pole of egg & zygote
- Maternal effect gene products (RNA & proteins present in egg; required for embryonic dev.) organize asymmetric divisions up to 16-cell stage (e.g. PAR proteins, homologs in insects & vertebrates)
- Asymmetric divisions partition P granules ultimately to P₄, founder cell of germ line (Fig. 21-18) (flies, fish & frogs show similar partitioning of germ line fate determinants including RNA binding protein Vasa)
- Laser ablation and genetic analyses reveal Wnt/Frizzled and Delta/Notch signaling pathways critical for early cell fate decisions (Fig. 21-20)
- Fig. 21-21: Heterochronic mutations (e.g., *lin-14* mutation) affect timing of cell fate decisions

Terms to know:

cell determination

cell differentiation

positional value

asymmetric vs symmetric cell divisions

inductive signal, inductive interaction, sequential inductions

morphogen

sonic hedgehog, limb bud, *Tbx4* and *5*

maternal-effect genes, PAR genes, P granules

Wnt, Frz, Notch, Delta

loss of function mutation, gain-of-function mutation

heterochronic mutation