Developmental Biology Exam 2-Key
Dec. 7, 2012

1. [20 pts] Define 10 of the following for full credit. Extra credit [1 pt/ea] for additional definitions.

a. **Meroblastic** – Clevage that doesn't go all the way through the fertilized egg.
b. **Hensens node** – analogous to the primitive knot, acts as an organizer for gastrulation.
c. **Bicoid RNA** – maternal effect gene that establishes a morphogen gradient that is important for anterior patterning during *d. melanogaster* embryonic development.
d. **AER** – Apical ectodermal ridge, structure that forms at the distal end of each limb bud and acts as a major signaling center to ensure proper limb development.
e. **Number regulation** – Relating to the reaction diffusion model in developmental biology, it describes a system where the inhibitor diffuses far relative to the field size.
f. **enhancer** - a region of DNA that can be bound by proteins to enhance transcriptional levels of a gene or genes in a gene cluster.
g. **Homeotic mutation** – mutation in a gene that disrupts normal specification of body parts.
h. **midblastula transition** – stage of development when zygotic gene transcription is activated. (maternal to zygotic transition of gene expression)
i. **Syncytial blastoderm** – in insect development, a stage in which all the cleavage nuclei are contained with in a common cytoplasm.
j. **Fate map** – a method of understanding the embryonic origin of various tissues in the adult organism by establishing the correspondence between individual cells or groups of cells at one stage of development and their progeny at later stages of development.
k. **Trophoblast** – cells forming the outer layer of a blastocyst and will develop into a large part of the placenta.
l. **Notochord** – rod shaped body in all chordates that is derived from mesoderm and defines the primitive axis of the developing embryo.
m. **Rhombomere** – In the vertebrate embryo, a rhombomere is a transiently divided segment of the developing neural tube within the hindbrain region.
n. **floorplate** – Located at the ventral midline of the embryonic neural tube. Functionally the structure serves as an organizer to ventralize tissues in the embryo as well as guide neuronal positioning and differentiation along the dorsal/ventral axis of the neural tube.
o. **Ubx** – is a member of the homeobox gene family that functions as a transcription factor. In *d. melanogaster* it is expressed in the T3 and A1 segments to regulate the number of wings and legs in the adult.

2. [10 pts] compare human and chick oocyte characteristics and describe the pattern of **early** cleavages. What are the similarities and differences between the **late** blastocyst stages? Suggest a reason for the differences and similarities.

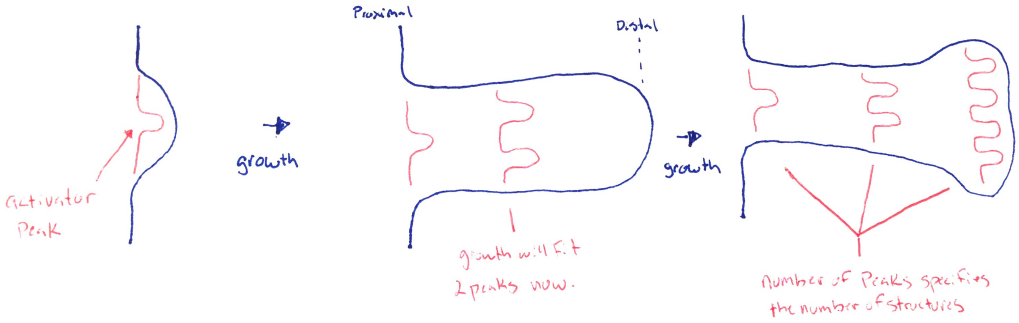
    - Human oocytes are isolecithal and undergo rotational holoblastic cleavage. Early cleavage is very slow, asynchronous and regulated by zygotic transcription from the start.
    - Chick oocytes are telolecithal and undergo discoidal meroblastic cleavage, which is regulated by maternal effect genes early in development and transitions to zygotic transcription at the midblastula transition.
    - During later cleavage events, both human and chick embryos form similar structures that direct tissue organization during gastrulation like the primitive streak and primitive knot.
    - However, only human embryos develop a trophectoderm layer which is an adaptation in placental mammals that allows the mother to supply the developing embryo with nutrients and get rid of waste. Chick embryos have a finite nutrient supply, the yolk, which must be sufficient for all of development.

3. [15 pts] What is the primitive streak? What determines it's position and how would you experimentally prove this? What does it become? Describe the migration of cells associated with its later function.

   - The primitive streak will establish bilateral symmetry, determine the site of gastrulation and initiate germ layer formation.
   - Cells of the hypoblast determine the position of the primitive streak during development. Rotating the orientation of the hypoblast cells by resection and transplantation will cause the primitive streak to align along this new axis. Also you can ablate the hypoblast cells and see if the primitive streak forms at all.
   - The primitive streak becomes the cells of the forgut endoderm, head mesoderm and chordamesoderm (notochord).
   - Ingressing cells migrate ventrally and laterally to form presumptive mesodermal and endodermal precursors.

4. [15 pts] The SCIENCE REVIEW on Turing's Reaction diffusion model suggests that limb skeletal development is a good candidate for a "Turing System". What molecule did they suggest for the activator? Propose a Turing Model for specification of all limb P-D cartilage. Two clues that should help you: Incorporate growth of the limb in your model and the proximal distal sequence of skeletal elements specification, i.e. humerus, radius and ulna, metacarpals, and digits. I suggest drawing a sketch to go with your description (you do not need to know the suggested activator to get credit for your model).

- The activator is *Tgf*-β.



- The smaller bone field in the developing limb bud will allow for only one activator peak and therefore only the development of one structure (humerus). As growth proceeds, the increasing bone field allows for more activator peaks to arise that will specify more distal structures (radius/ ulna) ultimately leading to the largest field with the largest number of boney structures at the most distal end (carpels/metacarpels).

5. [15 pts] I deleted the bithorax complex in a fly. What genes did I delete? What segments do they specify? If a fly could survive with this deletion speculate what it would look like? Explain your assumptions.

   - The genes of the bithorax complex include *ultrabithorax*, *abdominal-A* and *abdominal-B*.
   - This complex specifies the thoracic segment T3 and the all the abdominal segments.
   - This bithorax complex represses *antennapedia*, which is expressed in the next most anterior thoracic segments (T2) to inhibit the conversion of more posterior segments T3 and A1 into T2 segments. It inhibits the T3 segment from duplicating the structures that will normally arise from the T2 segment (think of the fly with two wing segments from the lecture).
   - If the deletion of ubx alone causes T3 to adopt a T2 fate, then the deletion of all the bithorax complex genes (*ubx, abd-A, abd-B*) may cause all the abdominal segments to adopt a T2 fate. (i.e. each abdominal segment will have a set of wings).

6. [15 pts] Describe the three axial patterning systems in vertebrate limb development. What is the phenotype of the Wnt-7a KO mouse and what important concept of "axial" patterning is illustrated by the fact that the KO phenotype is more complex than you might have expected?

- Proximal-Distal axis – is established by exposure to the Fgf morphogen gradient from the AER. The longer cells stay in the zone of polarizing activity (Pz) the higher the exposure to Fgf. When cells leave the Pz their P-D positional values are fixed and they differentiate appropriately.
- Anterior-Posterior – Retinoic acid induces the ZPA to express Shh and the distance from the posterior ZPA dictates what structures will form.
- Dorsal-Ventral – Dorsal mesoderm induces rFng and Wnt7a in the limb bud. The ventral mesoderm induces engrailed-1 expression in the ventral limb bud. The inhibitory relationship between rFng and engrailed-1 in the dorsal and ventral mesoderm determines the position of the AER at the equatorial margin.
- The Wnt7a KO mouse has a ventralized limb that is also missing posterior pattern elements and is truncated.
- It is the coordination among axial patterning systems that ensures that the right structures develop. This is illustrated by the complexity of the Wnt7a KO mouse. Wnt7a is a positive regulator of the Shh pathway and the loss of the activator and its targets lead to both A-P and P-D defects.

7. [10 pts] What early structure induces the neural plate? What are the molecules secreted by this structure and how do they induce neural plate formation?

- The chordamesoderm (notochord) is the organizer that induces the neural plate.
- Chordin, noggin and follistatin are the molecules secreted by the underlying mesoderm that inhibit Bmp and as a result cause the overlying cells of the ectoderm to develop into neural cells. The cells in the ectoderm that circumvent these inhibitory signals express Bmp and will induce these cells to adopt an epidermal fate.