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1. (10 pts) Draw or describe the fate map of a late blastula stage sea urchin embryo. Draw or describe the corresponding fate map of the pluteus stage larva. Describe the sequence of gastrulation events that lead to the pluteus stage larva.

*Primary mesenchyme (micromeres) form skeletal rods (spicules). Secondary mesenchyme form muscle. Vegetal plate (Veg1 and Veg2 layers) form gut tube. An1 and An2 form epidermal layer and nerve cells.*

1. *Thickening of vegetal plate*
2. *ingression of primary mesenchyme*
3. *Invagination of vegetal plate to from blastopore*
4. *Convergent extension to form archenteron*
5. *Ingression of secondary mesenchyme cell from tip of archenteron.*
6. *Contact of archenteron with blastocoel ectodermal wall and induction of mouth.*

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2. (10 pts) Describe Spemann and Mangold's Nobel prizing winning experiments and the implications of their experiments for embryonic pattern formation.

*They showed that the only tissue specified in the late blastula was the dorsal lip of the future blastopore by transplantation experiments. Further, they put forth the idea that this tissue behaved as an "organizer" and because it would alter the patterning of the surrounding host cells. They showed this tiny bit of transplanted tissue could induce an embryonic pattern duplication.*

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3. (10pts) What are the most important maternal effect genes specifying the patterning of the fly embryo? Briefly describe how they function to set up the major axis and termini of the embryo.

*Bicoid and Nanos morphogen gradients effectively antagonize each other to set up the A-P embryo allocation. Torso is activated only at the termini to specify terminal structures. Default is telson. Acron develops due to Bicoid acting with Torso. The opposing morphogen gradients of DPP (from dorsal midline) and nuclear Dorsal from the ventral midline antagonistically allocate pattern along the dorso-ventral axis.*

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4. (10 pts) Describe the sequence of events and molecular mechanisms of hydra HEAD regeneration based on the required review reading assignment. What cellular process is "both necessary and sufficient" for head regeneration? What is the suggested head morphogen?

*Increased apoptosis is associated with early phases of head regeneration. After mid-gastric bisection in Hydra, MAPK signaling leads to rapid activation of the transcription factor CREB in fragments regenerating a head. MAPK/CREB activity is required for stimulating a wave of apoptosis in interstitial cells near the site of injury. These apoptotic cells secrete Wnt3, inducing a (head organizer) zone of proliferation below the region of apoptosis.*

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5. (15 pts) We discussed two major models of pattern formation in developing embryos. Are they necessarily independent, i.e., can the embryonic field use both patterning mechanisms simultaneously? Provide and example.

1. *Alan Turing"s Reaction Diffusion Model*
2. *Simple morphogen gradient model with defined source of morphogen.*

*These two mechanism can both act simultaneously within an embryonic field and rely on threshold values of morphogens that specify positional information and differential cell fates. One example would be pattern of bone development in the limb. Reaction diffusion model would determine the number of bones as the limb field grows, while the gradients from the ZPA, e.g. sHH would specify bone identity via threshold values for HOX gene expression.*

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6. (10 pts) Describe how you might generate a fly that has halteres associated with each thoracic and abdominal segment, but localized too far ventrally in each of the segments.

*Delete (use CRISPR or gene targeting by homologous recombination, etc.) Antp, Ubx, AbdA and AbdB. Or you can say delete all Hox genes posterior to Scr or to misexpress Scr in segments T1-A8. This will give a fly with all T1 segment identities posterior to T1. Next cause the gradients of either Dorsal to be too small or DPP to be too big to alter the DV location of the halteres, e.g., add extra copies of the DPP gene to the fly.*

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7. (15pt) 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 and the more distal their identity when they leave the Pz and they differentiate appropriately.*

*Anterior-Posterior – Retinoic acid and Hox genes induce the ZPA to express Shh and the distance from the posterior ZPA dictates what A-P structures will form. Limb field cells closer to the ZPA and exposed to higher concentrations of sHH will differentiate into more posterior pattern elements.*

*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 and D-V patterning across the limb field.*

*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.*

8. (10pt) What is the default fate of all the cells that **do not** pass through the blastopore during mammalian gastrulation? How are the separate differentiated fates of these cells determined? How is the anterior to posterior pattern of the midline non-gastrulating cells determined?

*Default state is neural ectoderm. The organizer (and chordomesoderm) secretes Chordin, Follistatin, and Noggin which binds to and blocks the anti-neuralizing affect of BMP secreted by the lateral plate mesoderm (and later the epidermal ectoderm). Anterior posterior patterning of the neural axis is by the morphogen gradients of retinoic,FGF and Wnt from the organizer (posterior pattern) and Cereberus, Dickkopf, and Tlc from the Anterior Visceral Endoderm.*

*(Students do not have to list all morphogens from organizer and AVE. 2 from each is enough for full credit.)*

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9. (10pt) Define 10 of the following for full credit. Extra credit [1 pt/ea] for additional definitions.

a. cyclopamine– toxin from Corn Lily inhibits sHH and causes cyclops lambs

b. Koller's sickle – posterior margin hypoblast cells involved in A-P patterning of chick blastodisc

c. nanos mRNA – fly posterior group determinant

d. N-cadherin — Ca++ dependent cell adhesion molecule whose expression correlates with neural plate segregation from epidermal ectoderm.

e. Space regulation – Turing Reaction-Diffusion model where inhibitor diffuses a short distance relative to field size, e.g., scales on a fish, hairs on your arm.

f. TBX5 - transcription factor specifies forelimb identity

g. Homeo Domain– highly conserved DNA binding motif share by all HOX and HOM genes

h. Maternal effect gene –- Phenotype of embryo is dependent on maternal gene and not zygotic gene.

i. NFkb – mammalian Dorsal homolog critical for immune function

j. organizer – group of cells that release morphogen gradient to specify pattern of nearby cells, e.g., ZPA, Speman's Oranizer, micromeres, midbrain-hindbrain junction, anterior cut edge of hydra.

k. – Ed Lewis—identified and characterized the homeotic mutations in fly that specify the identify of each segment.

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l. AVE – anterior visceral endoderm. Important for induction signal for patterning anterior neural axis

m. Toll – maternal effect gene required for Dorsal activation

n. Chordamesoderm – mesoderm at dorsal midline that induces neural plate formation. Becomes notochord which patterns DV neural axis.

o. Ubx– ultrabithorax. First gene of the Bithorax Complex and famous because its deletion leads to the 4 winged fly.