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Biology 411 - Developmental Biology
Winter Quarter 2012

Midterm 1

100 Total Points
Open Book

Choose ***20*** out the 25 questions to answer (5 pts each). Only the first 20 questions that are answered will be graded. Cross out answers that you do not wish to be graded.
Provide answers using full sentences, unless instructed otherwise.

1. (Chapter 1) What are the uses of vital marking in developmental biology?

Vital marking allows the migration and developmental fates of single cells, or groups of cells, to be followed through embryogenesis.

2. (From discussion section) In the film Life's Greatest Miracle, you saw an abstract, animated representation of how the *SRY* gene on the Y chromosome contributes to sexual dimorphism in the developing human fetus. In the space below, draw a rough diagram of a fetal gonad cell including chromosomes, cytoplasm, and the nuclear membrane. Draw the cytoplasmic pathways via which the *SRY* gene's product is generated, trafficked, and processed in order to induce the male phenotype. For your information, the SRY gene encodes a transcription factor. More credit will be given to more complete drawings.

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3. (p. 26) A long-haired Dachshund zygote normally has two copies of a mutated *Fgf5* gene. Assume for this question, that the *Fgf5* gene is located on the end of an autosome. Imagine the situation where the tip of one the autosomes containing the *Fgf5* gene is lost. The zygote is thus hemizygous for the trait. Draw the most probable phenotype of a Dachshund dog with this deletion. Explain the reasoning for your drawing.

The dog would have long hair and short legs. The Dachshund dog breed has an extra copy of *Fgf4*, which terminates cell division in the cartilage of the long bones of the legs of the dog femurs. The long-hair phenotype that results from a mutation of *Fgf5* would be unchanged by loss of one the *Fgf5* genes (because it is a recessive trait).

4. (p. 48) What effect would the NRSE sequence have on gene expression in the neural rudiment? Explain why.

NRSE stands for Neural Restrictive Silencing Element. This element prevents non-neural genes from being expressed in neural tissues. NRSE has no effect on gene expression in non-neural tissues.

5. (pp. 62-64) What would most likely happen if you silenced miR181 expression in a lymphoid cell line? (Figure 2.36).

B cells would probably be specified, but would probably not differentiate.

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6. (p. 628, p. 27) The *KIT* gene is necessary for the specification of neural crest cells. Melanocytes are derived from neural crest cells. In piebald mutants, some regions of the body fail to form neural crest cells, leading to patches of unpigmented skin. Provide an explanation for the mosaic phenotype of piebald mutants using the concept of "induction."

Regional defects in signals necessary to activate the expression of the *KIT* gene may explain regional losses of skin pigmentation. Gene action in non-neural crest cells is needed for activation of *KIT* in neural crest cells. This is an example of induction.

7. (p. 28) Why is there variability in the phenotype among individuals exposed to thalidomide *in utero*?

Thalidomide is a teratogen that alters the development of appendages. Appendages are initiated during development at different time windows. If thalidomide is present during the time window of an appendage's initiation, malformation is likely to occur. Variation in the time of exposure to thalidomide is a major determinant in the phenotype of the affected individual.

8. (p. 35) Why does "deacetylation" of histones promote coiling of DNA? Describe the process and explain the mechanism.

DNA is negatively charged. This negative charge attracts positively charged histones, which cause the DNA to condense. This electrostatic interaction can be reversed by acetylation of lysine groups on histones, which changes their charge from positive to negative. Removal of acetyl groups of lysine residues on histones restores net positive charge to histones. This causes the nucleosomes to coil, and the chromatin to condense.

9. (pp. 48-51) Why would a null mutation of *Dnmt3* be probably be lethal to an embryo?

Dnmt1 is the enzyme that locates regions of methylation and adds methylation to the complementary DNA strand. Without methylation of complementary strands duringsemi-

conservative DNA replication, genes would not remain inactivated in a lineage of cells. This would lead to of abnormal gene expression. Abnormal cell specification and abnormal cell behavior would likely result, leading to embryonic death.

10. (Chapter 2) How could methylation of enhancers located within introns affect gene regulation? Using molecular detail, explain your reasoning.

Methylation of an enhancer anywhere could reduce, or block, the expression of a gene. Transcription factors must bind to enhancers to help activate the expression of a gene. Methylation of enhancers could block binding of critical transcription factors necessary for a given gene's expression.

11. (pp. 32-34; 50-52) The coloration pattern of the calico cat and its clone are different in Figure 2.2 because of random X chromosome inactivation in early embryonic cells. Explain why X chromosome inactivation is essential for the normal development of a female embryo.

X inactivation is the process by which the mammalian embryo achieves gene dosage compensation in the female embryo.

12. (p. 52) In a **male** individual with Prader-Willi Syndrome (PWS), is the Angelman Syndrome (AS) locus active? Is the Prader-Willi Syndrome (PWS) locus active? Explain why.

The Angelman Syndrome locus is active in an individual with Prader-Willi Syndrome. The individual lacks a portion of paternal chromosome 15, which includes both the PWS locus and the AS locus. However, the intact maternal chromosome 15 has both loci. The PWS locus is inactive, owing to imprinting (probably via methylation) of the gene that occurred during gametogenesis. The AS locus is active on maternal chromosome 15.

13. (pp. 90-91) Explain how ingestion of cholesterol could interfere with the teratogenic effects

of cyclopamine.

Cholesterol is needed to stimulate the cleavage of Sonic Hedghog. Cholesterol also restricts the diffusion of the Sonic Hedghog in the extracellular space, thereby enhancing its signaling capabilities. Cyclopamine blocks cholesterol synthesis. Ingested cholesterol could provide the needed cholesterol to prevent cyclopia.

14. (p. 103-105) Explain what could happen if the soluble peptide RGD was added to mammary gland cells cultured on the surface of a basal lamina. Which genes would be activated, and which genes who be turned off?

The RGD binding sites of beta-integrin would become occupied by the soluble peptide. The beta-integrin receptor would no longer be able to bind to fibronectin on the basal lamina. The mammary gland cells would not be stimulated to form secretory epithelia, because they coiuld not be enveloped by a basal lamina. However, c-myc and cyclin D1 would be turned off. Lactoferrin and p21 would be turned on.

15. (p. 99) If the *lin-3* gene product was overexpressed in anchor cells in *C. elegans*, how many VPCs would form? Explain where these cells would come from.

6 VPCs would be still be specified. However, increased levels of Lin-3 protein would most likely induce P8.p and P4.p into the central vulval cell linage. P8.p, P4.p, and P3.p could potentially be recruited into the lateral vulva cell lineage, in the Lin-3 levels were high enough.

16. (p. 60) How can the enzyme polyA polymerase affect gene regulation in fertilized oocytes?

polyA polymerase can extend the polyadenylated tail of mRNA transcripts stored in oocytes, allowing the mRNA transcripts to be translated into protein.

17. (p. 57) Draw the morphology of a Drosophila neuron that had two alternative splicings of *Dscam* expressed in its cell membrane?

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Alternative splicing allows different versions of proteins to be made from the same mRNA transcript. This allows different isoforms (i.e. versions) of the protein to be expressed in different neurons. Dscam prevents dendrites of a given neuron from forming synapses on themselves. If two different versions of the Dscam protein were expressed uniformly in a given neuron, the neuron would not be able to form synapses on itself. Self-repulsion would still operate.

18. In terms of X inactivation, provide a possible reason why human females are more prone to autoimmune disease? (Discussion section, JAMA paper)

In females, organs are composed of a mosaic of cells, with some expressing the maternal gene product and other cells expressing the paternal gene product. In the thymus, T cells and B cells that have surface receptors for self-antigens may not be recognized and eliminated. If these cells escape destruction in the thymus, they are capable to becoming activated in the body and initiating autoimmune disease.

19. (p. 93) Describe the effects a null mutation in GSK3 would have on the canonical Wnt pathway.

GSK3 inhibits beta-catenin by phosphorylating the protein. Phosphorylation targets beta-catenin for degradation. A null mutation in GSK3 would block GSK3 ability to phosphorylate beta-catenin, thus allowing beta-catenin to translocate to the nucleus and participate in gene activation.

20. (p. 89) Think about the transcription of casein. If the cytoplasmic tails of the Prolactin receptors were mutated to become constitutively activated, what would happen to the transcription of the casein gene?

Transcription would occur independently of the binding of Prolactin.

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21. (pp. 80-82) In terms of specific genes, why does a lens fail to form if an optic cup is placed near the trunk epidermis of a developing embryo?

Trunk epidermis is not component to express Pax6 in response to inductive signals from the optic cup.

22. (pp. 125-127) What does the germinal vesicle become in a dog primary oocyte during gametogenesis.

The germinal vesicle matures to become the female pronucleus and the first polar body after fertilization. The germinal vesicle is diploid, and progresses through meiosis I after fertilization.

23. (Chapter 4) What are the contents of an acrosome? What type of organelle is it?

The acrosome contains digestive enzymes. It is a specialized lysosome.

24. (pp. 54-59) The Greek god Zeus decided to give Ajax an abnormally strong body, so that he could help defeat the Trojans in the Trojan war. Assume Zeus knew molecular genetics. What mutation do you think Zeus gave Ajax to be so powerful.

A null mutation in *myostatin* could have provided Ajax with hypertrophied muscles.

25. (Discussion section) What is the utility of forming alternative hypotheses?

Alternative hypotheses allow questions to be examined without restricting attention to a specific viewpoint. Alternative hypotheses provide better avenues to discuss critical tests that can be developed to invalidate the proposed hypotheses.