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Biology 411 - Developmental Biology
Winter Quarter 2008

Midterm 1

100 Total Points
Open Book

25 questions - 4 pts each 1 extra-credit question - 4 points
Provide answers using full sentences, unless instructed otherwise.

1. (pp. 6-7) Why did Malpighi question the Aristotlean theory of epigenesis?

Using a microscope, Malpighi observed structures in an unincubated chick embryo before the time at which Aristotle claimed the egg was merely chaos. Malphigi therefore concluded that the embryo must be preformed.

2. Why are fate maps useful to developmental biologists?

Fate maps provide information about changes in cell movement and cell fate. Understanding changes in cell fate and cell movement in the embryo are key elements to the study of pattern formation and morphogenesis.

3. (p. 17) Is the hyomandibular bone in jawed fishes "homologous", "analogous", or "both", to the incus of the human inner ear? Explain the reasoning of your answer.

The hypomandibular bone in jawed fishes is homologous to the human incus, because it is derived from the 1st pharyngeal arch. The two bones are not analogous in function: the hyomandibular bone provides structural support to the fish skull, the incus is involved in the transduction of hearing.

4. (pp. 21-22) What would happen in a reaction-diffusion reaction if the activator diffused faster and/or farther than the inhibitor? Explain your answer.

If the activator diffuses farther and faster than the inhibitor, no individual peaks in activator concentration would be expected to arise. However, because the activator in auto-catalytic, the activator would eventually increase its concentration everywhere, by overpowering the inhibitor.

5. (p. 21) What would happen if the rate of allometric growth of the human head matched the rest of the body? Draw the figure of the resulting adult.

The head would become enormous, and could not be supported by the body.

Place the head of a 8-week embryo on p. 21 on a slightly reduced version of the adult body in the same figure.

6. (p.33) What would be the phenotype of a Volox colony that possessed a null mutation in the *gls* gene?

gls is important for the asymmetrical part of the cell division to make either gonidia or somatic cells. If there is no gls, there is an equal cell division instead. Over multiple rounds of cell division there would be rounds of smaller and smaller cells, resulting in a juvenile that is lacking gonidia, as the gene gonidialess (gls) implies.

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7. (pp. 36-37) If the center of an aggregating mass of *Dictyostelium* amoebae was transplanted into the dish of starved *Dictyostelium* amoebae, what would happen? Explain why.

The starved *Dictyostelium* amoebae would aggregate because the transplanted center is release the chemoattractant cAMP in a pulsatile fashion. This provides a chemotactic gradient to guide the migration of starved amoebae.

8. (p. 41) Draw two possible results from a single fertilization in an angiosperm plant egg. Label the ploidy of each nucleus in egg following a single fertilization.

Possible outcome 1: diploid zygote; haploid endosperm nucleus

Possible outcome 2: haploid egg nucleus; triploid endosperm nucleus

9. (pp. 43-45) Name 5 morphological characters that can be found in members of Lophotrochozoa.

The Lophotrochozoa have spiral cleavage, a common larval form (the trochopore), and a distinctive feeding apparatus (the lophophore). They are also have a mouth derived from a blastopore, and bilateral symmetry. (The answer, multicellular, is too general for credit)

10. What would happen if an a.4.2 blastomere of an 8-celled tunicate embryo was injected with yellow crescent cytoplasm, then mechanically separated from the rest of the embryo? Why would this occur?

The a.4.2 blastomere would differentiate into muscle cells because the yellow crescent cytoplasm biases blastomeres to adopt a muscle cell fate.

11. Explain the difference between prospective and presumptive.

Prospective means capable of becoming something. Presumptive means about to become something.

12. What is the definition of a stem cell?

A stem cell is a pluripotent cell type that is capable of producing copies of itself through cell division, as well as producing cell types that have a more restrictive cell fate than the stem cell.

13. What is the difference between differential affinity and differential adhesion?

Differential affinity refers to the property of heterotypic cells to sort out into homotypic distributions. Differential adhesion is the property of homotypic cells to preferentially bind to each other over other cell types. Differential adhesion is viewed a probable mechanism to explain differential affinity.

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14. How could one dissociate a mass of cells held together by cadherins?

If the cells were placed in a calcium-free solution, the cadherins would loose their homotypic intercellular adhesion and the cell aggregate would fall apart.

15. Why is a neomycin resistance gene inserted along with a transgene when making a knockout strain of mice? (p. 95)

The neomycin-resistance gene is inserted into embryonic stem cells along with other transgenes in order to have a functional marker to determine whether the transgenes have integrated into the genome of the recipient cells. Neomycin resistance allows a researcher to easily determine whether transfection has occurred. Cells that do not possess the neomycin resistance gene are destroyed *in vitro* when neomycin in added to the culture media. Surviving cells containing the transgenes are then transplanting into the inner cell mass of recipient mouse embryos, to begin the process of establishing a transgenic line of mice.

16. (p. 118) What phenotype will result from a human zygote that has both a deletion of paternal chromosome 15 and a methylated Angelman Syndrome locus on maternal chromosome 15? Explain why.

The embryo, fetus, or infant resulting from this zygote will die. Methylation of the AS locus will inactivate it. With the PWS locus being absent on paternal chromosome 15, critical genes for survival are not transcribed.

17. (p. 122) Explain why genetic imprinting, which occurs during gametogenesis, is not transmitted to the progeny (i.e. offspring) of a zygote.

Gene inactivation that is established in the early blastocyst is removed during the establishment of the germ line.

18. What would the coloration pattern of a XXY kitten be if it had parents of the calico cat breed?

The XXY male kitten would have a coloration pattern similar in tri-color pattern to female calico cats, but the exact spatial pattern would be unique to that kitten. Random X-inactivation in different cells of the blastocyst would generate the unique pattern. Presence of the Y chromosome would not change this.

19. (pp. 134 and 682) Propose how a viral vector could be used to transiently treat a patient using miRNA.

A adenovirus could be used to insert a RNA sequence encoding a therapeutic miRNA into the patient's cells. The miRNA would be cut by the Dicer protein, and the resulting miRNA fragments would combine with RISC to block translation of targeted mRNA, as well as to degrade the targeted mRNAs of the patient's cells. The therapy would terminate when the inserted RNA sequence is degraded.

20. (p. 151) Explain why human growth hormone cannot be used to successfully treat achondroplasic dwarfism.

Human growth hormone cannot reverse the effects resulting from the mutation of the FGF receptor, which underlies achondroplasic dwarfism. Premature ossification of cartilage is the pathology that results from this mutation. Human growth hormone therapy would not affect this aberration.

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21. (p. 152) What teratogenic risks are there for a fetus exposed to cholesterol-lowering drugs in utero? Explain your answer in molecular terms.

Cholesterol is needed to enhance the cleavage and diffusion of the Sonic Hedgehog signaling protein. A deficiency of cholesterol, resulting from cholesterol-lowering drugs, could produce cyclopia.

22. (pp. 162-163) What would happen in the C. elegans LIN-12 gene product was mutated that it could not be cleaved by a protease? Draw the altered phenotype.

P7.p and P5.p would become central vulval cells along with cell P6.p. Normal activation of Lin-12 signaling in P7.p and P5.p from P6.p represses genes that specify central vulval fate, so when Lin-12 is mutated, those central vulval genes are allowed to be expressed in appropriately.

23. A. Where in a cell are primary polypeptides usually folded into their final structure?

Proteins are usually folded in the rough Endoplasmic Reticulum.

B. Name three ways a protein can be modified post-translationally.

Cleavage, phosphorylation, glycosylation, acetylation, methylation

24. Describe how you would use a gel mobility phase-shift assay to determine whether a transcription factor necessary for vocal cord formation in *Homo sapiens* interacted with a DNA fragments isolated from a *Homo floresiensis* bone. What technique would have been used to obtain enough *Homo floresiensis* DNA for the gel mobility assay? Why would scientists be interested in performing this type of study?

Using primers that flank the genomic DNA sequence of *H. floresiensis* that is homologous to the vocal chord transcription factor binding region in *H. sapiens*, perform a PCR reaction using radiolabeled nucleotides to generate a large quantity of radiolabeled DNA in the region of interest. Then you would mix the radiolabelled *H. floresiensis* PCR product and human vocal chord transcription factor protein. You would compare the amount of binding between *H. floriensis* DNA and *H. sapiens* vocal chord transcription factor to transcription factor alone, and transcription factor + *H. Sapiens* radiolabeled DNA, by running the mixtures on a gel and exposing to film. If the first and third band were both shifted to a higher molecular weight, than the DNA alone that implies that *H. floresiensis* may have had the capacity for complex language the same as *H. sapiens*.

25. Why is the androgen receptor so important to the development of a human male fetus?

The androgen receptor binds testoterone during human gestation. The activated androgen receptor activates numerous target genes that are critical for the development of the male phenotype.

<u>Extra Credit Question (4 pts)</u>

26. Using transgenic technologies, explain how one could modify calico cats to study X-linked human diseases. Use your imagination to answer this question. A logical answer and justification is required for this extra credit.

Examples:

1. Human transgenes suspected of causing recessive human diseases could be inserted into the X-chromosome of a calico cat breed, using embryonic stem cells technology. Using gene recombination, a mutated null version of XIST could also be inserted into the same X-chromosome. Female offspring would then be studied.

Instead of random X-inactivation occurring during the blastocyst state, the genetically-modified X-chromosome would be expected to remain active and force the inactivation of the other X-chromosome. Matings of the transgenic breed could be chosen to result in progeny in which female offspring would have either the selective inactivation of the maternal, or the paternal, X-chromosome. The effects of a mutant human X-linked gene could thus be examined in a non-mosaic female individual. This may reveal a stronger (i.e.

more penetrant) phenotype than in human females (who are mosaic in their pattern of X-inactivation)

Question: What color would the genetically-modified calico female cats be? Answer: not calico! Note: the loss of calico phenotype would be an easy way to screen for transgenesis in this study.

2. You could insert a mutant X linked gene alongside a specific coat color gene in a calico cat. Once this cat line has a stable homozygous transgene, you will be able to follow in any heterozygous offspring where the mutated gene is unmasked by following the corresponding coat spot. This cat could be useful for studying mutations in selected tissue types. However, it would be random what tissue spot you get to study depending on what spots the mutant gene and color you end up with.