Problem Set 10-2011

1. In each of the following situations, select all answers that are correct. Consider ALL consequences of these changes on limb patterning. What would happen to limb development if :

(.5) An embryo had a loss of function mutation in the gene *radical fringe?*

i. no or reduced proximal-distal outgrowth
ii. duplication of A-P structures
iii. loss of A-P patterning
iv. posteriorization of digits
v .Limb identity altered
vi. limb placement along body altered

2. (.5) An embryo had overexpression of Tbx4 throughout the flank of the developing embryo.

i. no or reduced proximal-distal outgrowth
ii. duplication of A-P structures
iii. loss of A-P patterning
iv. posteriorization of digits
v .Limb identity altered
vi. limb placement along body altered

3. (.5) An embryo had high levels of Shh expression throughout the limb.

i. no or reduced proximal-distal outgrowth
ii. duplication of A-P structures
iii. increase in number of digits
iv. posteriorization of digits
v. Limb identity altered
vi. limb placement along body altered

4. (1) If an embryo had a homozygous loss of function mutation in Engrailed 1, you would expect to see:

i. alteration of proximal-distal outgrowth
ii. anteriorization of digits
iii. posteriorization of digits
iv. dorsalization of limb
v. ventralization of limb
vi. limb placement along body altered

5. (1.5) There are many different kinds of Fibroblast Growth Factor ligands and receptors with varying roles in development. In class, we mentioned FGFs 4,8 and 10, all of which were present in the limb bud. A dominant, gain of function point mutation in the FGF3 receptor gene results in Achondroplastic Dwarfism in humans: markedly shortened limbs with a normal length torso. Postulate a general role for FGF3 in this process and indicate how such a mutation can result in shortened limbs.

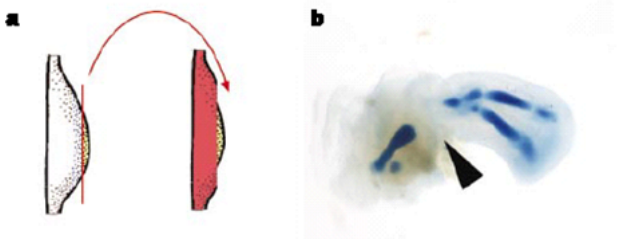
6. After graduating from MCDB, you have been hired by a biotech company that believes there is a demand for 6-legged cats. For each of the following questions, focus on the molecules you would need to manipulate to make these cats (not the actual procedure for producing them!)
(.5) How could you induce an additional 2 legs in cats?

7. (.5) You realize that the cats may be more mobile if they have 4 forelimbs and 2 hindlimbs. What type of gene might be useful to manipulate to cause the extra limbs to be forelimbs?

8. (1) One customer thinks cats with extra toes (polydactyl) are cute. How could you produce this phenotype?

9. (1) Another customer wants the limbs to be covered in fur (no ventral side). Explain to the customer why this manipulation may lead to other problems.

10. (1.5) In the experiment shown, cells from the very distal end of an early limb bud were transplanted onto the stump of a limb bud of the same stage (basically the new limb bud contains some very proximal cells and some very distal cells, but no middle limb bud cells). The result of this transplantation is shown in b. The arrow marks the juxtaposition between the two sets of cells. What can you conclude from this experiment? Does this support the progress zone model or the prepattern model of limb outgrowth? Explain briefly.



11. (1.5)
The figure shows the result of adding a bead containing Noggin into interdigital spaces (F=ID3, G=ID2) of a developing limb bud. What affect does Noggin have, and why? Explain.