

EXAM 3 12/5/02

1. (4 pts) If both alleles of the Xist gene were unmethylated (methylation is normal elsewhere), what would happen to expression of the Xist alleles and inactivation of the X chromosomes in an XX embryo and why? Be sure to consider both Xist alleles and both X chromosomes.

Methylation is required to silence the Xist allele on the active X chromosome. So, without methylation of Xist, both copies of Xist would be active, and both chromosomes will be inactivated.

2. (4 pts) Analysis of a human female fetus by amniocentesis indicates that the baby will have a normal XX karyotype but is heterozygous for a mutation that inactivates the Tsix promoter. Explain how dosage compensation will be affected by this mutation. What can you tell the parents about the baby's chances for survival, normal sex determination, and normal dosage compensation based on this evidence?

*Since Tsix is mutant on one X chromosome and wild type on the other, the chromosome with the mutant (non functional) Tsix will **always be inactivated** (since Tsix will never be produced). Thus, the baby will be fine and have normal sex determination. In terms of dosage compensation, the only thing that will be different is that the individual will not be mosaic, but rather will have the same X chromosome active in each cell.*

3. (4 pts) List two experiments or observations originally supporting the hypothesis that SRY is the primary sex determining gene in mammals.

SRY transgene converts XX mice to males

SRY mutations found in human XY females

SRY expression in XY gonads

Name _____

4. (4 pts) For proper sex determination, it is important that the inappropriate development of gonadal or ductal structures in the "wrong" sex (e.g., the development of a testis in an XX female) does not occur. Give **two** examples (including molecule involved) of how mammals normally repress the development of inappropriate gonadal or ductal structures during development of the reproductive tract.

MIS prevents development of Mullerian duct structures in males

DAX1 prevents formation of testicular tissue in female gonads

Wnt-4 blocks Leydig cell formation (production of testosterone) in ovaries

A few other possibilities, but you had to talk about repression!

5. a. (4 pts) List two functions of the apical ectodermal ridge (AER) during limb development.

Promotes proliferation of progress zone cells (or limb outgrowth), prevents differentiation of progress zone cells, maintains ZPA (via FGF-4/Shh feedback loop), permits survival of mesenchyme cells.

b. (2 pts) If the AER were surgically removed, how could you replace AER function and rescue limb development? (Grafting another AER is not a valid answer)

AER function could be replaced with a bead expressing an FGF.

6. Suppose that an experimental chick limb combined wing ectoderm and leg mesenchyme.

a. (3 pts) Would this limb be more like a wing or a leg? Why?

Leg because mesenchyme determines the fate, not ectoderm.

b. (2 pts) Name one molecule that helped to determine whether the experimental limb was a leg or a wing.

Pitx1 OR Tbx4 determine hindlimb

Name _____

7. (6 pts) A limb bud has two types of defects. First, some bones and tendons, normally found only on the dorsal half of the limb, are duplicated in the ventral half of the limb. Second, placement of the apical ectodermal ridge appears abnormal. Explain how a loss of function mutation in one gene could cause both of these defects.

An engrailed-1 mutation would explain both defects. First, loss of En-1 would lead to ectopic Wnt-7a expression in the ventral ectoderm and dorsalization of the limb bud.

Second, loss of En-1 would also lead to ectopic radical fringe expression. This would disrupt the AER which is normally formed at the boundary between cells expressing radical fringe and cells not expressing radical fringe. This second part is a little trickier. Saying that loss of En-1 would disrupt placement of AER is sufficient.

A mutation in radical fringe would not fully account for this defect, but we gave partial credit

8. (5 pts)

a. (1 pt) What is the phenotype of a ced-3 loss of function mutant?

No apoptosis

b. (1 pt) What is the phenotype of a ced-9 loss of function mutant?

All cells die

c. (2 pts) How do these two proteins interact in a cell that is not undergoing apoptosis?

Ced-9 binds to Ced-3 (and Ced-4) to prevent the activation of ced-3

d. (1 pt) How is the study of apoptosis relevant to cancer?

Multiple possible answers....most likely, cancer cells don't undergo apoptosis. Or, if we could figure out how to make cancer cells undergo apoptosis, we could get rid of cancerous cells.

9. (6 pts) The mouse **Kit** and **SCF** genes regulate the differentiation of melanocytes, pigment cells in the skin. From the following experimental evidence, determine which gene product is expressed in which cell type, fibroblasts of the dermis or neural crest cells that give rise to the melanocytes.

When neural crest cells from an SCF mutant mouse embryo are transplanted into a wild-type host embryo, descendants of the transplanted cells differentiate into melanocytes.

When neural crest cells from a wild type embryo are transplanted into an SCF mutant host embryo, descendants of the transplanted cells do not differentiate into melanocytes.

Which of these genes is expressed in

a) (1 pt) fibroblasts of the dermis: *SCF*

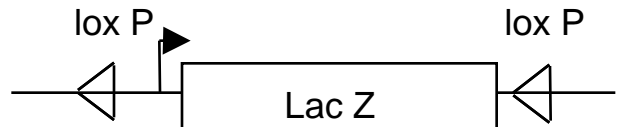
b) (1 pt) neural crest cells: *Kit*

c) (4 pts) What do you predict would be the outcome of injecting SCF mutant neural crest cells into a Kit mutant host embryo? Briefly explain your answer.

The resulting embryo would have normal neural crest cells and normal dermal fibroblasts; therefore melanocytes would differentiate normally.

10. (5 points) Suppose you have developed a strain (strain 1) that carries the *Cre* recombinase gene, expressed under the control of a brain-specific promoter. You have also constructed a strain (Strain 2) that is homozygous for the reporter construct diagrammed below, comprised of a *lacZ* gene driven by an actin promoter that is expressed in all cells, flanked by two *loxP* sites. All tissues of these mice (strain 2) stain blue with an X-gal stain for β -galactosidase activity. If you mate a male of Strain 1 with a female of Strain 2, and analyze tissues of the resulting progeny for staining with X-gal, you will find that (choose the one most likely answer):

- All tissues stain blue.
- Only the brain stains blue.
- All tissues except the brain stain blue.
- None of the tissues stain blue.



Answer C

Briefly explain your answer:

Lac z is cut out preferentially in cells where the brain specific promoter is active; thus the cells in the brain will not stain blue.

11. (4 pts) Name two developmental processes that involve signaling by Delta and Notch or their homologs (from either vertebrates or invertebrates).

Vulval fate determination

AC vs. VU cell.

PNS and CNS neuronal precursor determination

Segmentation of somites

Determination of which cell will migrate away from ventricular zone in mammalian cortex development

12. (3 pts) Hox genes

a) What is the general function of Hox genes in all animals?

Specify anterior posterior identity

b) Name a similarity between the Hox genes of flies and mice (besides function).

Best answer: colinearity (ie, expressed in same order along chromosome as along organism)

Other possible answers: same structure; similar regulation.....

c) Name a difference between the Hox genes of flies and mice.

One complex of Hox genes in flies; 4 complexes in mice

others....

13. (6 pts) Briefly explain what is meant by the following two terms, and give a general example that illustrates each.

a) Forward genetics:

Mutagenize animals and look for a phenotype that interests you. Clone gene, figure out it's function. Example: anything that shows they understand the concept: ie, screen for vulval defects; discover ras pathway and N/Dl are involved in that process.

b) Reverse genetics:

Start with a gene of interest from another organism, clone it in your organism, figure out the phenotype of your organism when that gene is mutated.

E.g. Apoptosis: find ced-3 or ced-9 homolog; discover the function of caspases