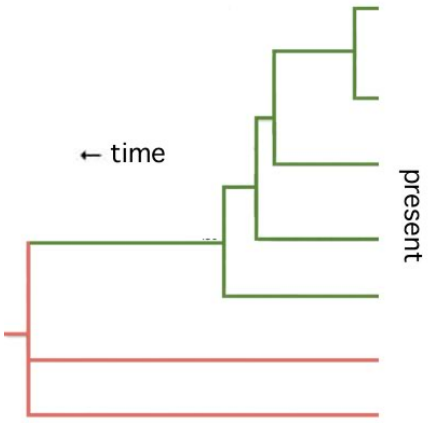
DEVO Midterm 2 review questions **March 2019**

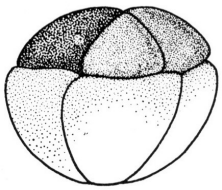
class 10:

- What features of embryonic development that make various model systems (frog, fly, worm, fish, chick, mouse) useful and what are there limitations (for understanding human development)?
- Draw a model in which you place these organisms in a phylogenetic (evolutionary) tree, what is the order (as a function of time) of common ancestors, explain your diagram?
- Xenopus laevis has ~twice as many genes as humans, while Drosophila has about half as many genes as *C. elegans.* Explain the relationship between gene number organismic complexity.



class 11/12 Xenopus

- Someone tells you that gene loss **always** leads to a deleterious phenotype, explain why this is or is not necessarily the case.
- What does the term "essential" mean when it comes to a gene? How can a "non-essential" gene be conserved?
- Amphibian embryos were used to demonstrate that in vertebrates, genes are not lost during development and cellular differentiation. What types of experiments were used to support this conclusion?
- Why are genetic markers needed to characterize the ability of a nucleus from a differentiated cell to generate a normal embryo (adult)?



- Predict (and justify) whether the blastomeres of an 8 cell Xenopus embryo are totipotent.
- Map out the processes that lead from an oocyte to an embryo with an anterior-posterior and dorsal ventral axis in Xenopus.
- Why do eggs rotate so that there pigmented animal hemispheres are all pointing up after fertilization?
- How is sperm entry related to the site where gastrulation starts and the future dorsal-ventral axis?
- How can you induce a second anterior-posterior axis in Xenopus
- How could you "dorsalize" or "ventralize" a Xenopus embryo?
- Predict how mutations in the Wnt / Dsh pathway influence target gene expression.
- Summarize what one can learn from single cell RNA SEQ studies of cells at various stages during (Xenopus) embryogenesis.
- How is the generation of iPSCs similar to and different from the generation of an embryo?
- How might mitosis give rise to an asymmetry in the resulting daughter cells?
- What type of experiment could let you know whether there was mixing of cells during embryo formation?

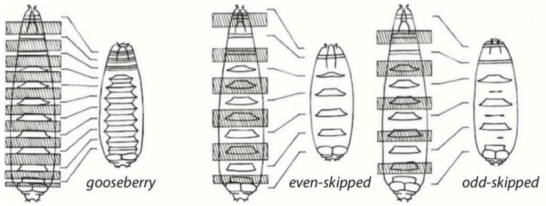
class 12/13 - experimental manipulation

- How could an antibody influence the activity of a protein or a gene?
- What is the main effect of RNAi? What can a morpholino be used for?
- What can CRISPR-CAS9 or dCas-chimeras be used for? (What is a chimeric protein?)

  - Why is CRISPR so specific?
  - Why is a morpholino stable in a cell or embryo?
- Which reagent(s) can be used to specifically examine maternal versus zygotic effects ?

class 13/14 - Drosophila

- How could a gene have more than one activity?
- How might an amorphic allele have a dominant phenotype?
- Would you expect an anti-morphic or a neomorphic allele to be dominant or recessive (explain)?
- How does phenotype determine whether an allele is dominant or recessive?
- What made Drosophila a good system for Wieschaus and Nusslein-Volhard's approach?
  - What features of the *Drosophila* larvae did they exploit?
- Why carry out the screen looking at larval rather than adult phenotypes?
- Why did they not study dominant mutations?
- Why was the use of balancer chromosomes useful to them? what is a balancer chromosome?
- How would you identify a gene that acted maternally?
- How can you tell (using a graph) whether a mutational screen in a particular process (such as early embryonic patterning) is near or has reached saturation?
  - What does "saturation" mean exactly.
- If the early Drosophila embryo were patterned only by a simple and single gradient, would you expect the classes of mutant phenotypes observed?
- What does it mean that two mutant alleles complement each other? Are they in the same or different genes?



- Define what is necessary for autocrine, paracrine, juxtacrine signaling.
- A cell emits a signaling molecule, it does not respond to the molecule but nearby cells do, what can you conclude about these different types of cells?
  - What if cells on the posterior side of the signaling cell respond, but those on the anterior side do not; what can you conclude?
- Given a signaling pathway predict the outcome of null mutations.
- How does a enhancer-GAL4 / UAS-target shRNA system work?

class 14/15 - Hox-Homeobox

- You discover a gene with a homeobox domain - what do you think it does? how would you test your hypothesis?
  - How would you determine whether it is a HOX gene?
  - Predict the plausible effects of various mutations in a protein's homeodomain (given what is know about homeodomain conservation).
- What is a "homeotic" mutation? What do such mutations look like in a mammal?

class 15 - *C. elegans*

- What features of *C. elegans* development facilitate genetic studies. How is this similar to the bristle / segment pattern in Drosophila larvae?
- What does it mean to be a hermaphrodite?
- How could you tell whether a gene is involved in a process (such as apoptosis)?

- Why is it that you could not identify all genes that might be involved in such a process?
- Again, given a signaling network / pathway predict outcomes of mutations.

class 16/17 - Early mouse embryogenesis, asymmetries, and the neural crest

- Draw a schematic of the process driving the specification of cell types (trophectoderm, epiblast, primitive endoderm) - where and how do these asymmetries arise?
- Given a signaling network / pathway predict outcomes of mutations.
- When a mouse (mammalian) embryo undergoes compaction, what types of cellular processes are likely to be involved? Justify your suggestion(s).
- During the process of neural crest formation, what would happen if cells could not "disconnect" their various adhesion systems?
- What factors influence the initial state and ultimate fate of a neural crest cell?
- What do the terms totipotent, pluripotent, differentiated (or committed) mean?
- Epidermis (skin), neural crest, and neural tube (nervous system) are derived from a common embryonic epithelium- how do they become different (in broad terms).
- You discover a mutation that allows for the EMT event of neural crest formation to occur normally, but the neural crest cells fail to migrate. Propose a possible mechanism, and suggest how you might test it; what cellular system(s) could be malfunctioning?
- In the trunk, neural crest migration is restricted to one half of the somite; you find a mutation in which neural crest cells migrate over the entire somite. Propose a possible mechanism, and suggest how you might test it (what cellular system(s) could be malfunctioning?

Thinking about cell fate commitment and the use of tissue transplants. To understand whether two different neural crest cell populations (e.g. trunk and cranial neural crest) are pluripotent or committed to different fates, you realize that you might be able to get the answer by carrying out transplantation experiments.

Heterotopic: different location, same time: Neural crest cells that normally make trunk derivatives (from an older donor) could be put into the cranial position (and visa versa).

Heterochronic: different time, same location: Neural crest cells that would have a later fate (from older host, ie. melanoblasts) could be transplanted into the equivalent position in a younger host.

How will they behave if they are or are not "committed" based on their site of origin or the time of their appearance.

Think about interactions between tissue layers: Birds are related to reptiles (and dinosaurs), which have teeth. Bird ancestors had teeth, while all modern birds do not. In organisms like mouse, teeth form from cranial neural crest and adjacent epidermis. Birds have both of these tissue types, but they do not form teeth. To study tooth formation, consider a number of experimental results: 1) when either mouse or chick neural crest cells are grown in isolation, teeth are NOT formed; 2) when mouse jaw epidermis is combined with chick neural crest: teeth are NOT formed; 3) when bird jaw epidermis is combined with mouse neural crest: teeth ARE formed. Propose (and diagram) a simple model for a system that generates teeth and a plausible mechanism to explain how birds have lost the ability to form teeth. When (in terms of evolutionary ancestry), did the tooth-less phenotype appear.