BIO-411 **Mock open questions** **12 DEC 24**

A) You happen upon a spontaneous mutation in an inbred mouse line that doubles its lifespan. You find that the mutation is inherited in a dominant fashion. Biochemical experiments indicate that the lifespan extending factor is a protein, but when you sequence the genome of the mutant mice you find no changes in the open reading frames of any protein coding gene.

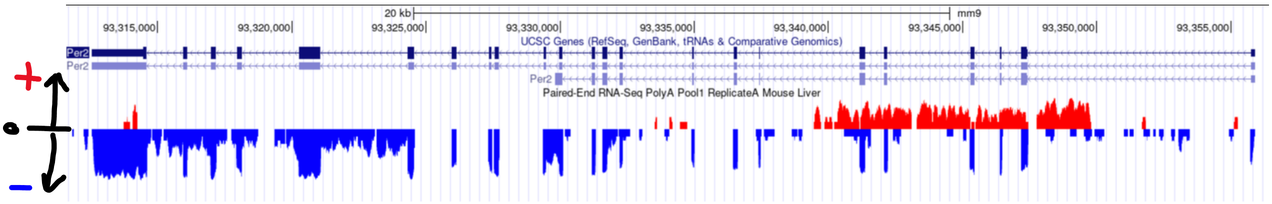
Can you speculate on the molecular nature of the mutation might have occurred in the mutant mouse line providing at least two examples of different types of mutations that could explain the phenotypes you observe?

You identify a candidate protein that could be linked to lifespan extension in the mutant mice. How would prove that this protein is really is causing the increase in lifespan?

You find the candidate protein is expressed in many tissues in the body but suspect some cell types are critical. Using modern technologies, how would you identify these cell types? Having identified them, how could you confirm expression in only these cells is critical for lifespan extension?

B) Sampling the ocean off the coast of Japan, you recover a male and a female of what looks like a new species of octopus, characterized by four brown arms and four purple arms. You name this species *Octopus bicolorus* and decide to develop it as a new model system. Inspired by what you have seen in class, describe the sequence of steps you would take -some of which could take months or even years- to discover genes that are necessary for the unusual color dichotomy in this new model system (mention at least four)?

C) This plot represents the density of a polyA selected RNA-seq experiment in mouse liver (log-scale), here for the Per2 gene. Reads on the positive strand of the genome are shown in the positive y-scale in red, while reads on the negative strand are shown in blue on the negative y-scale.



a) Explain the properties of the blue signal, on what gene features do you find the highest read coverage? (1 point)

b) What is the red signal? Speculate on what its function could be. (1 point)

c) What would you expect to be different if you had sequenced total RNA instead of the poly-A selected fraction? (1 point)

d) Say you're sequencing total RNA at different time points in mouse liver. Draw possible intron and exon density profiles in function of time for a gene that's known to have a maximum to minimum mRNA amplitude of 5 fold, and a mRNA half-life of 1 hour. (1 point)