Rieder - Genetics
Worksheet 8
Due: 11/14/17 at the beginning of class

Name: ____

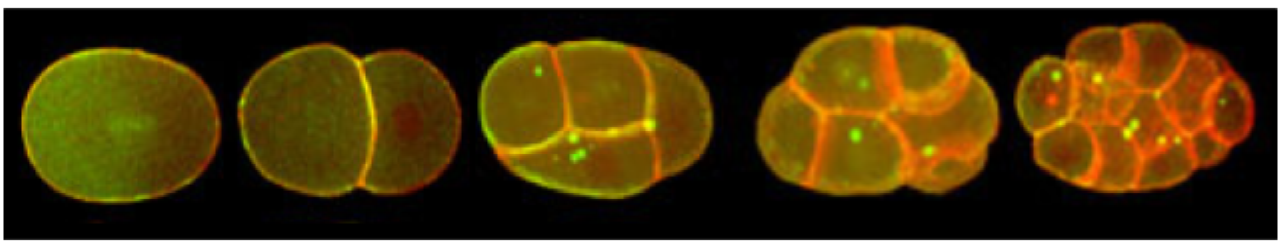
About how long did this homework take you? ______________________________________

I consulted/worked with: ____

I will not accept late homework. Special exceptions will be made **only** in the event of illness or if you contact me at least 24 hours ahead of when the assignment is due (at my discretion).

POINTS: / 50

Below are photos of the earliest developmental stages of a *C. elegans* (worm) embryo:



1. Label the fertilized egg "**1**" (2 pts).

2. The fertilized egg divides through ______________________(2 pts) to make a multicellular embryo.

3. Indicate the product of a single cell division "**2**" (2 pts).

4. If the final embryo in the picture has 16 cells, how many rounds (cycles) of cell division has it undergone (2 pts)?

____

5. Are the 16 cells in the last stage genetically identical (Y/N)(2 pts)? ________________

6. If you separate a single cell from the 16 cell embryo on the right, it can--by itself!--develop into a whole *C. elegans*. This is because the cells early during development are **totipotent.** Have any of the 16 cells **differentiated** (Y/N)(2 pts)?

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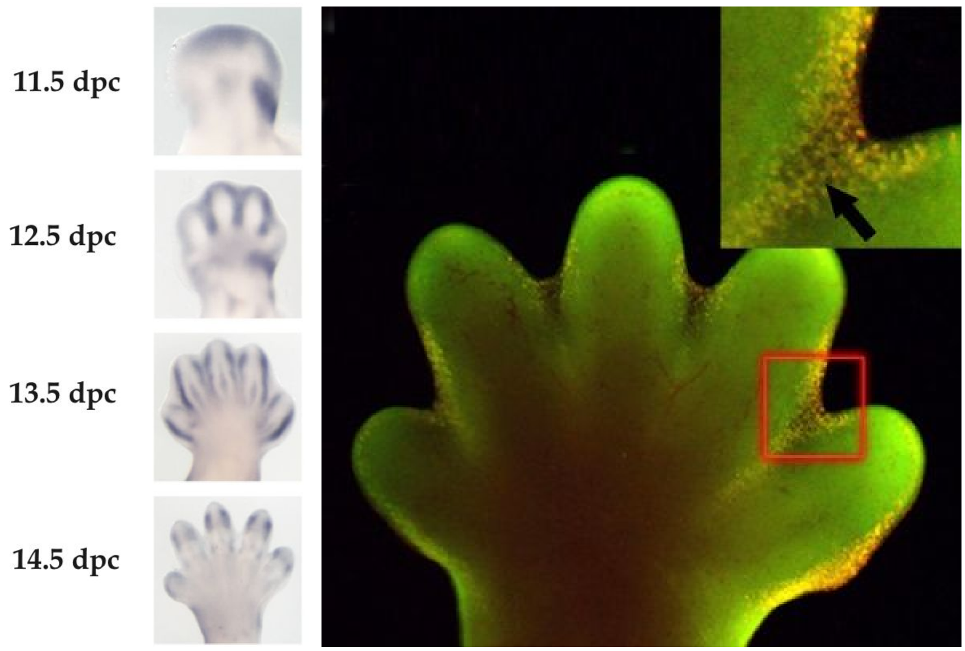
The below photos show development of a mouse embryo paw (dpc = days post copulation).

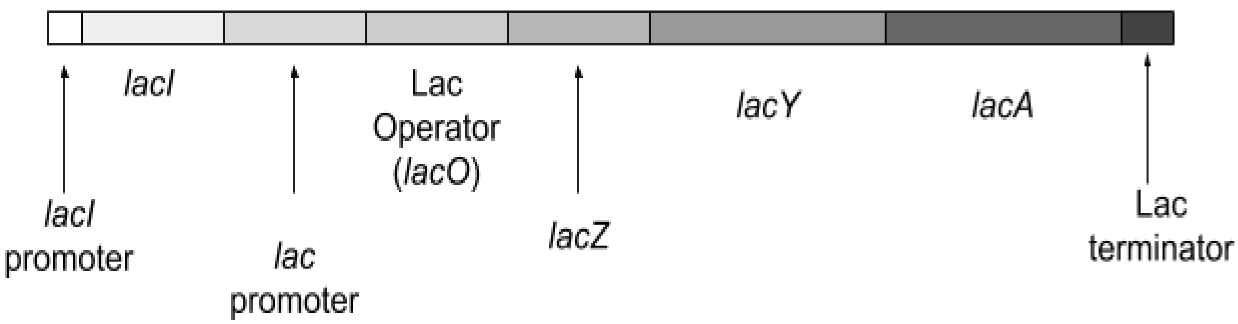


Human hands develop similarly in utero! Early during development, human and mouse embryos have only "limb buds" (see 11.5 dpc), but eventually, five digits begin to form. The fingers do not *grow* out of the limb bud, but rather the bud is *split* into 5 fingers when the cells *between* the fingers die. In the picture on the right, the yellow cells are dying while the green cells remain alive.

7. Cell death is called **apoptosis**, and is controlled during development by the **expression** of "apoptotic" genes. What would the limb look like if these apoptotic genes did NOT turn on during development (4 pts)?

8. What would happen to the organism if <u>all</u> the cells in the embryo expressed their apoptotic genes (4 pts)?

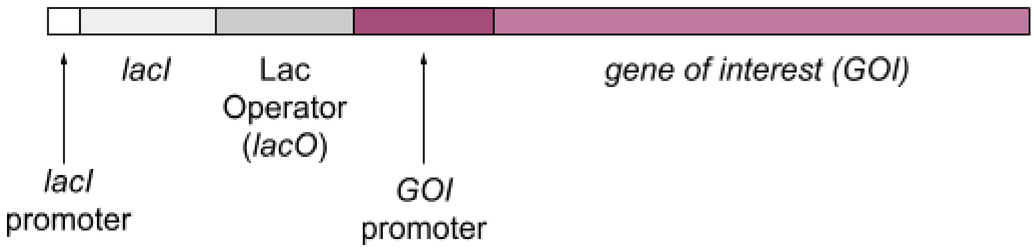
Below is the basic structure of the **Lac operon**, which is found in the genomes of *E. coli* and other **prokaryotes:**



9. WHEN is the LacI ("Lac Inhibitor") **repressor** transcription factor <u>expressed</u> (3 pts)?

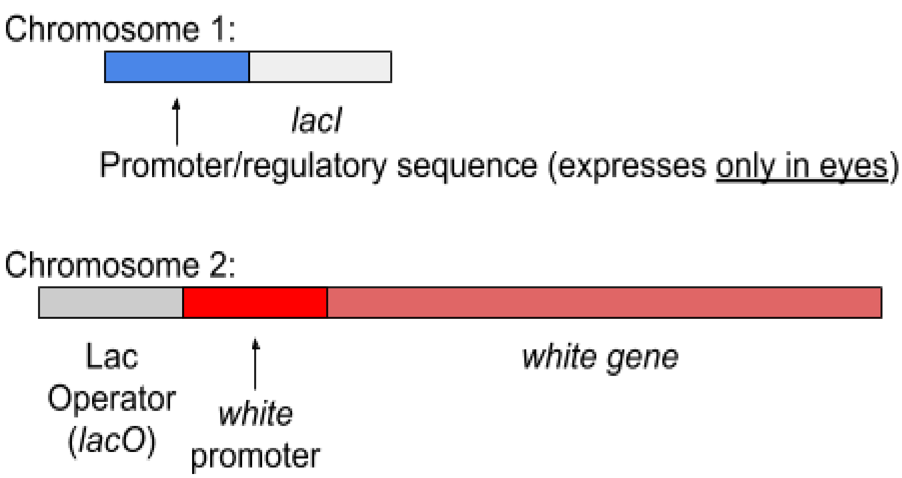
10. When the **effector** molecule **lactose** is present in the environment, which genes (*lacI, lacZ, lacY,* or *lacA*) are expressed (3 pts)?

The ***lac* operon** is normally found in prokaryotic genomes, but because the DNA code is universal, it can also be used in **eukaryotic** systems! The *lac* operator is also modular--you don't need to use all the components. For example, just the *lacO* (***lac* operator**-- the regulatory sequence) and LacI (Lac Inhibitor, the **repressor transcription factor)** components can be used in other contexts (no lactose is present in these contexts).



11. Above, the *lacO* sequence has been placed "upstream" (before) a gene of interest (GOI). Will the GOI be **expressed** if no lactose is present? How do you know (3 pts)?

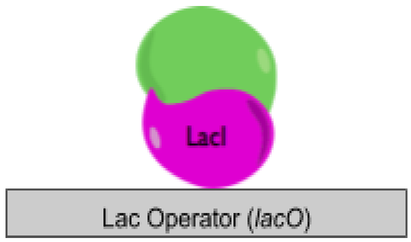
The *lacI* gene and the *lacO* regulatory sequence don't even have to be located on the same chromosome to work! In addition, we can control where (in what body part) the LacI **repressor** protein is expressed by giving it a new **promoter/regulatory sequence**:



12. What color will a fruit fly's eyes be if it has the genes shown above in its genome (3 pts)?

13. Will the *lacI* gene be **expressed** in the fly's leg? How do you know (3 pts)?

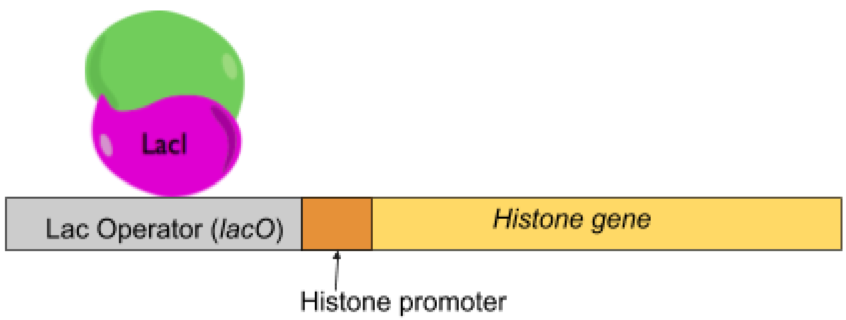
Finally, we can use the LacI/*lacO* system simply as a way of telling another protein where to go in the genome. The green protein is a **transcription factor.**



Let's say I want to artificially bring the green protein to a place in the genome it does not normally go to. I can take advantage of the affinity that the LacI protein has for the *lacO* sequence.

I can fuse the green protein to the LacI protein. This drags the green protein to the *lacO* sequence, no matter where I put it in the fruit fly genome!

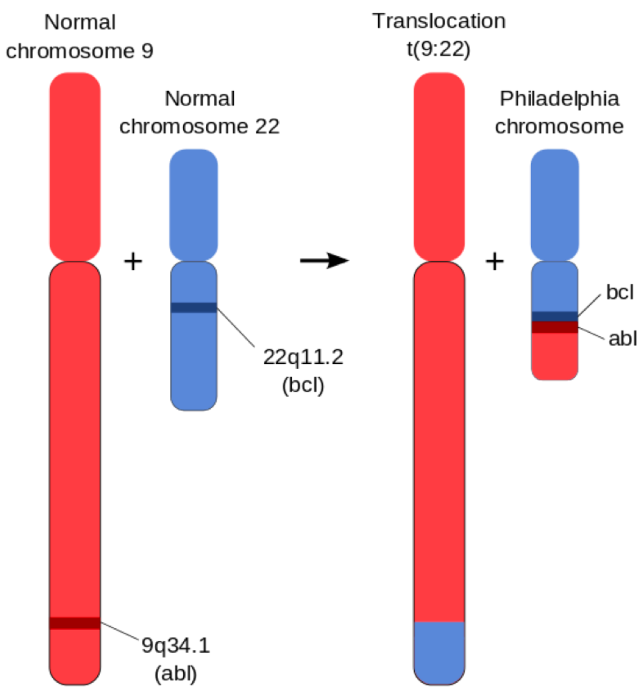
In this case, LacI no longer acts as a **repressor**; we are using it simply for its ability to locate the *lacO* sequence. Let's say the green protein is an **activator**.

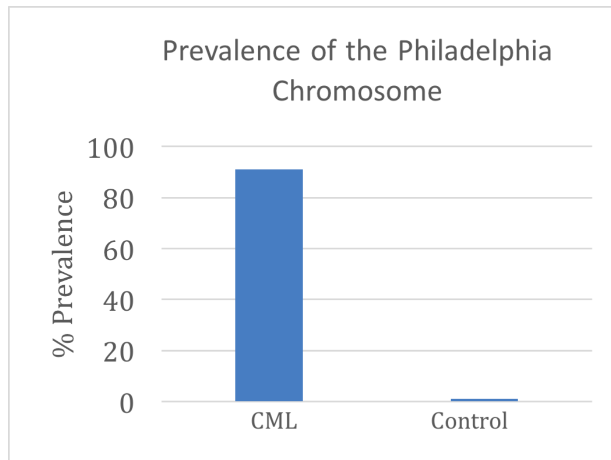


14. Above, I put the *lacO* sequence "upstream" of a histone gene (yellow). In the above picture, will the histone gene be expressed or not? How do you know (3 pts)?

Chronic myelogenous leukemia (CML) is a **cancer** (unchecked cell division) of white blood cells. Until recently, the average lifespans of patients with this disease was 3-5 years from onset, unless they received a bone marrow transplant.

The Philadelphia chromosome is formed by a **translocation** event (rearrangement of chromosome pieces), and contains the majority of chromosome 22 with a piece of chromosome 9 attached to one end (see below, left).





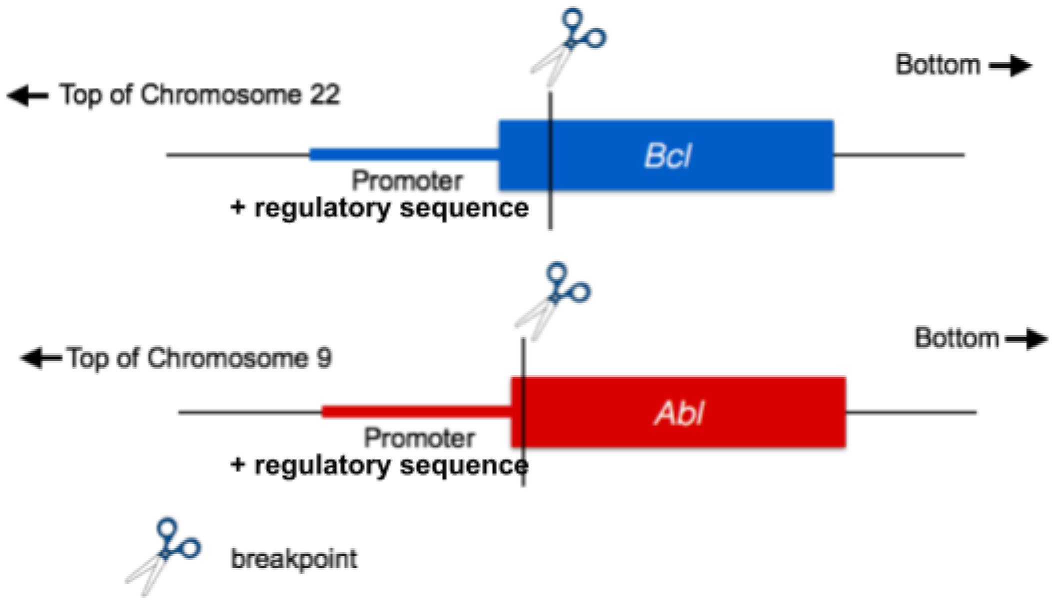
Prevalence of the Philadelphia chromosome is extremely common in patients with CML, but unusual in healthy patients (see above, right).

The breakpoints of the translocation occur in the middle of two genes:

1) The *Bcl* gene encodes a protein of unknown function that is *continuously expressed* in the cytoplasm of white blood cells. The gene is normally found on chromosome 22. The breakpoint on the Philadelphia chromosome occurs just after the start of the coding region (that encodes amino acids). See below.

2) The *Abl* gene is found near the end of chromosome 9. The breakpoint in chromosome 9 occurs in the very first part of the coding region of *Abl.* See below.

   The *Abl* gene encodes a protein involved in promoting **mitosis**. Because of its important role in cell division, *Abl* is usually only expressed for a short period of time at the beginning of **mitosis**.



15. Above are the breakpoints in *Bcl* and *Abl.* Below, sketch the region where the TOP of chromosome 22 fuses to the BOTTOM of chromosome 9. In other words, <u>what is the NEW gene that is produced when the *Bcl* and *Abl* genes fuse</u> (4 pts)?

16. WHEN/WHERE will the fusion protein you drew above be expressed (4 pts)?

17. Below, explain how the **translocation** that results in the Philadelphia chromosome leads to CML (4 pts).