Rieder - Genetics
Worksheet 10
Due: 12/5/17 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

1. Please describe the major differences between **euchromatin** and **heterochromatin**. Use the word "**histone**" in your explanation (2 pts).

2. Genes located within (**eu/hetero**)_____**chromatin** are usually **expressed** ("turned on") (1 pt).

Genes located within (**eu/hetero**)_____**chromatin** are usually not **expressed** ("turned off") (1 pt).

3. What color eyes do flies have when the the *white* gene is **expressed** (1 pt)? _____

4. The flies pictured below both have a copy of the *white* gene, but the genes are located in different places within the flies' genomes. In which fly is the *white* gene located in **heterochromatin**? In which fly is the *white* gene located in **euchromatin** (2 pts)?

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Prader-Willi syndrome (PWS) is a rare genetic disorder. People with PWS are constantly hungry, so they are often obese and have type 2 diabetes. PWS is due to a problem with chromosome 15, but it is not an **aneuploidy** (like Trisomy 21); instead PWS occurs when an individual has two copies of chromosome 15 from his/her mother and none from his/her father!

We learned about **epigenetics** in class: *changes in gene expression that are not due to changes in the DNA sequence*. PWS is due to a specific form of epigenetics called **imprinting**: *genes are expressed in a parent-of-origin specific manner*. In other words, normally an individual will inherit two copies of each gene, one from his/her mother and one from his/her father, but sometimes (and this is normal) only the mother's copy of the gene is expressed, while the father's is silenced through packaging of the DNA around **histones**. In other cases only the father's copy of the gene is expressed, while the mother's gene is silenced. This is the **epigenetic** phenomenon called **imprinting**.

5. People without PWS have an active copy of two important genes on chromosome 15: the SNRPN and necdin genes. Despite having two copies of chromosome 15, people with PWS do not have active SNRPN and necdin. Please explain below how **imprinting** causes PWS (3 pts).

6. Another chromosome 15-associated disorder is called **Angleman syndrome** (AS). Those with AS are very smiley, laugh constantly, are fascinated by water, and have seizures and intellectual disability. In AS, the genetic problem is due to one gene on chromosome 15, UBE3A. In individuals without AS, only the mother's copy of the UBE3A gene is active; the father's copy is inactivated through epigenetic mechanisms. Like those with PWS, people with AS have two copies of chromosome 15. From which parent(s) were these chromosomes inherited (2 pts)?

7. Like humans, female cats have two X-chromosomes, while males are XY. The gene that governs fur color is carried on the X-chromosome, and there are two **alleles**, X^o, which gives orange fur, and X^B, which gives black fur. In class, we discussed how tortoiseshell (black and orange spots) cats are all female (with very rare exceptions). Below are three FEMALE cats. What are their sex-chromosome **genotypes** (2 pts)?



_____ _____ _____

8. Below are three MALE cats. What are their sex-chromosome **genotypes** (2 pts)?



_____ _____ _____

9. What are the possible fur color **phenotype**(s) of a <u>female</u> cat with the equivalent of human **Turner syndrome** (1 pt)?

10. Please explain why we cannot determine which of the <u>orange</u> and <u>black</u> alleles (X^o and X^B) is **dominant** or **recessive** (2 pts).

11. Let's say that the X^o and X^B alleles are (magically) no longer located on the X-chromosome; instead we have moved them to an **autosome**. Two black cats mate and have 8 kittens (below). Which **allele** is dominant and which is recessive (1 pt)?

12. What were the **genotypes** of the parent black cats (1 pt)?

13. Now, two orange cats mate. What will be the ratio of fur colors of their kittens (1 pt)?

Many weeks ago, we discussed how **DNA polymerase** has **3' to 5' proofreading** ability. **RNA polymerase** has no such ability--if it makes a mistake, it will only impact a single RNA molecule (no big deal), whereas when DNA polymerase makes a mistake, it results in a **mutation** (a big deal).

14. Viruses can have either DNA or RNA genomes. Which kind of virus (DNA or RNA) do you think mutates faster (1 pt)?

15. Every year you get a new flu vaccine that is slightly different than the vaccine from the years before. What kind of genome (DNA or RNA) does the influenza virus have and why do you think the vaccine from last year may not protect you against the influenza virus this year (2 pts)?

In class we discussed my favorite virus, hepatitis **δ** (delta). Its short, single-stranded RNA genome contains only a single gene that encodes a single protein, called HDAg. The HDAg gene contains an **UAG stop codon** at codon 196. There is another stop codon later on in the gene. The genome is actually circular, but here I have drawn it linearly for clarity:

16. What happens when **RNA polymerase** encounters a **stop codon** (2 pts)?

Yet another cool thing about hepatitis **δ** virus: even though there is only one gene in the genome, the HDAg protein comes in two forms: large and small! Different forms of the same protein are called **isoforms**. The stop codon at codon 196 leads to the small-HDAg.

17. On your last exam, you learned about a phenomenon called **RNA editing** in which an adenosine (A) is changed to a guanosine (G) in an mRNA sequence. Please explain how RNA editing leads to the long form of the HDAg protein (3 pts).

While bacteria can be (relatively) easy to kill using antibiotics, viruses are *really* difficult to combat. Remember that they are just little protein shells housing a genome!

Some viruses, like HIV (single-stranded RNA genome), act by integrating their own genomes into the genomes of their host cells. To do this, RNA viruses first have to make their genomes

into DNA using a protein called **reverse transcriptase**. Please read about HIV reverse transcriptase in this article from the Protein Data Bank (http://pdb101.rcsb.org/motm/33).

18. Reverse transcriptase is a common antiviral drug target. Drugs that target reverse transcriptase are called **antiretroviral** drugs. Why won't antiretroviral drugs harm your cells (2 pts)?

19. Based on the reading, describe how one antiretroviral drug works in your own words (3 pts).

Scientists use **reverse transcriptase** as a biotechnology tool in the laboratory! That's because DNA is very stable and easy to work with, but RNA falls apart easily-- it is difficult to work with. We would rather convert volatile RNA into stable DNA.

Let's say I want to know if a certain gene is expressed in a cell. To do this, I:

1. Isolate all the mRNA molecules from a cell
2. Use **reverse transcriptase** to make **copy DNA** ("**cDNA**") molecules from the mRNA
3. Sequence all the cDNA molecules
4. Match the cDNA sequences to the corresponding genes.

20. Please explain why cDNA from a **prokaryotic** cell will be the same length as the corresponding gene, but cDNA from a **eukaryotic** cell will be shorter than the corresponding gene (3 pts).

21. RNA interference is a cell's defense mechanism against double-stranded RNA viruses. Why is it easier for a cell to defend itself against double-stranded RNA viruses than it is to defend itself against DNA or single stranded RNA viruses (2 pts)?

All of the biotechnology tools that scientists use were first discovered in natural systems. For example, scientists often use **RNAi** as a tool in the laboratory.

22. Below are two flies. Both have the *white* gene in their genomes. In one of these flies, scientists have injected single-stranded RNA ("**sense**" RNA) encoding the White protein. In the other fly, scientists have injected both **sense** and **antisense** RNA. Which is which (2 pts)?

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You suspect that Rudolph the red nosed reindeer expresses a gene that all the other reindeer (who laugh and call him names) do not express.

To test your hypothesis, you take a sample of cells from Rudolph's nose and another sample from the nose of his friend, who has a **wild-type** black nose.

You isolate all the mRNA from both nose cell samples, use **reverse transcriptase** to make

cDNA, and then sequence all the cDNA molecules.
You compare the cDNA sequences to the reindeer genome (sequenced just this year!) and find that the samples are identical except for one thing:

Some cDNAs are present in Rudolph's sample that are not present in the wild-type sample. The sequences of these cDNAs all correspond to a gene of unknown function. You name this gene "*shinynose.*"

23. The *shinynose* gene exists in the genomes of all reindeer. Which reindeer, Rudolph or all-the-other-reindeer, are **expressing** *shinynose* (2 pts)?

24. How might **epigenetics** be responsible for the difference in *shinynose* expression (2 pts)?

The best way to confirm that differential expression of the *shinynose* gene is responsible for Rudolph's unique red-nosed phenotype is to artificially change the expression of *shinynose* and see if you can predict the phenotype.

25. For example, you begin with a wild-type black-nosed reindeer. If you could somehow turn "on" the *shinynose* gene, what nose phenotype would you expect to observe (1 pt)?

26. Using RNAi, we can turn "off" a gene by preventing **translation** of mRNA. How would you test your *shinynose* hypothesis using both Rudolph and RNAi (3 pts)?