Name: _____ May 21, 2008

Biology 4, Exam 2

*In compliance with the Dartmouth honor principle, all the work you hand in on this exam is to be your own. Please remember to be **precise** in your wording – scientific descriptions rely on accurate use of specific terms. Also, try to keep your answers **concise**. If you can say something briefly there is no need to create a lengthy answer just to fill up space. Use the space provided and the point values for each question as indicators of the amount of detail your answer should contain. If you really need extra space for an answer, turn the page over and continue your answer on the back of the same piece of paper. To facilitate grading, we separate the exam by page; if your answer is on a different sheet of paper we will not see it. **Please put your name on each page now**.*

If something is not clear to you, please ask me during the exam. That is why I stay in the room. Good luck. - Prof. Gross

1. We watched a video called "Making Perfect Babies" in which a case was presented about Molly Nash. Molly has Fanconi's anemia and was destined to a premature death without a bone marrow transplant. Discuss what choice her parents made to save her life and what were the ethical concerns raised about their choice. ***(10 points)***

   (you can use the back of this page if you absolutely must, but please try to keep your answer brief)

Parents had child through IVF. They selected against Fanconi's and FOR the new child to be a compatible donor. Question revolves around the ethics of selecting for a trait to allow a newborn to be a donor, rather than selecting AGAINST a non-wanted deleterious trait.

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2. Operon theory was developed around the Lac operon and resulted in Nobel prizes for Jacob and Monod. This question deals with some of the original experiments done to test operon theory. Cells with mutations were created and Lac operon regulation was tested in those cells.

a. What would be the effect of a mutation in the gene coding for repressor so that it can no longer recognize lactose? ***(2 points)***

It could not be "de-repressed" and would bind to operator to permanently turn of the operon.

b. What would be the effect of a mutation in the operator so that it can no longer recognize repressor? ***(2 points)***

If repressor cannot bind to operator, the operon would be permanently on.

c. What would be the effect of a mutation in the beta-galactosidase gene so that it no longer makes a functional enzyme? ***(2 points)***

If lactose is present, it would bind to repressor to de-repress the operon. Beta-galactosidase, a product of the operon, would not function and therefore could not metabolize lactose. This means the operon would be permanently stuck on because there would always be lactose bound to the repressor. In the absense of lactose, the operon would be off.

d. What would be the effect on lac operon regulation if the cell has a normal lac operon (and lac repressor gene) present on its chromosome, but you place into the cell a mutated version of the lac repressor gene on a plasmid. This mutated version of the repressor is always turned on and makes a repressor that cannot recognize lactose? ***(3 points)***

Since the cell will always be making repressor and at least some of the repressor (from the plasmid gene) cannot be de-repressed by lactose, the lac operon will always be off.

3. Phage are viruses that can infect bacterial cells. We discussed three mechanisms that allow a phage genome to switch from one phase to another (early, delayed early, middle, and late phases). Describe two of those mechanisms. (6 points)

• switch from host RNA polymerase to phage RNA polymerase to recognize new promoter

• switch different sigma factors to cause host RNA polymerase to recognize different promoter

• make product that block action of rho-termination factor. This blocks transcription termination and allows downstream genes to be transcribed.

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4. What are the three eukaryotic RNA polymerases and what do they do? **(6 points)**

I: makes rRNA
II: makes mRNAs/pre-mRNAs, snRNAs
III: makes tRNAs

5. What are the three major modifications that happen during pre-mRNA maturation in the eukaryotic nucleus? ***(6 points)***

placing a cap on the 5' end, placing a poly(A) tail on the 3' end, and splicing out introns

6. What is meant by chromatin remodeling and what purpose does it serve? ***(4 points)***

Chromatin remodeling is the rearrangement of chromatin components to change the accessibility of transcription factor (and other) binding sites. Chromatin needs to be "opened up" so that it can become available to transcription factor activation. Conversely, "compacting" chromatin makes in inaccessible to regulatory factors and transcriptionally silent.

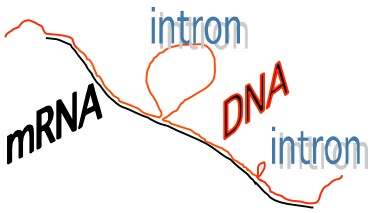
7. a. Explain how transcription factors and their binding sites on DNA regulate expression of genes. ***(5 points)***

TFs recognize specific binding sites on DNA, usually in upstream regions of the genes they regulate. If the upstream region has a number of TF binding sites, the level of expression of the gene will depend on the number of TFs that can bind to the sites for that gene. Each gene will have a different set of TF binding sites and so will be transcribed at a different level from other genes.

b. What is the major difference in the way prokaryotic RNA polymerase + sigma factor + DNA interact in comparison to the way eukaryotic RNA polymerase + transcription factors + DNA interact? ***(3 points)***

Prokaryotic RNA polymerase must interact with sigma before it can bind to DNA. In eukaryotes, transcription factors must interact with DNA before an RNA polymerase can bind.

8. The famous picture at the right shows the hybridization between a globin mRNA and the DNA that coded for it. Label the different parts of the figure and explain the loops. ***(4 points)***



loops are introns in the gene

9. Dr. Judy Stern discussed several cases of in vitro fertilization (IVF), surrogate mothers, and other complex situations. It used to be simple to think of what it meant to be a mother, but when IVF is involved that is no longer true. Discuss two different situations in which a woman might legitimately be defined as the mother of a child even though she did not provide any genetic material to the child. ***(8 points)***

For sake of discussion, call the male and female couple intending to raise the child, the intended parents.

- *surrogate mother might carry baby with genetic info from both the intended parents.*
- *female of intended parents might carry a donor egg (not hers) fertilized by the male of the intended parents*
- *surrogate mother might carry baby with donor egg fertilized by male of intended parents*
- *others are possible.*

10. What is meant by alternative splicing. ***(3 points)***

Alternative splicing is the result of different pathways for splicing a pre-mRNA. The different (alternatively spliced) pathways would each choose different exons from the original pre-mRNA to produce a final mRNA product.

11. Many biologists believe that life first evolved as an RNA World. Explain what this means and give some current day evidence to support this theory. ***(6 points)***

It suggests that the first "living' things were actually RNA molecules. The original RNA molecule could replicate itself and not much more. Through errors, the RNAs developed additional abilities including protein synthesis. Eventually DNA evolved into the genetic material. Remnants of this world still exist as seen by the major role played by RNA in protein synthesis (rRNAs, mRNA), telomere maintenance (telomerase RNA), the use of RNA primers in DNA replication, and finally siRNAs.

12. What is PCR and what can it be used for? ***(6 points)***

Polymerase chain reaction is a method used to amplify a piece of DNA by using short primers to anchor DNA replication and repeating the process many times. It is used often in forensics or in paleontological studies to examine trace amounts of DNA.

13. Dr. Marty Cetron from the CDC discussed some of the ethical dilemmas concerning modern day quarantine in case of a possible flu epidemic. There are also economic issues. Let's say there is a quarantine imposed on a supermarket so no employees can come to work (this can actually be any business). Is the supermarket obligated to pay their workers during this time? After all, the workers are willing to work and it is the store that is closing. The workers need to support their families. On the other hand, without customers, how will the supermarket be able to take in the money necessary to pay their workers? What do you think is the right thing to do in this case? Remember that the whole town might be in the same condition. ***(10 points)***

14. Reporter genes are often used to study gene regulation, but can sometimes be used as indicators of environmental changes.
    a. What is a reporter gene? ***(2 points)***

A reporter gene make a product that is easy to identify (such as a fluorescent protein).

    b. How were zebrafish used to indicate the presence of hormones/pesticides or toxic metals in the water? ***(4 points)***

A green fluorescent protein was placed downstream of an estrogen promoter so that if there are steroids or some pesticides in the water, the gene is activated and the fish glow green.
A red fluorescent protein was placed downstream of a stress promoter so that if there are toxic chemicals in the water, the promoter is activated and the fish glow red.

15. Explain how pharmacogenetics can be used to help determine the best chemotherapy treatment for a patient. ***(5 points)***

Each tumor will have a characteristic set of genes being expressed (or not) at specific relative levels. By biopsying a sample of the tumor and assaying it with microarray technology it is possible to characterize the expression profile of that tumor. It is then possible to choose the best chemotherapy treatment based on past experience of which expression profiles are most amenable to treatment with different chemotherapy drugs.

16. You have cloned a piece of eukaryotic DNA (DNA-X) that, although it is not transcribed, has some unusual properties you wish to explore. To do this, you transfect various kinds of eukaryotic cells with this DNA and observe how the newly inserted DNA-X alters the recipient cell's behavior. In each different cell you observe that different genes are activated after DNA-X insertion. In each case the activated genes are near each other in the genome and had been expressed at very low levels before transfection, but after DNA-X is inserted nearby, the genes get transcribed at a high level. How is DNA-X functioning? Explain your answer. ***(3 points)***

Since the inserted DNA is not transcribed it cannot be responsible for making any product (either RNA or DNA) that causes the changes. It therefore must be acting as a regulatory sequence in the DNA itself. Since DNA-X does not activate any genes that are silent, but it does increase the level of gene transcription, and the genes that are stimulated are near each other, it is most likely that DNA-X is an enhancer.