Biochemistry 465 **Your Name:** _____

Biological Information Processing **Prof. Jason Kahn**

Final Exam (170 points total) **May 15, 2006**

You have 120 minutes for this exam.

Exams written in pencil or erasable ink will not be re-graded under any circumstances.

Explanations should be concise and clear. I have given you more space than you should need, but just in case there is a blank page at the end.

You do not need a calculator for this exam, and no other study aids or materials are permitted.

Generous partial credit will be given, *i.e.*, if you don't know, guess.

Honor Pledge: At the end of the exam time, please write out the following sentence and sign it, or talk to me about it:

"I pledge on my honor that I have not given or received any unauthorized assistance on this examination."

1. DNA repair (36 pts):

(a; 15 pts) Draw the structure of an abasic site in DNA. This is the common intermediate for what type of DNA repair? Given that this type of repair exists, and that it's much simpler than NER, why do you think NER evolved as well?

Score for the page_____

(b; 6 pts) What is the source of the information needed for error-free DNA repair via (1) direct repair, (2) NER, and (3) DSB repair? (Very short phrase each)

(c; 15 pts) Sketch the MutSHL complex on DNA just after incision, and indicate the function of each protein. We argued that through-solution looping does not make sense as a mechanism for establishing the MutSHL complex, that tracking makes more sense. What is the reasoning? (Note that while there's some experimental evidence for tracking, this is not a done deal.)

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2. Translation (38 pts):

(a; 9 pts) In kinetic proofreading during aa-tRNA selection on the ribosome, there is a branched pathway for acceptance vs. rejection. What is the acceptance branch called and what happens during acceptance? What is the rejection branch?

The existence of tradeoffs among speed, energy cost, and fidelity is a general theme of biological information processing. Translation offers an example. Streptomycin is an antibiotic that inhibits growth by markedly increasing the error rate of tRNA selection in translation. The mechanism is complex but the bottom line is that rejection of tRNAs becomes much less efficient.

(b; 6 pts) Why would an increased error rate for protein biosynthesis hurt the cell (not a trick question)? What name did we give the corresponding effect of inaccurate DNA polymerases?

(c; 8 pts) Streptomycin-resistant (SmR) ribosomes are hyperaccurate, i.e. they make fewer mistakes than wild type ribosomes. Recall that hyperaccurate DNA polymerases (antimutators) have very active _____**(fill in the blank)**. Analogously, how might the EF-Tu•GTP•aa-tRNA kinetic proofreading mechanism above be altered to make a hyperaccurate ribosome?

Score for the page_____

(d; 9 pts) The SmR ribosome is not the wild type: in other words, hyperaccuracy is actually selected against in the absence of the antibiotic. Give two possible reasons, one based on economy and one based on speed; we will not consider the possibility that the errors per se can be useful. Based on what you know about ribosome function and abundance, and general themes from the course, is the argument from economy or the argument from speed more likely to be correct?

(e; 6 pts) Some SmR mutants are actually streptomycin-dependent (SmD), i.e. they die in the absence of the antibiotic. Why might this happen?

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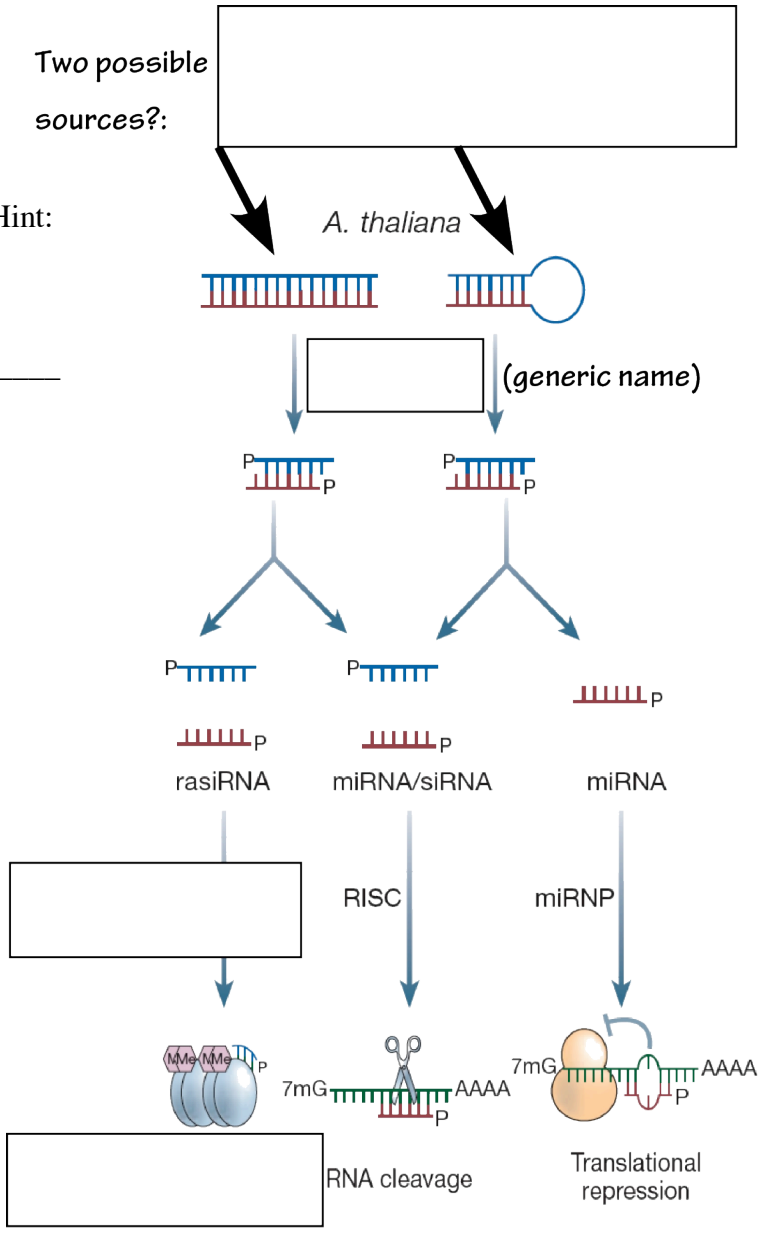
3. RNA Biology (40 pts):

(a; 15 pts) Fill in the boxes in the schematic at the right of three possible outcomes of RNAi in plants.



(b; 6 pts) How might RNAi have evolved? Hint: administering long dsRNA molecules to mammalian cells sets off an

_____

(fill in the blank) response.

(c; 9 pts) What are two of the main attractions for oligonucleotide-based therapeutics as opposed to e.g. small-molecule inhibitors of enzymes? What is one serious difficulty with administering oligonucleotides to patients?

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(d; 10 pts) RNA has been suggested as the primordial self-perpetuating macromolecule, because it can combine information carrying and catalytic function. In the last few billion years, RNA has specialized mainly in transesterifications of one kind or another. Why has DNA taken over information storage? Why has protein taken over most catalytic functions? Why does RNA retain primacy in nucleic acid transactions like splicing?

3. Eukaryotic Transcription (27 pts):

We've seen that eukaryotic transcription involves combinatorial regulation by sets of transcription factors, and that chromatin remodeling activities are recruited as part of the process.

(a; 6 pts) Wouldn't it be simpler to have a single transcription factor dedicated to each gene? Give two simple reasons hasn't life evolved this way.

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(b; 12 pts) In general, give two ways in which one transcription factor bound at a promoter/enhancer can potentiate the activity of another, and two ways in which one can repress the other. Some possible activate/repress answers rely on similar mechanisms, that's okay.

(c; 9 pts) What do SWI/SNF ATPases do? How can they either activate or repress transcription depending on the gene in question? How might they end up repressing some genes indirectly as opposed to directly?

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4. Connections and Miscellaneous (29 pts)

(a; 24 pts) We have seen several examples of potentially dangerous macromolecules with cryptic activities that are delivered or activated by molecular matchmakers. Describe two examples: for each, list (A) the molecule with the cryptic activity, (B) the nature of the activity (i.e. a restriction enzyme, which is not otherwise an answer I am looking for, would be described as "cuts DNA at a palindromic recognition site"), (C) the partner that loads/activates molecule (A), and (D) one reason that molecule (A) doesn't just do everything itself without help.

(b; 5 pts) Suggest an improvement I could make in the coverage of a topic of your choice.

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