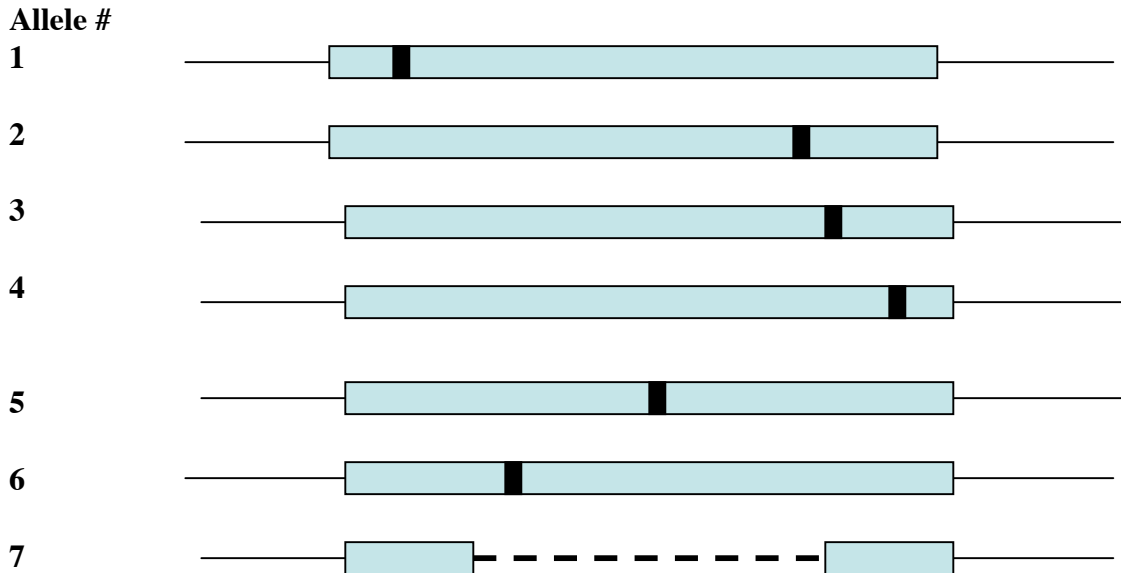


**You Must Type Out Your Answers where your answers involve words.**

1. List the three reasons given in class for “drug side effects”.  
(This is a “regurgitation” question, of which there will be very few on an exam!)
2. ORFs. Refer to a Table of the Genetic Code (there is one in your text book. pg240)
  - A. Start with an “ATG” (the nearly-universal “start” codon). Not using the same codon twice, write out 30 consecutive “sense” codons. You have just generated a new “open reading frame”. Underline consecutive triplet bases, each encoding an amino acid, in this open reading frame.
  - B. Calculate the probability that, if you wrote down bases in random order (A,T,C,G) , that you would generate an open reading frame (i.e. one having no stop or non-sense codons”) that was 30 codons long.
  - C. Now delete the 4th base from the left. Underline the new reading frame. Is it “open”..encoding amino acids? Circle the first (if any) nonsense codon. By my calculation, about 4 in 5 of you should have sequences that end in a nonsense codon. Write down the amino acids that this new reading frame encodes. If your sequence did not result in an in-frame nonsense codon, go back to your original sequence, now add a base after the third base (the G of ATG), underline the new reading frame and circle the first (if any) nonsense codons.
  - D. Without considering your specific sequence, what is the probability that you will reach a stop codon by the 10th triplet? Hopefully you now understand why a “frameshift mutation” frequently eliminates a proteins function (as opposed to a missense mutation that may change one amino acid), either because of a nonsense codon or different amino acids.
  - E. If genome #1 is “AT rich’ compared to genome #2 (say an obscure yeast versus cow). That means that genome #1 has, say, 60% AT and 40% GC, while genome #2 is 50%AT and 50% GC. If a frameshift mutation occurs, is a nonsense codon more likely, less likely, or just as likely to occur in the new reading frame in a gene in the AT-rich genome #1 compared to genome#2. Explain briefly.
3. On the structure of mutational intermediates caused by base modification.
  - A. See Slide 23. Draw a G and a C base-paired, complete with their correct chemical structures and hydrogen bonding. Draw the ethylated G base-paired with T see in slide 23. The mechanisms of how ethylation causes a mutation by altering base pairing should now be clear.
  - B. Now look up and write down a second example that illustrates the chemistry of how a base pair mutation come about by base modification.
4. Fluctuation Test: Imagine you have 1000 bacterial haploid cultures that each started from 1 cell. The cells were Amp<sup>R</sup>, and you screened for Amp<sup>S</sup> in each culture. You allowed the cells to complete 10 cell divisions (to generate cultures of 1024 cells each.)
  - A. Calculate the number of cultures with no mutants (the “0” class) and with >256 mutants if the mutation rate is 0.01 per cell division; if the mutation rate is 0.001 per cell division .
  - B. A fellow student comes to you and explains that he thinks he discovered a bacterial mutant that causes a higher frequency of mutation in the Amp<sup>R</sup> gene. He bases this conclusion on the observation that, in mutant and wildtype cultures of 10<sup>6</sup> cells he identified 200 and 20 mutants, respectively. What do you tell him?

5. Recombination Problem. You are given these 7 *Leu1*- alleles. The site of the mutation in 1-6 is shown in each allele by a vertical bar. For the “bar” mutations, the mutation is a missense. A deletion is shown for allele 7 by a dotted line....this represents the DNA that is missing from that allele.



Imagine that pairs of alleles are present in a diploid eucaryotic cell, so the cell is *Leu*-.

You can determine the frequencies of intragenic mitotic recombination by selecting for *Leu*+ progeny.

- Which single pair of alleles will give the highest rate of recombination, and why? Draw out the recombination reaction and the resulting diploid cells.
- Which single pair of alleles will give the lowest rate of recombination and why?
- If you have homozygous strains (in which both alleles are the same), which allele will most frequently revert to wildtype, and why?
- Which homozygous strain (in which both alleles are the same) will revert at the lowest frequency, and why?
- Will X-irradiation increase or decrease the recombination frequency? Explain why.