Mutation, Repair, and Recombination

1. You need to know the reading frame of the possible message.

2. The mutant has a deletion of one base and this will result in a frameshift (–1) mutation.

3. Proline can be coded for by CCN (N stands for any nucleotide) and histidine can be coded for by CAU or CAC. For a mutation to change a proline codon to a histidine codon requires a transverion (C to A) at the middle position. Therefore, a transition-causing mutagen cannot cause this change. Serine can be coded for by UCN. A change from C to U at the first position (a transition) would cause this missense mutation and would be possible with this mutagen.

4. Assuming single base-pair substitutions, then CGG can be changed to CGU, CGA, CGG, or AGG and still would code for arginine.

5. **a. and b.** By transversion, CGG (arginine) can be become AGG (arginine), GGG (glycine), CCG (proline), CUG (leucine), CGC (arginine), or CGU (arginine).

6. The enol form of thymine forms three hydrogen bonds with guanine.

7. **a. and b.** After the first round of replication, the enol form of thymine will be paired with guanine. At the next round, the guanine will pair with cytosine to result in the TA•CG transiton.

8. **a.** Acridine orange causes frameshift mutations and frameshift mutations often result in null alleles.

b. A +1 frameshift mutation can be reverted by two further single insertions so that the reading frame is re-established.

9. Apurinic sites have lost either an A or G. If thymine is preferentially inserted opposite these sites, GC•AT transitions should be produced.

11. One of the mechanisms for repair of UV-induced photodimers is the enzyme photolyase. This enzyme requires visible light for function and would therefore be expected to be more active on bright sunny days.

12. The mismatched "T" would be corrected to C and the resulting ACG, after transcription, would be 5´ UGC 3´ and code for cysteine. Or if the other strand was corrected, ATG would be transcribed to 5´ UAC 3´ and code for tyrosine.

13. Gene conversion is the result of regions of heteroduplexes that form as part of the recombination process. Consequently, in meioses that produce aberrant ratios (gene conversions), there is a crossover between flanking genes at much higher frequencies than expected.

14. The formation of heteroduplex DNA is part of the double-strand break model. If the allelic mismatch is not repaired, a 5:3 ascus will result. However, if the mismatch is repaired prior to cell division, a 6:2 ascus results. If 6:2 asci are more

frequent than 5:3 asci, it indicates that repair of the heteroduplex mismatch is more likely to happen than not.

17. Frameshift mutations arise from addition or deletion of one or more bases in other than multiples of three. When translated, this will alter the reading frame and therefore the amino acid sequence from the site of the mutation to the end of the protein product. Also, frameshift mutations often result in premature stop codons in the new reading frame, leading to shortened protein products. A missense mutation changes only a single amino acid in the protein product.

19. Depurination results in the loss of the adenine or guanine base from the DNA backbone. Because the resulting apurinic site cannot specify a complementary base, replication is blocked. Under certain conditions, replication proceeds with a near random insertion of a base opposite the apurinic site. In three-fourths of these insertions, a mutation will result.

Deamination of cytosine yields uracil. If left unrepaired, the uracil will be paired with adenine during replication, ultimately resulting in a transition mutation.

Deamination of 5-methylcytosine yields thymine and thus frequently leads to C to T transitions.

Oxidatively damaged bases, such as 8-OxodG (8-oxo-7-hydrodeoxyguanosine) can pair with adenine, resulting in a transversion.

Errors during DNA replication can lead to spontaneous indel mutations.

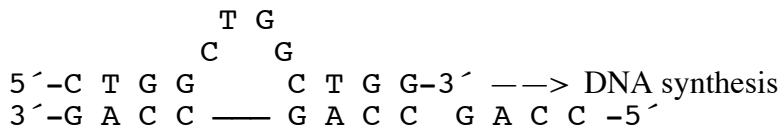
22. There are many repair systems that are available: direct reversal, excision repair, transcription-coupled repair, and non-homologous end-joining.

24. Depurination results in the formation of an AP site. AP endonucleases introduce chain breaks by cleaving the phosphodiester bonds at these sites. Some exonuclease activity follows, so that a number of bases are removed. The resulting gap is filled by DNA pol I and then sealed by DNA ligase.

Deamination of cytosine and adenine yields uracil and hypoxanthine, respectively. Specific glycosylases remove these bases, creating an AP site that is then repaired as above. Deamination of 5-methylcytosine yields thymine, and because this cannot be distinguished from any other thymine in the DNA, 5-methylcytosines represent mutational “hot spots.”

25. The Streisinger model proposed that frameshifts arise when loops in single-stranded regions are stabilized by slipped mispairing of repeated sequences. In the *lac* gene of *E. coli*, a four-base-pair sequence is repeated three times in tandem, and this is the site of a hot spot.

The sequence is 5´-CTGG CTGG CTGG-3´. During replication the DNA must become single-stranded in short stretches for replication to occur. As the new strand is synthesized, transient disruptions of the hydrogen bonds holding the new and old strands together may be stabilized by the incorrect base-pairing of bases that are now out of register by the length of the repeat, or in this case, a total of four bases. Depending on which strand, new or template, loops out with respect to the other, there will be an addition or deletion of four bases, as diagrammed below:



In this diagram, the upper strand looped out as replication was occurring. The loop is stabilized by base pairing on either strand. As replication continues at the 3´ end, an additional copy of CTGG will be synthesized, leading to an addition of four bases. This will result in a frameshift mutation.