1. (2 pts.) Recall the article entitled: Human Genetic Variation
   By each statement circle True/False/Not addressed in the paper. Answer false if any part of the statement is false.
   T  F  N  This article states that copy number variations (CNVs) have turned out to be very unusual in humans.
   T  F  N  People with high starch diets – such as in Japan – have extra copies of a gene encoding a starch-digesting enzyme as compared with members of hunter-gatherer societies.

2. (4 pts.) Circle True or False. If there are two statements, the first statement is true and you are to decide whether the second statement is True or False. No credit if no explanation.
   T  F  Both spontaneous and induced mutations are random events. For this reason, most non-neutral mutations in the proto-oncogene class of genes will not result in cancer-inducing (driver) alleles.
   One sentence explanation:

   T  F  The tumor suppressor class of genes (often found mutated in cancer cells) are named for their loss-of-function phenotype.
   One sentence explanation:

3. (3 pts) Reactive oxygen species such as hydrogen peroxide and hydroxyl radicals are produced as by-products of normal aerobic metabolism. Such species can cause damage to the bases of DNA. Consider an oxidative lesion to guanine (G\(^{ox}\)). G\(^{ox}\) can pair with adenine or cytosine. Based on this information, what kind of mutation(s) can result from the oxidation of a guanine either before or after it is incorporated into a DNA polymer?
   i. This type of DNA damage will result in (circle all correct answers)
      a. a transition mutation
      b. a transversion mutation
      c. an indels (of a few bases)
      d. none of the above
   ii. This type of DNA damage will result in the following point mutations (circle all correct answers)
      a. GC \(\rightarrow\) AT
      b. GC \(\rightarrow\) CG
      c. GC \(\rightarrow\) TA
      d. AT \(\rightarrow\) GC
      e. AT \(\rightarrow\) CG
      f. none of the above are likely
Huntington disease (HD) is caused by a variable expressed but fully penetrant autosomal dominant mutation that causes late onset (post-reproductive) neurodegeneration. The mutations that cause HD involve an expansion of a triplet repeat located in the coding region of the gene (HTT --see below). Normal alleles of this gene have 27-35 CAG repeats. Alleles with >40 repeats confer a clear HD phenotype. Interestingly, as the number of repeated triplets increases, the age of onset in the patient decreases. Furthermore, because the unstable trinucleotide repeat can lengthen when passed from parent to child, the age of onset can decrease from one generation to the next.

Homo sapiens huntingtin (HTT), mRNA (in cDNA language)
>gi|90903230|ref|NM_002111.6| Homo sapiens huntingtin (HTT), mRNA
GCTGCCGGAGCGGGTCCAAAGATGGACGGCCGCTCAGTTCTGCTTTTACCTCGGCCAGAGGCCCACTTCATTGCCCGTGCTGAGGCCTCCGGGACTGCCTGGGCCGAGCCTCCGCCATGGCGACCCTGGAAAAGC

\[\text{\textcircled{a}}\]

a. (2 pts.) The 5’end of the huntsintin mRNA is shown above. Note that by convention all database sequence files are in DNA language.  **Circle the translation start codon.**

b. (4 pts. all or nothing since one correct and one incorrect primer will not give you a partial PCR product…)  You are planning to set up PCR to amplify the shaded region between the \[\text{\textcircled{a}}\]'s. The PCR product should include all of (but not extend beyond) the designated region. **List the first five bases of each primer.** Your primer sequences must read in the 5’ to 3’ direction.

Primer A: 

Primer B:

c. (1pt.) DNA polymerase is a special needs enzyme. What property common to all DNA polymerases is critical to the amplification specificity of a PCR? **One complete sentence.**

d. (2 pts.) Will an expansion or contraction of the number of CAG repeats result in a frameshift at the protein level:  **Circle YES or NO**

One sentence defense of your answer (no credit if no explanation):

Problem continues on the next page…
e. (2 pts.) On the sequence below, label the strand that acts as the template during transcription.

f. (6 pts.) DRAW a clearly labelled diagram to show how an increase of one repeat unit can occur as a spontaneous mistake during DNA replication:
   • Be sure to label the 5’ and 3’ ends of all DNA strands.
   • Be sure to label the parental and daughter DNA strands.
   • Only show relevant parts of sequence
   • Hint: the initial mistake can occur during the replication of either parental strand so follow the replication of just one of the parentals

PARENTAL DNA

- --------------- CTCAAGTCCTCCAGCAGCAGCAG ---------------
- --------------- GACTTCAGGAAAGGTGTCGTCGTC ---------------
5. (14 pts.) See pedigree and PCR data on the extra sheet.
Both families shown have mutations in the GATA gene. The affected individuals have similar
symptoms including heart defects, immune deficiencies, deafness and renal malformations. The
data for genotyped individuals is shown directly below their pedigree symbol. N1 and N2
represent normal control individuals. A codon table is on the extra sheet.

a. (1 pt.) Examine panel a. At the protein level, what type of mutation is seen in this
family? One word. No explanation. ______________________

b. (1 pt.) Answer the same question for family 12/99. ________________

Circle True/False/Not enough info to decide. 1 pt if no explanation is required. 2 pts if an
explanation is required. For the latter, no credit given if there is no explanation.

T  F  N  The mutation in Family 12/99 could have been originally generated by environmental
exposure to a base analog mutagen such as 2 aminopurine.

T  F  N  In family 12/99, the mutant allele is codominant at the molecular level of assessment
but dominant (completely or incompletely) at the organismal level of assessment.

T  F  N  The GATA gene is likely to be X-linked.
One sentence defense of your answer:

T  F  N  In both families the mutant alleles are likely to result in a gain-of-function.

T  F  N  The mutant GATA allele is recessive in Family 26/99 and dominant in Family 12/99
One sentence defense of your answer:

T  F  N  Based on the data presented here, GATA mutations are completely penetrant.

T  F  N  In family 12/99, the mutant phenotype results from an extra copy of the chromosome
that the GATA gene is located on.

T  F  N  Setting niceties aside, if individual I #1 from family 26/99 mates with I #2 from
family 12/99, the probability of a normal offspring is 1/4.

T  F  N  If the parents in either family have additional children, there is a 50:50 probability of
an affected offspring.
One sentence defense of your answer: