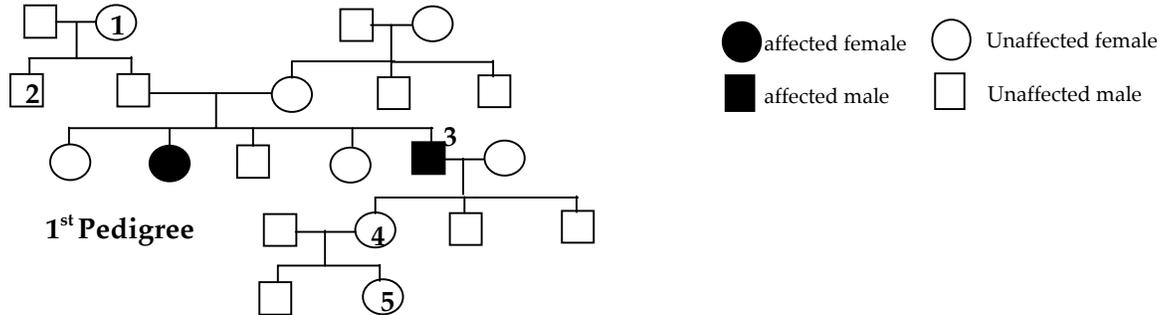


# Solution Key- 7.016 Problem Set 3

## Question 1

The following human pedigree shows the inheritance pattern of a specific disease within a family. Assume that the individuals marrying into the family for all generations (except the parental generation) do not have the allele associated with the disease phenotype and that no other mutation arises spontaneously. Also assume complete penetrance.



a) Circle the **most likely** mode of inheritance for this disease. Choose from: autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive.

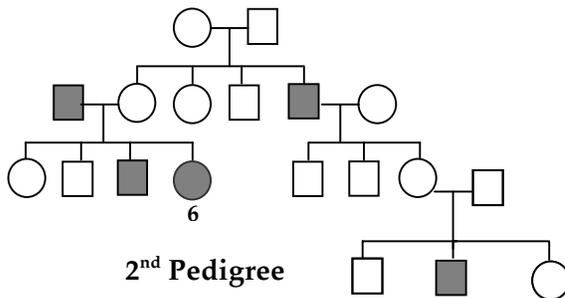
b) Write **all possible** genotypes of the following individuals in the pedigree. Use the uppercase "A" or "X<sup>A</sup>" for the allele associated with the dominant phenotype and lowercase "a" or "X<sup>a</sup>" for the allele associated with the recessive phenotype.

Genotype(s) of **Individual 2**: AA, Aa

Genotype(s) of **Individual 4**: Aa

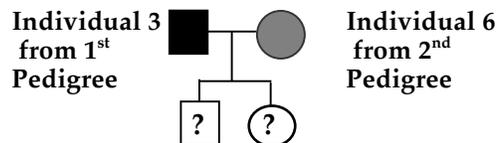
c) What is the probability that Individual 5 will be a carrier? 50%

d) The following human pedigree shows a family affected by a **different disease**. Assume that the individuals marrying into the family do not carry any allele associated with the affected phenotype and that no other mutation spontaneously occurs. Also assume complete penetrance



Note: Use the notation such as "R or X<sup>R</sup>" for the allele associated with the dominant phenotype and "r or X<sup>r</sup>" for the allele associated with the recessive phenotype.

Individual 3 from the 1<sup>st</sup> pedigree has a second marriage with Individual 6 from the 2<sup>nd</sup> pedigree. They have a son and a daughter as shown below.

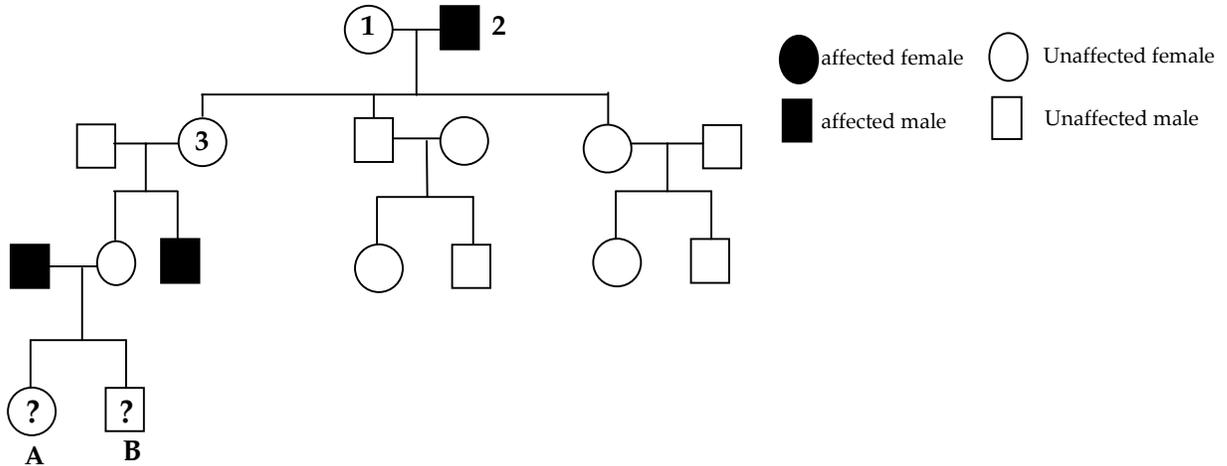


i. What would be the **genotype** of their **son** for the two genes? X<sup>Y</sup>Aa

ii. What would be the **genotype** of their **daughter** for the two genes? X<sup>R</sup>X<sup>r</sup>Aa

### Question 2

You are analyzing the following human pedigree. Assume that the individuals marrying into the family (except the parental generation) do not carry any allele associated with the disease phenotype and that no other mutation spontaneously occurs. Also assume complete penetrance. Use the letter "R or  $X^R$ " for the allele associated with the dominant phenotype, "r or  $X^r$ " for the allele associated with the recessive phenotype.



a) Circle the **most likely** mode of inheritance of this disease? Choose from: autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive.

b) List **all possible** genotypes of the following individuals in the pedigree.

Genotype(s) of Individual 1:  $X^R X^R$  or  $X^R X^r$

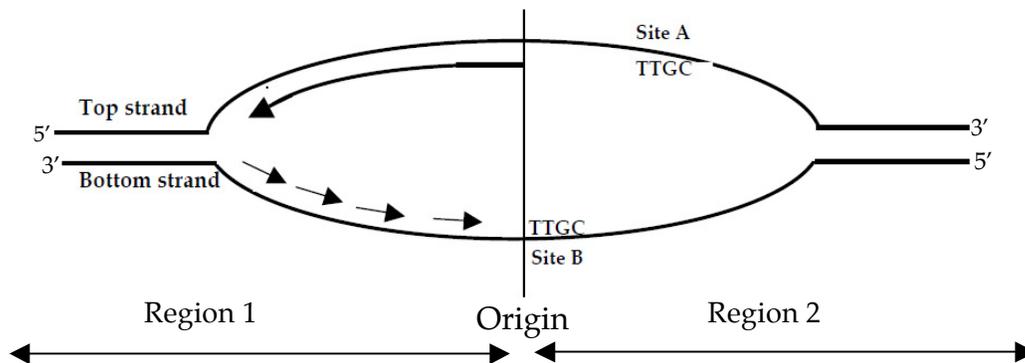
Genotype(s) of Individual 3:  $X^R X^r$

c) What is the probability of **Individual A** being affected? 25%

d) What is the probability of **Individual B** being affected? 25%

### Question 3

Shown below is the schematic of a replicating DNA in a bacterial cell.



a) On the diagram, label the 5' and the 3' ends of the parental DNA strands.

b) Identify the strand(s) (choose from *Top*, *bottom*, *both* or *neither*)...

i. Which serves as a template for the synthesis of a **continuous** strand in **Region 2**. *Bottom*

### Question 3 continued

- i. Which will not replicate if the cells have a **non-functional helicase** in Regions 1 & 2. **Explain** why you selected this option.

If the helicase is non-functional the two strands of DNA duplex will not unwind and hence will not be available to serve as the templates for the synthesis of the complementary strand strands. So neither the top nor the bottom strand in region 1 and Region 2 will be able to replicate.

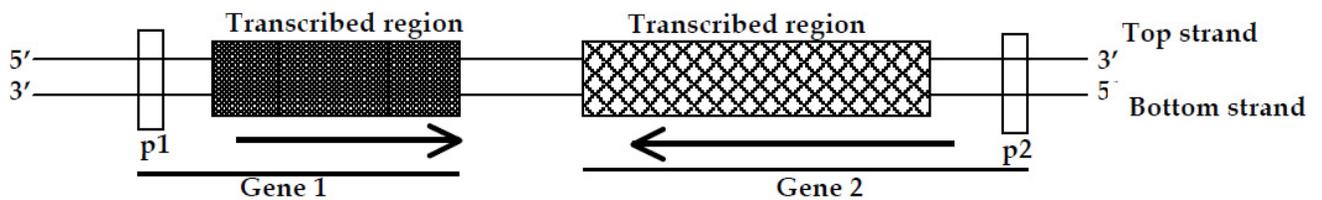
c) To which site (**A or B or both**) can primer 5'AACG3' bind during replication? *Site B*

d) Each replication cycle, during each cell division in eukaryotes, results in the shortening of chromosomal ends. This process is slowed down by the action of telomerase enzyme that adds telomere repeats (5'TTAGGG3') to the chromosomal ends. **Explain** how the telomerase activity may regulate the number of mitotic divisions a cell can have during its lifetime.

In the absence of a functional telomerase in adult somatic cells, the chromosomal ends continue to shorten with each cell division. This eventually results in the loss of genetic information, which is crucial for cell division and survival.

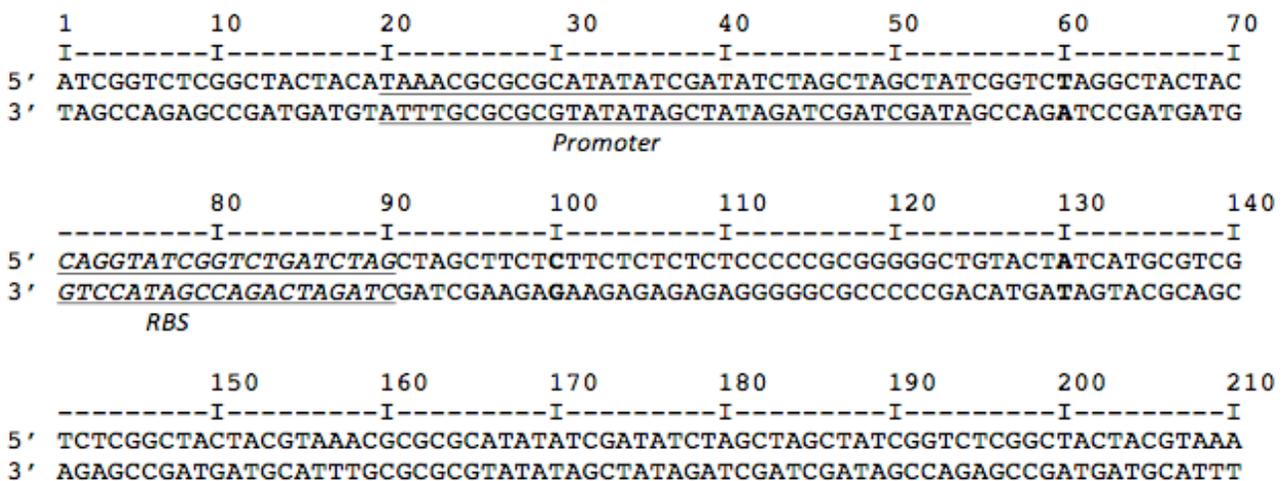
### Question 4

The following schematic shows the chromosomal location of Gene 1 and Gene 2. The corresponding promoters for Gene 1 (p1) and Gene 2 (p2) are shown.



a) On the schematic, use arrows to show the direction of transcription of **Gene 1** and **Gene 2**.

b) The following is the partial DNA sequence of Gene 1. **Note:** The underlined sequence (from position 20-54) represents the promoter for Gene 1 and the underlined and italicized sequence (from position 71-90) represents its ribosomal binding (RBS) site. Transcription begins at and includes the bold T (Top)/A (bottom) base pair at position 60.



- i. Which strand (*Top/ bottom*) is the template strand for transcription of Gene 1? *Bottom strand*
- ii. What are the first 6 nucleotides of the mRNA transcribed from Gene 1? *5'UAGGCU3'*

iii. What are the first 4 amino acids encoded by Gene 1? *N-met-arg-arg-leu-C*

**Question 4 continued**

c) You have found mutant alleles of Gene 1 that have insertion of the following three base pairs immediately **after** the C/G base pair at positions, 70, 100 and 150. Complete the table below for each of the following mutations.

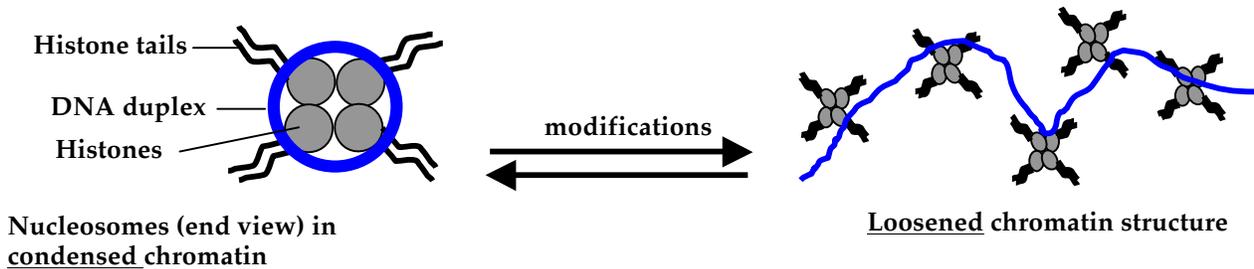
5' CGA 3'  
3' GCT 5'

	Positions of insertions of the above sequence		
	After 70 <sup>th</sup> base pair	After 100 <sup>th</sup> base pair	After 150 <sup>th</sup> base pair
Effect on the length of protein (longer than/ shorter than/ same as the protein produced by the wild-type allele of Gene 1). <b>Explain.</b>	Same as the original protein since the insertion of the bases is prior to the ribosomal binding site.	Same as the original protein. Although this insertion is after the ribosomal binding site it is prior to the start codon and hence is not a part of the open reading frame.	Longer than the original protein by one amino acid since it is after the start codon. But it does not change the reading frame.
If the protein is produced, will it be functional? <b>Explain.</b>	Yes, since the translation of the protein following this insertion remains unaffected for the reasons described above.	Yes, since the translation of the protein following this insertion remains unaffected for the reasons described above.	Functional, if the extra amino acid does not change the 3D conformation of the protein. Inactive if you do not make this assumption.

d) Chromatin is a dynamic structure comprised of DNA and histone proteins. Chemical modifications of histones affect state of chromatin condensation and gene transcription. More than a fifth of histone's amino acids are lysine and arginine. **Explain** why this is crucial to the packing of DNA.

*The DNA is negatively charged due to the phosphates in the sugar phosphate backbone. Therefore it is most likely to interact with the amino acids that are polar and have positively charged side-chains.*

e) The schematic below represents the chromatin in a *condensed* or *loosened* state.

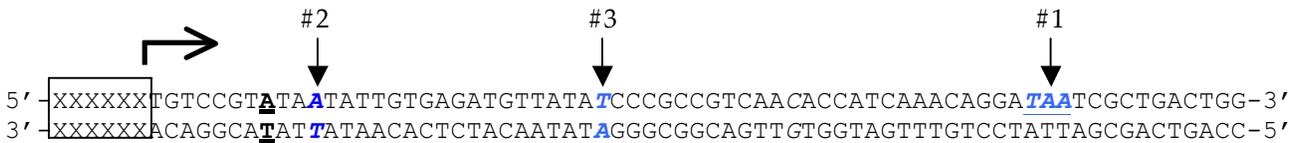


- i. Which of the above states (*condensed*/*loosened*) represents a replicating DNA molecule?
- ii. Which of the above states (*condensed*/*loosened*) represents the DNA that is being transcribed?
- iii. Which state (*condensed* / *loosened*) of chromatin would you expect to see in a cell that has been treated with DNA methylase that adds methyl groups to the cytosine bases in the promoter region of a gene? **Explain** why you selected this option.

*The chromatin will be in the condensed. So the promoter will not be available to bind to the RNA polymerase and other factors that are a part of the transcription initiation complex thus resulting in inhibited or reduced transcription i.e. transcription silencing.*

### Question 5

You are looking at the sequence of a eukaryotic gene that encodes a small peptide. Part of the promoter specific for this gene is indicated by the boxed sequence and the direction of transcription is shown by an arrow. Transcription starts at and includes the bold and underlined A/T (top strand/bottom strand) base pair.



a) Give the mRNA sequence of the first 15 bases transcribed from this gene and label its 5' and 3' ends.

5' AUAUUGUGAGAUGUU3'

b) Give the first five amino acids of the peptide that would be translated from the mRNA for this gene and label its N and C ends?

5' met- leu- tyr- pro- ala- C

c) Give the base sequence and label the 5' and the 3' ends of the anti-codon on the tRNA that inserts the 2nd amino acid into the nascent polypeptide.

The 2<sup>nd</sup> codon is 5'UUA3' so the corresponding anticodon on the tRNA should be 3'AAU3' and the codon – anticodon should undergo complementary base pairing.

d) Would a 3<sup>rd</sup> base substitution within the codon for the second amino acid in the above mRNA transcript always change the resulting protein sequence? **Explain** your answer.

No. Leucine is coded by six different codons. Any change in the third base of the codon would still result in leucine. In addition, if the first position has a change from U → C or C → U, the codons will still code of leucine.

e) Do the italicized and underlined nucleotides TAA (shown in blue and indicated as #1) correspond to a stop codon for the peptide that is encoded by this gene? Briefly **explain** your answer.

No, the TAA is not in frame so it does not correspond to a stop codon.

f) For each of the following mutations, indicate how the change in the DNA alters the resulting peptide as it compares to the normal functioning peptide. Your choices are: longer than, shorter than, of the same size but different sequence, or no change compared to the normal functioning peptide. For each, **explain** your answer.

- You add an extra G/C (top strand/bottom strand) base pair after the A/T base pair that is shown in blue, italicized and labeled as #2.

No change. The addition of the G/C base pair is upstream of the start of the first 5'AUG 3', so there will be no change in the peptide size or sequence.

- The T/A base pair, which is shown in blue, italicized and labeled as #3, is changed to a G/C base pair.

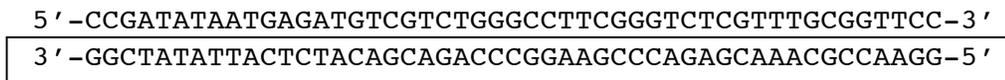
The addition of the T/A base pair results in a change from 5' UAU 3' to 5'UAG 3'. This results in a premature stop codon so the peptide will be truncated.

### Question 6

You are studying transcription in a plant whose leaves fluoresce blue in response to touch. You have the information that the TATA binding factor in this plant specifically binds to the 5'-TATAAT-3' sequence and recruits other components of the transcription apparatus to form a transcription initiation complex. Once RNA polymerase has bound to this region, it begins transcribing **from** the 25<sup>th</sup> nucleotide **downstream** of 5'-TATAAT-3' sequence.

a) You decide to examine the following **segments of chromosomal DNA** from this plant. For each of the sequences below **box** the template strand of the DNA.

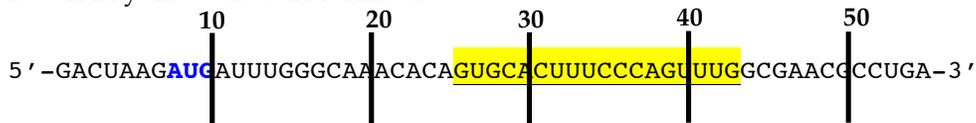
#### Chromosomal DNA segment I



#### Chromosomal DNA segment II



b) Following is an mRNA transcript that encodes a small peptide. The start codon is shown in blue and the intron is shown in yellow and underlined.



You create the following mutants. **Circle** the mutant from the choices below, which will generate a premature stop codon.

- The 6<sup>th</sup> base in the **above transcript** was changed from **A** to **U**.
- The 16<sup>th</sup> base in the **above transcript** was changed from **G** to **A**.
- The 12<sup>th</sup> base in the **above transcript** was changed from **U** to **C**.

c) The fidelity of transcription is far less compared to replication. **Explain** why is this so. Also **explain** why the cell can tolerate the errors in transcription much better than the errors in replication. *DNA polymerase has 3'-> 5' exonuclease activity that proofreads and repairs any mismatched base pair at the time of replication. If there is an error in replication, it gets repeated in all daughter cells and it results in incorrect mRNA transcripts and presumably a non-functional proteins. However, when a gene is transcribed many mRNA copies of the same mRNA transcripts are produced some of which may have errors. These transcripts are short-lived meaning that the error is not persistent. Besides, even if there are some transcripts with errors the remaining mRNA transcripts may produce protein that is sufficient for the normal functioning of the cell*

**Codon Chart (You can detach this page)**

	<b>U</b>	<b>C</b>	<b>A</b>	<b>G</b>
<b>U</b>	UUU Phe (F)	UCU Ser (S)	UAU Tyr (Y)	UGU Cys (C)
	UUC "	UCC "	UAC "	UGC "
	UUA Leu (L)	UCA "	UAA <b>Stop</b>	UGA <b>Stop</b>
	UUG "	UCG "	UAG <b>Stop</b>	UGG Trp (W)
<b>C</b>	CUU Leu (L)	CCU Pro (P)	CAU His (H)	CGU Arg (R)
	CUC "	CCC "	CAC "	CGC "
	CUA "	CCA "	CAA Gln (Q)	CGA "
	CUG "	CCG "	CAG "	CGG "
<b>A</b>	AUU Ile (I)	ACU Thr (T)	AAU Asn (N)	AGU Ser (S)
	AUC "	ACC "	AAC "	AGC "
	AUA "	ACA "	AAA Lys (K)	AGA Arg (R)
	<b>AUG</b> Met (M)	ACG "	AAG "	AGG "
<b>G</b>	GUU Val (V)	GCU Ala (A)	GAU Asp (D)	GGU Gly (G)
	GUC "	GCC "	GAC "	GGC "
	GUA "	GCA "	GAA Glu (E)	GGA "
	GUG "	GCG "	GAG "	GGG "

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