7.013 Problem Set 3- 2018

Question 1
Our hair color is determined by the relative amounts of two types of melanin pigment in hair follicles: **pheomelanin** (which promotes red or blond hair color) and **eumelanin** (which promotes black or brown hair color). In humans, the type of melanin produced depends on the activation of the melanocortin 1 receptor (MR-1), which triggers a series of chemical reactions within a cell that stimulates it to make eumelanin. However, if the MR-1 receptor is blocked or inactive, the cells can only make pheomelanin.

a) Represent the above information as a flowchart using -> for activation and –I for inhibition.

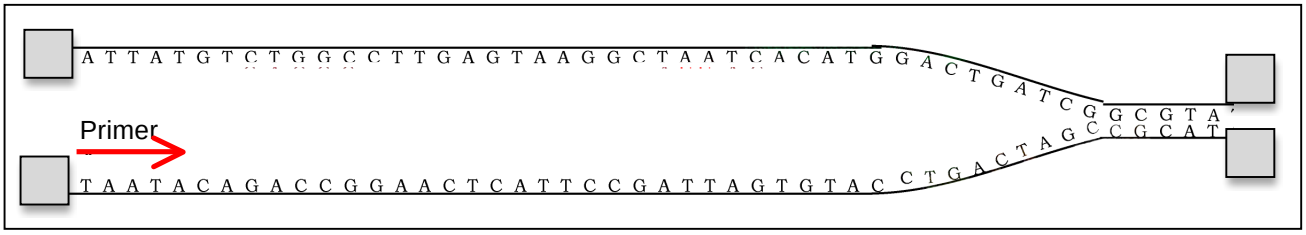
b) The *MR1* gene, on chromosome 16 codes the MR-1 receptor.

Beside DNA, which other class of macromolecules contributes to chromosome structure: **proteins/ lipids/ carbohydrates**? Identify the most likely **non-covalent interaction** between the sugar-phosphate backbone of DNA and the class of macromolecule that you identified.

i. Class of macromolecules: _____

ii. Likely non-covalent interaction: _____

The diagram below depicts a replication fork at one origin of replication site (ori) on Chromosome 16 in a cell undergoing DNA replication. **Note:** *The primer is shown by an arrow i.e. 5->3'.*



c) On the DNA diagram above, label the 5' and 3' ends of the template DNA strands by filling in the shaded boxes and show the direction of movement of the replication fork by an arrow.

d) Label the parental strands as the templates for **leading (continuous)** or **lagging (discontinuous)** strand synthesis.

e) Give the sequence of the five base long primer that is shown as an arrow in the diagram above:
5' _____3'

f) Give the sequence of the **next four bases** that would be added to the growing end of the primer: **5'**_____**3'**

g) Explain why **Sequence 2** shown to the right, is more likely the "**ori "** site as opposed to **Sequence 1**.

5′CGGGGACGCCGCGT3′
3′GCCCCTGCGGCGCA5′
Sequence 1

5′ATATATCGTTATAA3′
3′TATATAGCAATATT5′
Sequence 2

Question 1 continued

h) You grow the normal, healthy melanin producing cells in the presence of nutrients and the following compounds. ***Note:*** *For this question you may assume that these compounds are able to get into the cells.*

- **Plate 1** contains TA-65, a compound that prevents the shortening of chromosomes.
- **Plate 2** contains doxorubicin, a compound that promotes DNA supercoiling.
- **Plate 3** contains an RNAse inhibitor.
- **Plate 4** contains papilloma virus E1 protein that mimics the effects of DNA helicase.

For each plate, **explain** if the cells will be able to replicate their DNA.

Plate 1:

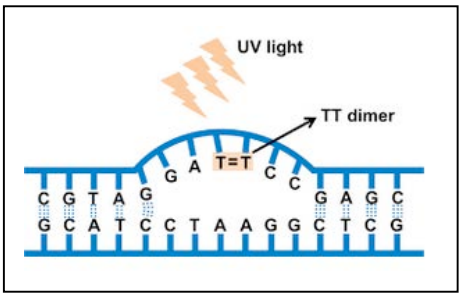
Plate 2:

Plate 3:

Plate 4:

Question 2

UV radiation from the sun or tanning salons can result in the formation of thymidine dimers (T-T) in the DNA of skin and hair follicle cells. These T-T dimers, if left unrepaired can result in rapid aging of skin, freckles and even melanoma (a form of skin cancer).



a) Which process will repair the T-T dimers: **DNA Proofreading/ mismatch repair/ Nucleotide excision repair**? **Explain** why you selected this process over the others.

b) Does the formation of T-T dimers impact the process of …

i. **Replication**? If so, how? **Note:** *Your explanations may vary.*

ii. **Transcription**? If so, how? **Note:** *Your explanation may vary.*

Question 2 continued

c) Once the T-T dimer has been removed…

i. Name the enzymes/ proteins that will elongate the DNA strand and seal the gap.

- **Enzyme elongating the DNA:** _____
- **Enzyme that seals the gap:** _____

ii. DNA ligase is required in all the processes listed below except one. Circle this process: **Replication/ Proofreading/ Mismatch repair/ Nucleotide excision repair.**

Question 3

The *MR-1* gene is comprised of four exons (Exon 1, 2, 3, and 4) that are each 1.5 kilo base (kb) long and three introns (Introns 1, 2, and 3) that are each 3kb long.

a) Based on the information provided, draw the *MR-1* gene in the box below. Label its 5' and 3' ends, draw and label the promoter, the transcription start and stop sites, exons 1-4 (as blank boxes) and introns 1-3 (as shaded boxes). ***Note:*** *The arrow in the schematic shows the direction of transcription.*

b) Draw the **nascent (pre-spliced/ newly synthesized) mRNA** transcribed from the *MR-1* gene. Label its 5' and 3' ends, exons 1-4 and introns 1-3. Label each splice donor site with a "D" and each splice acceptor site with an "A".

c) Assuming all introns are spliced out, give **all** the possible **mature (spliced) mRNA transcripts** resulting from the *MR-1* gene.

I. Label the 5' and 3' ends of each mature transcript.

II. Specify the exons that make the transcripts and give the size (in terms of kb) for each mature transcript.

III. List any modification(s) to the 5' and the 3' ends of the mature mRNA transcripts and **briefly describe** their significance.

Question 3 continued

d) Complete the table below. ***Note:*** For Column 3, choose from: *chromatin structure, transcription, splicing, mRNA stability, and translation. Please take a look at the information on eumelanin, pheomelanin and MR-1 provided thus far in the problem set.*

Alteration	**Hair color (*Red/ black*)?**	**Process/ feature that is the affected FIRST**
Histone proteins bound to the *MR-1* gene are phosphorylated		
Activating transcription factors (TF) that bind to the promoter region of *MR-1* gene are absent		
Promoter region of *MR-1* gene is NOT methylated		

Question 4

The following is the DNA sequence for the transcription initiation region of the *MR-1* gene. ***Note:*** *Part of the **promoter region** is boxed and the dashes represent bases that are not shown. Transcription **begins at and includes** the bold and underlined **T/A** base pair.*

5′--TGGACTGCTATGATAGCAGTTCTGCTGAGACGATGGCCATACGGCCATGG**T**TCATAAAGT----3′ **TOP**
3′--ACCTGACGATACTATCGTCAAGACGACTCTGCTACCGGTATGCCGGTACC**A**AGTATTTCA----5′**BOTTOM**

a) Identify the template strand for transcription: **Top / Bottom**?

b) Write the **first 6 nucleotides** of the newly transcribed *MR-1* mRNA: **5’**_____**3’**

c) Using the codon chart on the last page of this problem set, write the **first 3 amino acids** of the newly synthesized MR-1 receptor: **N-**_____**-C**

d) The last (C-terminal) **5 amino acids (296-300)** of the **wild-type** form of the **MR-1 receptor** are:
N –Val^{296}-Ser^{297}-Asn^{298}-Ser^{299}-Met^{300}- C

The DNA sequence encoding the C- terminus of the wild- type and mutant forms of the *MR-1* receptor is included within the sequence below. The **point mutations** in mutants 1 and 2 are bold & shaded and the stop codon is underlined. ***Note:*** *The codon table is provided on the last page of the problem set.*

Wild- type: 5′-TCGTATCGAATTCCATGTAGC-3′
3′-AGCATAGCTTAAGGTACATCG-5′

Mutant 1: 5′-TCGTAT**A**GAATTCCATGTAGC-3′
3′-AGCATA**T**CTTAAGGTACATCG-5′

Mutant 2: 5′-TCGTATCGAA**C**TCCATGTAGC-3′
3′-AGCATAGCTT**G**AGGTACATCG-5′

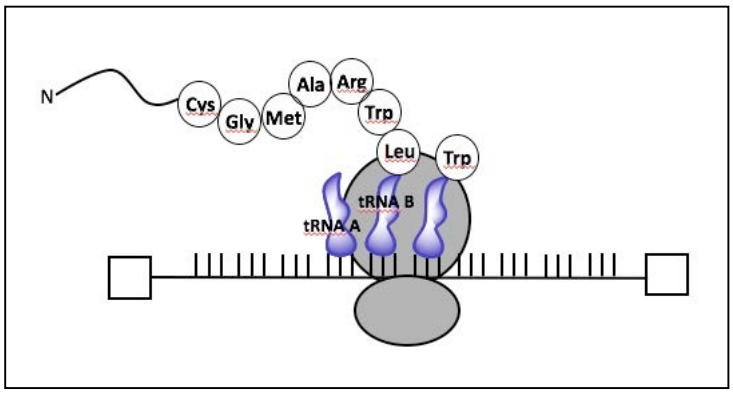
Compared to the wild- type, which mutant allele will most likely promote red hair color and **why**?

Question 4 continued

e) Approximately 5% of *MR-1* mRNA transcripts have errors relative to the *MR-1* gene sequence. However, a cell can still produce a normal concentration of functional MR-1 receptor. Why can a cell better tolerate mutations in mRNA compared to the mutations in DNA?

f) Your friend mentions that because you know the amino acid sequence of the MR-1 receptor, you can determine the length (in terms of base pairs) and the sequence of the *MR-1* gene. Do you agree with your friend? **Why or why not?**

g) Below is a drawing of a ribosome actively translating *MR-1* mRNA. The horizontal line represents the mRNA, each vertical line represents a base (A, U, G, C) and two tRNA molecules (tRNA A and tRNA B) are labeled and drawn in purple on the posted version of the problem set.



i. Draw an arrow to indicate the movement of mRNA relative to the ribosome during translation.

ii. Label the 5' and the 3' ends of the mRNA.

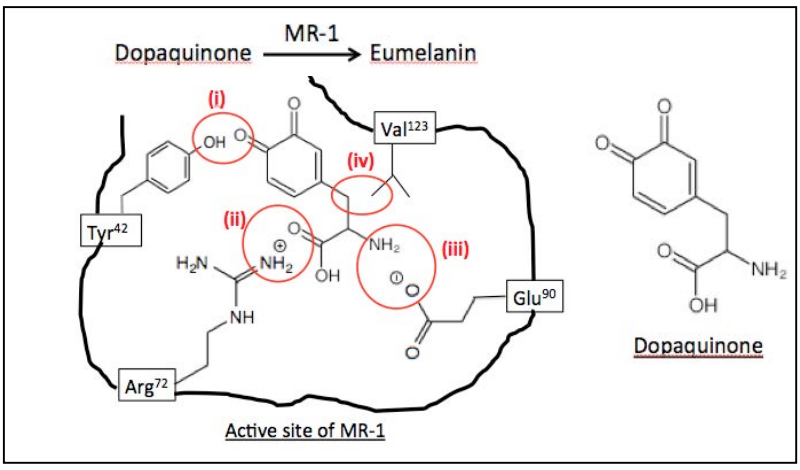
iii. Name the amino acid that was originally bound to **tRNA A**: _____

iv. Give the sequence of the anti-codon loop of **tRNA-Trp**: **5'**_____**3'**

Question 5

The MR-1 receptor catalyzes the conversion of dopaquinone to eumelanin as shown in the schematic below. ***Note:*** *Each circled interaction is critical for dopaquinone-MR-1 binding.*

a) For each position (i)–(iv), name the **non-covalent interactions** between MR-1 receptor and dopaquinone by choosing from ***ionic/ hydrogen/ hydrophobic interactions***



(i): _____

(ii): _____

(iii): _____

(iv): _____

Question 5 continued

You analyze both alleles of the *MR-1* gene in four individuals (1-4). Each of these individuals has a specific mutation in one or both alleles of the *MR-1* gene as specified in the table below. ***Note:*** *You should assume that the inheritance of the MR-1 gene shows an autosomal recessive mode. You can refer to the information at the beginning of Question 1 of this problem set.*

Individuals	Allele 1	Allele 2
1	5'UAU3' (Tyr) -> 5'UAG3' at (i)	Same as the wild-type
2	5'CGU3' (Arg) -> 5'CGG3' at (ii)	5'GAA3' **(Glu)** -> 5'GAG3' at (iii)
3	5'GAG3' (Glu) -> 5'AAG3' at (iii)	5'GUU3' (Val) -> 5'GCU3' at (iv)
4	Promoter sequence is highly methylated	5'UAU3' (Tyr) -> 5'UAG3' at (i)

b) Which of the above individuals are most likely to have black hair color and **why**?

c) Which of the above individuals are likely to be most sensitive to UV radiation and **why**?

CODON CHART

	U	C	A	G	
U	UUU **phe**	UCU **ser**	UAU **tyr**	UGU **cys**	U
	UUC **phe**	UCC **ser**	UAC **tyr**	UGC **cys**	C
	UUA **leu**	UCA **ser**	**UAA STOP**	**UGA STOP**	A
	UUG **leu**	UCG **ser**	**UAG STOP**	UGG **trp**	G
C	CUU **leu**	CCU **pro**	CAU **his**	CGU **arg**	U
	CUC **leu**	CCC **pro**	CAC **his**	CGC **arg**	C
	CUA **leu**	CCA **pro**	CAA **gln**	CGA **arg**	A
	CUG **leu**	CCG **pro**	CAG **gln**	CGG **arg**	G
A	AUU **ile**	ACU **thr**	AAU **asn**	AGU **ser**	U
	AUC **ile**	ACC **thr**	AAC **asn**	AGC **ser**	C
	AUA **ile**	ACA **thr**	AAA **lys**	AGA **arg**	A
	AUG met	ACG **thr**	AAG **lys**	AGG **arg**	G
G	GUU **val**	GCU **ala**	GAU **asp**	GGU **gly**	U
	GUC **val**	GCC **ala**	GAC **asp**	GGC **gly**	C
	GUA **val**	GCA **ala**	GAA **glu**	GGA **gly**	A
	GUG **val**	GCG **ala**	GAG **glu**	GGG **gly**	G

7.013 Introductory Biology

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