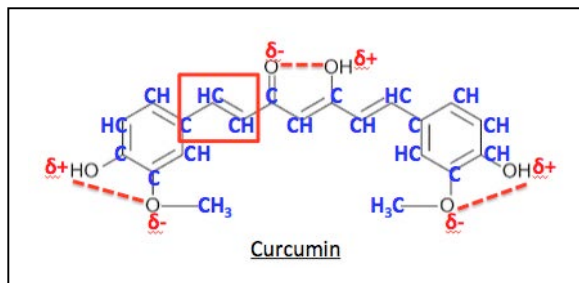


## Solution key- 7.013 EXAM 1

### Question 1 (14 points)

Anemia is a very common condition in which the body does not have sufficient number of red blood cells (RBC) or hemoglobin protein (Hb). The following is the line angle drawing of **curcumin**, an ingredient derived from turmeric plant, which is often given to patients with pernicious anemia (PA).



a) Clearly write in the position of **ALL** carbon (C) and hydrogen (H) atoms that are implied in the line angle drawing. (4pts, 2 for all Cs and 2 for Hs)

b) Circle an **intramolecular hydrogen bond** (an H-bond within the curcumin molecule) and label the proton donor (as  $\delta^+$ ) and proton acceptor (as  $\delta^-$ ) on the appropriate atoms of the circled groups. (4pts, 2 for the

bonds and 2 for the dipoles, any OH bond is fine)

c) Explain, in terms of the possible non-covalent interaction, why curcumin dissolves in water.

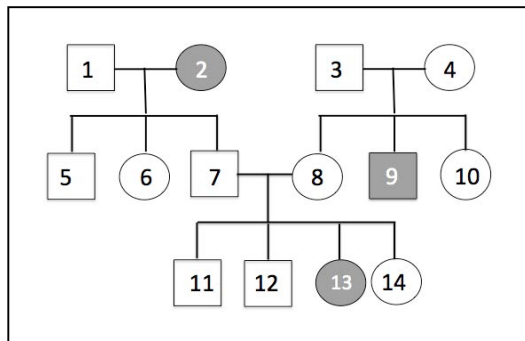
*Curcumin has multiple hydroxyl group that can hydrogen bond with the surrounding water molecules allowing it to dissolve in water. (2pts, 1 for the concept of polarity of OH groups and 1 for H bonds with HOH)*

d) What does the boxed region in the line angle drawing above represent: **saturated or unsaturated** hydrocarbons? Explain why you selected this option.

*This represents an unsaturated hydrocarbon since all the carbons are not saturated by the hydrogens i.e. there is a double bond present between two carbons. (4pts, 2 for unsaturated & 2 for explanation)*

### Question 2 (14 points)

The following pedigree represents the mode of inheritance of a juvenile form of PA. **Note:** The circles represent females and squares represent males. Filled squares or circles represent PA patients. Assume that no other mutation arises within the pedigree. Assume complete penetrance.



a) Give the mode of inheritance of juvenile PA:

*Autosomal recessive (4pts)*

b) Give all the possible genotypes of **Individual 11** using "A" for the allele regulating the dominant phenotype and "a" for the allele regulating the recessive phenotype.

*Aa or AA (4pts)*

c) Individual 10 marries a male who has the same genotype as Individual 7. Together they have a son.

i. What is the probability that their son will have the same genotype as his father? **Show your work.**

*#10 can either have the genotype AA (probability= 1/3) or Aa (probability= 2/3). But her partner will be a carrier (genotype= Aa). If #10 is carriers, the probability of the son having the genotype Aa is 2. If #10 has the genotype AA the probability is 1/2. Taken together the probability is  $1/3 \times 1/2 + 2/3 \times 1/2 = 1/6 + 1/3 = 3/6$  or  $1/2$ . (4pts)*

ii. If their son has juvenile PA what is the probability that their second child will have juvenile PA? *Then #10 has the genotype Aa and NOT AA. So the probability is 1/4. (2pts)*

### Question 3 (24 points)

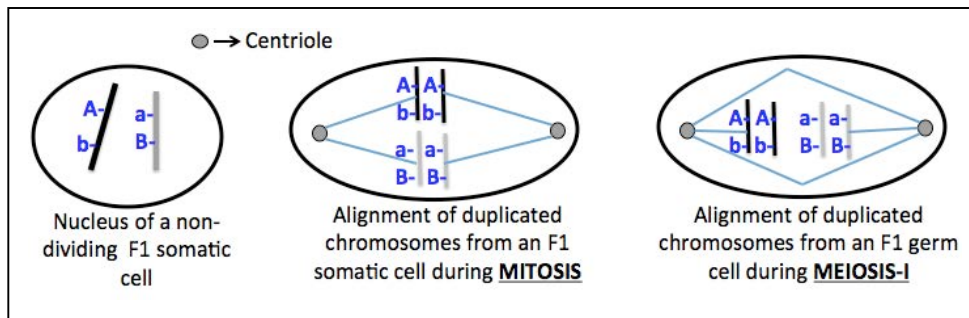
You decide to study two traits in a variety of turmeric plant: **powdered root color (regulated by autosomal Gene A)** and **taste (regulated by autosomal Gene B)**.

You cross true breeding **P1 (yellow powdered roots that taste sweet)** and **P2 (white powdered roots that taste bitter)** and obtain F1 plants (**yellow powdered roots that taste bitter**) Give the genotypes of the following plants for both traits, using "A" and "B" for the alleles regulating the dominant phenotype and "a" and "b" for the alleles regulating the recessive phenotypes.

a) Fill in the **genotypes of P1, P2 and F1** plants.

- i. Genotype of P1 (yellow powdered roots that taste sweet): ***AAbb*** (2pts)
- ii. Genotype of P2 (white powdered roots that taste bitter): ***aaBB*** (2pts)
- iii. Genotype of F1 (yellow powder roots that taste bitter): ***Ab/aB*** (2pts)

b) Assume that Gene A and Gene B are located on the **same** autosome. In the diagram below, draw in the configuration of alleles of Gene A and Gene B for the following. (6pts: 2 for each diagram)



c) You cross an **F1 progeny (yellow powdered roots that taste bitter)** with another plant that gives **white powdered roots that taste sweet**. If Gene A and Gene B are **10cM** apart ...

- i. Complete the table below for each class of F2 plants (Total = 100). (8pts, 2 for each)
- ii. Circle the non-recombinant / parental classes in the F2 generation in the table. (2pts, 1 each)

| Genotypes?   | Corresponding phenotype?                   | Estimated numbers? |
|--------------|--|--------------------|
| <i>Ab/ab</i> | <i>Yellow powdered roots/ sweet taste</i>  | 45                 |
| <i>aB/ab</i> | <i>White powdered roots/ bitter taste</i>  | 45                 |
| <i>ab/ab</i> | <i>White powdered roots/ sweet taste</i>   | 5                  |
| <i>AB/ab</i> | <i>Yellow powdered roots/ bitter taste</i> | 5                  |

d) You also want to study Gene D in the same plant variety. Experiment shows that Gene A in this variety of turmeric plant is completely linked to Gene D. You cross a P1 plant (genotype: AADD) with P2 plant (genotype: aadd) to get an F1 plant (Genotype AaDd). If you cross two F1 plants, what would be the genotypes and corresponding ratios of the plants in F2? (2pts, 1 for each part)

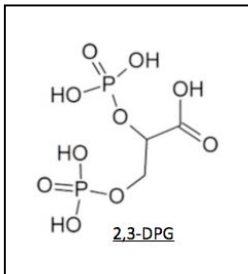
- i. Genotypes: ***AADD*** (1): ***AD/ad*** (2): ***ad/ad*** (1)
- ii. Expected genotype ratios: ***1 : 2 : 1*** as shown above

#### Question 4 (22 points)

Hemoglobin protein (Hb) is found in mature RBC.

a) The Hb has two  $\alpha$  and two  $\beta$ - globin polypeptide chains. What is the highest order of protein structure for the Hb tetramer: **primary/ secondary/ tertiary/ quaternary**? (2pts)

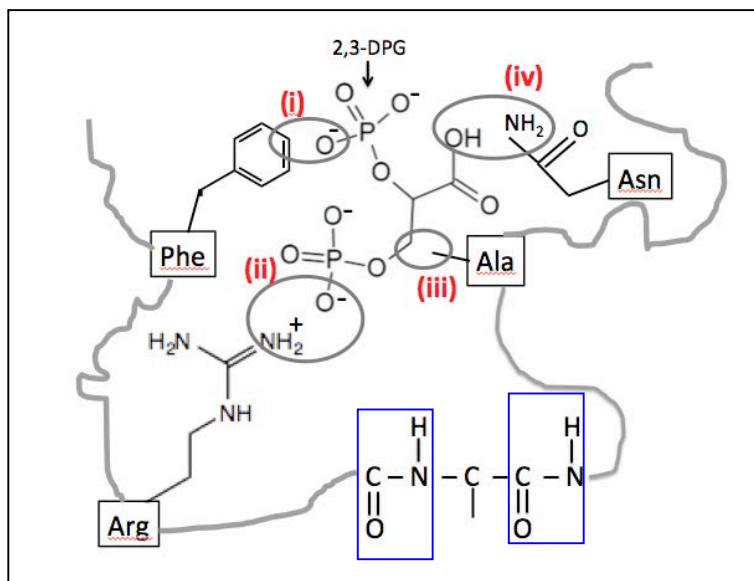
b) Each globin chain binds reversibly to one oxygen molecule ( $O_2$ ) to form oxyhemoglobin (Oxy-Hb). Experiments show that the **non-covalent binding** of 2,3-diphosphoglycerate (2,3-DPG) prevents the binding of Hb to  $O_2$ . Furthermore, increasing the concentration of  $O_2$  cannot reverse the effect of 2,3-DPG.



Based on this observation, would you classify 2,3-DPG as a **competitive/ uncompetitive/ allosteric/ reversible** irreversible inhibitor of Hb? Circle **all** that apply and **explain** why you selected these options.

*It is reversible since its binding to the Hb is non-covalent. It does not bind to Hb-O<sub>2</sub> complex, so it is not uncompetitive. Increasing the O<sub>2</sub> concentration cannot reverse the binding of 2,3DPG to Hb. Instead to a site on Hb that is different from its O<sub>2</sub> binding site to change the conformation of Hb. This makes it an allosteric inhibitor. (4pts, 2 for each with explanation)*

c) The binding of 2,3-DPG to Hb protein is shown below. **Note:** Each circled interaction is critical for 2,3-DPG mediated inhibition of Hb.



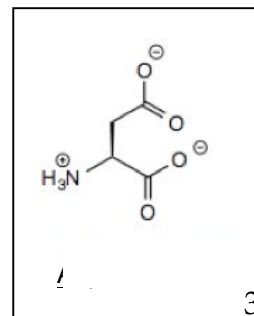
i. For each of the positions below, write the **strongest non-covalent interaction** between 2,3-DPG and Hb protein by choosing from the *hydrogen bond/ ionic interaction/ VDW forces/ hydrophobic interaction*. (8pts, 2 each)

- Position (i): VDW forces
- Position (ii): Ionic interaction
- Position (iii): Hydrophobic
- Position (iv): Hydrogen bond

ii. **Box all peptide bonds** on the drawing. (2pts, 1 each)

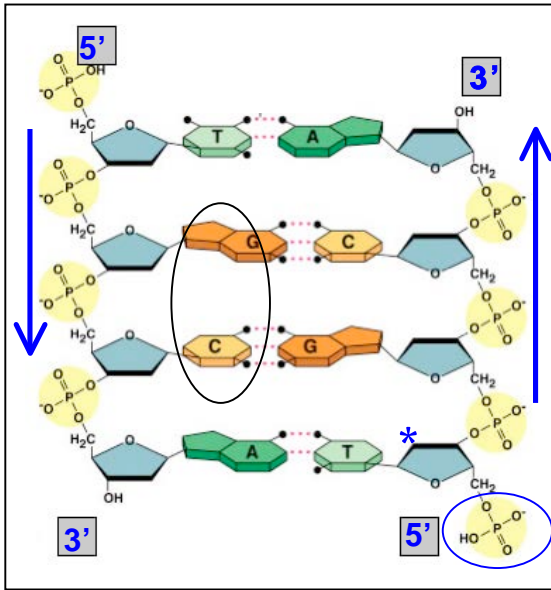
iii. In the diagram above, which amino acid was first added to the globin chain as it was being translated from the globin mRNA: **Phe or Asn**? Provide an **explanation** for selecting this amino acid. *Based on the orientation of the peptide bonds, the Phe is closer to the N terminus and Asn is closer to the C terminus of the Hb polypeptide chain that is shown. So the Phe must have been added first to the primary structure of the globin chain. (3pts)*

d) You identify a mutant version of globin chain in a PA patient where the Arg shown in the diagram in part (c) is replaced by Aspartic acid. Would the Hb protein in this patient be able to transport  $O_2$  even in the presence of 2,3-DPG? **Why or why not?** *The Aspartic acid has a negatively charged side-chain unlike Arg at position (ii) in the diagram above, so it will repel 2, 3DPG and prevent it from binding to the globin chain. So this mutant version of globin chain will bind to  $O_2$  even in the presence of 2, 3 DPG. (3pts)*



### Question 5 (12 points)

Below is a small portion of the gene that encodes the Globin chain of Hb protein. On the drawing...



a) Label the 5' and 3' ends by filling in the shaded boxes.

b) Show the direction of synthesis of each strand by drawing arrows.

c) To which end would the incoming nucleotide be added: 3' or 5'? **3' OH end**

d) Circle the group that may interact with the histone proteins that are rich in amino acids with positively charged side-chains.

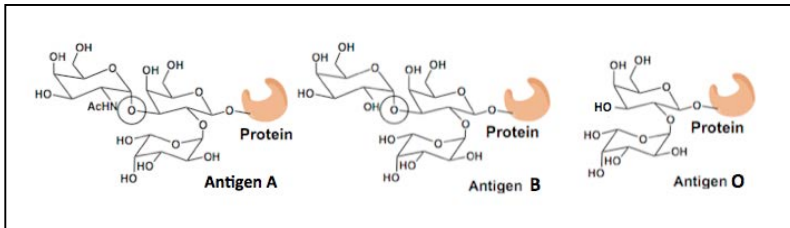
e) Put a "star" next to the carbon atom of the sugar that would differ between the nucleotides of DNA and RNA.

f) Name the circled non-covalent interactions between the bases of a DNA strand: **Hydrophobic interaction**  
(12pts total, 2points each)

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### Question 6 (14 points)

PA patients often need blood transfusions. We have four major blood groups based on the type of antigen located on the surface of circulating RBCs: Type A, Type B, Type O (universal donor) and Type AB (universal acceptor). The structure of A, B and O antigens are shown below. Matching blood groups is critical for successful blood transfusions.



a) Classify Antigens A/ B/ O as: **lipids/ carbohydrates/ proteins/ Nucleic acid.** (1pt)

b) Name an organelle where the antigens A/ B/ O would be covalently linked to the protein: **Golgi/ ER** (1pt)

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c) You want to use a specific enzyme(s) in order to hydrolyze the circled bonds in antigens A and B. Assuming that the hydrolysis reaction catalyzed by the enzyme has a  $\Delta G = -4 \text{ kcal/mole}$ , classify this reaction as **endergonic or exergonic** and **explain** why you selected this option.

*Here the energy of the substrate is more than the energy of the product as shown by the  $\Delta G = -4 \text{ kcal/mole}$  (4pts, 2 for option and 2 for explanation)*

d) Propose a mechanism that allows the enzyme to generate the transition state (TS) complex and **explain** why generating TS complex is critical for the reaction.

*The enzyme may change the orientation of the substrates to promote their interaction with each other, they may induce constrain on the substrates, they may temporarily add a group to the substrate to promote the transition state. The TS complex is unstable, so it will try to change into product that has the low free energy and is therefore stable. (4pts, 2 for mechanism and 2 for explanation)*

e) Assuming you are successful in hydrolyzing only the circled bonds, can you give the modified RBCs to patient of any blood type type? **Why or why not?**

*Yes, since this would produce Antigen O as the product of the hydrolysis reaction, which is a universal donor. (4pts, for the explanation)*

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Spring 2018

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