

## SSSS Protein Modeling TEST

By: Clements HS

Instructions to participants:

This exam is divided into 4 sections. You will have 45 minutes to complete this test. This test is completely free-response to better test your understanding of these concepts. Due to this, partial credit will be awarded for questions with point values greater than 1.

Section 1: Biochemistry(35%) - 25 points

- Covers protein structure and folding
- Biological principles of proteins
- Biotechnology

Section 2: CRISPR(20%) - 12 points

- CRISPR in bacterial immunity
- CRISPR-cas9 engineering
- Types of CRISPR

Section 3: Cytidine Deaminase (15%) - 8 points

- Cytidine Deaminase function

Section 4: Jmol Exploration(30%) - 15 points

## Part 1: Biochemistry

1. How do proteins maximize the strength of their hydrophobic interactions? (2 pts)
2. What two amino acids don't form alpha helices easily and why? (1 pt)
3. How many amino acids residues are there per turn of an alpha helix? How many angstroms in width is this? (1 pts)
4. How does hydrogen bonding in an alpha helix work? Draw a picture or explain in words. (1 pt)
5. What amino acid has the highest tendency to form a helix? (1 pt)
6. Which 2 amino acids are solely ketogenic? (1 pts)
7. What types of amino acids are found in the middle of Beta-sheets? (1 pt)
8. What is the relationship between  $K_a$  and  $K_d$ ? What is the relationship between  $K_d$  and the affinity of ligands for a protein? (2 pts)
9. How do enzymes catalyze reactions effectively? (2 points)
10. Derive the Michaelis-Menten equation. Hint - use the steady-state assumption as a starting point. (3 points)

11. Draw a titration curve for histidine. Designate the  $pK_1$ ,  $pK_2$ ,  $pK_3$ , and  $pI$ . (3 pts)

12. RNA and DNA are two important nucleic acids in eukaryotes. However, they differ in a considerable number of ways.

a) Identify how the sugar ribose differs from deoxyribose. (1 pt)

b) What are the implications of this difference in structure with regards to stability of both of these molecules? (2 pts)

c) Describe the reaction mechanism by which the process in (b) occurs. If you would like you can draw a picture or you may describe this process in words. (2 pts)

d) What amino acids preferentially bind to DNA and what structures are they commonly found in? (2 pts)

## Part 2: CRISPR

1. Where is CRISPR-CAS9 naturally found and what is its purpose? (1 pt)
2. What is the PAM sequence and why is it important? (1 pt)
3. What are the two possible repair pathways that might be activated after Cas9 cleaves the DNA? (2 pts)
4. What is the signature gene of the three most important types of CRISPR- Cas systems?(1.5 pts)
5. Name and explain the mechanism behind two other gene editing techniques other than CRISPR(3 points)
6. What are the two nucleases involved in DNA Repair? (1pt)

7. What is AcrII-A4 and what is its function in regards to CRISPR and genome editing? (2.5 pts)

### **Part 3: Cytidine Deaminase**

1. How does APOBEC3G cause a 5-methylcytosine to thymine mutation? (1 pt)

2. Is the APOBEC3 family part of the adaptive or innate immune system? What is their specific role? (2 pt)

3. What is the role of APOBEC1? (1 pt)

4. What compounds are formed by the deaminase of cytidine/deoxycytidine?(1 pt)

5. What is the function of the catalytic zinc section of the APOBEC3 protein? (2 pts)

6. Targeting the APOBEC3A and APOBEC3B offer promising treatments for aggressive cancers. Out of those two proteins, which one is able to cause mutations at a higher rate? What are two plausible ways to treat cancers in regards to APOBEC3A and APOBEC3B expression?

#### Part 4: Jmol Exploration

Directions: Use Jmol to explore the crystal structure of nanobody D3-L11 mutant Y102A in complex with hen egg-white lysozyme (form II) [6jb5.pdb]

1. The following questions refer to the entire structure [3 pts]
  - a. How many hydrophobic atoms are in this structure? (0.5 pts)
  - b. How many polar atoms are in this structure? (0.5 pts)
  - c. How many atoms are selected when the structure is restricted to water molecules? (0.5 pts)
  - d. How many chains are present in the structure? (0.5 pts)
  - e. How many atoms are selected when the structure is restricted to nucleic acids? (0.5 pts)
  - f. How many struts are in the structure? (0.5 pts)
2. The following questions refer to residue 35 of chain A [1.5 pts]
  - a. What is the one letter abbreviation of this amino acid? (0.5 pts)
  - b. What is the chemical formula of this amino acid? (0.5 pts)
  - c. How many chiral centers does this amino acid have? (0.5 pts)
3. The following questions refer to residue 23 of chain A [2 pts]
  - a. What is the full name of this amino acid? (0.5 pts)
  - b. Is the R-group of this amino acid aromatic or aliphatic? (0.5 pts)
  - c. Draw and label the two isomers of this amino acid (1 pt)
  
4. The following questions refer to residue 100 of chain A [1 pt]
  - a. What is the full name of this amino acid? (0.5 pts)
  - b. True or False: The positional variability of atom #787 is greater than that of atom #777. (0.5 pts)
5. The following questions refer to chain B [2.5 pts]
  - a. How many hydrogen bonds are in chain B? (0.5 pts)
  - b. How many atoms are in sheets? (0.5 pts)
  - c. How many 310 helices are present? (0.5 pts)
  - d. What ligands are present? List both the abbreviated ID and the name of the ligands. (1 pt)
6. What is the default color for sodium? (1 pt)

7. What is measured by an atom's "temperature factor"? What command would be used to color a structure's atoms based on their "temperature factor"? (2 pts)
8. What do struts represent? (1 pt)
9. What are disulfide bonds referred to in Jmol? (1 pt)