Protein Modeling Event

School Name: _____

School Number: _____

Team Member 1: _____

Team Member 2: _____

Team Member 3: _____

For Judges Use Only:	
Pre-Build Score:	
On-Site Build Score:	
Test Score:	
Tie Breaker:	
Total:	
Final Rank:	

Part I: Pre-Build (40% of total score)

Your Pre-Build Model should have been impounded the morning of the competition. You may pick up your Pre-Build model at the end of the competition after all models have been scored. **Please pick up your model no later than 4pm.** Unclaimed models will be thrown away.

Part 2: On-Site-Build (30% of total score)

The workstation should have the On-Site Model Competition Environment open on the computer. Using the 348cm Mini-Toober provided, construct a model of the MHC – amino acids 1-174 of chain A of 1hsa.pdb. The scale should be 2 cm per amino acid. A meter stick/ruler has been provided for you. Your Mini-Toober model of amino acids 1-174 of chain A of 1hsa.pdb should include the following:

A: Two amino acids: Cys101 and Cys164 (use metal clips to connect amino acids to your Mini-Toober)

B: Blue end cap indicating the amino terminus (N-terminal end) of this region (amino acids 1-174)

C: Red end cap indicating the carboxylic acid terminus (C-terminal end) of this region (amino acids 1-174)

Part 3: On-Site Exam (30% of total score)

The On-Site Exam consists of both multiple choice and short answer questions. You may use any materials provided at your work station as well as the five sheets you brought with you to answer these questions. You may NOT use the Internet to answer these questions.

There are ten multiple choice questions in the On-Site Exam (each worth 1 point for a total of 10 points). Clearly print the letter of the one BEST answer to each question in the blank provided for that question. Illegible answers will be incorrect.

There are also short answer questions in the On-Site Exam. The point value for each question is given in parentheses at the end of the question (20 pts total). The points for the tie-breaker questions (identified with ★ Tie Breaker) will be included in the final score but may be used to determine team placement in case of a tie.

On-Site-Exam

Multiple Choice Questions:

D 1. Which of the following amino acids contains an imidazole group?

A. Arginine (Arg)
B. Glutamic Acid (Glu)
C. Tryptophan (Trp)
D. Histidine (His)

A 2. Caspases cleave in a very specific location. Which of the following sequences of amino acids (using the one letter abbreviations) would be a potential substrate for caspase catalytic activity?

A. AFGHDQRTPK
B. QEFGALKPIVE
C. MERTSHGEQP
D. ASMTHKLRCV

C 3. In order to determine the cause of Nic Volker's symptoms, the doctors…

A. …sequenced all of the proteins within Nic's cells.
B. …sequenced Nic's genome.
C. …sequenced Nic's exome.
D. …sequenced the introns in Nic's DNA.

B 4. Which group of the 2nd amino acid is used to form its hydrogen bond in an alpha helix?

A. N-H
B. C=O
C. C-H
D. Sidechain

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B 5. Which of the following proteins is a target of caspase function?

A. Diablo
B. PARP
C. XIAP
D. MHC

A 6. Which two amino acids are involved in the catalytic activity of caspase-3?

A. Histidine (His) and Cysteine (Cys)
B. Histidine (His) and Aspartic Acid (Asp)
C. Cysteine (Cys) and Glycine (Gly)
D. Glutamic Acid (Glu) and Serine (Ser)

C 7. Which of the following characteristics describes necrosis?

A. Shrinking of cytoplasm
B. Condensation of nucleus
C. Loss of membrane integrity
D. Fragmentation of cell

B 8. Which amino acids are involved in stabilizing the transition state of the caspase-3/substrate complex?

A. Histidine (His) and Cysteine (Cys)
B. Cysteine (Cys) and Glycine (Gly)
C. Glycine (Gly) and Histidine (His)
D. Cysteine (Cys) and Aspartic Acid (Asp)

A 9. What is the name of the chemical reaction that catalyzes the cleavage of a peptide bond?

A. Amide Hydrolysis
B. Oxidation-Reduction Reaction
C. Substitution Reaction
D. Dehydration Synthesis

C 10. For your onsite model, you positioned two cysteines. What is the significance of these two amino acids in terms of structure and/or function of MHC?

A. The cysteines form the active site for the protease activity of the MHC protein.
B. The cysteines stabilize the interaction between caspase and MHC.
C. The cysteines form a disulfide bond that stabilizes the MHC structure.
D. The cysteines form the binding site for the substrate interacting with MHC.

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Short Answer Questions:

1. Sequencing Nic Volker's genome identified a mutation in the XIAP protein. (4 pts)

   What is the mutation at the DNA level? (1 pt)

   G→A

   What impact does this have on the amino acid sequence? (1 pt)

   Changes a cysteine to a tyrosine

   What is the functional significance of this mutation at the protein level? (2 pts)

   XIAP has a zinc finger motif, stabilizing the protein. (0.5 pt) The zinc ion is held in place by critical cysteine and Histidine amino acids. (0.5 pts) One of the cysteines is mutated in Nic's XIAP sequence. The mutation changes a cysteine to a tyrosine, a much larger amino acid. (0.5 pts) Tyrosine does not interact with zinc, and it may cause a structural defect due to the difference in size from Cysteine to Tyrosine. (0.5 pts)

2. For both a non-apoptotic and an apoptotic cell, describe the function, activity level, location and any protein interactions for the following proteins: Diablo, XIAP, Caspase, and PARP. (4 pts) ★ Tie Breaker

   Non-apoptotic Cell (2 pts)

   Caspase and XIAP are located in the cytoplasm of the cell. XIAP is bound to caspase, thus inhibiting the function of caspase. (1 pt)
   Diablo is sequestered in the mitochondria, and is not functional. (0.5 pts)
   PARP functions normally in the nucleus, detecting problems with the DNA and initiating repair as needed. (0.5 pts)

   Apoptotic Cell (2 pts)

   Diablo is released from the mitochondria after a signal has been given. (0.5 pts)
   Diablo binds to XIAP, thus breaking the interaction between XIAP and Caspase. (0.5 pts)
   Caspase is now active. (0.5 pts)
   Caspase can cleave PARP, thus inhibiting PARP's ability to repair DNA. (0.5 pts)

3. Caspases exist within our cells, poised to initiate the apoptotic response under appropriate conditions.

What is the inactive form of the caspase called?

Zymogen (1 pt)

What is the advantage to having this inactive form of caspase present within the cell? (3 pts)

With the zymogen form of the protein present within the cell, the activation process is much faster (1 pt). When a cell is responding to a signal to initiate the apoptosis process, a cleavage event to activate the zymogen form (1 pt) is a much quicker response, rather than needing to transcribe and translate a new protein in response to a signal (1 pt). If the protein is currently present in the cytoplasm, as the precursor form, a response will be faster than having to create the protein de novo.

4. In order to sequence Nic Volker's DNA, researchers used a technique called "Emulsion PCR" to create "hairy beads". This technique revolutionized the speed at which DNA sequencing was done. (4 pts) ★ Tie Breaker

How is emulsion PCR different from traditional, or standard, PCR? (2 pts)

The PCR reaction itself is the same in emulsion PCR as it is in standard PCR. The difference is that the reaction takes place in a water droplet that is suspended in an oil/water emulsion (0.5 pts). Each droplet is functionally equivalent to a test tube, or a well in a 96-well plate. Since a 100 µl drop emulsion might contain thousands of water droplets, this is equivalent to performing several thousand separate PCR reactions, in just one tube. (0.5 pts)

Each droplet of water contains one bead, with a single fragment of the DNA being sequenced attached to it. The other factors needed for the reaction (dNTPs, Taq polymerase and buffer components to support the reaction are included in the droplet as well (0.5 pts). As additional copies of the original DNA fragment are synthesized/polymerized (the DNA is amplified), they become bound to the bead as well, generating a "hairy bead" containing several thousand copies of the identical DNA fragment. (0.5 pts)

How does this technique enable the Next-Generation sequencing technology used to sequence Nic Volker's DNA? (2 pts)

The hairy beads generated by the emulsion PCR are passed over a slide containing a regular array of picoliter-sized wells, each one large enough to accommodate one (but not two) hairy bead. (0.5 pts) Even smaller beads are added to the well, trapping the one hairy bead in each well. The smaller beads are coated with enzymes that work together to generate light in the well every time a nucleotide is added to the end of the DNA that is being synthesized within the well. (0.5 pts) The light that is generated in each well by the combined action of the enzymes coating the smaller beads is detected by a camera and recording to determine the sequence of the DNA on each hairy bead. (1 pt)

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5. Why is it critical to match MHC types prior to a tissue transplant? (4 pts)

MHC molecules play a critical role in the immune system. These proteins are responsible for "displaying" antigens to the immune cells (T helper and cytotoxic T cells). (0.5 pts) These displayed antigens are then determined to be "self" or "non-self". (0.5 pts) If "self", nothing happens. (0.5 pts) If "non-self", the body mounts an immune response to the invading pathogen. (0.5 pts)

In a tissue transplant, the MHC molecules on the transplanted tissue could be potential antigens (foreign bodies to the host) and therefore, in order to minimize the risk of rejection, tissue typing is done to find a donor with the most similarities in the MHC molecules (1 pt). If the MHC molecules are too different, the host system will see the new MHC molecules as non-self, and mount an immune response against the tissues, thus leading to rejection of the organ. (1 pt)