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 1: 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 152cm Mini-Toober provided, construct a model of the Cas9 – amino acids 1263-1339 of chain B of 4un3.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 1263-1339 of chain B of 4un3.pdb should include the following:

A: Four amino acids: Ile1270, Phe1324, Arg1333 and Arg1335 (use 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 1263-1339)

C: Red end cap indicating the carboxylic acid terminus (C-terminal end) of this region (amino acids 1263-1339)

**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.
Multiple Choice Questions:

1. Which of the following amino acids contains an imidazole ring?
   A. Proline (Pro)
   B. Tyrosine (Tyr)
   C. Tryptophan (Trp)
   D. Histidine (His)

2. The CRISPR-Cas9 system in bacteria is akin to our body’s
   A. Digestive system
   B. Immune system
   C. Circulatory system
   D. Respiratory system

3. CRISPR refers to repeated sequences located in the
   A. Bacterial DNA
   B. Viral DNA
   C. Fungal DNA
   D. Viral RNA

4. As proteins fold, amino acids with carbon-rich sidechains, like leucine and phenylalanine, are usually placed
   A. on the surface of the protein
   B. inside the protein
   C. near positively charged residues
   D. near polar residues

5. Which of the following proteins have not been used in genome editing?
   A. ZFN
   B. TALENs
   C. CRISPR-Cas9
   D. MHC
6. The Berlin Patient inspired which of the following strategies for treating HIV infection?

A. Disrupting the CCR5 gene  
B. Blocking viral entry by interfering with the CD4-gp120 interaction  
C. Blocking integration of proviral DNA into the host cell genome  
D. Mimicking the reverse transcriptase enzyme substrate and binding to the active site

7. To direct a nuclease to a statistically unique DNA sequence on the human genome, it must be able to recognize a sequence that is at least

A. 10 base pairs long  
B. 16 base pairs long  
C. 32 base pairs long  
D. 5 base pairs long

8. The CRISPR sequences are recognized by

A. Zinc finger domains  
B. TALE repeats  
C. Guide RNA  
D. Leucine zippers

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

A. Oxidation  
B. Reduction  
C. Dehydration  
D. Hydrolysis

10. Which of the following statements is NOT true about the FokI enzyme:

A. It is a bacterial restriction endonuclease  
B. It recognizes specific DNA sequences and makes single stranded breaks  
C. It is derived from *Flavobacterium okeanokoites*  
D. It has DNA binding and nuclease domains
1. The CRISPR associated protein Cas9 is now being used as a molecular tool for genome editing. (4 pts)

   “CRISPR” is an acronym for what phrase? (1pt)

   What is the role of Cas9 in genome editing? (2pts)

   In a cell, what happens to a gene that has been cut by a genome editing system? (1 pt)

2. The structure of Cas9 that you are modeling on-site includes a target DNA strand, non-target DNA strand and guide RNA. (4 pts) ★ Tie Breaker

   How is the guide RNA made and what role does it play in this gene-editing method? (2 pts)

   What is the difference between the structures of DNA and RNA sugars? (1pt)

   What is the difference between the DNA and RNA bases? (1 pt)

3. Genome editing requires bio-molecular tools to specifically recognize a target sequence on the genome and cut it in a precise way. (4 pts)

   List 2 molecular tools other than the CRISPR Cas9 system that are available for genome editing. (2 pts)

   In what way is the CRISPR-Cas9 system different from the genome editing tools listed above (1 pt)

   The Cas9 protein needs to be engineered to add a specific signal so that it can be transported into the nucleus. What is this signal called? (1 pt)
4. Four amino acid side chains -- Arg1333, Arg1335, Phe1324 and Ile1270 -- were added to your on-site model of a region of the Cas9 protein. (4 pts) ★ Tie Breaker

How might Phe1324 and Ile1270 contribute to the structure and function of the Cas9 protein? (2 pts)

How do Arg1333 and Arg1335 contribute to the structure and function of the Cas9 protein? (2 pts)

5. In the last three decades, a number of different strategies have been developed to treat HIV infection. Current research is focused on finding cures and a vaccine against HIV (4 pts).

The current FDA approved drugs to treat HIV disrupt the HIV life cycle. Name three HIV Viral Enzymes that are targeted by these drugs. (1.5 pts)

Name two other types of drugs used to treat HIV and describe how each of these currently approved classes of drugs block the HIV life cycle. (1 pt)

List one genome editing approach and its target that is currently being tested for providing a functional cure for HIV infection and explain how it works. (0.5 pts)

List one genome editing approach and its target that can completely cure an HIV infection. (1 pt)