PROTEIN MODELING

1. **DESCRIPTION:** Participants will use computer visualization and online resources to construct a physical model of a protein that is being used with CRISPR Cas9 to edit plant and animal genomes. This year's event will focus on **modifications to Cas9 that make it useful for base-editing**.
   A TEAM OF UP TO: 3   **IMPOUND:** Yes   **APPROXIMATE TIME:** 50 minutes

2. **EVENT PARAMETERS:**
   a. Each **participant** may bring one 8.5" x 11" sheet of paper, **which may be** in a sheet protector **sealed by tape** or laminated, that may contain information on both sides in any form and from any source without any annotations or labels affixed along with writing utensils for each participant.
   b. Each team will impound a pre-built model of a **cytidine deaminase protein**.
   c. Event Supervisors will provide internet-connected computers, instructions for computer exploration of protein structure, and the written exams.

3. **THE COMPETITION:**

   Part I: The Pre-Built Model
   a. Participants will use the program Jmol/JSmol to visualize **cytidine deaminase (chain A, residues 214-310**) based on data found in the **5td5.pdb file**. The atomic coordinate data file can be downloaded for free from the RCSB Protein Data Bank (www.rcsb.org). A constructed model of this protein must be brought to all competitions; as the competition level increases, the scoring rubrics for the pre-built model will reflect higher expectations for model accuracy, detail and enhancements. (See SCORING for more details.) Jmol/JSmol can be accessed at http://cbm.msoe.edu/scienceOlympiad/ designEnvironment/prebuild.html for free.
   b. The pre-built model must be based on the alpha carbon backbone display of the protein, using a scale of 2 cm per amino acid. Students may use Mini-Toobers®, or other comparable bendable material (e.g., Kwik Twists, 12-gauge dimensional house wire, etc.), to manually fold their pre-built model.
   c. Three Dimensional (3D) printed materials may NOT be used to build the protein backbone but may be used for functionally relevant features.
   d. Participants will use materials of their own choosing to add functionally relevant features to their model (e.g., selected amino acid sidechains, DNA or associated molecules). Additions to the model should highlight the significance of structure to the function of the protein.
   e. Participants must explain their functionally relevant features using clear and concise descriptions on a 4" x 6" notecard, in the form of a table with 3 columns, headed:
      i. What is displayed?
      ii. How is it displayed?
      iii. Why is it important?
   f. Teams may use both sides of the notecard, and information must be legible.
   g. All models, including all functionally relevant features, must fit within a 61.0 cm x 61.0 cm x 61.0 cm space.
   h. The model must be sufficiently sturdy that judges can pick it up and rotate it for judging.
   i. Teams must deliver their pre-built model and 4" x 6" notecard for impounding. They may pick up pre-built models after the competition.

   Part II: Computer Exploration of Protein Structure
   a. **Participants will explore a new protein structure onsite using Jmol/JSmol.**
   b. **The Event Supervisor will provide the computer and give the participants the PDB file of a new protein.**
   c. **Participants will use Jmol/JSmol to display the protein and answer questions related to its structure.**

   Part III: Written Exam
   a. Teams will complete a written exam consisting of multiple choice and short answer questions.
   b. Topics addressed include:
      i. the principles of chemistry that drive protein folding
      ii. **chemical principles underlying stability and interactions in biological macromolecules (e.g., proteins, and nucleic acids such as DNA and RNA)**
      iii. **mechanism whereby CRISPR functions as an adaptive immune system in bacteria**
      iv. **ways in which the Cas9 protein has been engineered to make it more useful as a base-editing tool**

4. **SCORING:**
   a. High Score wins. Final score will be derived from all three parts of the competition:
   b. The pre-built model (Part I) accounts for 40% of the final score.
      i. **The pre-built score is based on the accuracy and scale of the secondary structures, tertiary arrangement of these structures, as well as relevant functional features added.**
      ii. **Features that are not relevant or do not explain the structure/function relationship of the protein will not receive credit.**
      iii. **The scoring rubric for the pre-built model will change with the level of each competition.**
         (1) **For Regional competitions, scoring will be based primarily on the accuracy of the 3D folded structure of the alpha-carbon backbone of the protein (secondary and tertiary structures).**
         (2) **For State competitions, 30% of the score awarded to the pre-built model will be based on functionally relevant features, such as inclusion of key sidechains, substrates, nucleic acids and so forth, that have been added to the alpha-carbon backbone model to explain the protein's function.**
         (3) **For the National competition, in addition to the folding of the protein and creative additions, scoring will focus on how the structure modeled fits within the larger fusion protein of the BE4 expression plasmid displayed at https://www.addgene.org/browse/ sequence/222010/. Note that it will be impossible to build the whole fusion protein to scale and fit within the space parameters. Teams are expected to include schematic representations of the other regions of the fusion protein and their connections to each other. Note that NO additional credit will be given to complete atomic models, but it is important that the additions are arranged in the correct linear order. This schematic fusion protein model will be worth 15% of the pre-built model score; the other 85% will come from the cytidine deaminase pre-built model. Both pre-built models must be impounded before the beginning of the event.**
   c. The computer-exploration of a protein structure (Part II) accounts for 30% of the event score.
   d. The written exam (Part III) accounts for 30% of the event score.
   e. Ties will be broken using identified questions from the written exam (Part III).

Recommended Resources: The Science Olympiad store (store.soinc.org) carries the Chem/Phy Sci CD (CPCD); other resources are on the event page at soinc.org.

This event is sponsored by Milwaukee School of Engineering (MSOE)