Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Vineet Kosaraju and Neerja Garikipati
High School: The Harker School and Huron High School
Mentor: Professor Rhiju Das
Project Title: *Towards Rational RNA Therapeutics: 3D RNA Engineering in a Massive Open Laboratory* (Biophysics)

Rationally designed therapeutics based on ribonucleic acid (RNA) molecules have begun to emerge after years of research, with applications to cancer and viral infection. Unfortunately, each drug has taken years to develop due to poor understanding of how RNAs fold to specific secondary structures and then to 3D structures required for their function. This study aims to uncover the missing design rules using a game-based crowdsourcing approach, the 'massive open laboratory'. EteRNA has succeeded in recruiting 100,000 players to generate sequences that match a given RNA secondary structure and, through actual experimental feedback, discovering empirically validated design rules. Here, we present a new game EteRNA3D that expands EteRNA from the secondary structure level to design of atomically precise 3D folds. A pilot study tackles two foundational 3D problems: stabilizing binding pockets for small molecules to enable external control of RNA therapeutics, and building an RNA 'arm' to lock a desired conformation into place. To evaluate success, twelve player and three computer designs have been experimentally synthesized; all were successful in achieving their design targets. Previously unknown rules for 3D design have already emerged, suggesting that a massive open laboratory will be a powerful paradigm for engineering and testing RNA therapeutics.