# Computer-Aided Investigation of Methoctramine-ExoU Interactions

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Pseudomonas aeruginosa (P. aeruginosa) is a ubiquitous, gram-negative bacterium associated with a wide variety of infections in the human body. As an opportunistic pathogen, P. aeruginosa most commonly infects individuals with severe burns, deep wounds, cystic fibrosis, and compromised immune systems. Due to its surplus of natural defenses, P. aeruginosa has a high drug resistance that makes it difficult to combat directly. An alternate approach is to target ExotoxinU (ExoU), the effector protein responsible for the cell lysis and infections caused by P. aeruginosa. By inhibiting the protein before it can damage the host's cells, high-risk individuals will be protected from P. aeruginosa-caused infections. As Methoctramine is a known inhibitor of ExoU (whose interactions with the protein are under investigation), the objective of the research project was to locate the potential binding sites of Methoctramine and analyze the interactions between the binding sites and different configurations of the ligand. This information will be used for the optimization of Methoctramine as it is not selective to ExoU and can competitively bind to M2 receptors, preventing neurotransmitters from interacting with these muscle receptors. With the assistance of a computer molecular modeling program, three viable binding sites and two Methoctramine configurations were discovered that contained a multitude of amino acid interactions and displayed strong binding affinities. The binding sites will be verified using Nuclear Magnetic Resonance and the residue interactions of the Methoctramine configurations will be used to render the ligand a safer, more effective ExoU inhibitor.

**Awards Won:**
American Committee for the Weizmann Institute of Science: Two finalists will be selected to receive a scholarship to attend the Bessie Lawrence International Summer Science Institute, which will be held virtually for 2021.