Fighting Zika: Computational Discovery of New Drugs to Inhibit the NS2B-NS3 Protease of the Zika Virus

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Purpose: The purpose of this experiment is to use computational methods to dock compounds onto a Zika virus protease and find stable inhibitors, as indicated by a low binding and interaction energy. The compounds were proposed by modifying the P1 and P2 side chains, and the backbone of the protein's natural substrate. These compounds can potentially become drugs to inhibit the growth of the virus. Procedure: ChemDraw was used to draw molecules with two different backbones and 31 different structures in the P1 position. Avogadro was used to build 3D coordinates for these molecules. AutoDock Vina computationally docked 62 different compounds onto the NS2B-NS3 protease from the Zika virus and predicted the conformation of the compound-protein complex with their binding energies. 41 lowest binding energy compounds were chosen for further modification. Next, P2 side chains were changed to 10 variations chosen from the Chem-Impex database. AutoDock Vina was used again to dock these 410 compounds on the Zika protease. Molecular dynamics simulations were run in GROMACS on lowest binding energy compounds. Their interaction energies were recorded. Results and Conclusion: Compounds that had low interaction energies were identified as potential drugs for the Zika virus. Two such compounds were 7HS, with an interaction energy of -581.67 ± 3.72 kJ/mol, and compound v7v1 with an interaction energy of -438.06 ± 10.32 kJ/mol.

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