Novel Inhibitors of Glucose Transporter 1 (GLUT1) for Cancer

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The goal of the project was to identify effective targeted drugs for inhibiting Protein Glucose Transporter 1 (GLUT1). Findings would be a big step towards curing cancer. GLUT1 transports glucose across the cell membrane, plays an important role during several stages of cancer progression, and is essential to the survival of many types of cancer. After reviewing existing docking research on the 4 known inhibitors of GLUT1, 23 docking positions were determined and then tested in 10 trials. The best docking position identified was then used for a High Throughput Molecular Docking Study of 40 million ligands with GLUT1. Thousands of ligands found had much more effective docking results than the 4 existing drugs. Top novel-inhibitor candidates (40%-60% improvement in binding-affinity compared to existing inhibitors) were chosen after toxicity-testing and 5 trials of tests with 7 optimal-docking positions. Among them, ZINC19798821 has an almost identical structure as CHEMBL564972, which has been previously reported as an Inhibitor of Protein Kinase B (Akt) for Breast Cancer. Both ligands could be dual-inhibitors of GLUT1 and Akt. MK-2206 (Merck's product in clinical-trials stage for Akt) is another dual-inhibitor candidate of GLUT1 and Akt. ZINC09711897 had very high binding-affinity but failed the toxicity-test. However, by altering the structure slightly, a new non-toxic ligand was created that ranked near the top. This offered valuable insight into how to design new ligands. These are all breakthrough discoveries. Results were verified in vitro, and the next steps are mouse model testing and clinical trials.

Awards Won:
Second Award of $2,000
American Committee for the Weizmann Institute of Science: First Award of $3,000