Assessment of Diabetes Clinical Trial Candidates Using Systems Pharmacology

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Curating molecular interactions is crucial to understanding how drugs work on molecular systems implicated in a disease and could provide future prospects for applications such as drug repositioning. For this project, we curated disease-specific drugs and protein interactions to help us understand Type II Diabetes in light of systems pharmacology. The pharmacological efficacy of drugs can be assessed based on their ability to regulate gene expressions in diabetic patients to resemble those of a healthy individual at a pathway level. Two drugs with a high level of similarity should share similar pharmacological effects, including drug target, side effects, mechanism of action, structure, and up or down-regulation of genes associated with diabetes. We focused on the relationships between drugs, proteins, and the disease, utilizing drug-drug similarity networks, a disease-specific protein-protein interaction network model, and the standardized curation of protein interactions by mining primary databases to visualize these relationships as they relate to Type II Diabetes. First, drugs were gathered from primary databases using proteins associated with the disease. From there, a drug-drug similarity network was constructed by examining similar targets, structures, side effects, and mechanism of action between drugs. To construct a disease-specific pathway model, proteins associated with Type II Diabetes were gathered from databases, PAG Electronic Repository and Connectivity-Maps, and analyzed from protein studies from the Diabetes Genome Anatomy Project and microarray datasets from Gene Expression Omnibus, generating a validated list of disease-specific proteins. Then, interactions and regulations within the proteins were determined to generate a disease-specific protein-protein interaction model to provide insights to the disease itself and mechanisms of action of drugs related to Type II Diabetes. In the future, the drug-drug similarity network, the protein-protein interaction network model, and the protein and drug interactions could possibly aid in the repurposing of drugs for Type II Diabetes.

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