Rapid Development of Clinical Trial Candidates Using Cancer Systems Pharmacology: a Lymphoma Case Study

Matthew Arkenberg[2,4] , Kylee Johnson[3], Palakpreet Kaur[1], Kelly Moors[5,6], Michael Weisman[3]

[1]Department of Biology, Purdue School of Science, IUPUI; [2]Biomedical Engineering, Purdue School of Science, IUPUI; [3]Department of Chemistry & Chemical Biology, Purdue School of Science, IUPUI; [4]Department of Chemistry, Butler University; [5]Department of Psychology, Purdue School of Science, IUPUI; [6]Department of World Languages and Cultures, IU School of Liberal Arts, IUPUI

Due to intrinsic complex molecular interactions, the "one disease – one target – one drug" strategy for disease treatment is no longer the best option to treat complex diseases such as cancers. To assess drug pharmacological effects, we assume that "ideal" drugs for patients can treat or prevent the disease by modulating its gene expression profile to a similar level of those in healthy people. A drug that may not have been approved to treat a cancer yet, based on its gene expression target profile is the most successfully at modulating the gene expression to being of similar level to a healthy person is known as drug repurposing. The goal of this study was to develop an *in silico* framework which would determine which drug(s) could be repurposed to treat more complex disease of interest such as cancers. Using three subcategories of Non-Hodgkin's Lymphoma (Burkitt's, Mantle, Diffuse Large B-Cell) as case studies, manual curation was done to collect data on drug-protein interaction, drug similarity analysis based on structure and protein target, and curation; disease-protein interactions, and protein-protein interactions. A network will be created from the curated data known as a Pharmacology Effect Network (PEN). The Pharmacological Effect on Target (PET) algorithm will then be used to rank the curated drugs. This ranking will help determine which of the investigated drugs not currently used to treat one of the three subsets of Non-Hodgkin's lymphoma could possibly be recommended to treat them. Although this project was primarily done using manual curation, the framework of each curated relationship used by each curator has been incorporated into a web interface. This webpage will allow for more automation of the curation process with little help from the curator and should improve the speed and accuracy of the curation process.

Mentors: Jake Chen[7], Xiaogang Wu[7], Walter Jessen[8]
[7]IU Center for Systems Biology and Personalized Medicine, IUPUI; [8]Informatics, Covance, Greenfield