# Finding drugs with common downstream effects, using direction information in biological pathways

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**Abstract.** Drugs aim at compensating for a biological process or processes that are not behaving as desired. Drugs frequently do this by binding to proteins in pathways, causing immediate or downstream changes in the pathway affecting the biological process. WikiPathways is an open resource for curating biological pathways. Interactions in the pathway, capture information that connects biological entities. WikiPathways RDF representation captures the participants of a specific interaction, the type of interaction (inhibition, stimulation, catalysis, etc.), and also the direction of the interaction. The increasing availability of this directionality enables answering a new class of research questions programmatically. For instance, this knowledge can be used to show how a combination of two drugs affects common downstream processes. This list of drug combinations with common downstream effects is important because drug combination therapies may be used to minimize the side effects of single drug treatments where higher doses need to be administered.

We will present work that answers this question by combining data from WikiPathways, ChEMBL, and Uniprot. ChEMBL is used to extend the knowledge base with drug data annotations linking drugs to protein targets in the pathway. While Uniprots endpoint is used to map ChEMBL target information to Uniprot IDs. The interaction directional information defines what is upstream and downstream in the pathway of the protein targets. Analysis of the combined data results in a list of drug combinations that share common downstream effects. The analysis was implemented as a series of queries against the SPARQL endpoints of ChEMBL, Uniprot, and WikiPathways.

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