Adverse drug reactions (ARs) are among the top-10 reasons for death in the US (Lazarou, JAMA, 1998) and are estimated to cost up to $30.1 billion annually (Sultana, J Pharmcol Pharmacother, 2013). While clinical trials test novel therapeutics in patients before marketing, the average drug exposure is only 1500 individuals (Friedman, JAMA, 1999) and clinical trials are unable to fully characterize a drug’s safety profile. In silico techniques, specifically protein interaction network methods, have uncovered associations of drug targets to AR phenotypes including severe ARs that could remove drugs from the market. Towards understanding potential safety risks, we developed a novel network interaction algorithm, PathFX, and a complementary web-server (PathFX-web) in collaboration with FDA scientists. We demonstrated that PathFX identified associations to efficacy and safety phenotypes for marketed drugs, and further that safety and efficacy associations shared interaction pathways. Yet, it is unknown if these pathway associations represent any mechanistic insight about the sources of drug-induced ARs. Through meta-analysis, we investigated patterns across networks of drugs with the same DME. After discovering shared interactions across these drugs, we considered that non-DME associated drugs could influence DMEs if they bound proteins within these shared interaction pathways and would represent novel drug combination effects. For instance, this analysis predicted that an anti-thrombotic agent would combine with a subset of anti-psychotics to exacerbate myocardial infarction, which is listed on the antipsychotic drug labels as a warning or precaution. Using a natural language processing method and published drug combination datasets, we’ve identified preliminary support for this drug combination effect. These results suggest that shared interaction paths contain mechanistic-like insights into sources of drug-induced adverse events, and that these paths represent a novel type of “long-ranging” drug combination effect.
from MIT, where she worked with Dr. Doug Lauffenburger. In her PhD, she demonstrated that network algorithms uncovered hidden gene candidates from RNAi screens and validated these predictions in two cancer contexts: acute lymphoblastic leukemia and growth-factor-driven cancer systems.