Driving Mutations: Lessons from Yeast and Cancer

In this talk we will discuss a new perspective on question "How does variation in genotype encode for phenotypic diversity?" We will discuss methods that harness gene expression to identify genetic variants that influence a trait of interest. Our premise is that much of the influence of genotype on phenotype is mediated by changes in the regulatory network and these can be inferred using gene expression. We will discuss 3 vignettes:

(1) We will demonstrate how biological modularity can be used to gain significant statistical power for linkage analysis of eQTLs (expression Quantitative Trait Loci). This will provide a refined map of linkages that provides new insight into non-additivity in genetic interactions and the influence of genetic variation on how a cell sees its environment.
(2) Camelot, an algorithm method that integrates genotype and gene expression collected in a reference condition (un-drugged) and phenotype data to predict complex quantitative phenotypes in entirely different conditions (drug response) and identify causal genes that influence these traits. We will discuss why gene expression gives such a large boost in power.
(3) Conexic, a novel Bayesian Network-based framework to integrate chromosomal copy number and gene expression data to detect genetic alterations in tumors that drive proliferation, and to model how these alterations perturb normal cell growth/survival. We demonstrate how this method can uncover an important role of protein trafficking in Melanoma