Center for Cancer Systems Biology (CCSB)

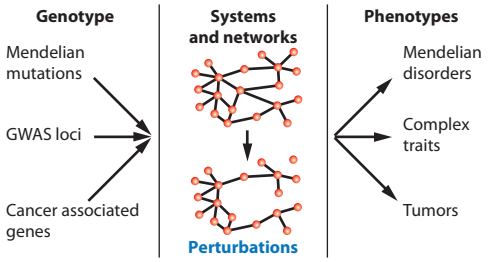
The long-term goal of CCSB is to understand how macromolecular networks control biological processes and how perturbations in such networks can explain phenotypes and human disease.

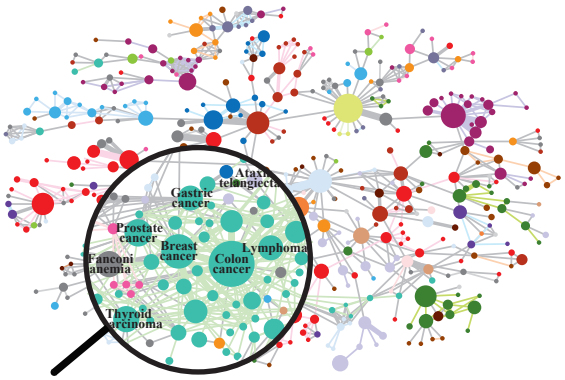
Physical protein-protein interactions are instrumental for all biological processes. We address several fundamental questions regarding protein interactions. How are protein interactions organized at the scale of the whole cell? Are there global principles that organize such complex networks of interactions? How to understand the global topological features of networks and what they mean? And how is the organization of cellular networks disrupted in human disease?

CCSB Guiding Principle

- Phenotypic effects of functional sequence variants are mediated through dynamic networks of gene products and metabolites.
- Understanding genotype-phenotype relationships requires that **phenotypes be viewed as manifestations of network properties**, rather than simply the result of genomic variations considered individually.

Vidal et al. Interactome networks and human disease, Cell 2011





Human Disease Network

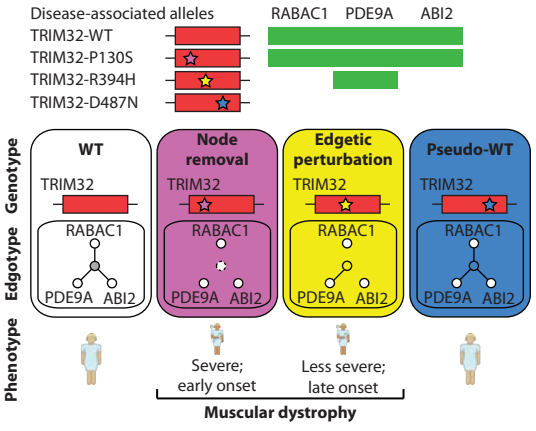
- We integrated known disease associated genes with our growing interactome map, resulting in a **global view of the "diseasome"**. Investigating the common genetic origin of diseases, we revealed that products of disease genes are part of highly interconnected cellular networks.
- Analysis of the diseasome network will **expand the list of disease-associated genes and highlight perturbations** of molecular pathways.

Goh et al. The human disease network, PNAS 2007

Edgotyping Initiative

- Perhaps half of Mendelian mutations in coding genes cause disruption of specific interactions, or **"edgetic" perturbations**, of the mutated gene.
- Differential loss of specific interactions can lead to different diseases as well as to different degrees of severity of a disease.
- Large-scale screening of edgetic events will allow design of **more efficient drugs targeting specific sub-phenotypes**.

Yildirim et al. Drug-target network, Nat. Biotechnol. 2007



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