BST281: Genomic Data Manipulation, Spring 2019

Wednesday 05: Protein-Protein Interactions

# Protein-protein interactions (PPIs)

Physical interactions between proteins that can be either stable or transient

## Stable PPIs

Typically co-complexes or part of the same structural or functional unit that persists over time.

Can be detected by two-hybrid methods:

 Separate functional domains of a reporter system into bait and activation units.

 Bait binds potential partners (prey), activation domain provides a readout.

 Originally transcriptional, but can be luciferase, FRET, signal cascade, etc.

Pros and cons:

 Can yield false positives (sticky proteins), false negatives (lack of localization, function).

Can also be detected by affinity capture:

 Generate an antibody or other attractor for one protein, pull it down, and then measure what comes along.

 Can be read out by gel (co-immunoprecipitation), but most often by mass spectrometry.

## Transient PPIs

Relative rapid interactions between protein partners for the purposes of regulatory information flow.

Typically modifications.

Phosphorylation (by phosphatases, removal by kinases): small high-energy group, regulatory.

Glycosylation: large, structurally complex sugar molecules (often cell surface).

Ubiquitination: targeting to protease for degradation.

Sumoylation, neddylation, others.

Can be difficult to both detect modification sites and the modifier-target pairs.

## PPI resources

Stable interactions from BioGRID, IntAct, MINT, Domine, BIND.

Transient interactions / modifications from PhosphoGrid, PhosphoElm, Phosphopep, Phosida, RESID, UniMod...

# Textbooks

Network analyses: Pevsner, Chapter 14 p670-685

Protein networks: Lesk, Chapter 11 p341-350, p361-365

# Literature

[Kim, Philip M., et al. "Relating three-dimensional structures to protein networks provides evolutionary insights." Science 314.5807 (2006): 1938-1941.](http://science.sciencemag.org/content/314/5807/1938)

[Rolland, Thomas, et al. "A proteome-scale map of the human interactome network." Cell 159.5 (2014): 1212-1226.](http://www.sciencedirect.com/science/article/pii/S0092867414014226)