Protein Interactions and Disease
What is a protein?
- A polymer of amino acids
- Basic functional unit within cells
- Responsible for phenotype

luciferase
Alpha amylase – breaks down carbs in saliva
Topo isomerase
GFP
ATP-Synthase
TP53

Protein-Protein Interactions (PPIs)
Types of PPIs
Biophysical

Transient
Biophysical Interaction Databases

- Human Protein Reference Database (HPRD)
- The Biological General Repository for Interaction Datasets (BioGRID)
- Search Tool for the Retrieval of Interacting Genes/Proteins (STRING)
- Molecular INTeraction database (MINT)
- IntAct
- Database of Interacting Proteins (DIP)
- Wiki-Pi
Genetic
Genetic Interaction Databases

- The Biological General Repository for Interaction Datasets (BioGRID)
- Molecular INTeraction database (MINT)
Krebs cycle
oxaloacetate
Metabolic Interaction Databases

- Kyoto Encyclopedia of Genes and Genomes (KEGG)
- REACTOME
- BioCyc/MetaCyc
- ConsensusPathDB
Co-localization & Co-expression
## Databases

**Co-localization**
- Molecular INTeraction database (MINT)
- Gene Ontology (GO)

**Co-Expression**
- Molecular INTeraction database (MINT)
- Gene Expression Omnibus (GEO)
Why do we care?
What happens when a protein “malfucntions”

Mendelian Diseases

Sickle Cell Anemia – Mutation in hemoglobin
Cystic Fibrosis – Mutation in CFTR
Marfan Syndrome – Mutation in FBN1 (Fibrillin 1)
Phenylketonuria – Can’t digest phenylalanine, mutation in PAH (phenylalanine hydroxylase)
Complex Diseases

- Pleiotropic phenotypes
- Multiple genes affecting same phenotype
- Environmental factors

Marfan syndrome – heart disease and hyper mobility
Complexity of heart disease
Twins, one with shingles
Identifying Disease Genes

• Select genes known or assumed to already be associated with the disease
  • Candidate Genes
• Examine interactions among candidates
• Rank genes by expected importance
Identifying Disease Genes
Limitations

- Human interactome very unknown
- Poor quality gene annotations