

Ontological Visualization of Protein-Protein Interaction


Harold J. Drabkin
Christopher Hollnbeck
David P. Hill
Judith A. Blake



Outline

- Proteomics
- Protein-protein interaction
- The Gene Ontology database
- Specific Vs Network Interactions
- Assigning protein function

Proteomics

- Genome  Proteome
- Genome is merely a parts list
- Identifying protein-protein interactions is one of the most challenging problems of the post-genomic era

Protein-Protein Interaction

- Aim is to understand the mechanism by which a set of proteins communicate and collaborate toward a common cellular function
- This will allow a broader outlook and a more comprehensive understanding of the biological processes occurring in cells

Protein-Protein Interaction

- Understanding protein interactions requires two steps
 - Identifying proteins that interact (experimentally and computationally)
 - Determining the significance of the interaction network

Protein-Protein Interaction

- There is enormous amount of specific protein-protein interaction data available (by studies focusing on a few interacting proteins)
- There is a need to extract data from different studies and accumulate all data into one databank

The Gene Ontology (GO) Database

- Provides a description of genes and how gene products behave in a cellular context
- Ontology (vocabulary set): cellular component, biological process, and molecular function
- Annotation is the characterization of gene products using terms from the ontology

The Gene Ontology (GO) Database

- Information encoded in GO annotations was used to develop protein interaction networks for mouse
- A gene product can be annotated to “protein binding” using the IPI (inferred from physical interaction)
- Ex: Ager protein binds to Q8BQ02

Gene Ontology Classifications

Symbol [Ager](#)
Name advanced glycosylation end product-specific receptor
ID MGI:893592

Category	Classification Term	Evidence	Inferred From	Ref(s)
Biological Process	transport	IDA		1
Cellular Component	extracellular space	TAS		1
Cellular Component	integral to membrane	TAS		1
Molecular Function	protein binding	IPI	SPTR:Q58Q02	1
Molecular Function	receptor activity	IEA		1

Gene Ontology Classifications

Symbol [Hmgbl](#)
Name high mobility group box 1
ID MGI:96113

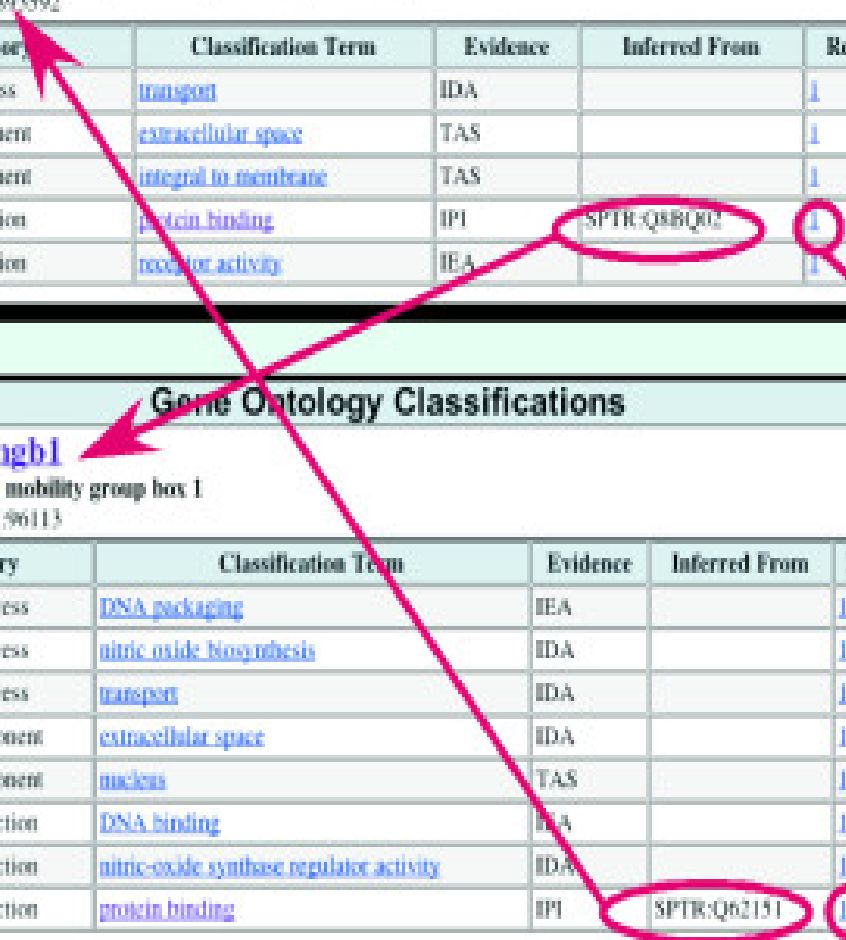
Category	Classification Term	Evidence	Inferred From	Ref(s)
Biological Process	DNA packaging	IEA		1
Biological Process	nitric oxide biosynthesis	IDA		1
Biological Process	transport	IDA		1
Cellular Component	extracellular space	IDA		1
Cellular Component	nucleus	TAS		1
Molecular Function	DNA binding	IEA		1
Molecular Function	nitric-oxide synthase regulator activity	IDA		1
Molecular Function	protein binding	IPI	SPTR:Q62151	1

J Number: J18721
Other Accession IDs:

- 12195785 ([PubMed](#))
- 22186637 ([MEDLINE](#))

Title: HMGB1 B box increases the permeability of Caco-2 enterocytic monolayers and impairs intestinal barrier function in mice.

Authors: Sappington PL, Yang R, Yang H, Tracy KJ, DeWitt DL, Park ME



Specific Interaction Vs Networks

- Ager with Q8BQ02
- Protein could have further annotations
- Ex. Of simple network
 - Hcph (hemopoetic cell phosphate) binds to jak 2 and klr1b. Jak2 not only binds to hcph but also SOCS1 which in turn binds with PIM2

Gene Ontology Classifications

Symbol: **Heph**
Name: heparin-binding epidermal growth factor receptor
ID: MIM:104737

Category	Classification Term	Evidence	Inferred From	Ratio
Biological Process	cytokine and chemokine mediated signaling pathway	TAS		1
Biological Process	intracellular signaling cascade	IDA		1
Biological Process	protein tyrosine kinase signaling pathway	IDA	SPTR:00011	1
Cellular Component	cytoplasm	TAS		1
Molecular Function	tyrosine activity	IDA	SPTR:00011	1
Molecular Function	phosphotyrosine phosphatase activity	IDA	SPTR:00011	1
Molecular Function	phosphotyrosine binding	IDA	SPTR:00011	1
Molecular Function	protein tyrosine kinase inhibitor activity	IDA	SPTR:00011	1
Molecular Function	protein tyrosine phosphatase activity	IDA		1
Molecular Function	protein tyrosine phosphatase inhibitor activity	IDA		1

Gene Ontology Classifications

Symbol: **Jak2**
Name: Janus kinase 2
ID: MIM:104233

Category	Classification Term	Evidence	Inferred From	Ratio
Biological Process	apoptosis			1
Biological Process	cell differentiation	MP		1
Biological Process	cytokine and chemokine mediated signaling pathway	TAS		1
Biological Process	intracellular signaling cascade	IDA		1
Biological Process	JAK-STAT cascade	IDA		1
Biological Process	JAK-STAT cascade	MP		1
Biological Process	negative regulation of cell proliferation	MP		1
Biological Process	protein tyrosine kinase signaling pathway	IDA		1
Biological Process	STAT cascade, nuclear translocation	IDA		1

Gene Ontology Classifications

Symbol: **Krb1b**
Name: killer cell lectin-like receptor subfamily B member 1B
ID: MIM:607333

Category	Classification Term	Evidence	Inferred From	Ratio
Biological Process	negative regulation of natural killer cell mediated cytotoxicity	IDA		1
Cellular Component	cytosolic side of plasma membrane	IDA		1
Cellular Component	integral to membrane	IDA		1
Cellular Component	integral to plasma membrane	IDA		1
Molecular Function	protein binding	MP	SPTR:00011	1
Molecular Function	protein binding	MP	SPTR:00011	1

Gene Ontology Classifications

Symbol: **Socs1**
Name: suppressor of cytokine signaling 1
ID: MIM:104636

Category	Classification Term	Evidence	Inferred From	Ratio
Biological Process	cytokine and chemokine mediated signaling pathway	IDA		1
Biological Process	cytokine and chemokine mediated signaling pathway	MP	SPTR:00011	1
Biological Process	intracellular signaling cascade	IDA	SPTR:00011	1
Biological Process	JAK-STAT cascade	IDA		1
Biological Process	regulation of cell growth	IDA	SPTR:00011	1
Biological Process	signal transduction	IDA		1
Cellular Component	cytosolic component	MP		1
Molecular Function	cytoskeletal activity	IDA		1
Molecular Function	protein binding	MP	SPTR:00011	1
Molecular Function	protein binding	MP	SPTR:00011	1

Gene Ontology Classifications

Symbol: **Ocd1 (Interin)**
Name: osteoblast inhibitory factor 1
ID: MIM:607334

Category	Classification Term	Evidence	Inferred From	Ratio
Biological Process	cellular differentiation, osteoblast	TAS		1
Biological Process	regulation of osteoblast differentiation	IDA		1
Biological Process	protection from natural killer cell mediated cytotoxicity	IDA		1
Cellular Component	cytosolic side of plasma membrane	IDA		1
Cellular Component	integral to plasma membrane	TAS		1
Cellular Function	natural killer cell lectin-like receptor binding	IDA		1
Cellular Function	protein binding	MP	SPTR:00011	1
Cellular Function	protein binding	MP	SPTR:00011	1
Cellular Function	protein binding	MP		1

Gene Ontology Classifications

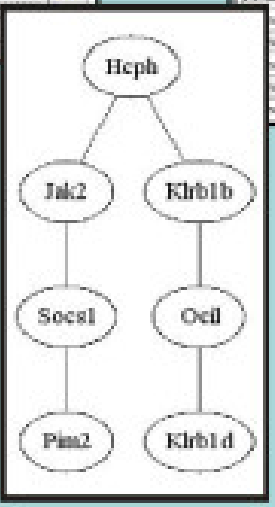
Symbol: **Pim2**
Name: protein tyrosine kinase 2
ID: MIM:104738

Category	Classification Term	Evidence	Inferred From	Ratio
Biological Process	cell apoptosis	IDA		1
Biological Process	apoptosis, nuclear factor kappa B	IDA		1
Biological Process	protein tyrosine kinase signaling pathway	IDA		1
Molecular Function	ATP binding	IDA		1
Molecular Function	protein binding	MP	SPTR:00011	1
Molecular Function	protein kinase activity	IDA		1
Molecular Function	protein tyrosine kinase kinase activity	IDA		1
Molecular Function	protein tyrosine kinase activity	IDA		1

Gene Ontology Classifications

Symbol: **Klrb1d**
Name: killer cell lectin-like receptor subfamily B member 1D
ID: MIM:607332

Category	Classification Term	Evidence	Inferred From	Ratio
Biological Process	negative regulation of natural killer cell mediated cytotoxicity	IDA		1
Cellular Component	cytosolic side of plasma membrane	IDA		1
Molecular Function	protein binding	MP	SPTR:00011	1
Molecular Function	protein tyrosine kinase activity	IDA		1
Molecular Function	protein activity	IDA		1
Molecular Function	signal binding	IDA		1



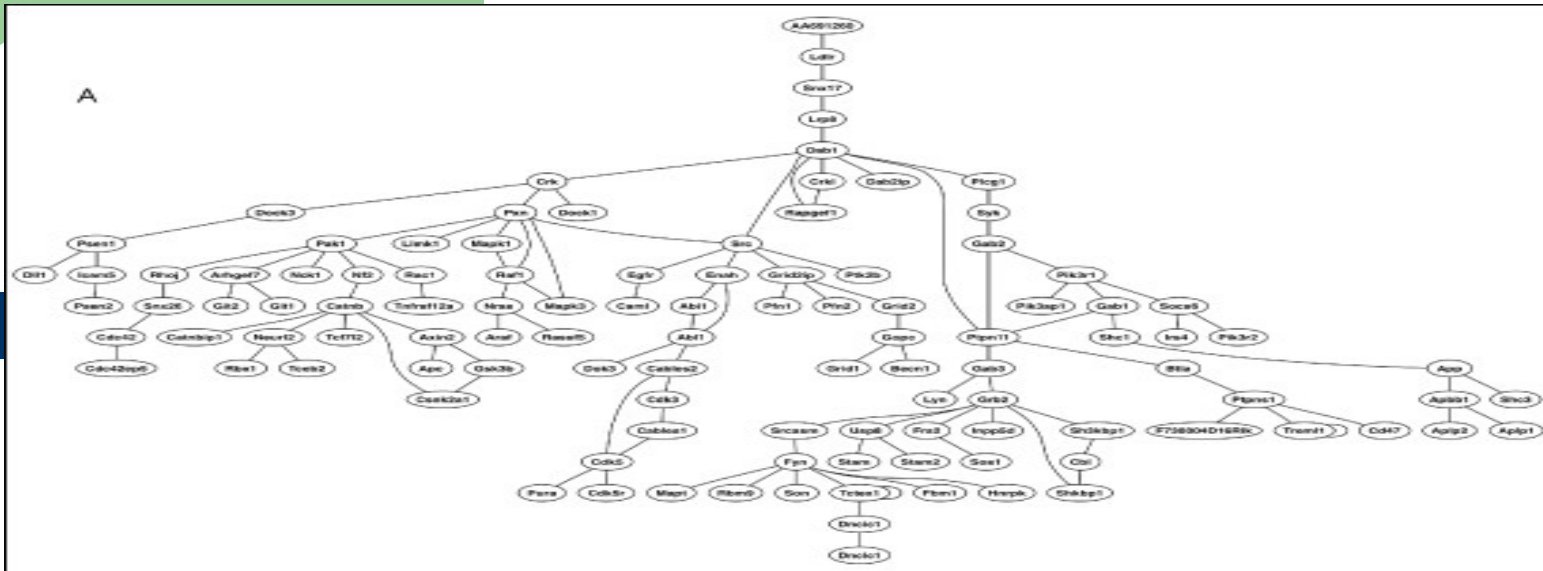
Proteins with unknown function

- A protein is known to interact with another protein but there is no information known about the biological role of this protein
- Use the GO annotation to determine the function of the interacting proteins and use this to assign a function to the unknown protein

GO Tools

- GO Term Finder and its graphical interface
Vlad searches for shared GO Terms and organizes information about the roles of proteins

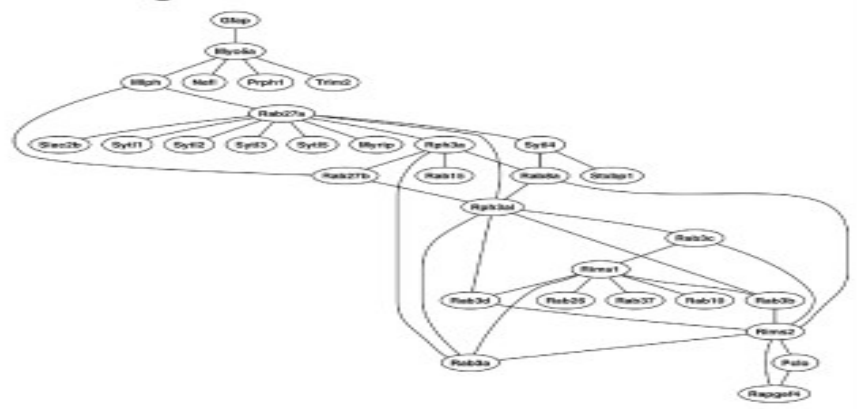
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B

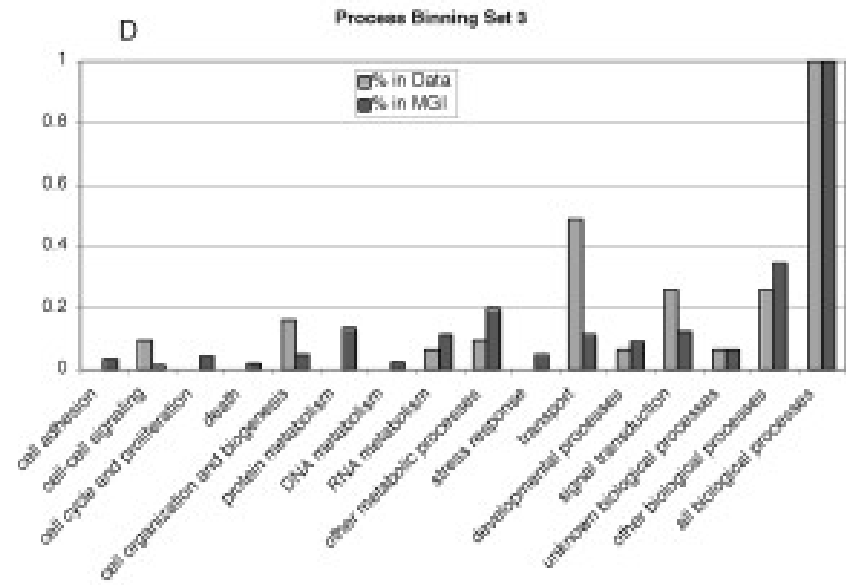
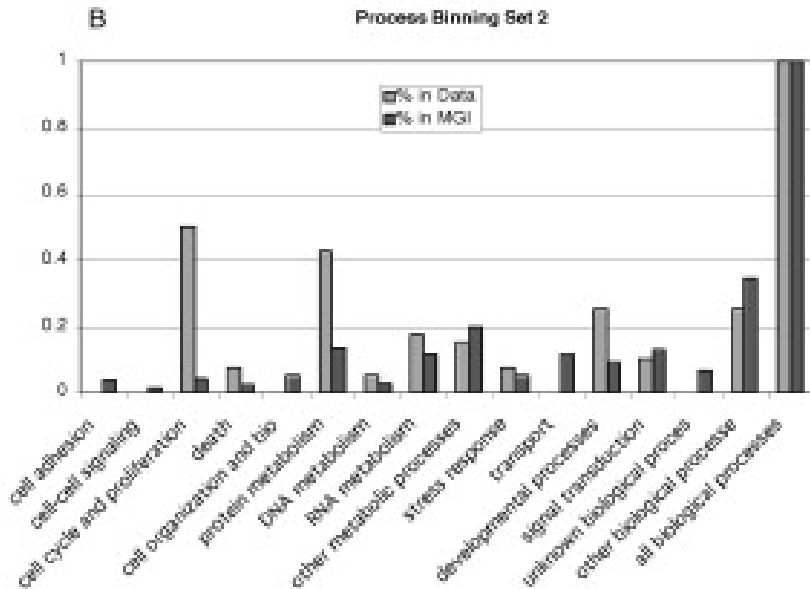
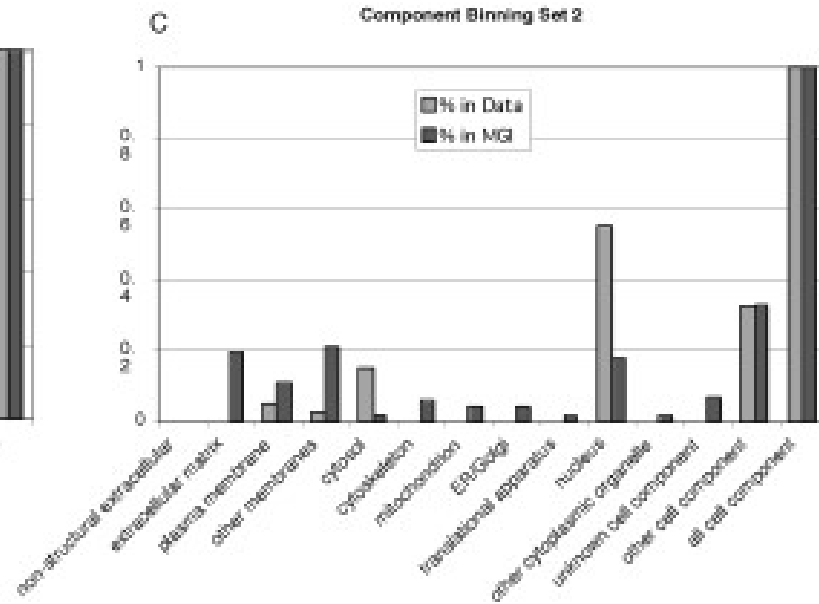
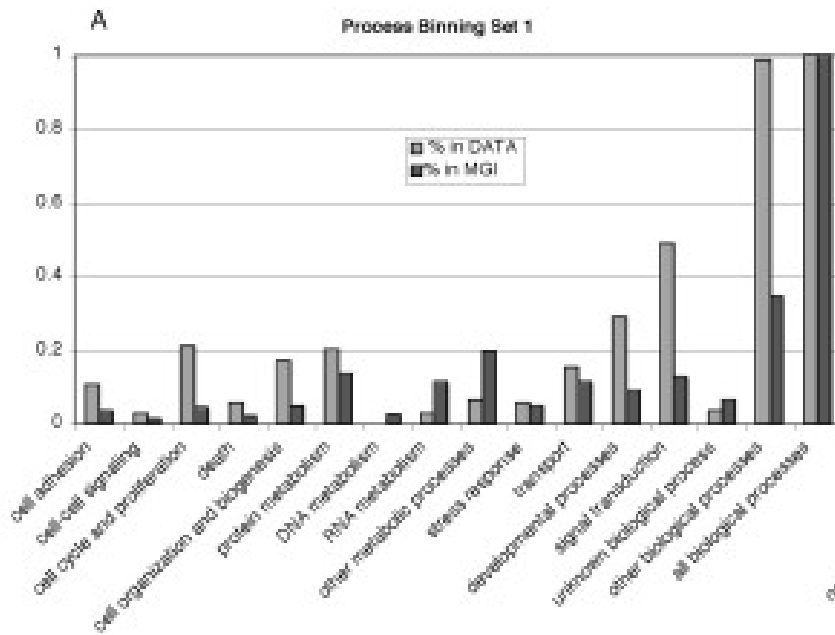


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GO Tools

- GO Slim Viewer provides a summary of the GO categories for a dataset based on specific annotations



Conclusion

- Gene annotations for protein binding interactions are based on published literature supported by experimental evidence
- GO annotations can be used to visualize and analyze protein-protein interaction networks