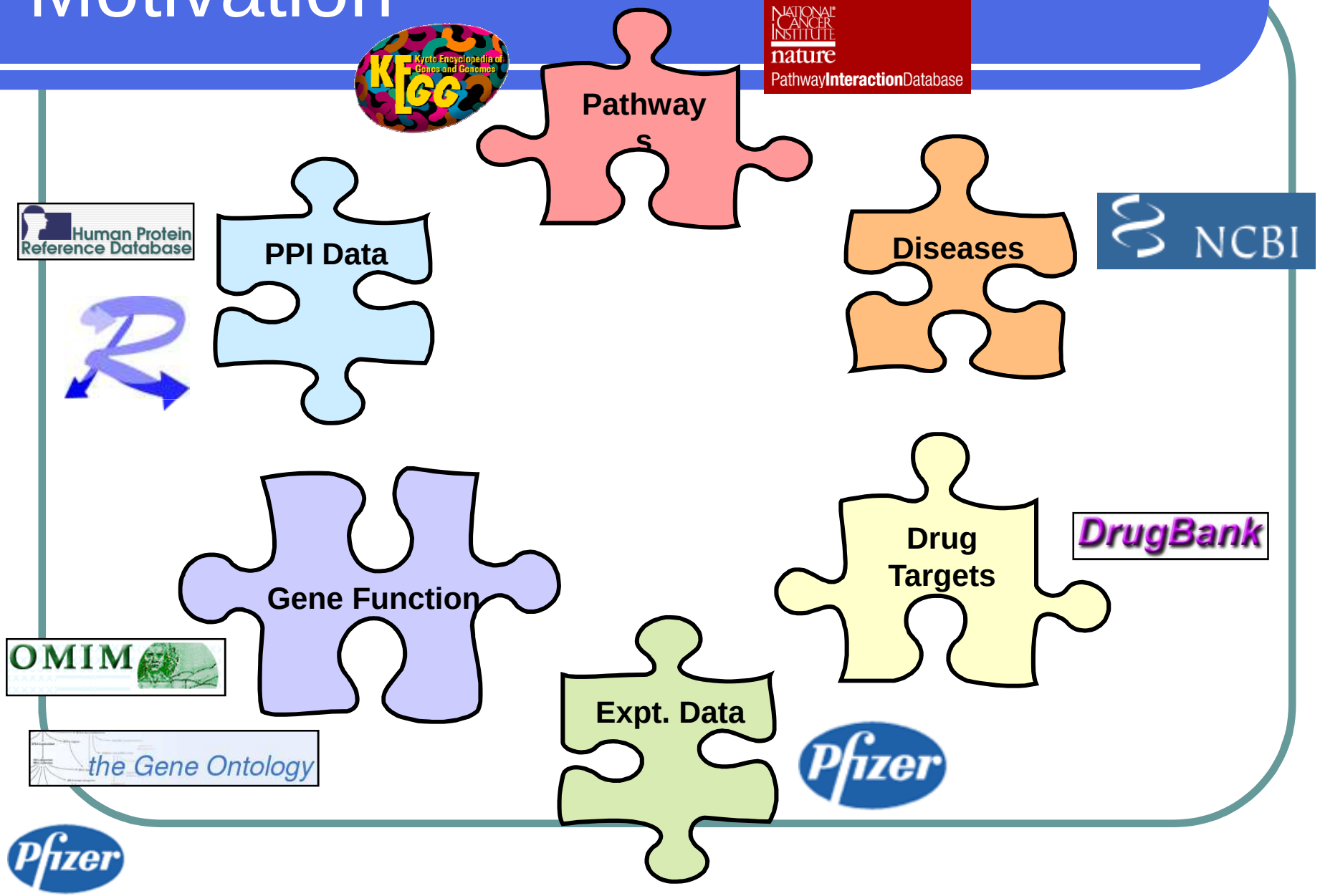
COBALT

Connection of Biological Lists

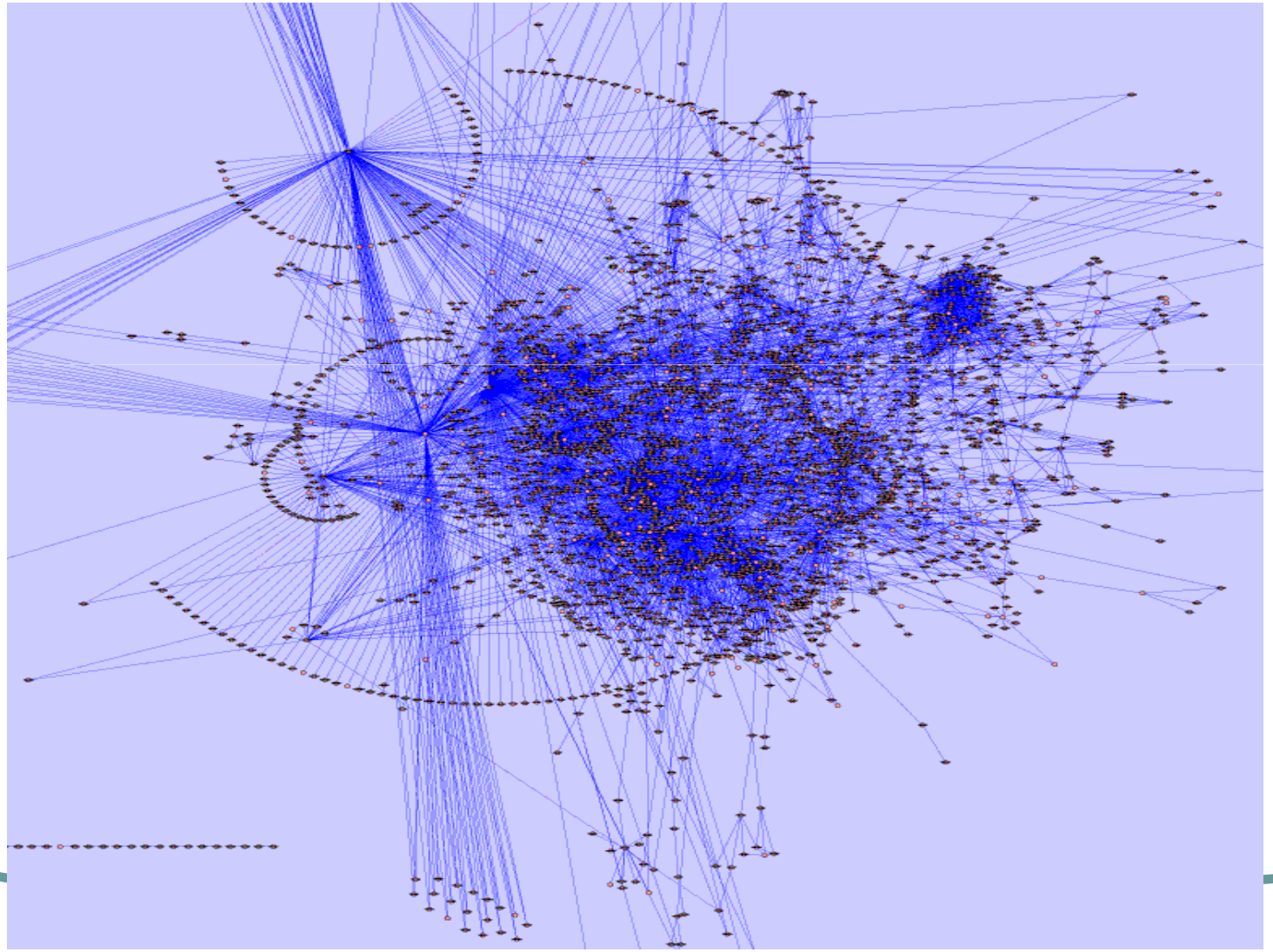
BioMANTA Meeting
November 15, 2007

Mike Schaffer & Victor Farutin

Motivation


KEGG
Kyoto Encyclopedia of Genes and Genomes
Pathways
NATIONAL CANCER INSTITUTE
nature
PathwayInteractionDatabase
Human Protein Reference Database
PPI Data
Diseases
NCBI
Gene Function
Drug Targets
DrugBank
OMIM
Expt. Data
the Gene Ontology
Pfizer
Pfizer

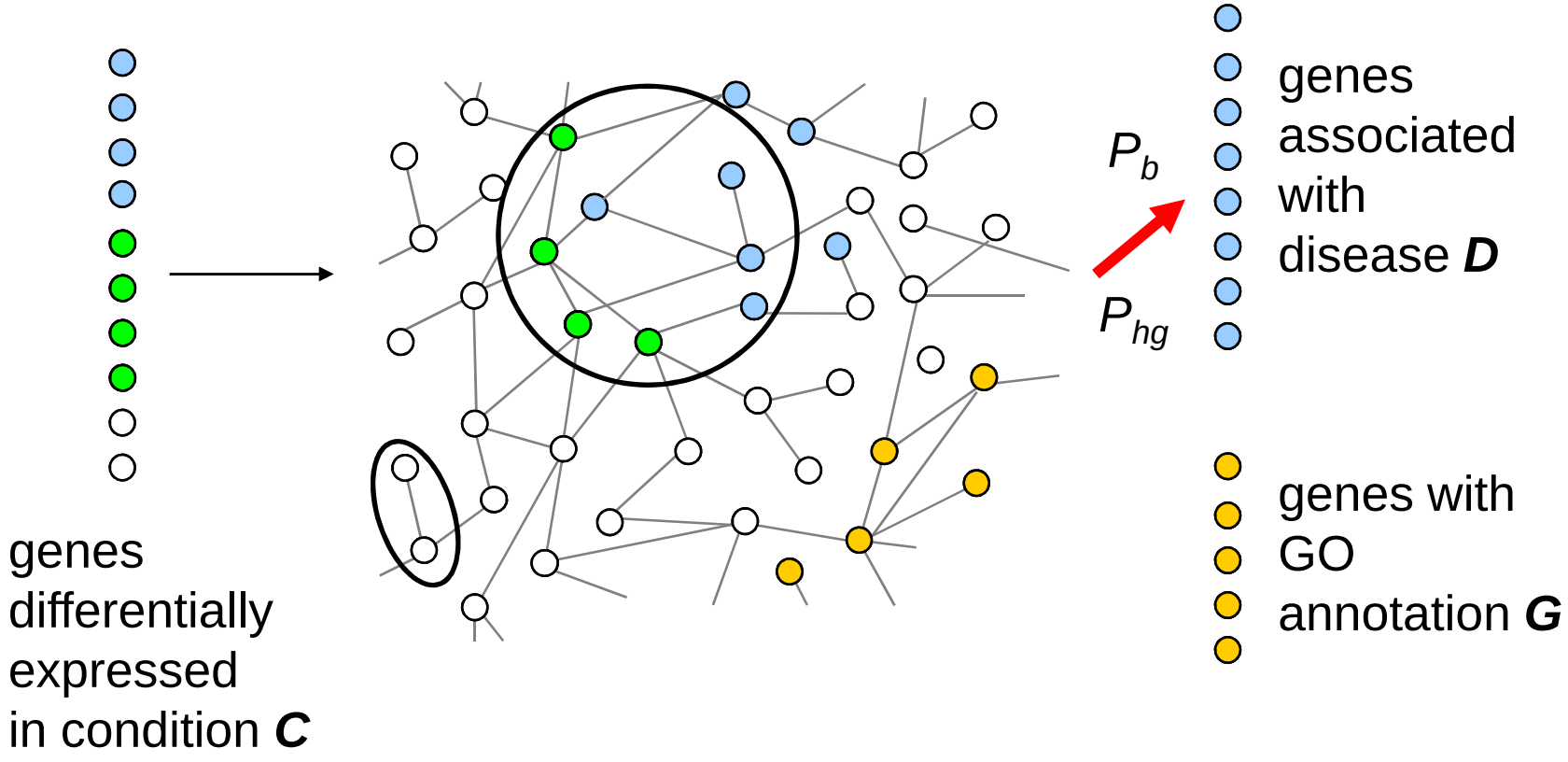
The “Hairball” Problem



COBALT

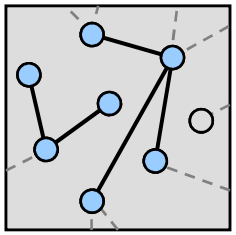
- A Java application being developed at the RTC
- Addresses “hairball” problem by using graph-based approaches to find connections between gene lists

COBALT Overview



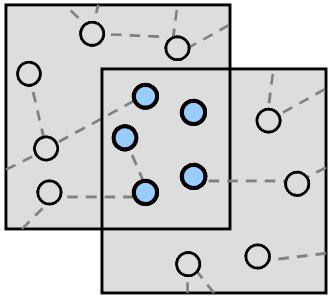
Statistics

P_L :



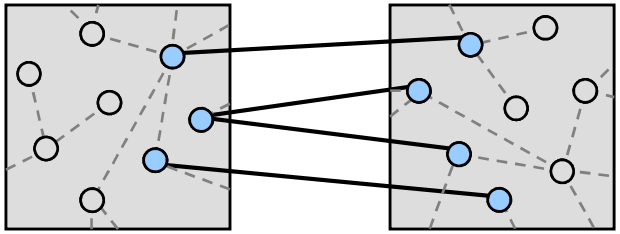
significance of within-set connections

P_{hg} :



significance of set overlap

P_b :



significance of between-set connections

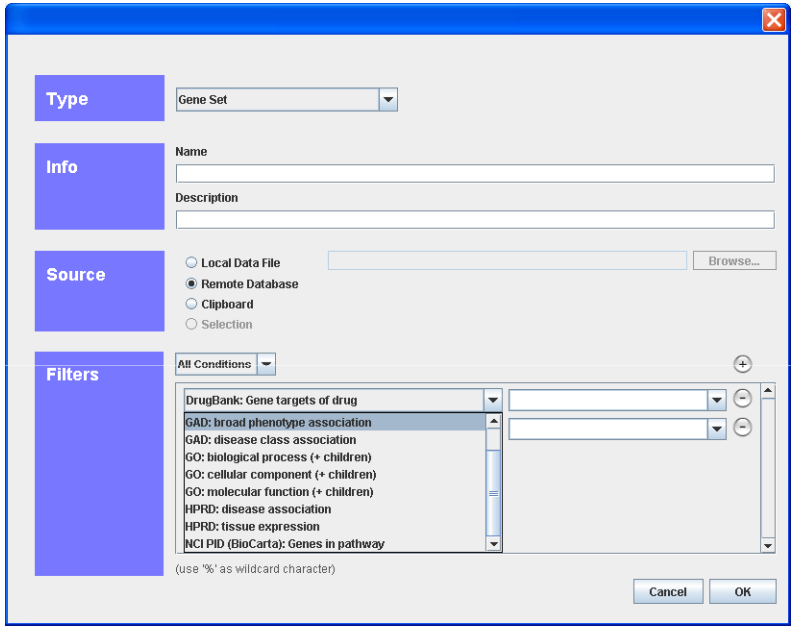
Joel R. Pradines, Victor Farutin, Steve Rowley, Vlado Dancik. (2005) "Analyzing Protein Lists with Large Networks: Edge-Count Probabilities in Random Graphs with Given Expected Degrees". Journal of Computational Biology. 12(2): 113-128.

Gene Sets

GAD:
- broad phenotype
- disease class
- MESH term

GO:
- biological process
- cellular component
- molecular function

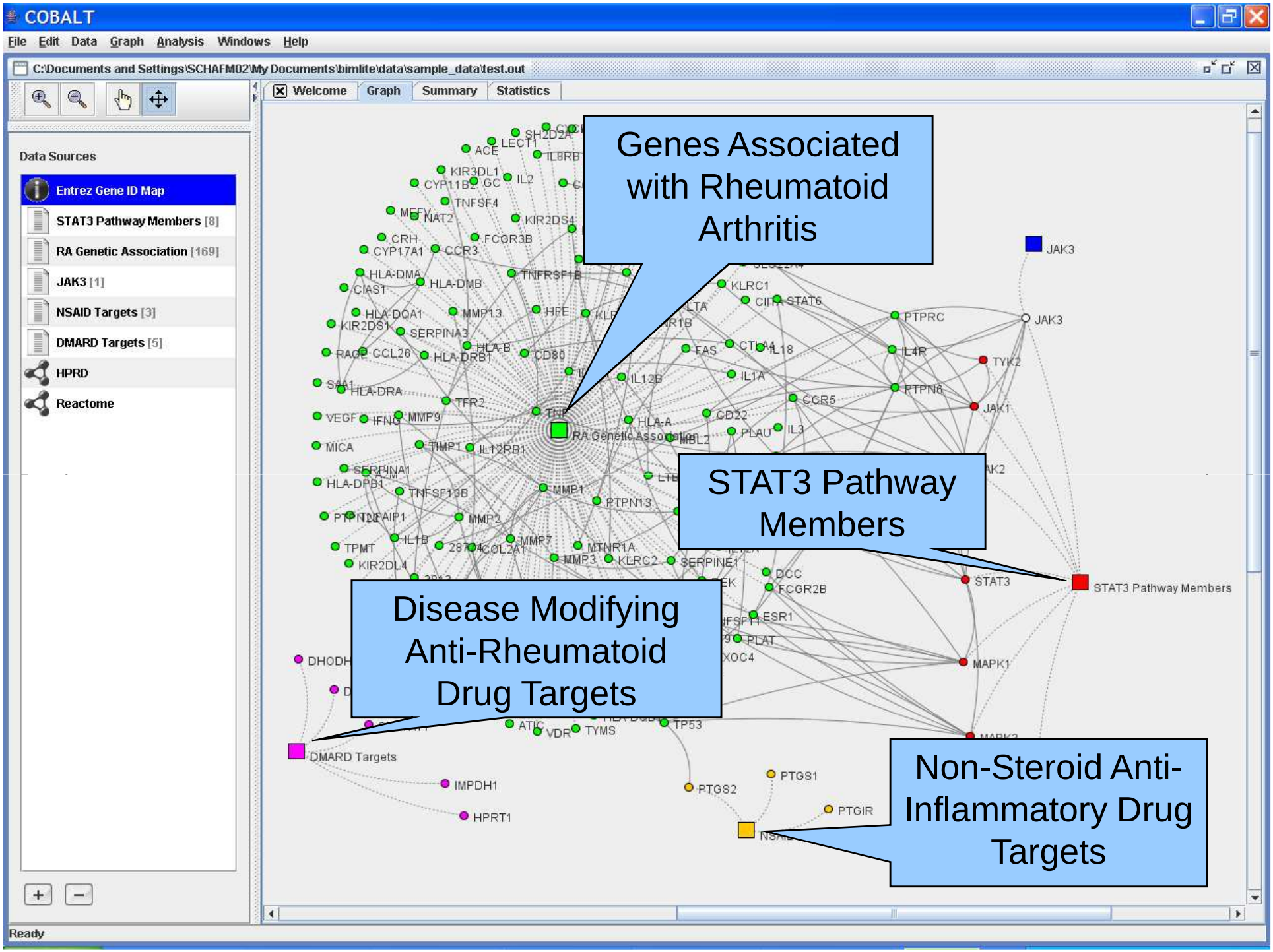
HPRD:
- disease association
- tissue expression



NCI PID/BioCarta: Canonical pathway genes

DrugBank: Gene targets of drug

Experimentally Derived: Microarray, KSS


COBALT
File Edit Data Graph Analysis Windows Help
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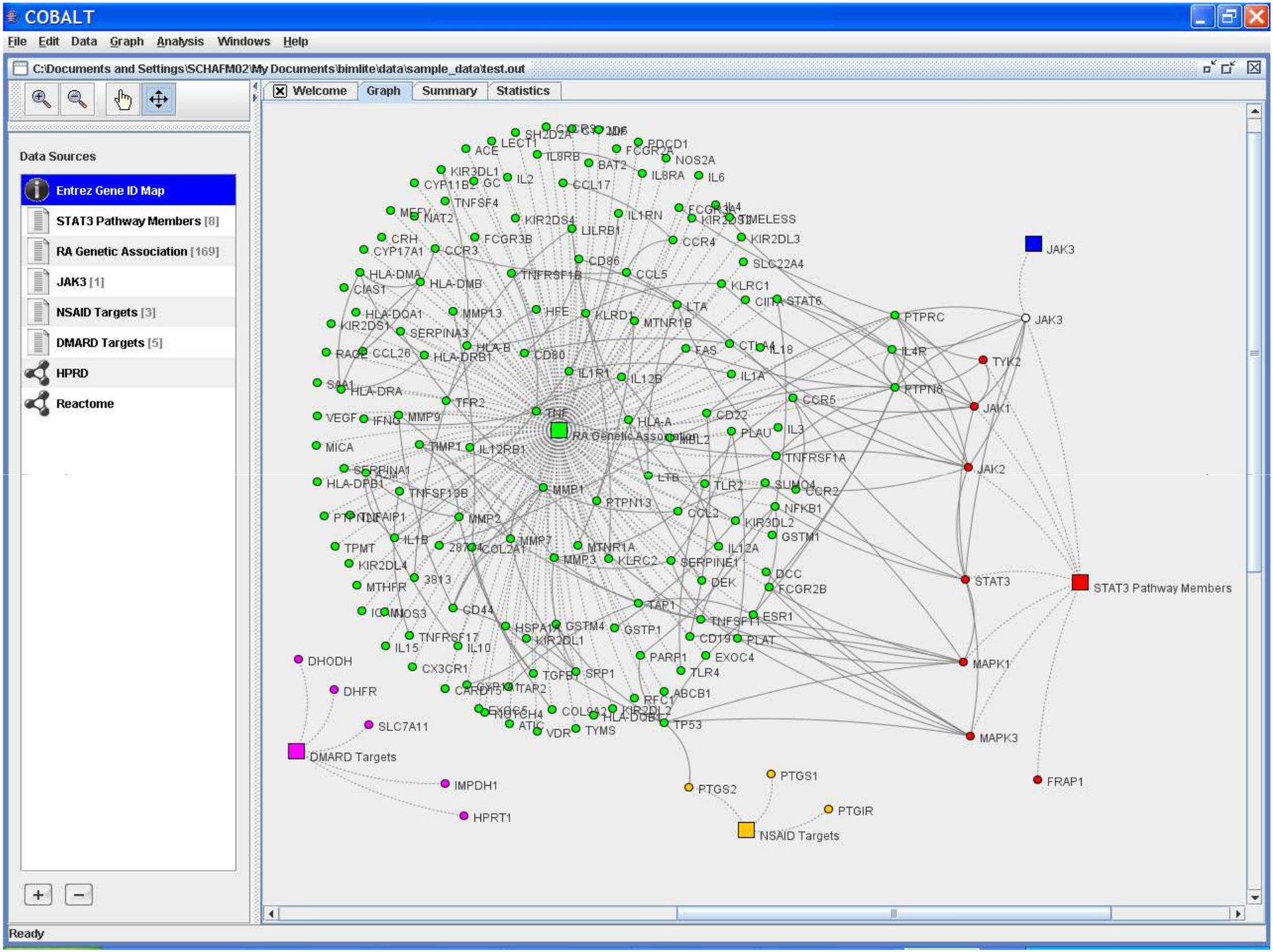
Welcome
Graph
Summary
Statistics
Data Sources
Entrez Gene ID Map
STAT3 Pathway Members [8]
RA Genetic Association [169]
JAK3 [1]
NSAID Targets [3]
DMARD Targets [5]
HPRD
Reactome
Genes Associated with Rheumatoid Arthritis
STAT3 Pathway Members
Disease Modifying Anti-Rheumatoid Drug Targets
Non-Steroid Anti-Inflammatory Drug Targets
JAK3
STAT3
STAT3 Pathway Members
DMARD Targets
NSAID Targets
RA Genetic Association
Ready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Welcome
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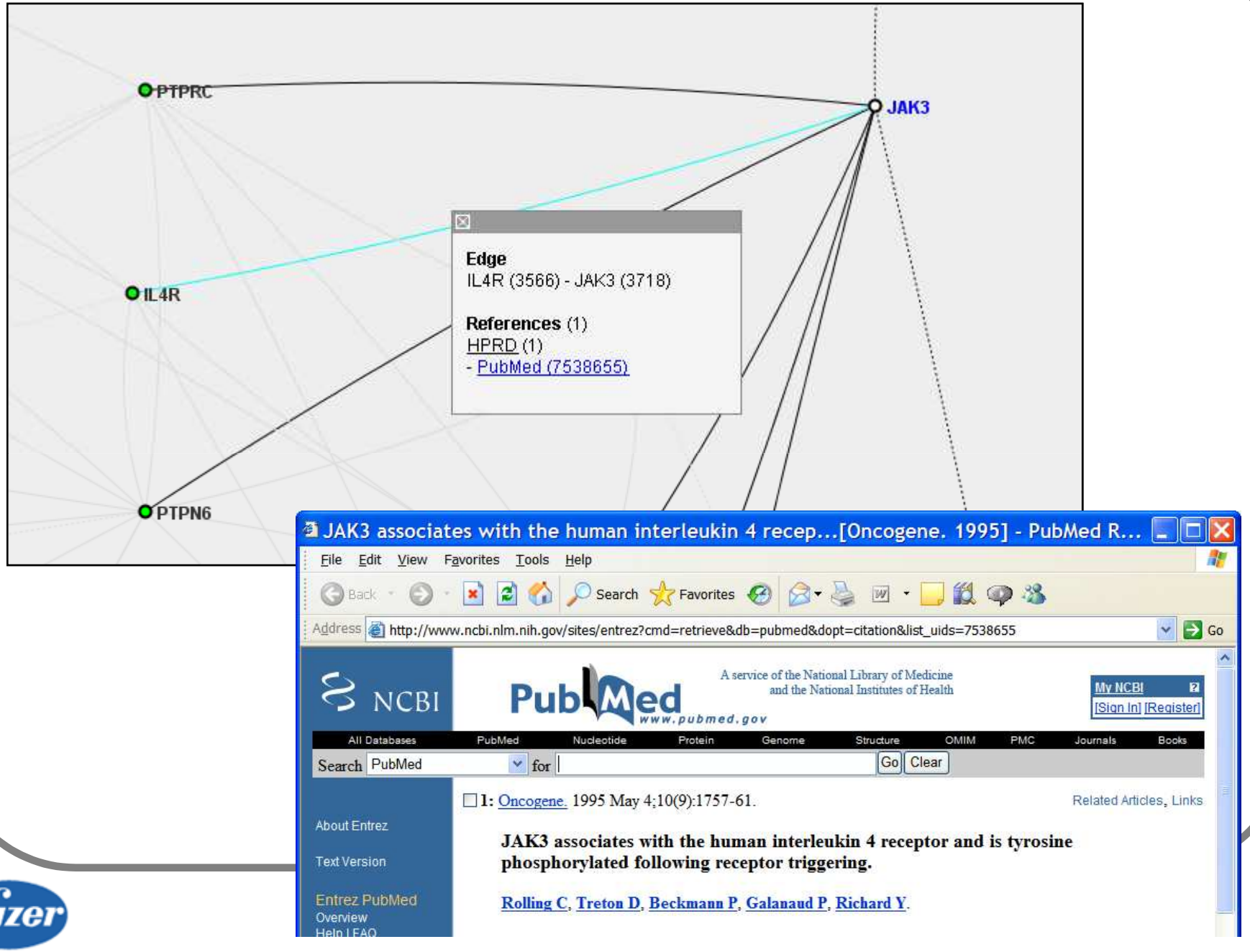
HPRD
Reactome
RA Genetic Association
JAK3
STAT3
STAT3 Pathway Members
MAPK1
MAPK3
FRAP1
DMARD Targets
NSAID Targets
Ready


PTPRC
JAK3
IL4R
PTPN6
Edge
IL4R (3566) - JAK3 (3718)
References (1)
HPRD (1)
- PubMed (7538655)
JAK3 associates with the human interleukin 4 recep...[Oncogene. 1995] - PubMed R...
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Address http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=retrieve&db=pubmed&dopt=citation&list_uids=7538655
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A service of the National Library of Medicine and the National Institutes of Health
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All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books
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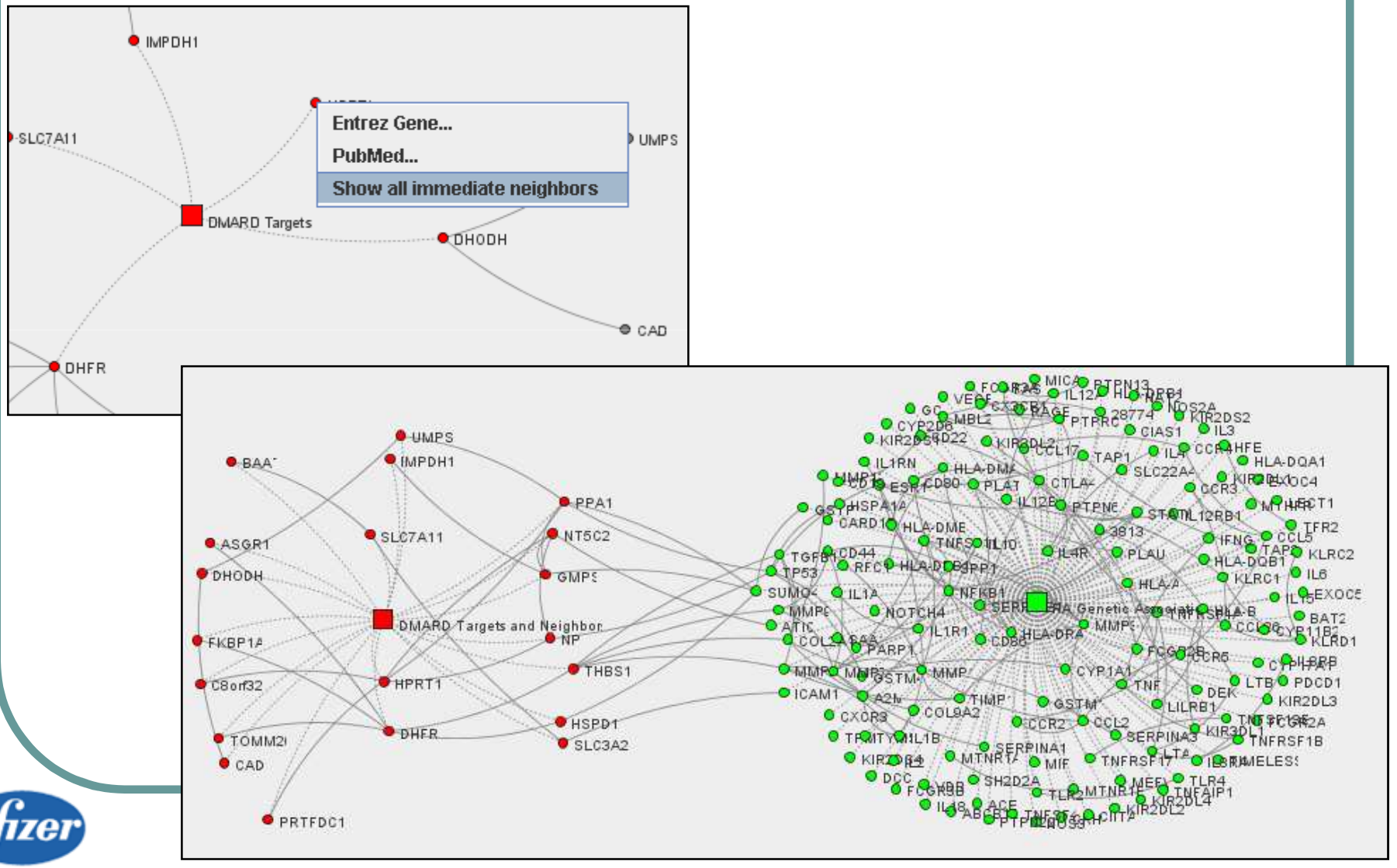
1: Oncogene. 1995 May 4;10(9):1757-61.
Related Articles, Links
JAK3 associates with the human interleukin 4 receptor and is tyrosine phosphorylated following receptor triggering.
Rolling C, Treton D, Beckmann P, Galanaud P, Richard Y.

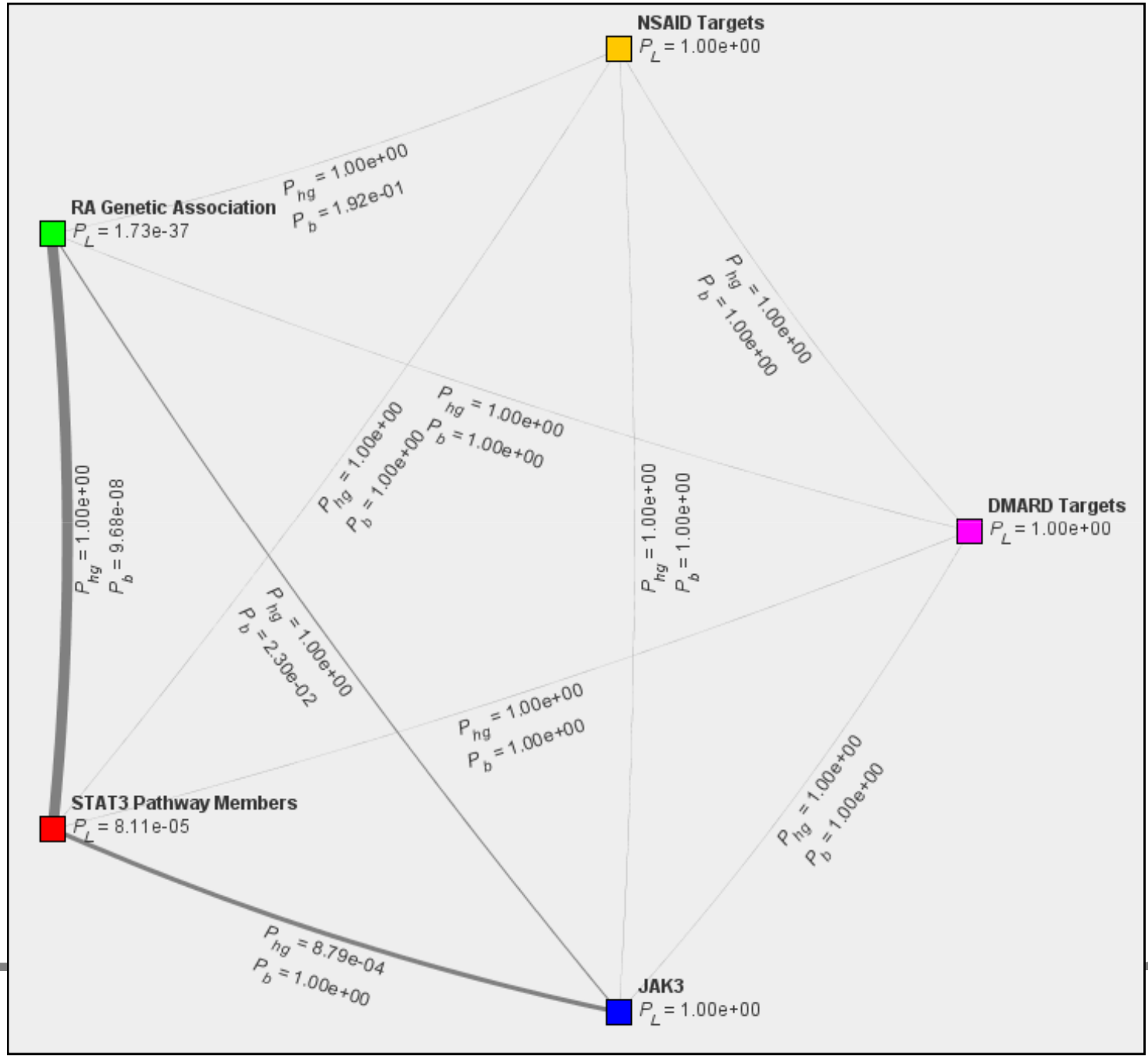
Interactions Between Sets

Bipartite Interactions Between Sets

	RA Genetic Association	JAK3	NSAID Targets	DMARD Targets
STAT3 Pathway Members	CCR2 - JAK2 CCR5 - JAK2 CTLA4 - JAK2 IL4R - JAK2 JAK2 - PTPN6 JAK2 - PTPRC JAK2 - TNFRSF1A ESR1 - MAPK1 FCGR2B - MAPK1 PLAT - MAPK1 MAPK1 - TNFRSF1A MAPK1 - TP53 MAPK1 - TNFSF11 MAPK1 - CD19 CCR5 - JAK1 IL4R - JAK1 JAK1 - PTPN6 JAK1 - PTPRC JAK1 - STAT6 JAK1 - TNFRSF1A PTPN6 - TYK2 PTPRC - TYK2 DCC - MAPK3 ESR1 - MAPK3 FCGR2B - MAPK3 PLAT - MAPK3 MAPK3 - TP53 MAPK3 - TNFSF11 IL4R - JAK3 JAK3 - PTPN6 JAK3 - PTPRC CCR5 - STAT3 SUMO4 - STAT3 NFKB1 - STAT3			
RA Genetic Association		JAK3 - PTPRC IL4R - JAK3 JAK3 - PTPN6	PTGS2 - TP53	
JAK3				
NSAID Targets				

Expand Sets to Neighbors




NSAID Targets
P_L = 1.00e+00
RA Genetic Association
P_L = 1.73e-37
P_{hg} = 1.00e+00
P_b = 1.92e-01
P_{hg} = 1.00e+00
P_b = 1.00e+00
P_{hg} = 1.00e+00
P_b = 1.00e+00
P_{hg} = 1.00e+00
P_b = 1.00e+00
DMARD Targets
P_L = 1.00e+00
P_{hg} = 1.00e+00
P_b = 9.68e-08
P_{hg} = 1.00e+00
P_b = 1.00e+00
P_{hg} = 1.00e+00
P_b = 2.30e-02
P_{hg} = 1.00e+00
P_b = 1.00e+00
P_{hg} = 1.00e+00
P_b = 1.00e+00
STAT3 Pathway Members
P_L = 8.11e-05
P_{hg} = 8.79e-04
P_b = 1.00e+00
JAK3
P_L = 1.00e+00