

# Networks and Interactions

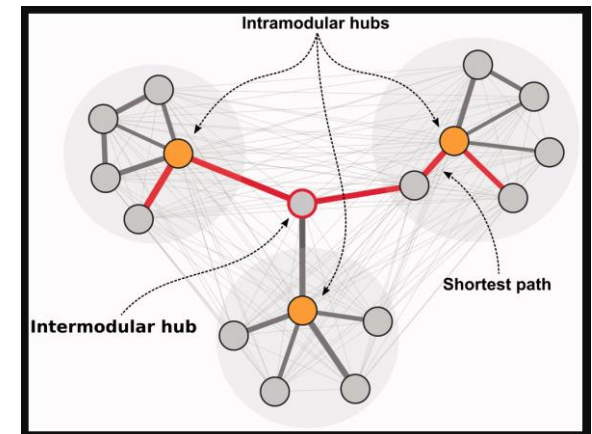
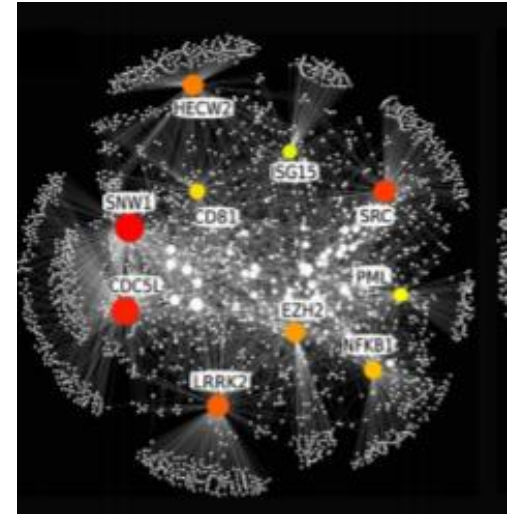
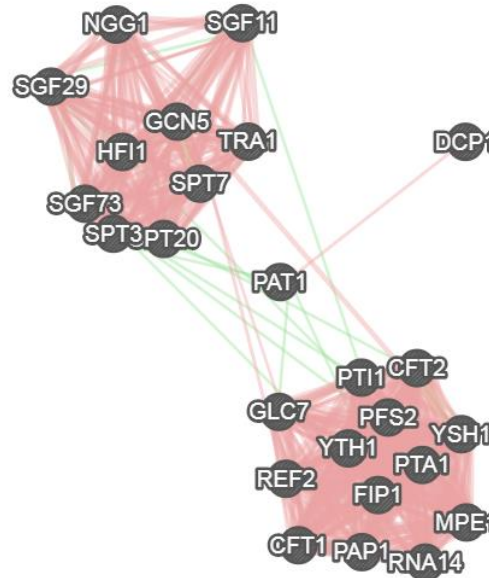
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v2017-07



# Why Networks?

- Biological processes are often controlled by a complex network of molecular interactions
- May identify important genes 'missing' from analysis
- May identify hub and bottleneck genes that are particularly important



# Network Analysis: Approach 1

Infer the network directly from the data generated

Algorithms used to generate novel networks

- Does not rely on published and curated data
- Can find novel interactions
- Various algorithms available
  
- Computationally intensive and complex
- Beyond the scope of this course

# Network Analysis: Approach 2

Use existing experimentally-supported (and computationally derived) interactions and relationships. Overlay data on to these.

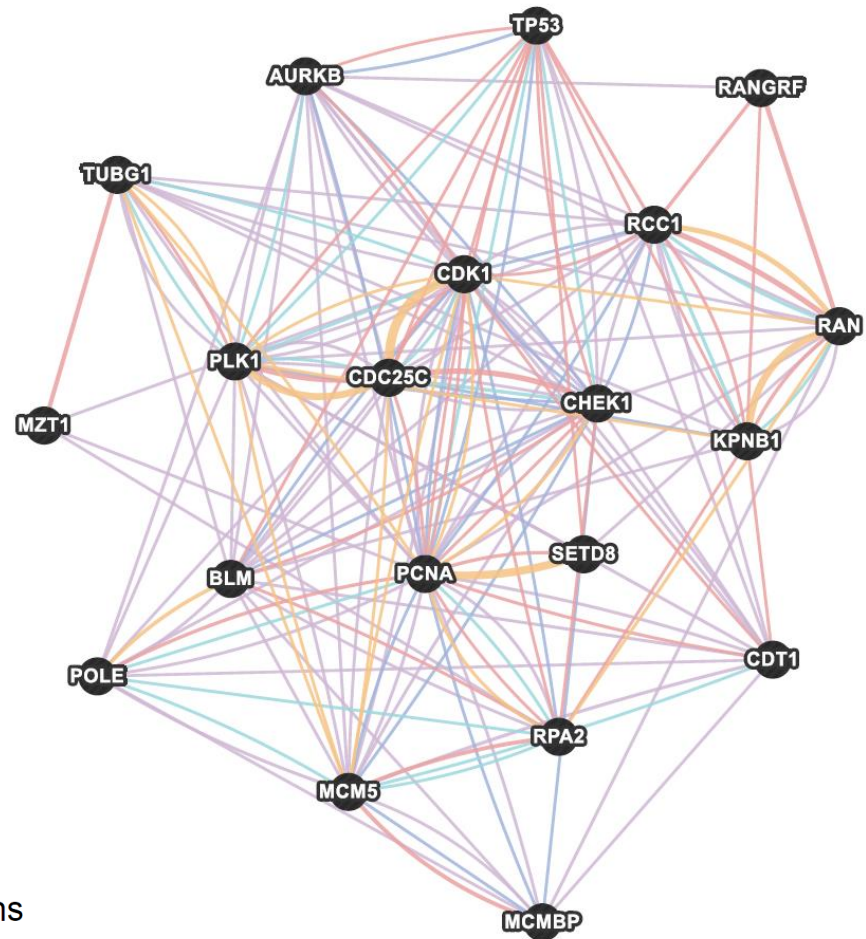
- A number of user-friendly software tools are available
- Simple and fast to perform analysis
- Various databases exist of different types of interactions
- Relies on published and curated data

# Types of interactions

Multiple sources  
and types of  
interaction data

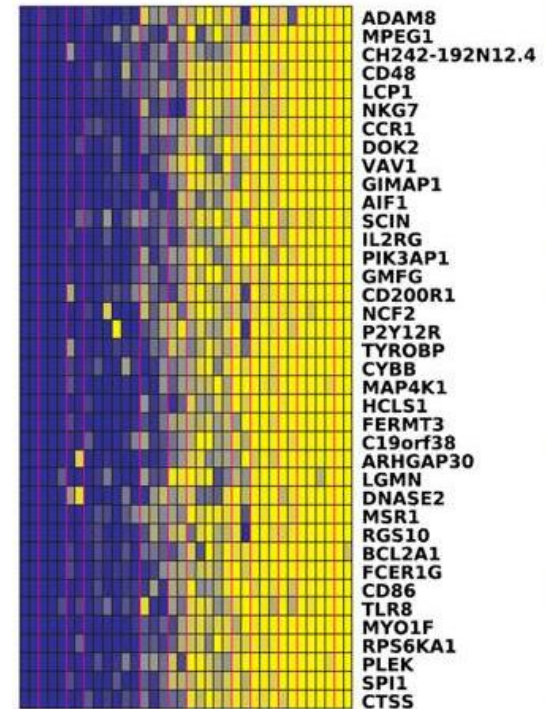
## Networks legend

- Co-expression
- Co-localization
- Pathway
- Physical interactions
- Predicted



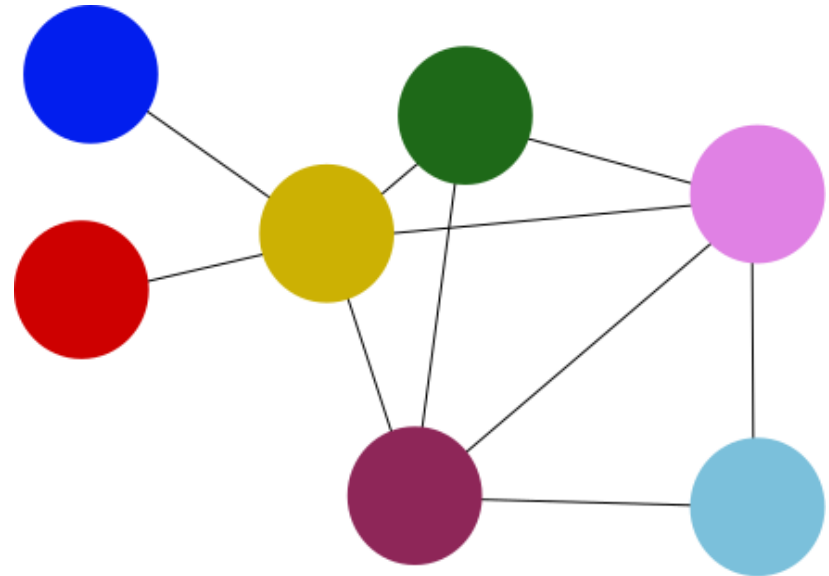
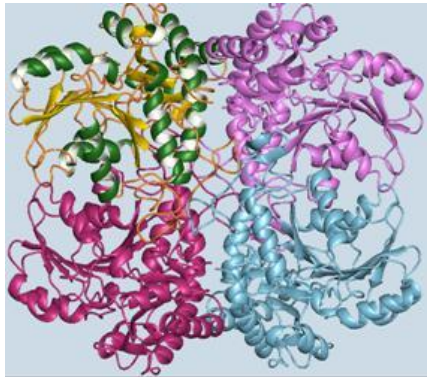
# Gene Co-expression

- Gene expression data
- Two genes are linked if their expression levels were similar across conditions in a gene expression study



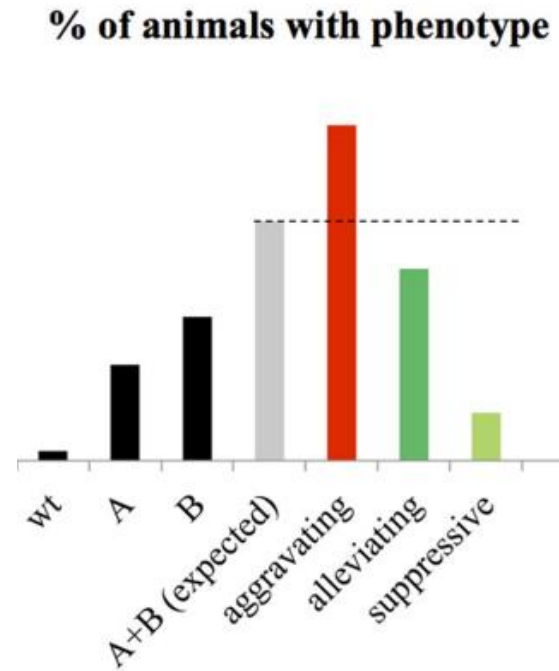
# Physical Interaction

- Protein-protein interaction (PPI) data
- Two gene products linked if found to interact in protein-protein interaction study



# Genetic Interaction

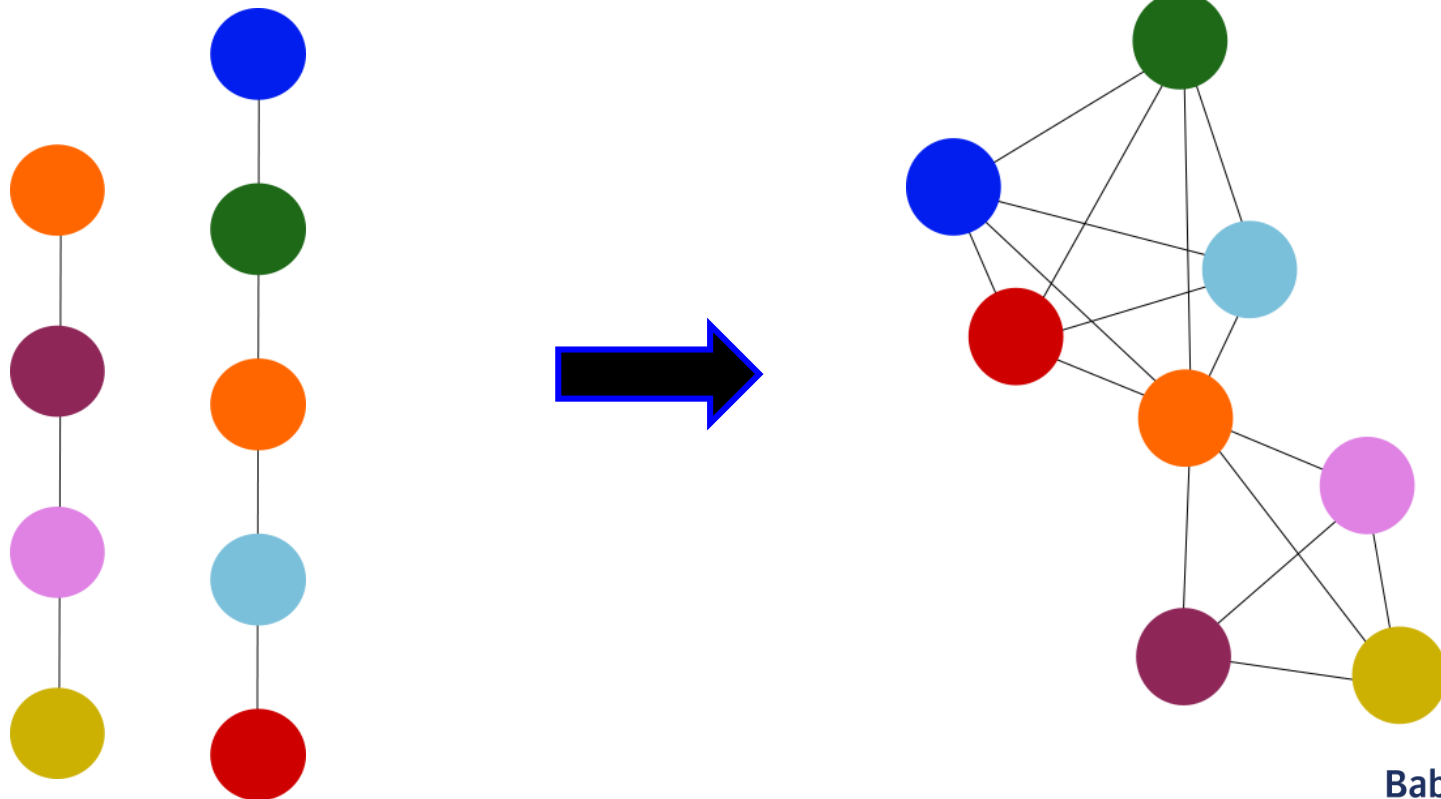
- Two genes are functionally associated if the effects of perturbing one gene were found to be modified by perturbations to a second gene
- i.e. phenotype of double mutant differs from that expected from each individual mutant





# Pathway

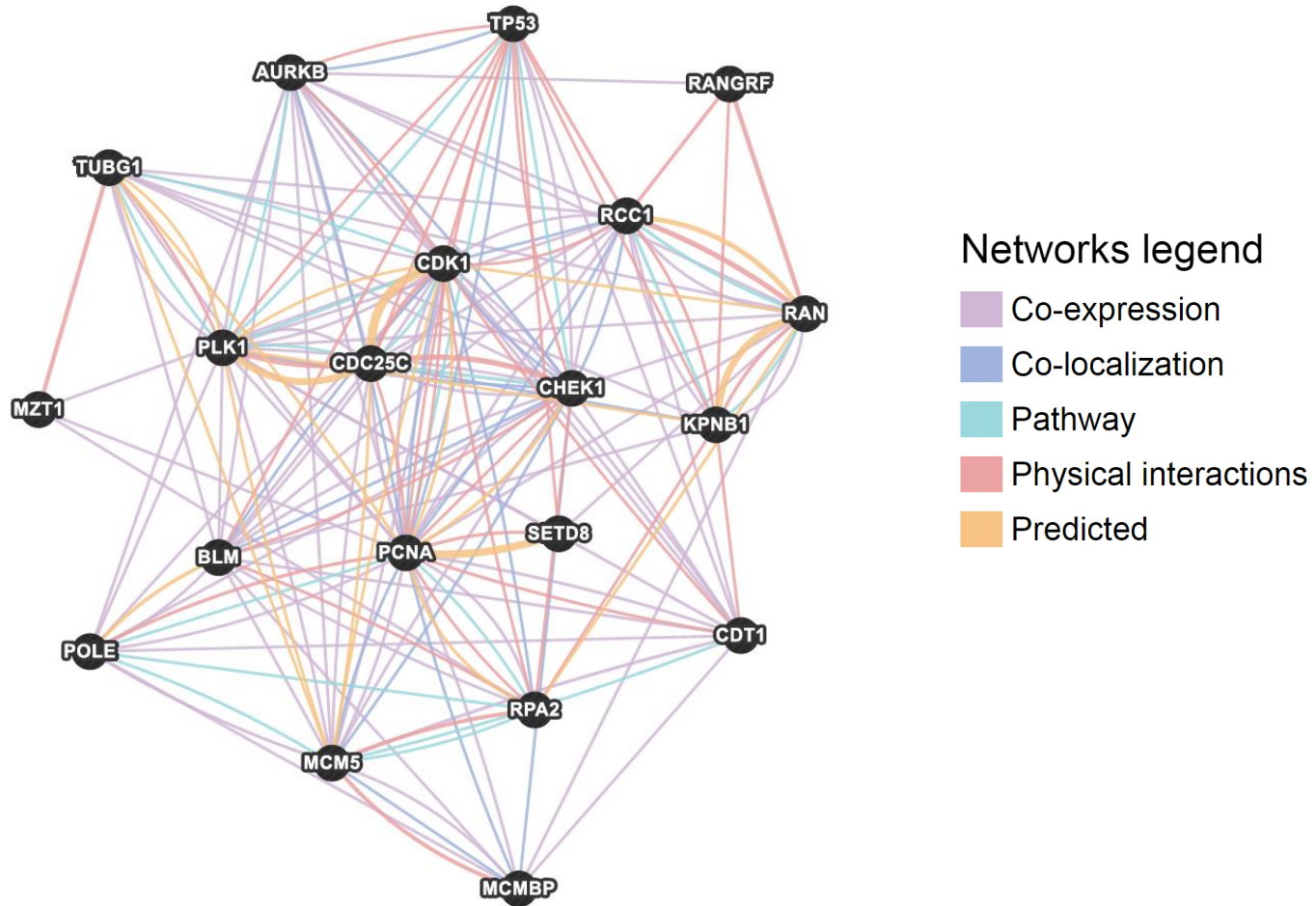
- Two gene products are linked if they participate in the same reaction within a pathway
- Unlike physical networks they don't have to directly interact



# Other Types of Network

- **Shared protein domain**
  - Two gene products linked if have the same protein domain
- **Co-localisation**
  - Two genes linked if both are expressed in the same tissue, or if their gene products are both identified in same cellular location

# Multiple Networks



# Constructing Networks





<http://www.cytoscape.org/>

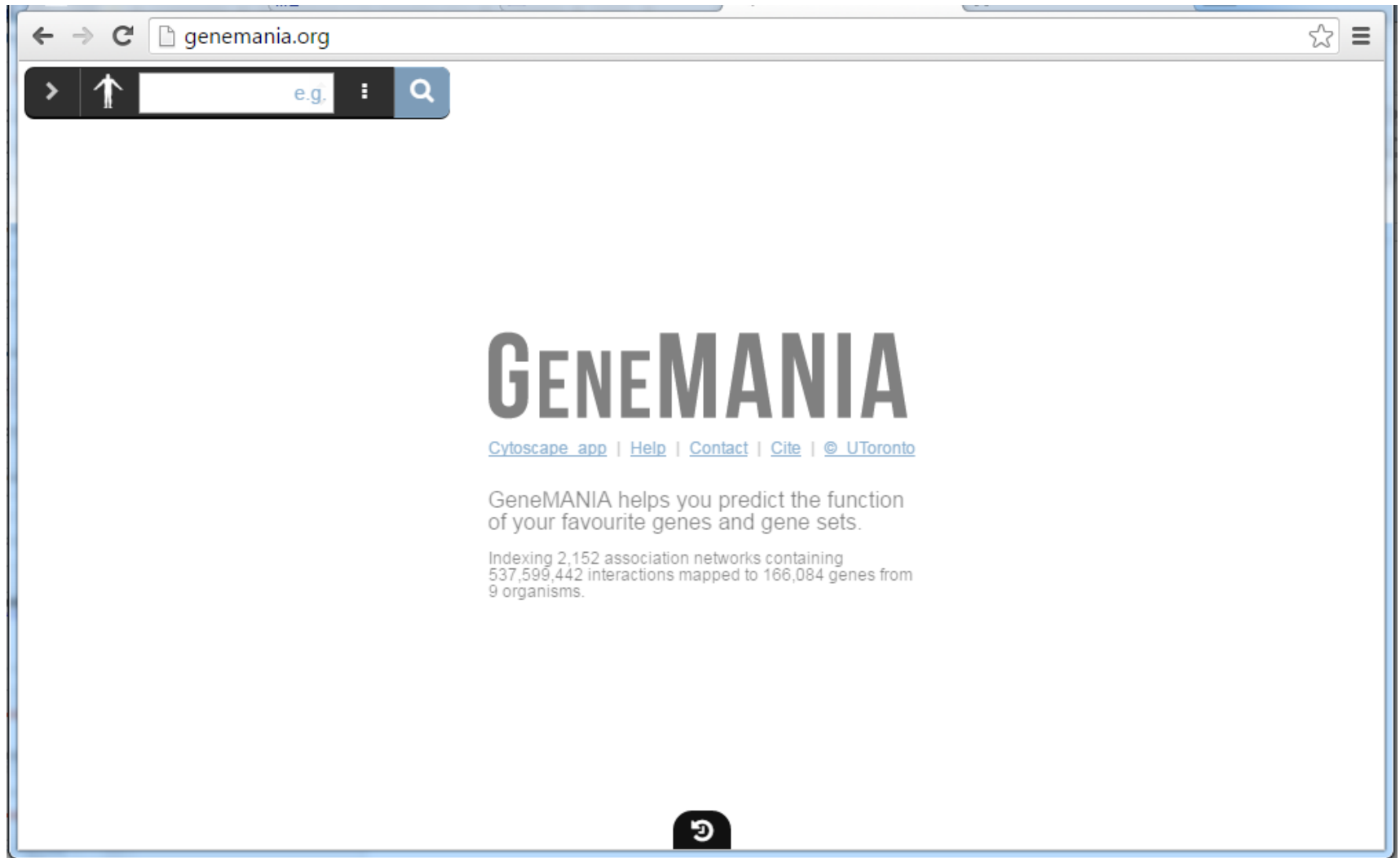
- Open source software platform
- Lots of functionality
- Visualize networks and biological pathways
- Integrate networks with annotations, gene expression profiles, etc
- Can import, edit and **analyse networks**
- Lots of Apps!
- Whole courses dedicated to Cytoscape – not covering it today

# GENEMANIA



- Free and easy to use web resources for network analysis
- Used in the practical today
- <http://www.genemania.org/>
- <https://string-db.org/>

# Genemania - demo





- Free to use web resource  
<http://string-db.org/>
- Direct and indirect associations from 4 sources:
  - co-expression
  - genomic context,
  - high throughput experiments
  - published/previous knowledge
- Over 2000 organisms (some more studied than others though)





# Welcome to STRING

## Protein-Protein Interaction Networks

ORGANISMS	PROTEINS	INTERACTIONS
2031	9.6 mio	1380 mio

SEARCH

# Genemania

- Association data include:  
Protein interactions, genetic interactions  
pathways, co-expression, co-localization,
- 9 Organisms available  
human, mouse, rat, worm, fly, zebrafish, E. coli,  
Arabidopsis, yeast
- Overlay functional enrichment  
information
- Precisely control the number of inferred  
genes
- No clustering options
- No network stats
- Export a report

# String

- More protein-centred  
Known interactions, predicted interactions, homology etc.
- Over 2000 organisms
- Overlay functional enrichment information –  
1 term at a time
- Control the number of inferred genes - bins
- Export various types of files
- Clustering options
- Basic network stats
- Export tables and figures
- Adjust minimum interaction score

# Network Practical