



Canadian Bioinformatics Workshops

www.bioinformatics.ca

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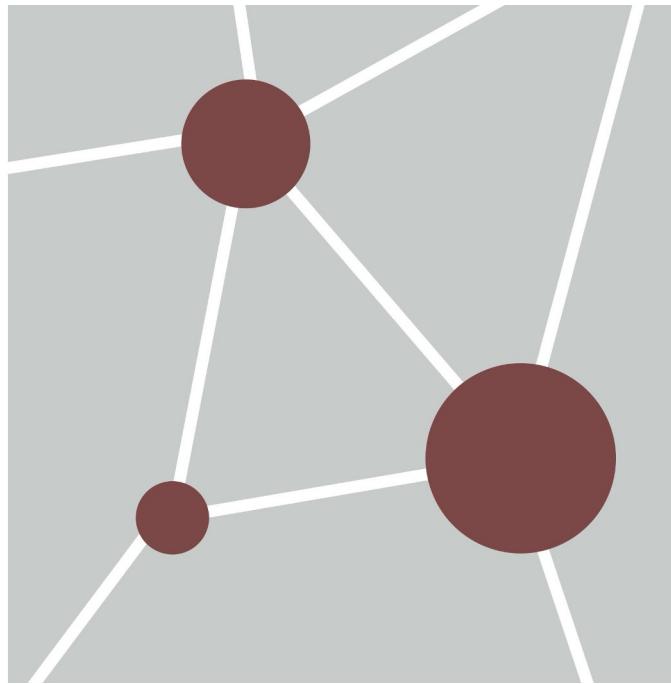
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Final Slides

Veronique Voisin
Pathway and Network Analysis of -omics Data
June 26-28, 2024



Summary

Cytoscape apps are organized by categories

cytoscape app store Submit an App ▾ Search the App Store Sign In

Wall of Apps 184 total

http://apps.cytoscape.org

network generation

online data import

graph analysis

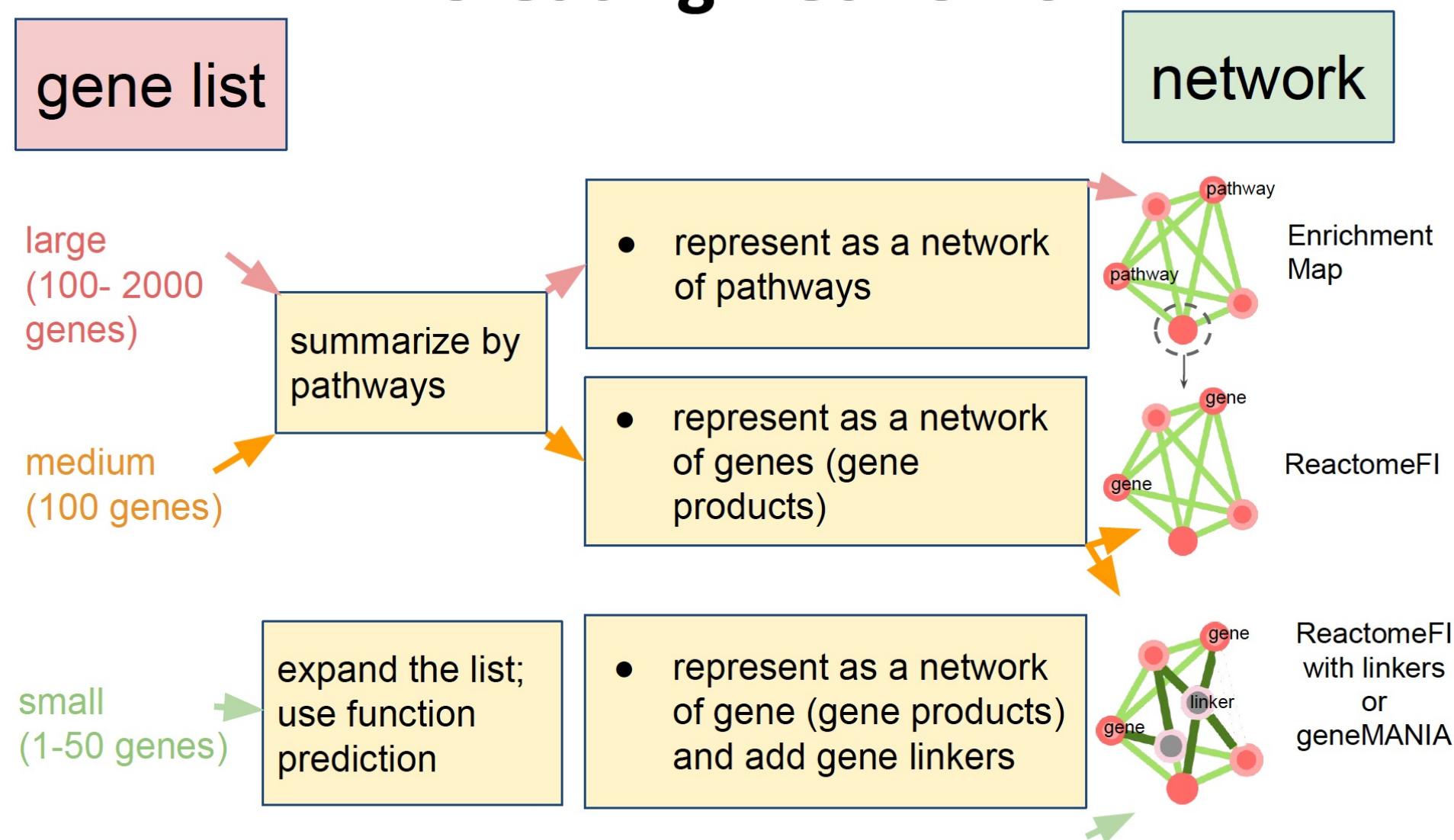
All Apps

Categories

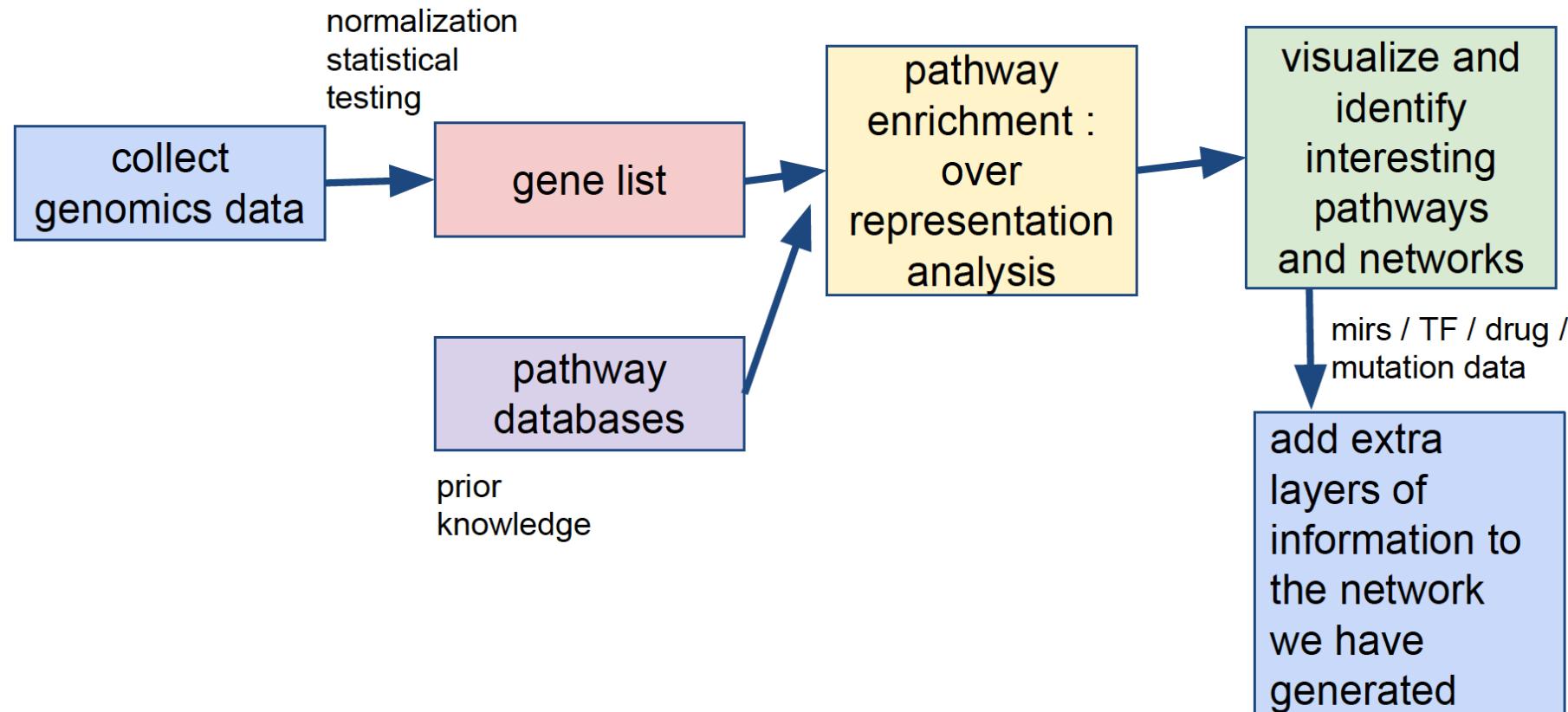
- data visualization**
- network generation
- graph analysis
- network analysis
- online data import
- automation
- integrated analysis
- clustering
- utility
- systems biology
- enrichment analysis
- visualization
- data integration
- core app
- layout
- annotation
- pathway database
- ontology analysis
- import
- gene expression

more »

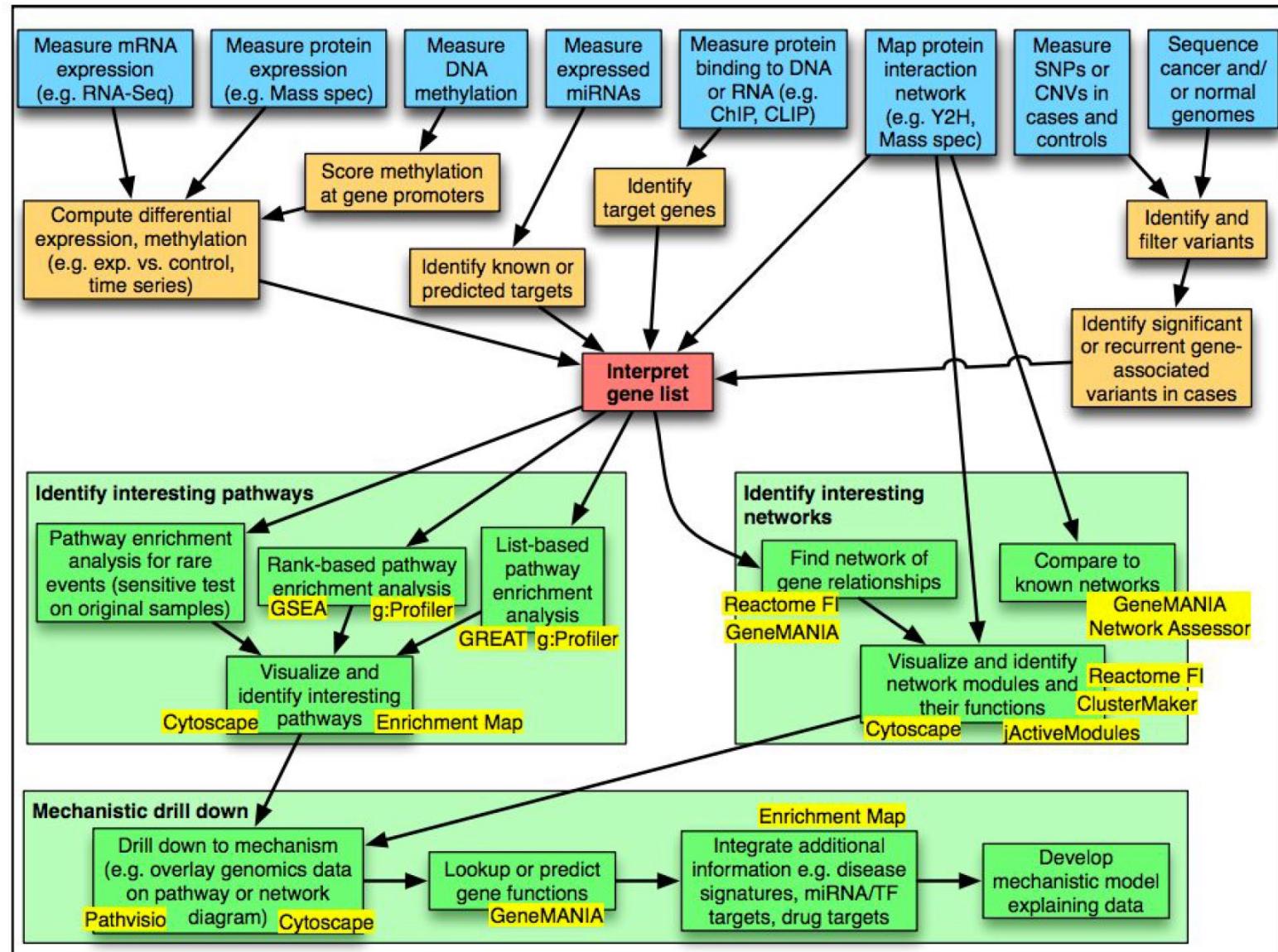
Creating Networks



WORKFLOW SUMMARY



ROADMAP



Mirs, pathways and targets

miRPathDB v2.0 Home About Documentation Download



miRPathDB 2.0

Search

Enter a miRNA or pathway name:

Fc gamma R-mediated phagocytosis

miRNAs that are significantly enriched for this pathway

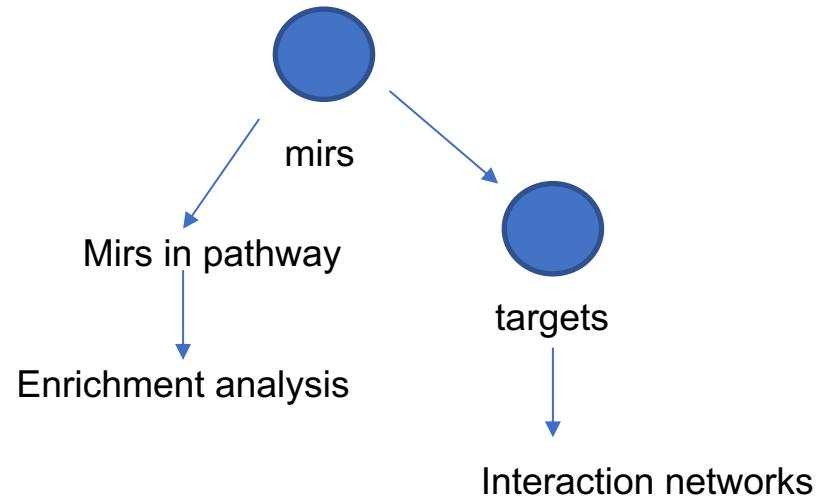
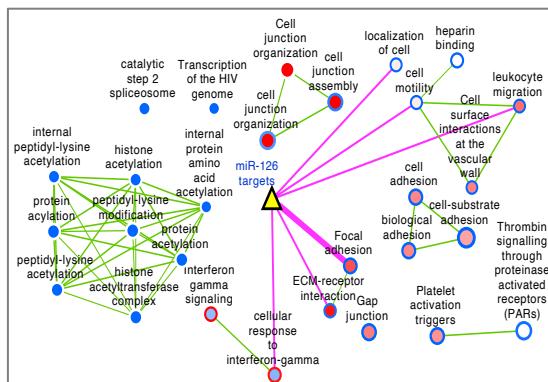
In this table miRNAs are depicted that have significantly more targets in this pathway than expected by chance.

Show 10 entries Search:

Database	miRNA	Evidence	Hits	Expected hits	P-value	Targets
miRBase	hsa-miR-126-3p	experimental (any)	7	0.281231	3.34e-8	AKT1,AKT2,CRK,CRKL,PK3CG,PKC
miRBase	hsa-miR-184	experimental (any)	5	0.297456	1.61e-4	AKT1,AKT2,INPL1,LPLP3,PRKCB
miRCarta	m-5765	predicted (union)	56	36.0553	3.01e-4	AKT2,ANPH,ARPC2,ARPC3,ARPC4
miRCarta	m-17942	predicted (intersection)	12	2.26763	3.89e-4	ARPC2,CRKL,ATM,MARK1,NCFL1,PIP5
miRCarta	m-152	predicted (union)	57	38.8709	4.14e-4	AKT2,ANPH,ARPC2,ARPC3,ARPC4
miRCarta	m-12614	predicted (union)	55	38.7072	4.47e-4	AKT1,AKT2,ARPC1B,ARPC2,ARPC4,ARPC5
miRBase	hsa-miR-184	experimental (strong)	5	0.336283	4.49e-4	AKT1,AKT2,INPL1,LPLP3,PRKCB
miRBase	hsa-miR-550a-3p	experimental (strong)	2	0.0053082	6.66e-4	MARK1,MARK3

EnrichmentMap
Post analysis
Mir targets

Post analysis:
Good for drug target
and transcription
factors



http://www.ccb.uni-saarland.de/mieaa_tool/

<http://www.lirmed.com/tam2/>

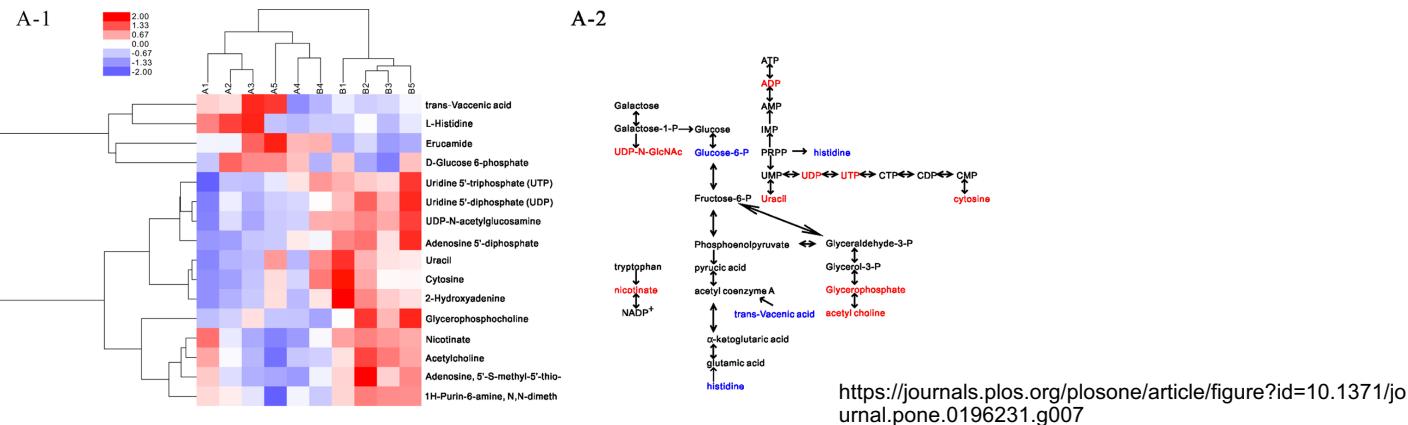
Result

Enrichment analysis results

Category	Count	Percent	Fold	P-value	Bonferroni	FDR
Cluster (4 Items)	1	0.33333	33.63889	0.0295	1	0.3755
Cluster (4 Items)	2	0.33333	33.63889	1.32e-3	0.3569	0.08
Cluster (4 Items)	1	0.5	50.45833	0.0197	1	0.3365
Cluster (4 Items)	1	0.2	20.18333	0.0487	1	0.479
Disease (194 Items)	1	0.16667	16.81944	0.0581	1	0.5292
Disease (194 Items)	2	0.14286	14.41667	7.67e-3	1	0.1858
Disease (194 Items)	2	0.04348	4.38768	0.0731	1	0.5944
Disease (194 Items)	1	0.14286	14.41667	0.0675	1	0.5676
Disease (194 Items)	2	0.08696	8.77536	0.0203	1	0.2926
Disease (194 Items)	1	0.04545	4.58712	0.1983	1	1
Disease (194 Items)	1	0.02632	2.6557	0.3191	1	1
Disease (194 Items)	2	0.0198	1.99835	0.2642	1	1
Adrenal Cortex Neoplasms (details)	1	0.08333	8.40972	0.1131	1	0.7828

Metabolomics Data Analysis

A) list of metabolites from your experiment



B) pathway: a set of metabolites known to be involved in metabolic pathways

The colored compounds indicate potential matches from the user's input, with red colors indicating significant hits and blue colors indicating non-significant hits.

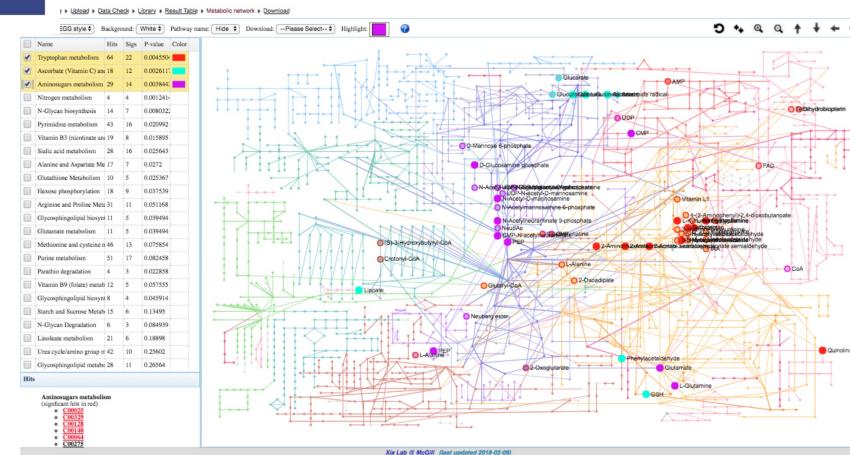
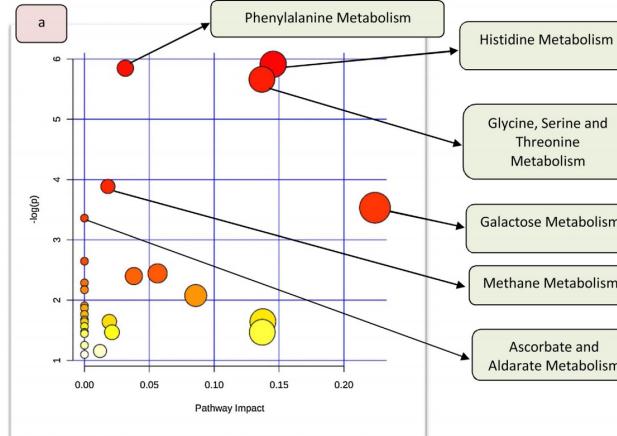
Pathway	Metabolites
Tryptophan metabolism	C00025; C00024; C00027; C00026; C00021; C00020; CE2119; C00028; C03722; C05647; C05645; CE1395; C05643; C05640; C00780; C05648; C00704; C01342; C00010; C00014; C00016; C00019; C15605; C00067; thbp4acam; C05651; C03512; C05653; C02693; C05660; C00398; CE5982; C00643; C02220; C00078; C00978; C00877; C05642; CE5860; C01252; C05637; C02406; C00108; C00272; CE1918; C01652; C02470; C01144; C06212; C06213; CE2949; CE2948; CE3140; CE2122; C00479; CE2947; C01717; CE3092; CE6205; CE5899; C03161; C00268; C00632; CE2152; CE2153; C02700; CE2095; C00328; CE3087; CE3086; C00322; C04409; C01352; C00051; C00058; C0030; C00331; C00332; C00936; C03824; C05636; C05635; C05634; C05639; C05638; C10164; C00637; C03227; C01598; C00525; C00527; C00041; C03024; C00954



Input Data Type	Available Modules (click on a module to proceed, or scroll down for more details)																																																																																																																																																																													
Raw Spectra (mzML, mzXML or mzData)	LC-MS Spectra Processing																																																																																																																																																																													
MS Peaks (peak list or intensity table)	Functional Analysis Functional Meta-analysis																																																																																																																																																																													
Annotated Features (compound list or table)	Enrichment Analysis Pathway Analysis Joint-Pathway Analysis Network Analysis																																																																																																																																																																													
Generic Format (.csv or .txt table files)	Statistical Analysis [one factor]	Statistical Analysis [metadata table]	Biomarker Analysis	Statistical Meta-analysis	Power Analysis	Other Utilities																																																																																																																																																																								
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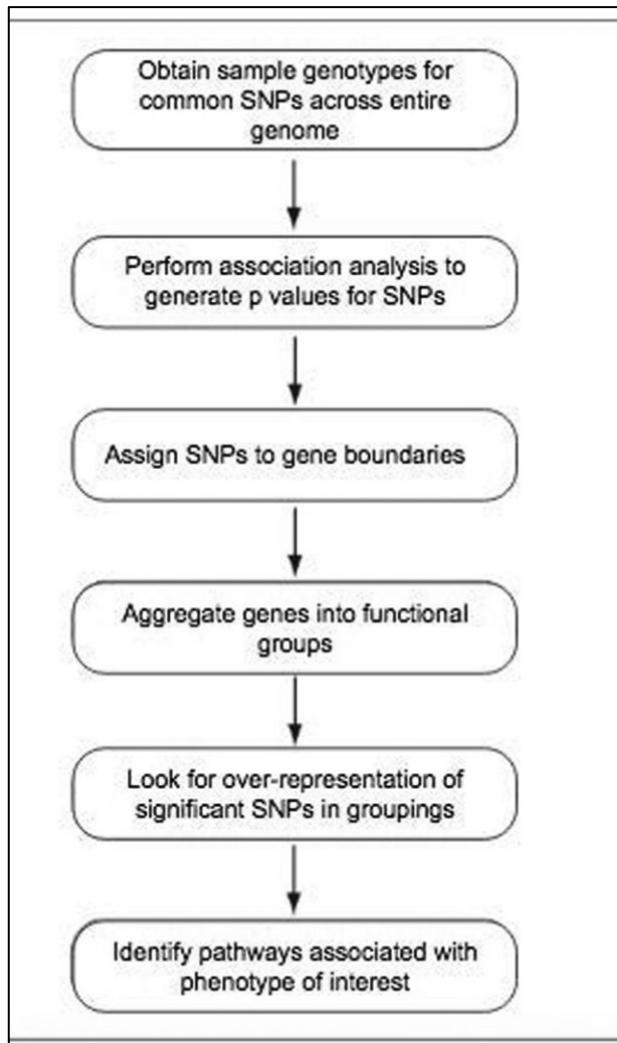
Download Result Tables: [Pathway Hits](#) [Compound Hits](#)

Metabolomics Data Analysis



List of metabolites: Fishers' exact test
If it is possible to rank all the metabolites: GSEA

Overall protocol for pathway-based GWAS / WGS analysis



GWAS --> MAGENTA
(Meta-Analysis Geneset Enrichment of variaNT Associations)
<https://software.broadinstitute.org/mpg/magenta/>

The only **input** required is a table with variant association p-values and their chromosome positions taken from a genome-wide association study or meta-analysis. **Optional:** pathway/s or gene set/s of interest. Otherwise, we provide a set of pathways from public databases (see below).

The main **output** of MAGENTA is a nominal **gene set enrichment analysis (GSEA) p-value** and a **false discovery rate** for each gene set or pathway tested. There are several options, including running MAGENTA in the absence of a subset of genes, such as a predefined set of disease or trait genes. Additional information is provided, such as the expected and observed number of genes above the enrichment cutoff, and the number and name of genes in each tested gene set that lie near validated disease or trait SNPs if inputted by the user.

Ref: <https://pubmed.ncbi.nlm.nih.gov/30387919/>

GWAS and pathway analysis

- **BridGE: a pathway-based analysis tool for detecting genetic interactions from GWAS.**
Published: 21 March 2024. Nature Protocol

ATACseq / CHIPseq

- GREAT (Stanford) is a recommended tool (from chromosomal position to gene + enrichment analysis)
- All tools compatible with EnrichmentMap

The screenshot shows the Great website homepage. At the top, there is a dark header bar with the 'GREAT' logo and links for Overview, News, Use GREAT, Demo, Video, How to Cite, Help, and Forum. Below the header, a dropdown menu shows 'GREAT version 4.0.4 current (08/19/2019 to now)'. The main content area has a title 'GREAT predicts functions of cis-regulatory regions.' followed by a detailed paragraph about the tool's purpose and methods. Below this, there is a 'News' section with a list of recent updates, each accompanied by a small sunburst icon. At the bottom of the news section, there is a link to 'More news items...'

Tips:

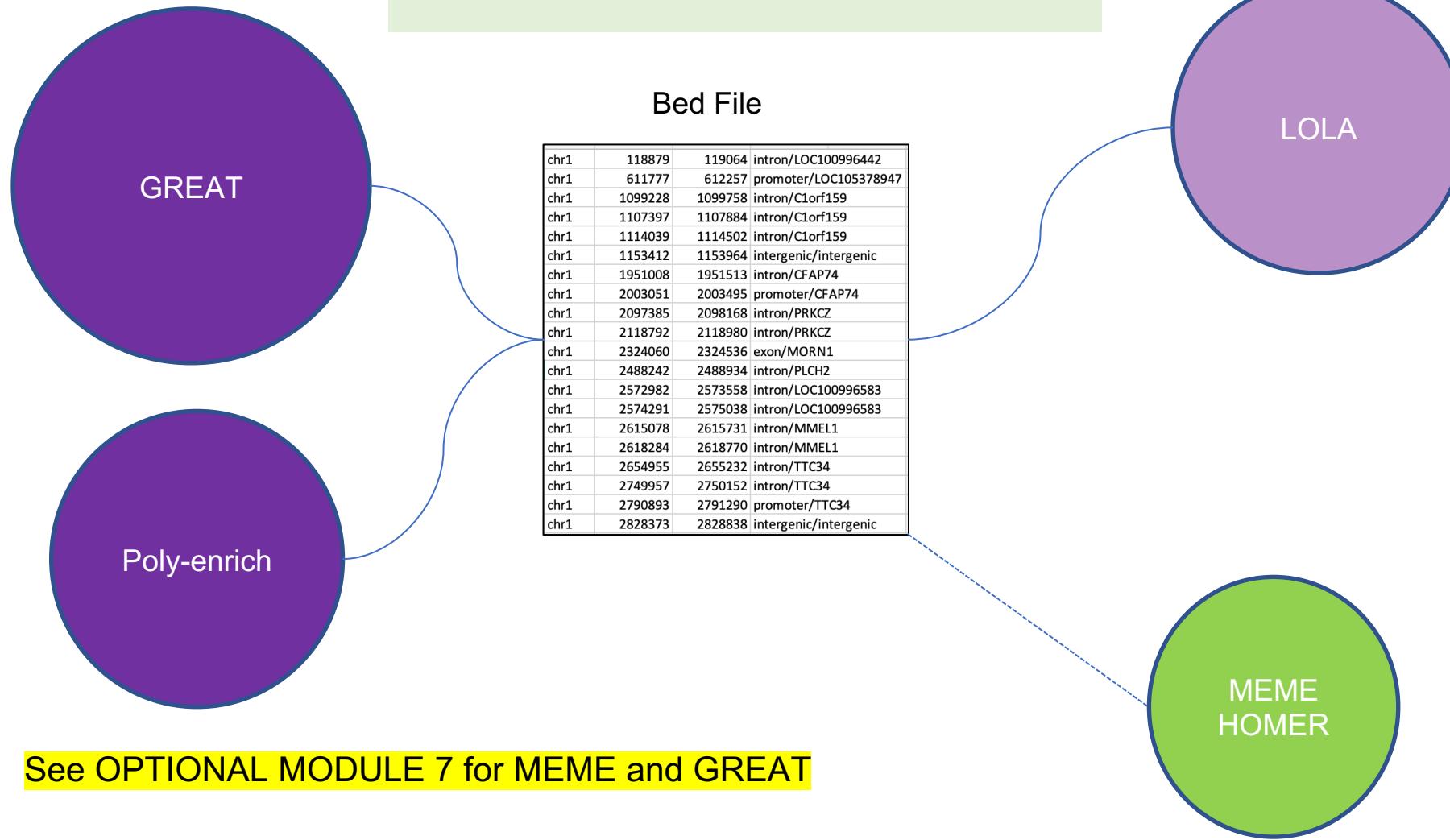
Do

- 1) Proximal analysis (+-2kb around TSS of genes)

And

- 2) Distal analysis (+-50kb around genes, filter genomic regions using tools like Segway or BEHST)

ATACseq / CHIPseq



See OPTIONAL MODULE 7 for MEME and GREAT

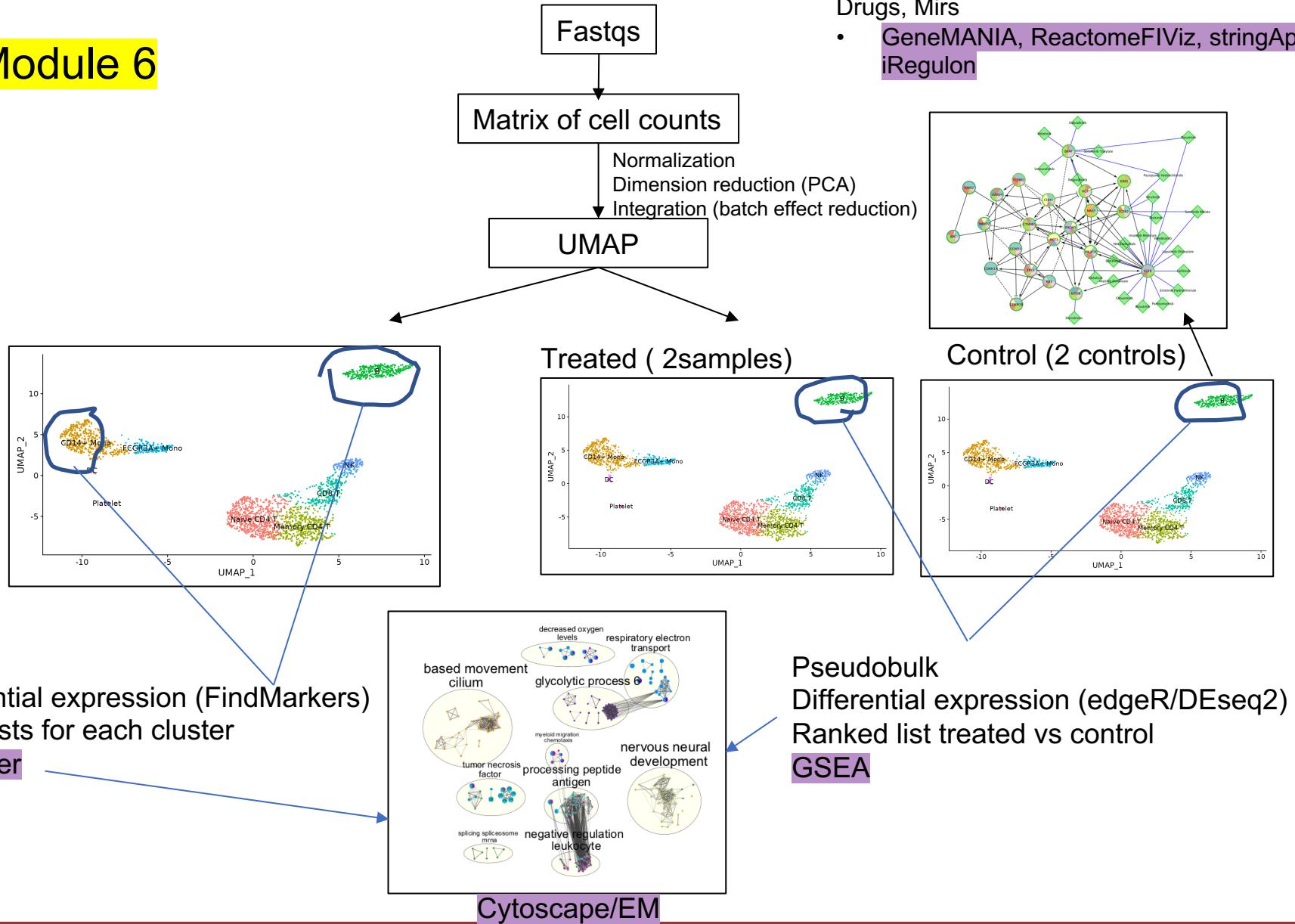
Included in module 7: iRegulon

Transcriptomics: bulk RNA-seq 2 class design

- Module 2 and 3:
- GSEA
- Enrichment Map

Module 6

scRNA-seq



Non model organisms

1. Find a pathway database/ gmt file which is the closest to your organism
2. Convert your gene identifier to the gene identifiers used in the gmt file that you found using g:Convert and g:Orth
3. Both GSEA and g:Profiler accept custom gmt file.
4. GeneMANIA offers several organisms and the option to build your interaction networks.

The screenshot shows the g:GOST functional profiling interface. At the top, there are four tabs: g:GOST (Functional profiling), g:Convert (Gene ID conversion), g:Orth (Orthology search), and g:SNPense (SNP id to gene name). Below the tabs, there are three input methods: Query (selected), Upload query, and Upload bed file. A note says "Input is whitespace-separated list of genes". On the right, there is an "Options" section with an "Organism:" dropdown set to "Homo sapiens (Human)". Underneath, a "Favourites" dropdown shows a list of organisms, with "Homo sapiens (Human)" highlighted in orange. Other listed organisms include Arabidopsis thaliana, Aspergillus fumigatus A1163, Bos taurus (Cow), Caenorhabditis elegans, Danio rerio (Zebrafish), Drosophila melanogaster, Gallus gallus (Chicken), Mus musculus (Mouse), Oryza sativa Japonica Group, Pyrenophora teres f. teres 0-1 (Pyrenophora teres), Rattus norvegicus (Rat), and Saccharomyces cerevisiae. At the bottom left, there are buttons for "Run query", "random example", and "mixed query example". A note at the bottom states: "g:GOST performs functional enrichment analysis, also known as over-representation".

Script to create a gmt file from the GO ontology:

<https://www.dropbox.com/s/wm3kq4lsdlfwcoq/creategmt.R?dl=0>

EnrichmentMap web app first release:

<https://enrichmentmap.org/>

EnrichmentMap:RNA-Seq

Recent Networks (1):

Demo Network
Jun 19, 2024

FAQ About Contact GET STARTED

...

Enrichment analysis for your RNA-Seq

Get a quick-and-easy, publication-ready enrichment figure for your two-case RNA-Seq experiment.

GET STARTED > View Demo Network

All Genes (6162)

	DOWN	UP
THY1	16.41	
COL6A3	16.21	
SESN3	15.49	
BCHE	15.13	
SPARC	14.99	
TGFB1	14.76	
COL1A1	14.75	
ADA2	14.66	
COL1A2	14.65	
EPHA7	14.47	
FXYD2	13.94	
RNF128	13.66	
COL5A2	13.67	
VCAM1	13.65	
HLPDA	13.56	
ERBB1I	13.54	
ADGRG1	13.51	
NRK	13.35	
PIKFB3	12.99	
ROBO1	12.89	
KCNJ15	12.88	

EnrichmentMap

Find pathways...

Pathway (453)

Pathway	NES	P value
peptide metabolic process	1.34	*
transmembrane transport	1.32	*
Nervous system development	1.32	*
regulation of proteolysis	-1.35	*
embryo development	-1.35	*

Module 7 (Review of the tools)

- Automation (R coding for advanced users)
- clusterProfiler (R coding for advanced users)
- Work with your own data
- Integrated Assignment
- Q and A with instructors

Module 7 (optional)

- Chipseq and ATAC data: MEME and GREAT, EnrichmentMap
- iregulon: TF network

Automated Enrichment and Visualization clusterProfiler



About Learn Packages Developers

Home > Bioconductor 3.19 > Software Packages > **clusterProfiler**

clusterProfiler

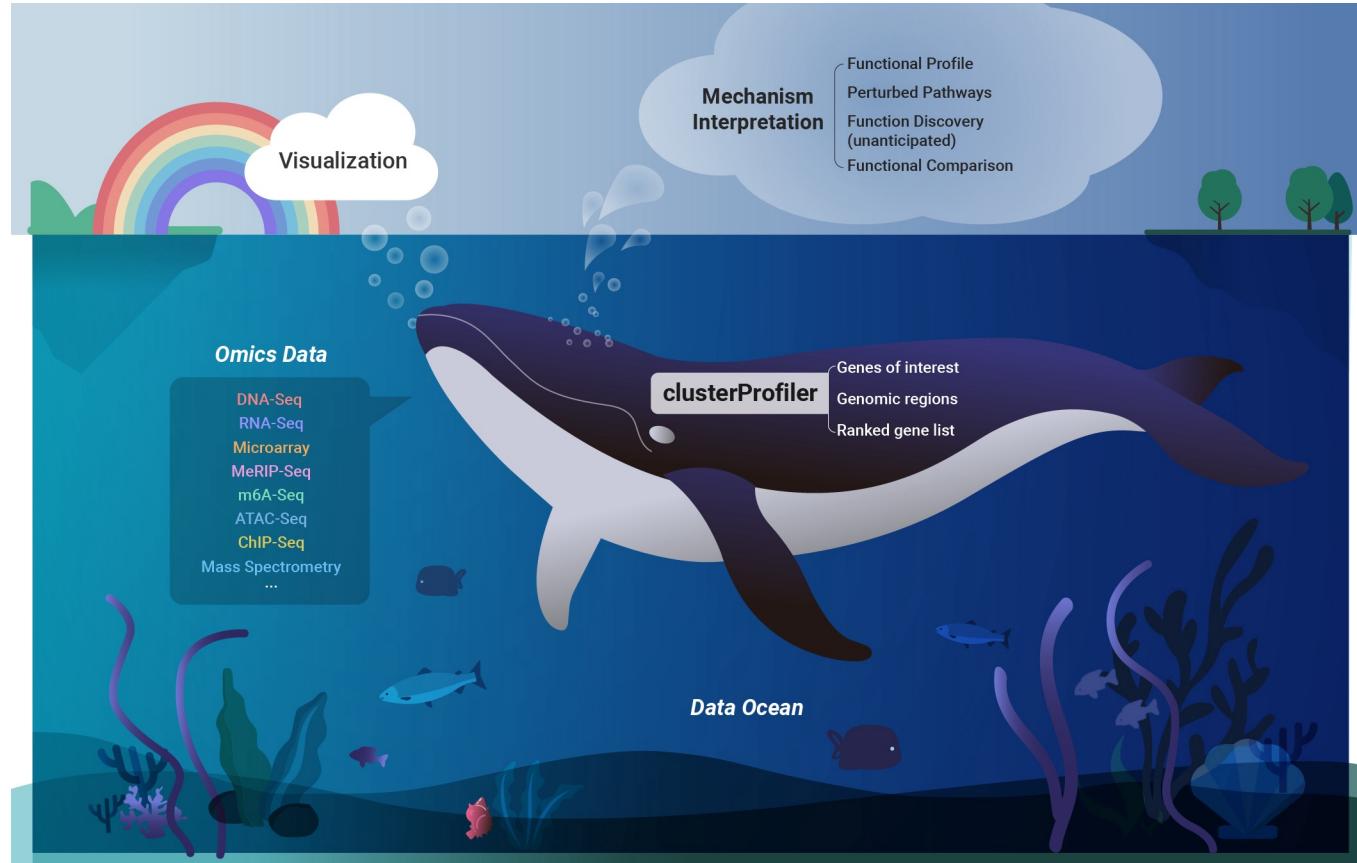
A universal enrichment tool for interpreting omics data

platforms all rank 37 / 2300 support 19 / 28 in Bioc 13 years build ok updated before release dependencies 128

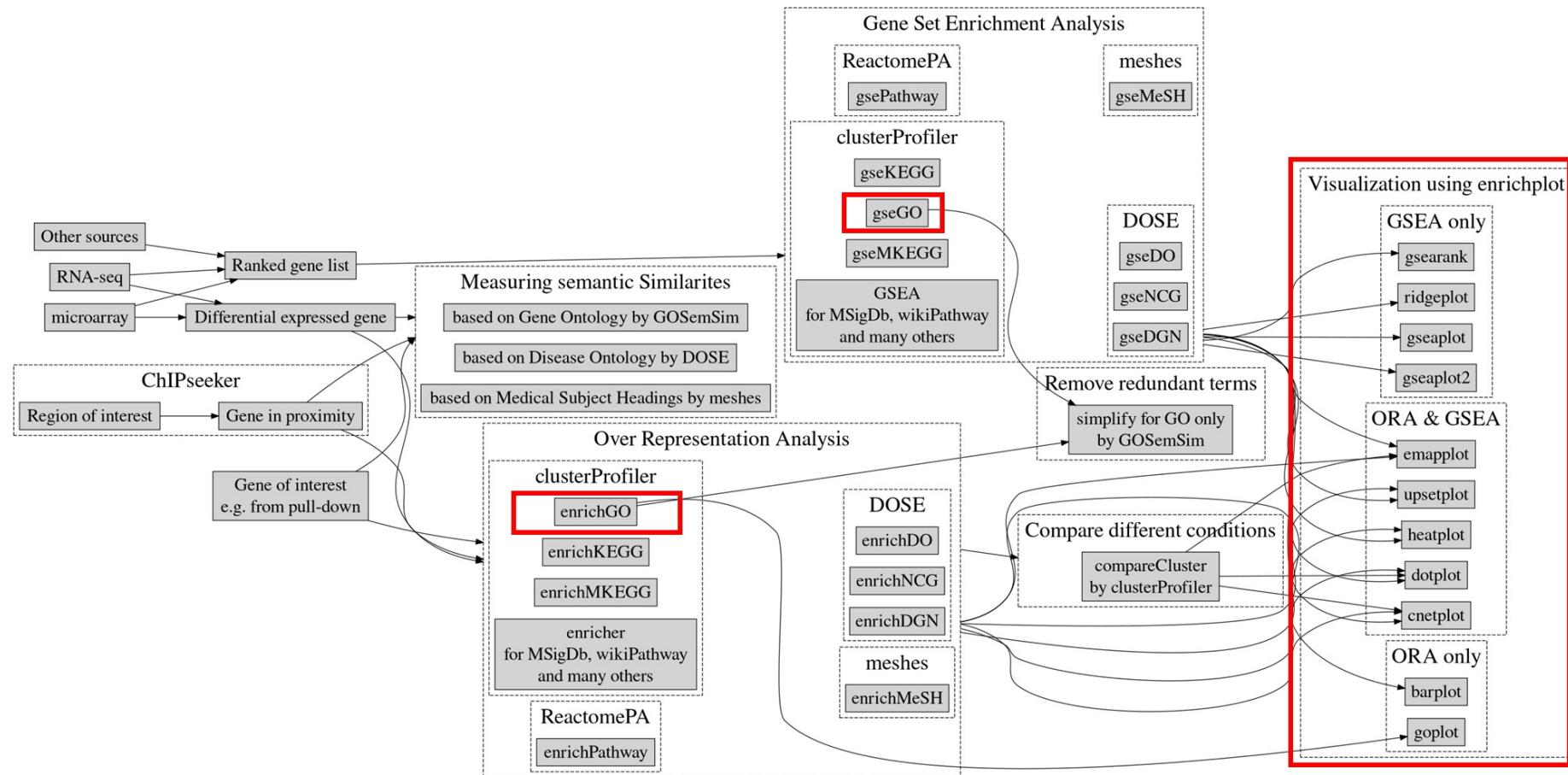
DOI: [10.18129/B9.bioc.clusterProfiler](https://doi.org/10.18129/B9.bioc.clusterProfiler)

- R package - tool for pathway analysis and visualization within R
- Helps interpreting omics data

Features of clusterProfiler



Day 3 lab clusterProfiler



We are on a Coffee Break & Networking Session

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