Clarke, D. J. B., et al. (2018). "eXpression2Kinases (X2K) Web: linking expression signatures to upstream cell signaling networks." Nucleic Acids Res.

While gene expression data at the mRNA level can be globally and accurately measured, profiling the activity of cell signaling pathways is currently much more difficult. eXpression2Kinases (X2K) computationally predicts involvement of upstream cell signaling pathways, given a signature of differentially expressed genes. X2K first computes enrichment for transcription factors likely to regulate the expression of the differentially expressed genes. The next step of X2K connects these enriched transcription factors through known protein-protein interactions (PPIs) to construct a subnetwork. The final step performs kinase enrichment analysis on the members of the subnetwork. X2K Web is a new implementation of the original eXpression2Kinases algorithm with important enhancements. X2K Web includes many new transcription factor and kinase libraries, and PPI networks. For demonstration, thousands of gene expression signatures induced by kinase inhibitors, applied to six breast cancer cell lines, are provided for fetching directly into X2K Web. The results are displayed as interactive downloadable vector graphic network images and bar graphs. Benchmarking various settings via random permutations enabled the identification of an optimal set of parameters to be used as the default settings in X2K Web. X2K Web is freely available from <http://X2K.cloud>.

Franz, M., et al. (2018). "GeneMANIA update 2018." Nucleic Acids Res.

GeneMANIA (<http://genemania.org>) is a flexible user-friendly web site for generating hypotheses about gene function, analyzing gene lists and prioritizing genes for functional assays. Given a query gene list, GeneMANIA finds functionally similar genes using a wealth of genomics and proteomics data. In this mode, it weights each functional genomic dataset according to its predictive value for the query. Another use of GeneMANIA is gene function prediction. Given a single query gene, GeneMANIA finds genes likely to share function with it based on their interactions with it. Enriched Gene Ontology categories among this set can point to the function of the gene. Nine organisms are currently supported (Arabidopsis thaliana, Caenorhabditis elegans, Danio rerio, Drosophila melanogaster, Escherichia coli, Homo sapiens, Mus musculus, Rattus norvegicus and Saccharomyces cerevisiae). Hundreds of data sets and hundreds of millions of interactions have been collected from GEO, BioGRID, IRefIndex and I2D, as well as organism-specific functional genomics data sets. Users can customize their search by selecting specific data sets to query and by uploading their own data sets to analyze. We have recently updated the user interface to GeneMANIA to make it more intuitive and make more efficient use of visual space. GeneMANIA can now be used effectively on a variety of devices.

Hamey, F. K. and B. Gottgens (2018). "Sorting apples from oranges in single-cell expression comparisons." Nat Methods **15**(5): 321-322.

https://www.nature.com/articles/nmeth.4675

Lee, J., et al. (2018). "Mutalisk: a web-based somatic MUTation AnaLyIS toolKit for genomic, transcriptional and epigenomic signatures." Nucleic Acids Res.

Somatic genome mutations occur due to combinations of various intrinsic/extrinsic mutational processes and DNA repair mechanisms. Different molecular processes frequently generate different signatures of somatic mutations in their own favored contexts. As a result, the regional somatic mutation rate is dependent on the local DNA sequence, the DNA replication/RNA transcription dynamics and epigenomic chromatin organization landscape in the genome. Here, we propose an online computational framework, termed Mutalisk, which correlates somatic mutations with various genomic, transcriptional and epigenomic features in order to understand mutational processes that contribute to the generation of the mutations. This user-friendly tool explores the presence of localized hypermutations (kataegis), dissects the spectrum of mutations into the maximum likelihood combination of known mutational signatures and associates the mutation density with numerous regulatory elements in the genome. As a result, global patterns of somatic mutations in any query sample can be efficiently screened, thus enabling a deeper understanding of various mutagenic factors. This tool will facilitate more effective downstream analyses of cancer genome sequences to elucidate the diversity of mutational processes underlying the development and clonal evolution of cancer cells. Mutalisk is freely available at <http://mutalisk.org>.

Li, J., et al. (2018). "TAM 2.0: tool for MicroRNA set analysis." Nucleic Acids Res.

With the rapid accumulation of high-throughput microRNA (miRNA) expression profile, the up-to-date resource for analyzing the functional and disease associations of miRNAs is increasingly demanded. We here describe the updated server TAM 2.0 for miRNA set enrichment analysis. Through manual curation of over 9000 papers, a more than two-fold growth of reference miRNA sets has been achieved in comparison with previous TAM, which covers 9945 and 1584 newly collected miRNA-disease and miRNA-function associations, respectively. Moreover, TAM 2.0 allows users not only to test the functional and disease annotations of miRNAs by overrepresentation analysis, but also to compare the input de-regulated miRNAs with those de-regulated in other disease conditions via correlation analysis. Finally, the functions for miRNA set query and result visualization are also enabled in the TAM 2.0 server to facilitate the community. The TAM 2.0 web server is freely accessible at <http://www.scse.hebut.edu.cn/tam/> or <http://www.lirmed.com/tam2/>.

Wong, A. K., et al. (2018). "GIANT 2.0: genome-scale integrated analysis of gene networks in tissues." Nucleic Acids Res.

GIANT2 (Genome-wide Integrated Analysis of gene Networks in Tissues) is an interactive web server that enables biomedical researchers to analyze their proteins and pathways of interest and generate hypotheses in the context of genome-scale functional maps of human tissues. The precise actions of genes are frequently dependent on their tissue context, yet direct assay of tissue-specific protein function and interactions remains infeasible in many normal human tissues and cell-types. With GIANT2, researchers can explore predicted tissue-specific functional roles of genes and reveal changes in those roles across tissues, all through interactive multi-network visualizations and analyses. Additionally, the NetWAS approach available through the server uses tissue-specific/cell-type networks predicted by GIANT2 to re-prioritize statistical associations from GWAS studies and identify disease-associated genes. GIANT2 predicts tissue-specific interactions by integrating diverse functional genomics data from now over 61 400 experiments for 283 diverse tissues and cell-types. GIANT2 does not require any registration or installation and is freely available for use at <http://giant-v2.princeton.edu>.

Ye, J., et al. (2018). "WEGO 2.0: a web tool for analyzing and plotting GO annotations, 2018 update." Nucleic Acids Res.

WEGO (Web Gene Ontology Annotation Plot), created in 2006, is a simple but useful tool for visualizing, comparing and plotting GO (Gene Ontology) annotation results. Owing largely to the rapid development of high-throughput sequencing and the increasing acceptance of GO, WEGO has benefitted from outstanding performance regarding the number of users and citations in recent years, which motivated us to update to version 2.0. WEGO uses the GO annotation results as input. Based on GO's standardized DAG (Directed Acyclic Graph) structured vocabulary system, the number of genes corresponding to each GO ID is calculated and shown in a graphical format. WEGO 2.0 updates have targeted four aspects, aiming to provide a more efficient and up-to-date approach for comparative genomic analyses. First, the number of input files, previously limited to three, is now unlimited, allowing WEGO to analyze multiple datasets. Also added in this version are the reference datasets of nine model species that can be adopted as baselines in genomic comparative analyses. Furthermore, in the analyzing processes each Chi-square test is carried out for multiple datasets instead of every two samples. At last, WEGO 2.0 provides an additional output graph along with the traditional WEGO histogram, displaying the sorted P-values of GO terms and indicating their significant differences. At the same time, WEGO 2.0 features an entirely new user interface. WEGO is available for free at <http://wego.genomics.org.cn>.