

Brief overview on how to start exploring functionality

Christian Werner

(Quantitative geneticist and biostatistician) EiB, CIMMYT, Texcoco (Mexico)

Filippo Biscarini



(Biostatistician, bioinformatician, and quantitative geneticist) CNR-IBBA, Milan (Italy)

Oscar González-Recio



(Computer biologist, and quantitative geneticist) INIA-UPM, Madrid (Spain)



Functional analysis



- Examining the function of genes and their role in biological processes.
 - by looking at how changes in a gene's sequence affect its function
 - by studying how different genes interact with each other to carry out specific functions in the cell.
 - using bioinformatics tools to analyze large datasets of genomic information, such as
 the sequence of an entire genome or the expression levels of thousands of genes in
 different tissues or under different conditions. This can help identify patterns and
 connections between genes that may be involved in specific functions or processes,
 such as disease development or response to environmental stimuli.

Overall, a genomic functional analysis can provide valuable insights into the roles that genes play in biological processes, and can help researchers better understand the underlying causes of diseases and other biological phenomena

Work Flow in FUMA



- •Download bkg genes: https://www.ensembl.org/info/data/ftp/index.html
- •Results overview in FUMA
- -https://fuma.ctglab.nl/snp2gene
- –Input file: GWASresults.txt
- Variant Effect Prediction in Ensemble
- -https://www.ensembl.org/Multi/Tools/VEP
- -Input file (significant SNPs): Map.selected.rs
- -Output file (Functional Info): Select 'Gene' column
- Enrichment analysis
- -https://fuma.ctglab.nl/gene2func
- -Input files: GENES from significant SNPs ('Gene' column from VEP)
- -Background genes from the specie (Canis familiaris.bkg genes from here

Work Flow in DAVID



- Visit the DAVID website and create an account, if you don't already have one.
 - https://david.ncifcrf.gov/
- Log in to your account and go to the "Functional Annotation" section of the platform.
- Choose the appropriate algorithms and methods for your analysis. DAVID offers a variety of options for functional analysis, including clustering, enrichment analysis, and pathway mapping.

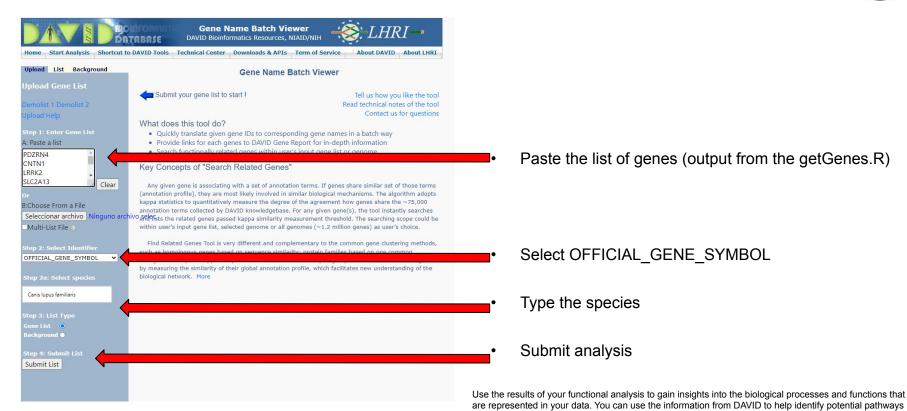


Work Flow in DAVID



and mechanisms involved in the development of diseases, for example, or to investigate how different

genes or proteins interact to perform specific functions in the cell.



Work Flow in DAVID



Functional Annotation Tool DAVID Bioinformatics Resources, NIAID/NIH Home Start Analysis Shortcut to DAVID Tools Technical Center Downloads & APIs Term of Service About DAVID About LHRI	
Upload List Background Gene List Manager	Annotation Summary Results Help and Tool Manual
Select to limit annotations by one or more species Help - Use All Species - Canis lupus familiaris(7	Current Gene List: List_1 7 DAVID IDs Current Background: Canis lupus familiaris Check Defaults Clear All Functional_Annotations (6 selected) COG_ONTOLOGY 28.6% 2 Chart UP_KW_BIOLOGICAL_PROCESS 42.9% 3 Chart UP_KW_CELLULAR_COMPONENT 42.9% 3 Chart
Select Species List Manager Help List_1 ^	UP_KW_MOLECULAR_FUNCTION 2 UP_KW_DTM 28.6% 2 Chart 2 UP_SEQ_FEATURE 100.0% 7 Chart 3 UP_SEQ_FEATURE 100.0% 7 Chart
Select List to: Use Rename	■ Pathways (1 selected) ■ KEGG_PATHWAY 42.9% 3 Chart ■ WIKIPATHWAYS 28.6% 2 Chart ■ Protein_Domains (0 selected) ***Red annotation categories denote DAVID defined defaults***
Show Gene List	Combined View for Selected Annotation Functional Annotation Clustering
	Functional Annotation Chart Functional Annotation Table

Go again to the Shortcut to **David Tools** and select **'Functional Annotation'**

You can select the different options to gain insights into the biological processes and functions that are represented in your data. You can use the information from DAVID to help identify potential pathways and mechanisms involved in the expression of the phenotype. For example, to investigate how different genes or proteins interact to perform specific functions in the cell.



Limitations



- FA relies on algorithms and methods that make assumptions and simplifications about the data being analyzed. These assumptions may not always hold true in all cases, and they can affect the accuracy and reliability of the results.
- FA are often based on large datasets that may not be representative of all possible scenarios. This
 can lead to bias in the results, and can make it difficult to generalize the findings to other situations
 or organisms.
- FA can provide valuable insights, but it is important to carefully consider the limitations and uncertainties of the methods and algorithms used, and to interpret the results with caution.