

Gene set enrichment

Jeff Leek

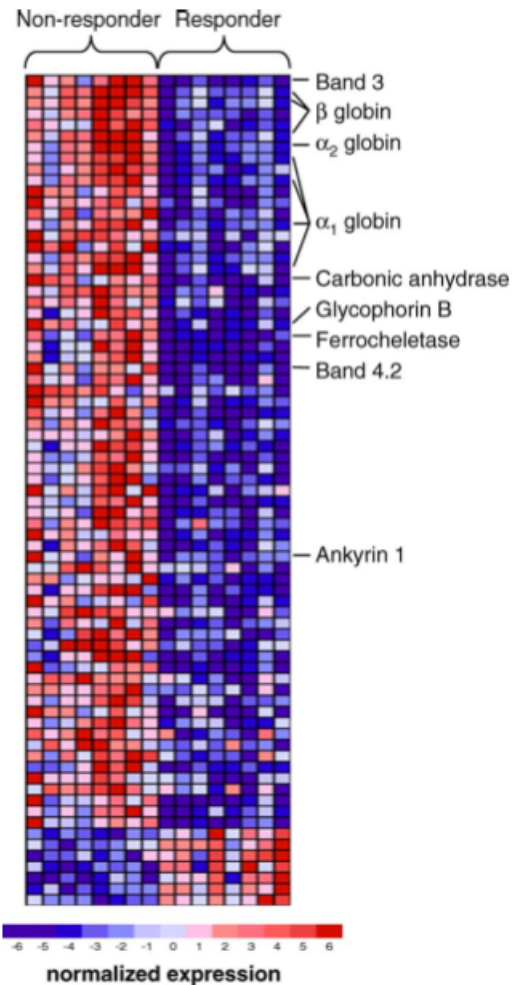
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An Erythroid Differentiation Signature Predicts Response to Lenalidomide in Myelodysplastic Syndrome

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47 Genes at $\text{FDR} \leq 10\%$

Gene set enrichment analysis

Looks for groups of genes that share function or other characteristics



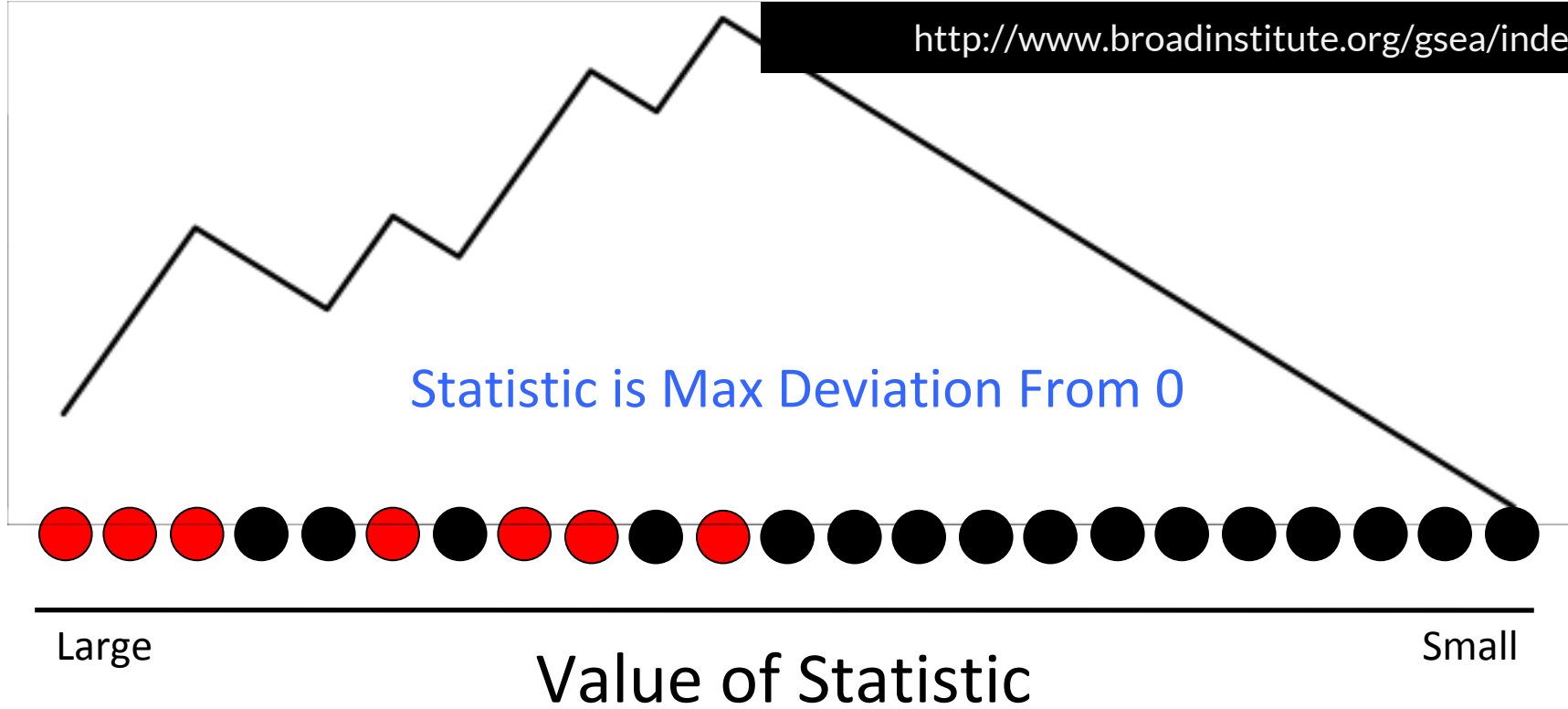
Large



Value of Statistic

Small

 Gene In A Relevant Set

 Gene Not In The Set



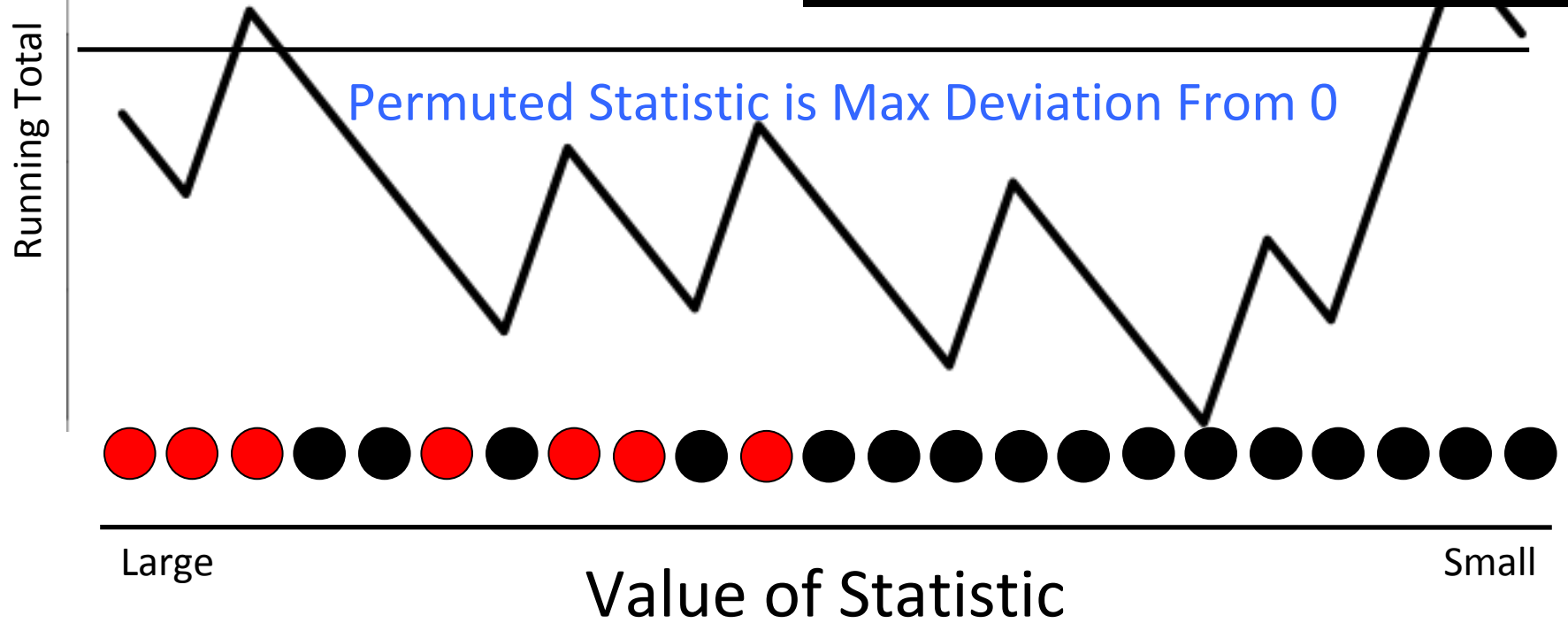
-  Gene In A Relevant Set
-  Gene Not In The Set

Measuring significance with permutation

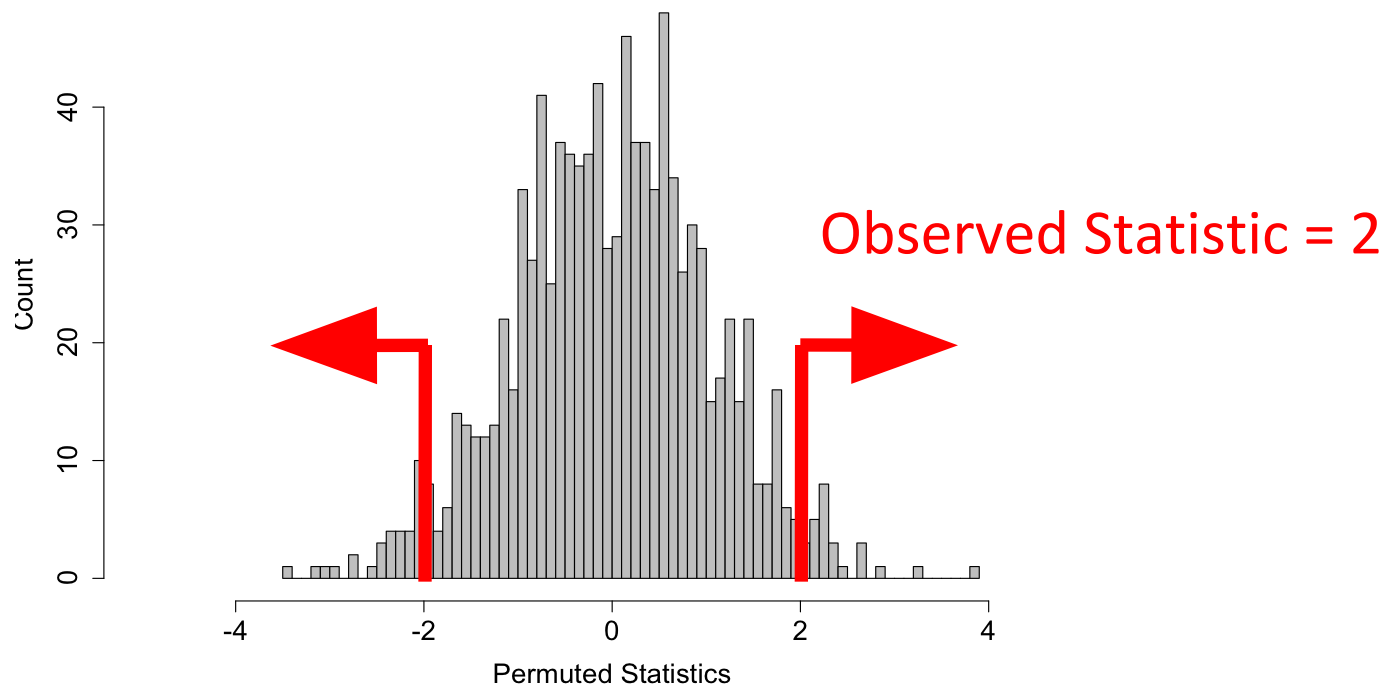


Response	R	R	...	NR	NR
	Patient 1	Patient 2	...	Patient n-1	Patient n
Gene 1	-1.64	-0.42	...	-1.39	-0.38
Gene 2	-3.12	-3.60	...	-3.80	-2.82
:	:	:	...	:	:
:	:	:	...	:	:
:	:	:	...	:	:
:	:	:	...	:	:
Gene m-1	-2.34	-0.22	...	-1.22	-2.76
Gene m	4.53	3.23	...	0.29	3.11

Response	NR	R	...	NR	R
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- Gene In A Relevant Set
- Gene Not In The Set



$$\{ \# \mid S^{perm} \mid \geq \mid S^{obs} \mid \}$$

$$\text{P-value} = \frac{\quad}{\# \text{ of Permutations}}$$

What gene sets?



Search GO data

[Search](#)

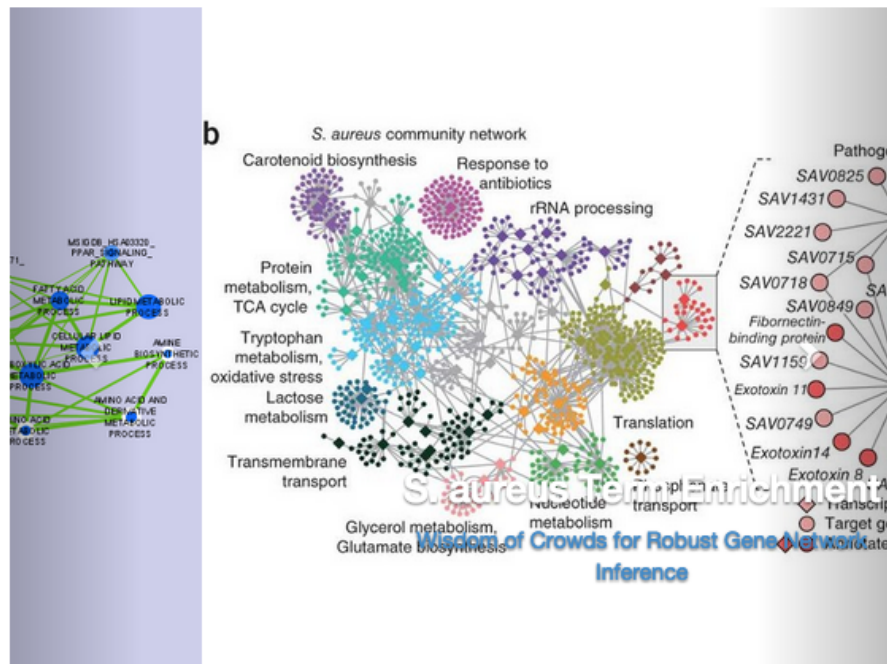
Enrichment analysis (beta)

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Statistics



Gene Ontology Consortium



What is the Gene Ontology?

[An introduction to the Gene Ontology](#)

Highlighted GO term

[Representing "phases" in GO biological process](#)

The GOC has recently introduced a new term [biological phase \(GO:0044848\)](#), as a direct subclass of biological process. This class represents a distinct period or stage during which biological processes can occur.

[more](#)

Random FAQs

- [What is an OWL file?](#)
- [Does the Term Enrichment tool have a limit on the number genes in the input file?](#)
- [What are the file formats used by the Gene Ontology?](#)

**MSigDB**Molecular Signatures
Database<http://www.broadinstitute.org/gsea/msigdb/index.jsp>

Molecular Signatures Database v5.0

Overview

The Molecular Signatures Database (MSigDB) is a collection of annotated gene sets for use with GSEA software. From this web site, you can

- ▶ **Search** for gene sets by keyword.
- ▶ **Browse** gene sets by name or collection.
- ▶ **Examine** a gene set and its annotations. See, for example, the [ANGIOGENESIS gene set page](#).
- ▶ **Download** gene sets.
- ▶ **Investigate** gene sets:
 - ▶ **Compute overlaps** between your gene set and gene sets in MSigDB.
 - ▶ **Categorize** members of a gene set by gene families.
 - ▶ **View the expression profile** of a gene set in any of the three provided public expression compendia.

Registration

Please [register](#) to download the GSEA software and view the MSigDB gene sets. After registering, you can log in at any time using your email address. Registration is free. Its only purpose is to help us track usage for reports to our funding agencies.

Collections

The MSigDB gene sets are divided into 8 major collections:

H

hallmark gene sets are coherently expressed signatures derived by aggregating many MSigDB gene sets to represent well-defined biological states or processes.

C1

positional gene sets for each human chromosome and cytogenetic band.

C2

curated gene sets from online pathway databases, publications in PubMed, and knowledge of domain experts.

C3

motif gene sets based on conserved cis-regulatory motifs from a comparative analysis of the human, mouse, rat, and dog genomes.

C4

computational gene sets defined by mining large collections of cancer-oriented microarray data.

C5

GO gene sets consist of genes annotated by the same GO terms.

Welcome to the Biological General Repository for Interaction Datasets

BioGRID is an interaction repository with data compiled through comprehensive curation efforts. Our current index is version **3.4.127** and searches **54,676** publications for **796,767** protein and genetic interactions, **27,034** chemical associations and **38,559** post translational modifications from major model organism species. All data are **freely** provided via our search index and available for download in standardized formats.

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By Gene

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AREAS OF INTEREST TO HELP YOU GET STARTED



**Build and Download
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Create custom interaction datasets by protein or by publication. You can also download our entire dataset in a wide variety of standard formats.



**Link To Us or Submit
Interactions**

Send us your datasets or link to the BioGRID directly from your own website or database. Full details on how to contribute are available here.



**Online Tools and
Resources**

We've developed tools that make use of BioGRID data. Check out the list of tools to see if we can help you work with our data.



**View Our Interaction
Statistics**

Find out how many organisms, proteins, publications, and interactions are available in the current release of the BioGRID.

BIOGRID FUNDING AND PARTNERS



[more partners](#)

Notes and further reading

- Sometimes still very hard to interpret, especially if the categories are broad/vague
- It is easy to “tell stories” if you aren’t careful
- Incurs a second multiple testing problem
- Can be simplified
 - <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3134237/>