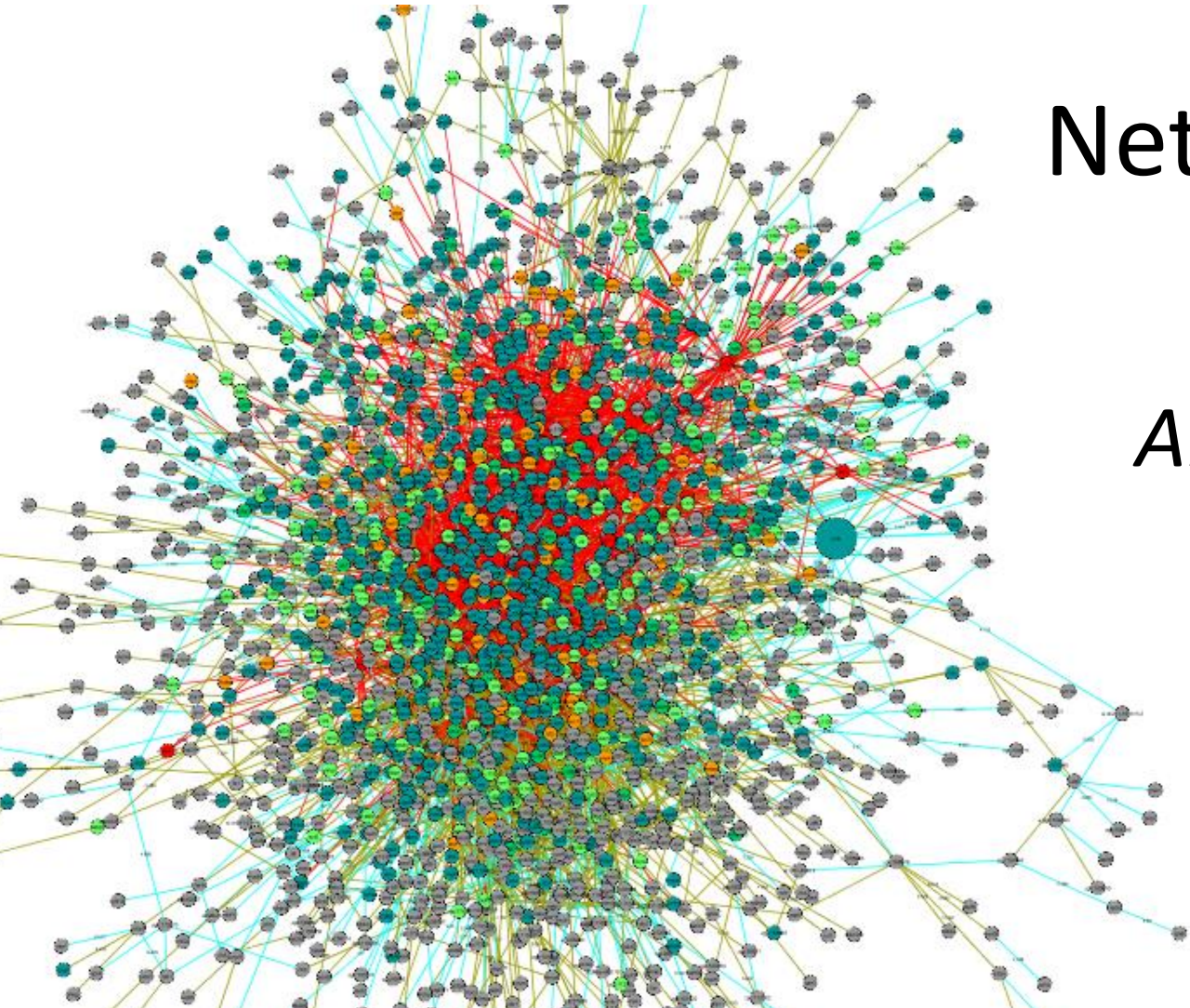


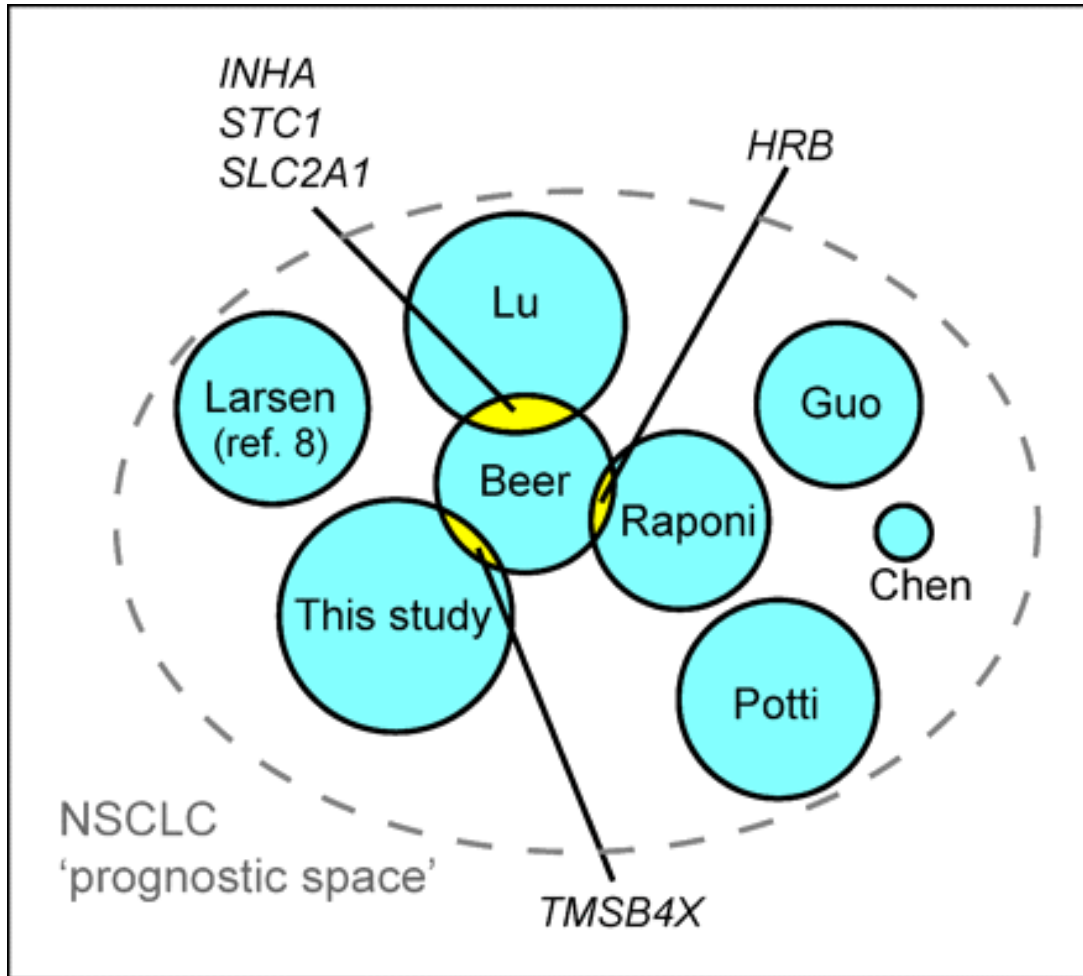


Robust Biomarkers via Network Enrichment Analysis of Molecular Profiles

Andrey Alexeyenko



Poor overlap between published biomarkers and signatures of clinical phenotype



Major, “unavoidable” reasons:

- Molecular heterogeneity between patients;
- $N \text{ genes} > N \text{ patients} \Rightarrow$ Dimensionality curse;

Other reasons:

- Different sub-types of patient population;
- Different microarray platforms;
- Technical noise.

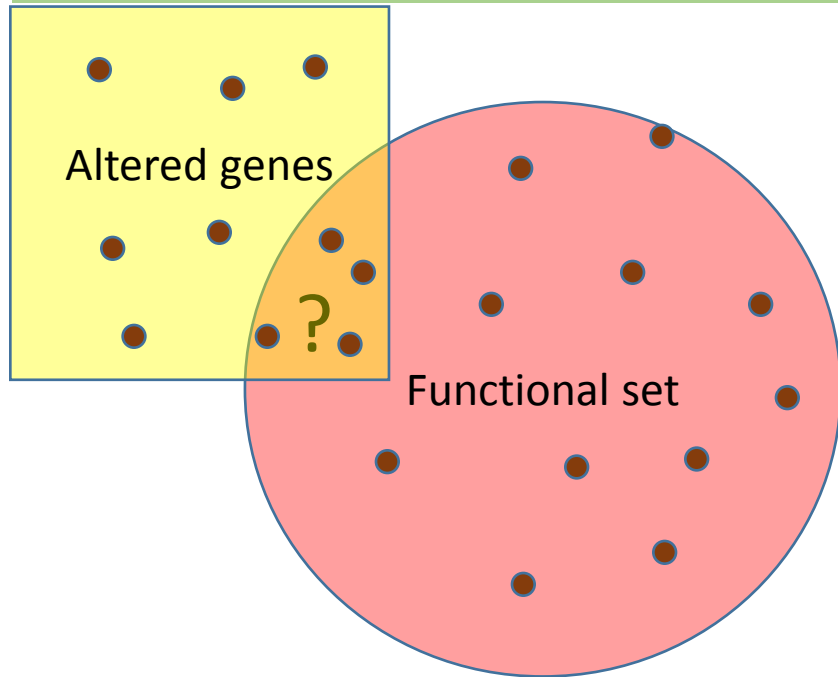
Gene expression signatures of lung cancer relapse

From: Roepman et al., 2007



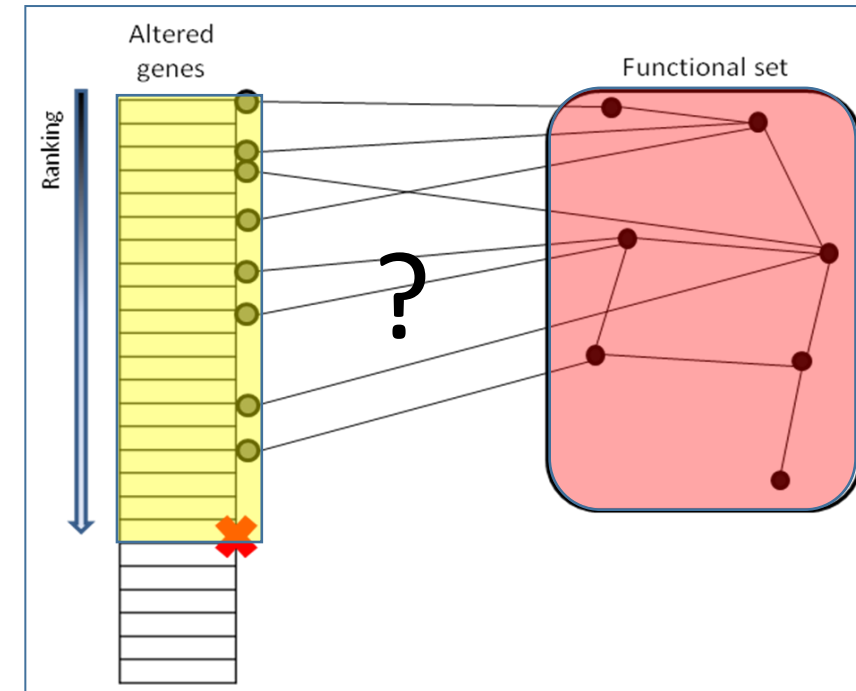
Enrichment analysis: characterization of novel gene sets

Gene set enrichment analysis



Huang da W, ... Lempicki RA. Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nature Protocols*, 2009
<https://david.ncifcrf.gov>

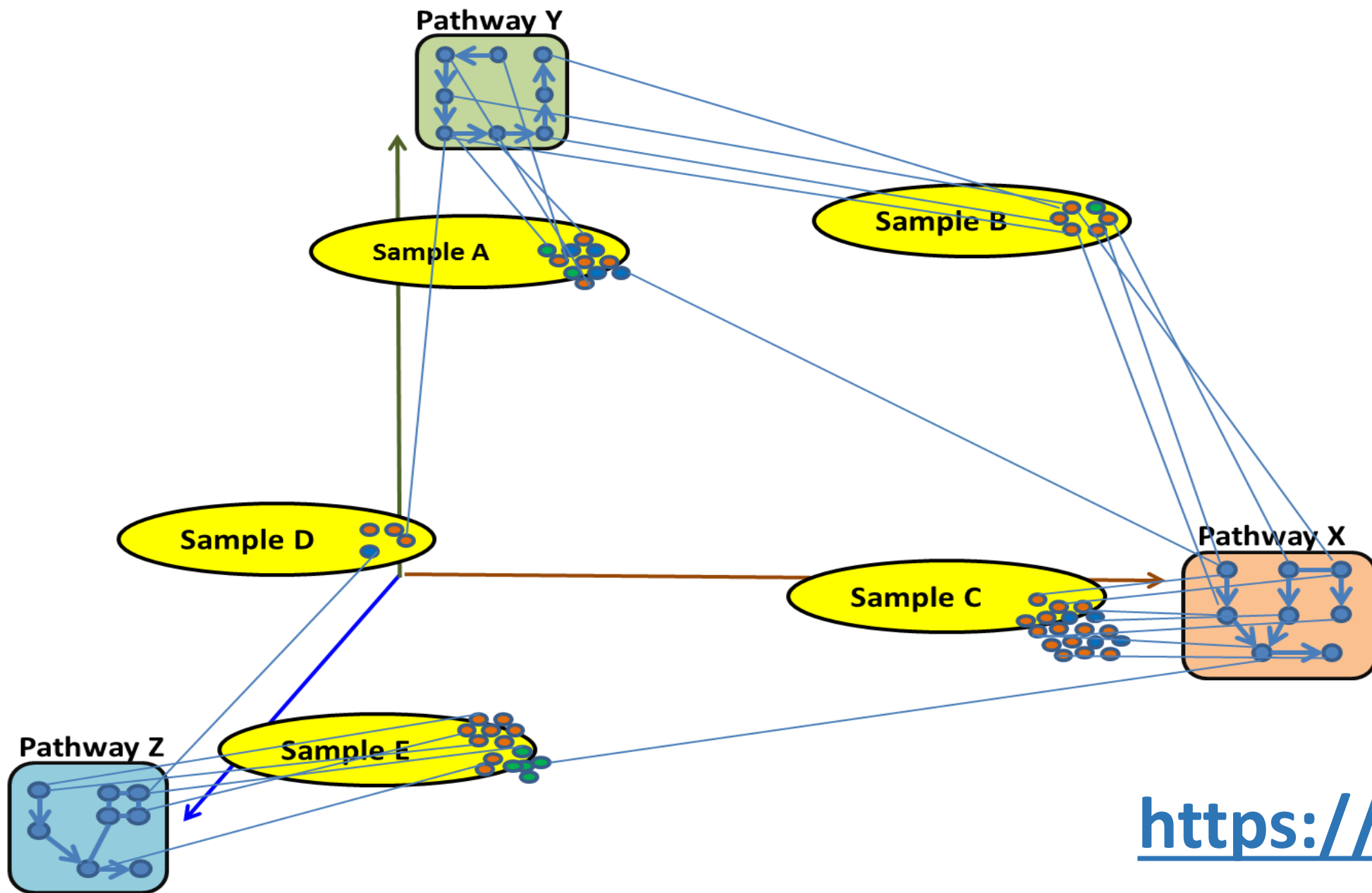
Network enrichment analysis



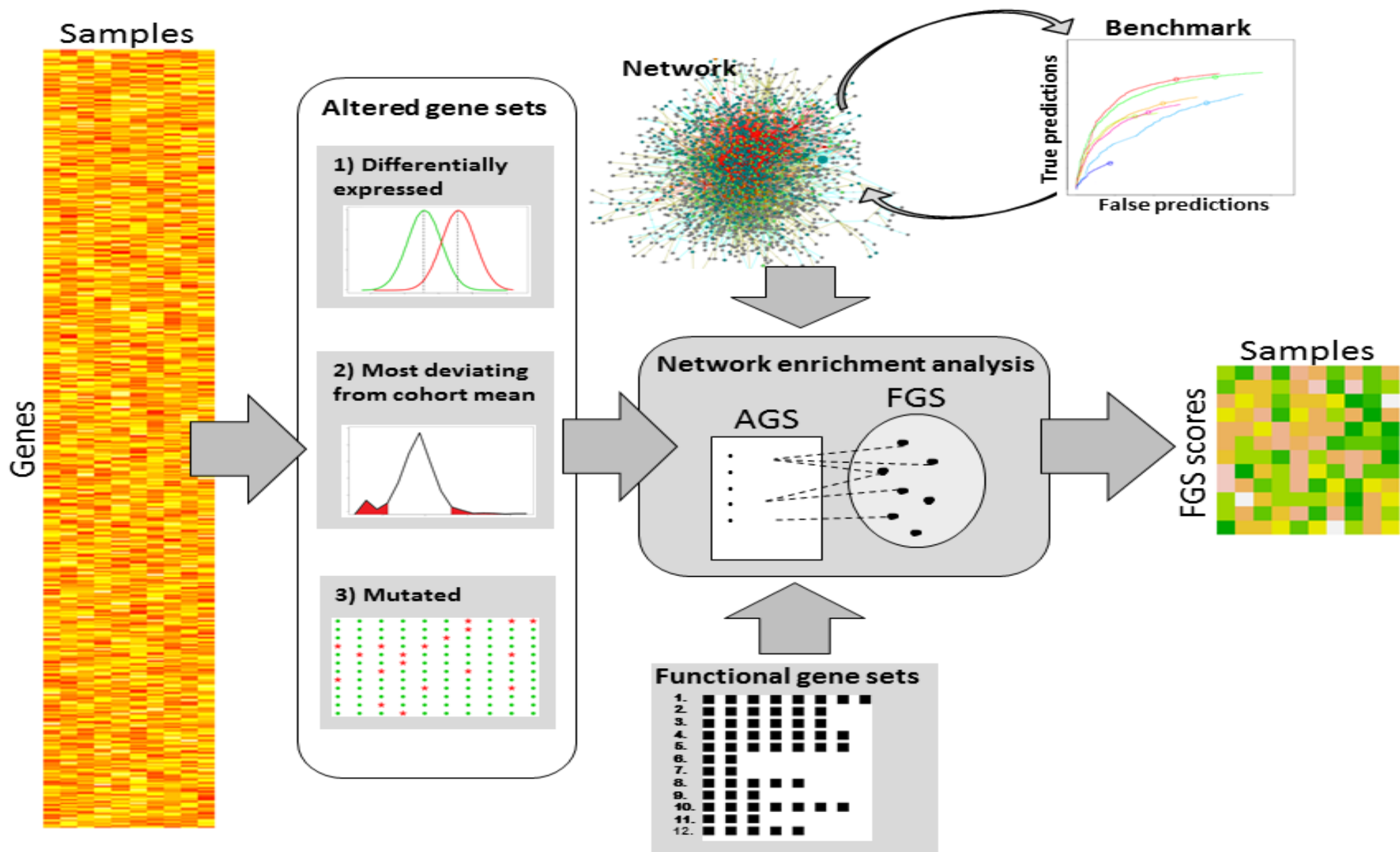
Alexeyenko A, Lee W, ... Pawitan Y. **Network enrichment analysis**: extension of gene-set enrichment analysis to gene networks. *BMC Bioinformatics*, 2012
https://research.scilifelab.se/andrej_alexeyenko/HyperSet/



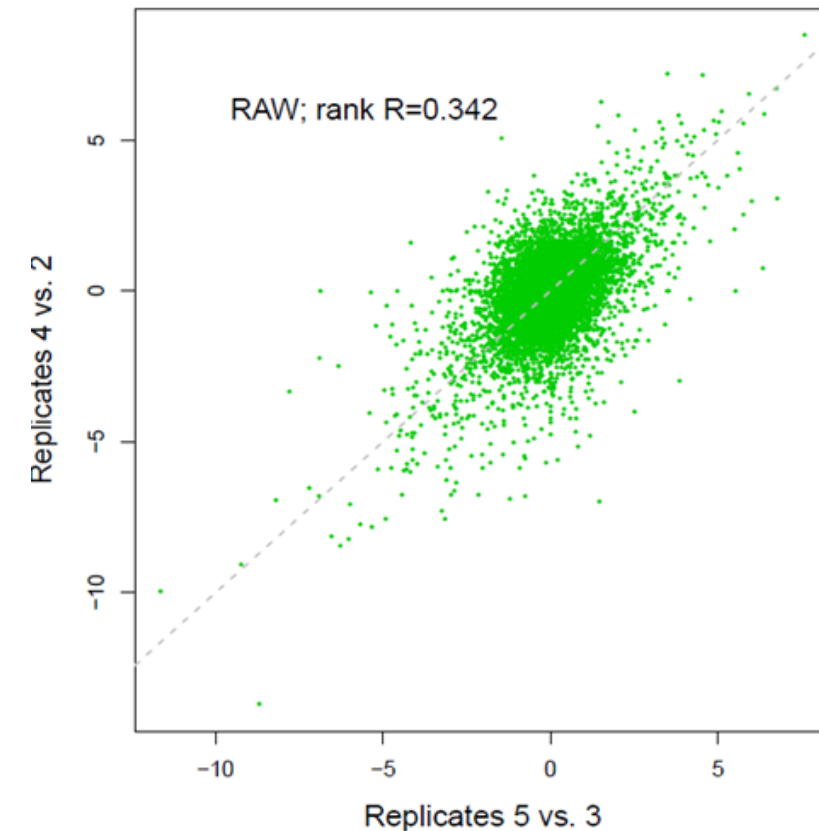
Samples in the pathway space



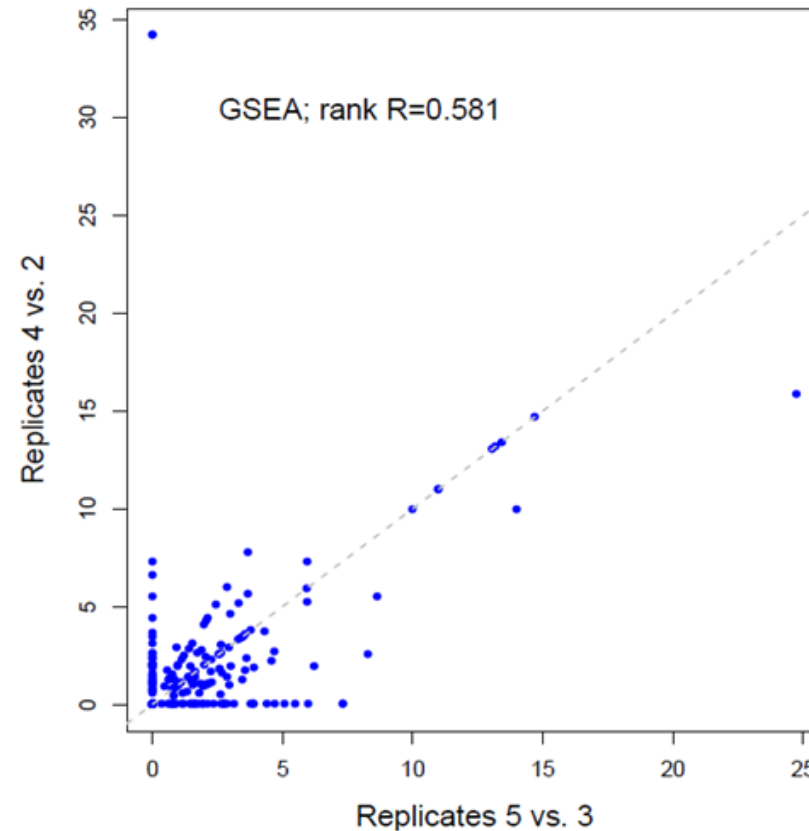
Analysis pipeline



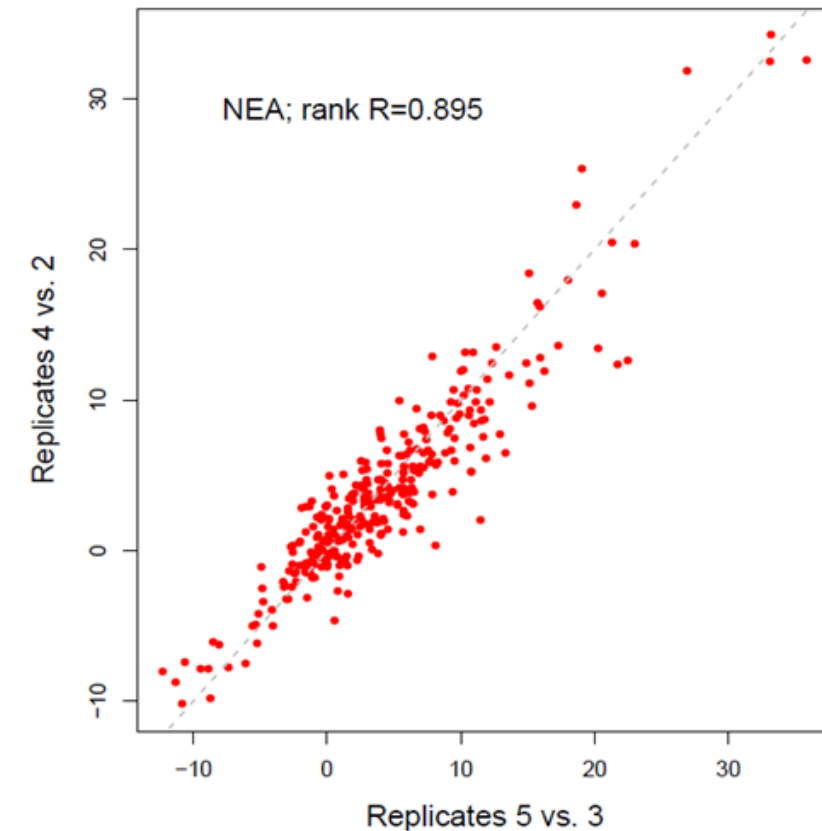
Consistency in differential expression analysis



Original differential
expression values



Gene set enrichment
of top DE genes



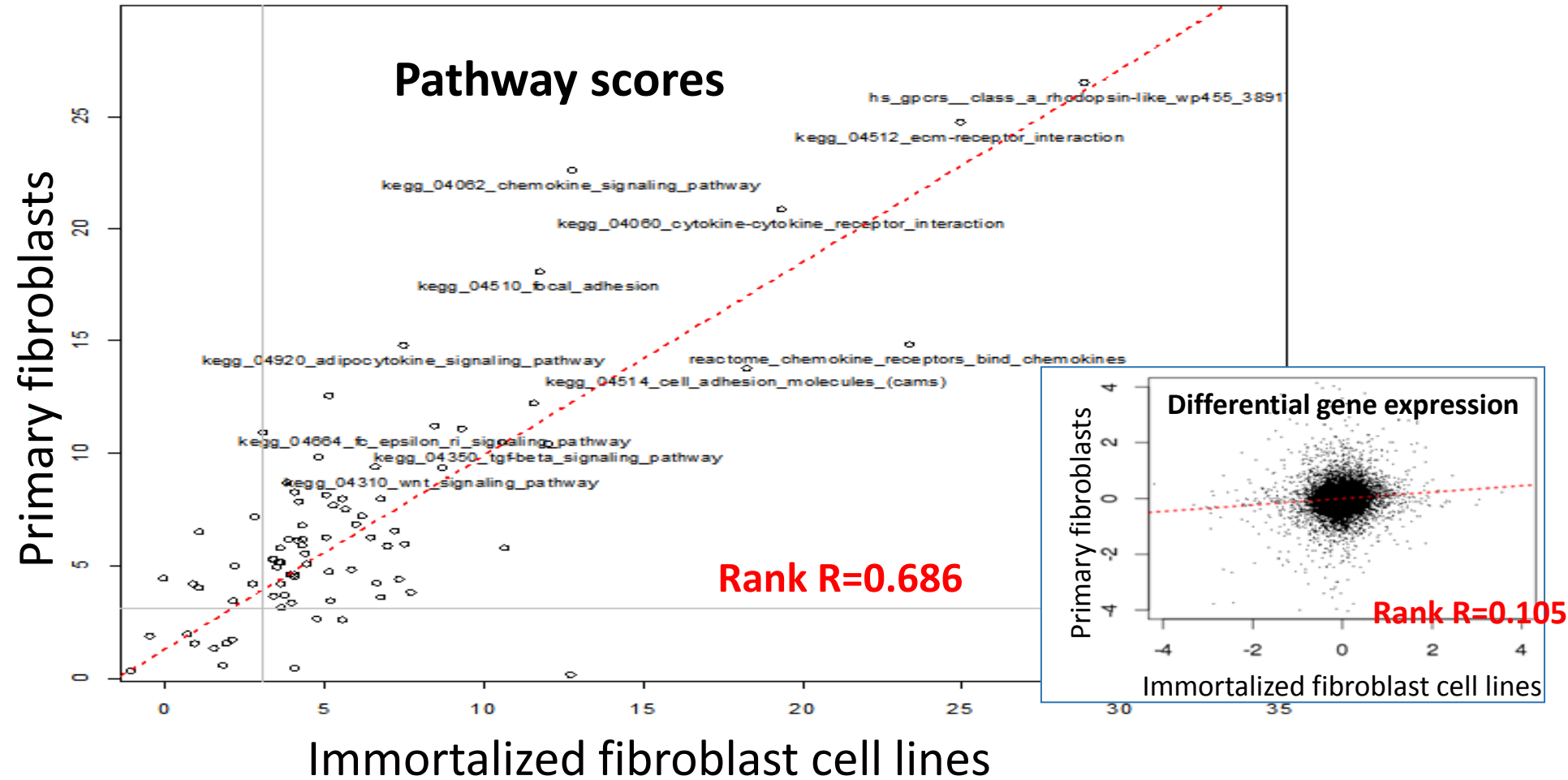
Network enrichment
of top DE genes

**FANTOM5: gene expression in gingival epithelial (GE) versus tenocyte cells (TC)
using samples from two different donor pairs (GE: #4 and #5; TC: #2 and #3)**

From: Jeggari A. and Alexeyenko A.

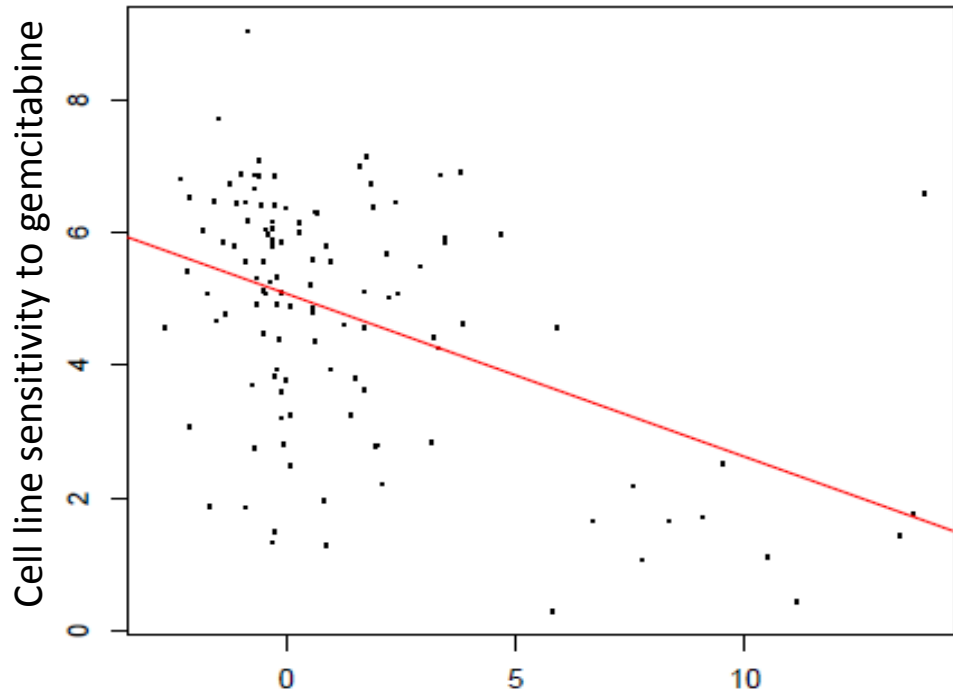


Two experimental models of tumor inhibition are similar at the pathway (and not gene) level



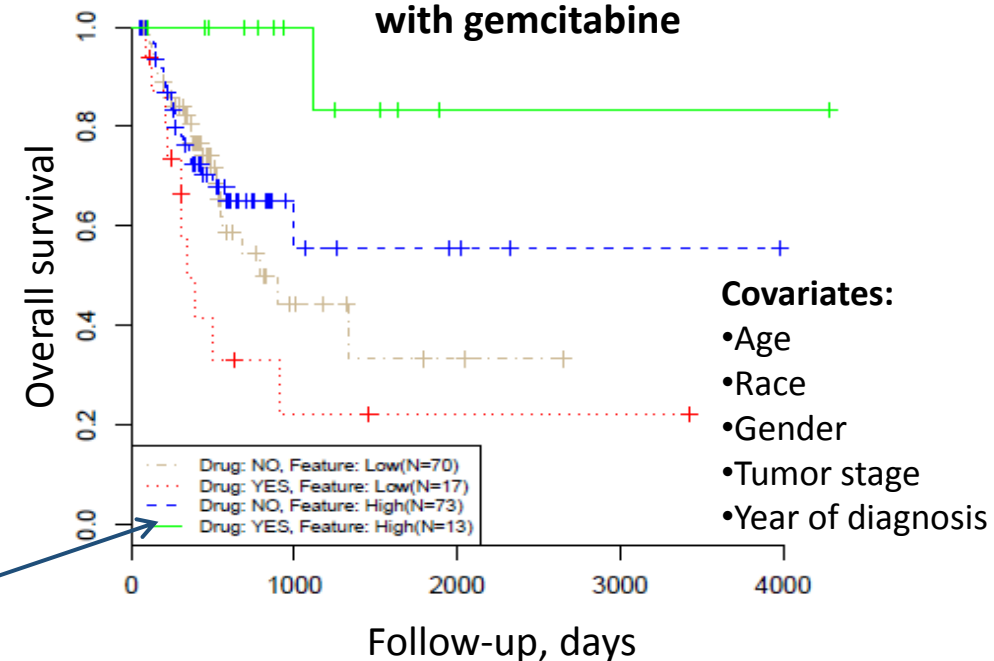
From: Alexeyenko A., Alkasalias T., ... and Klein G. [Confrontation of fibroblasts with cancer cells in vitro: gene network analysis of transcriptome...](#) J Exp Clin Cancer Res. 2015

Drug screen *in vitro* (Basu et al., 2013)

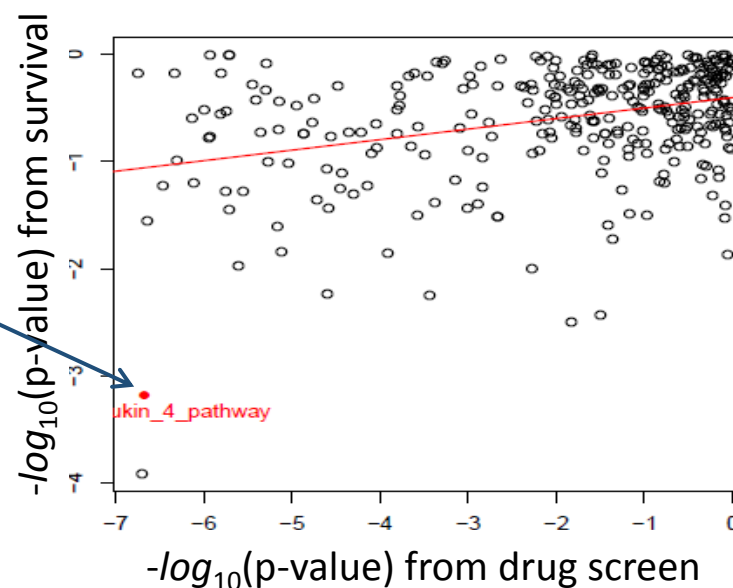


Cell line-specific "Interleukin-4 pathway" scores

Treatment of bladder carcinoma patients with gemcitabine



Performance *in vitro* and in the clinic, all pathways



Drug-pathway associations hold when followed from *in vitro* to the clinic

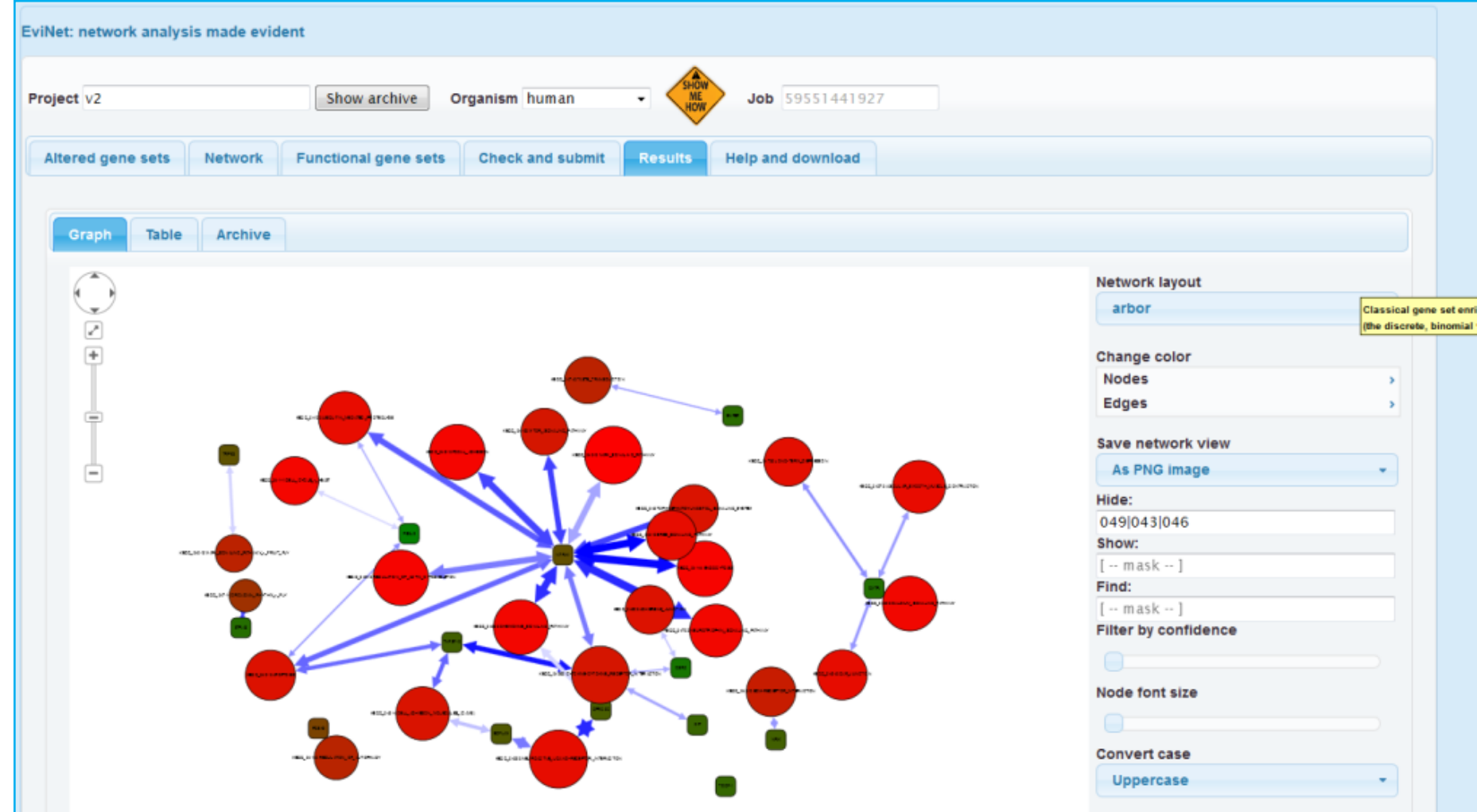
From: Franco M. et al.



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Jonathan Prince
Yudi Pawitan
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<https://evinet.org>

