Robust biomarkers from network-based data integration

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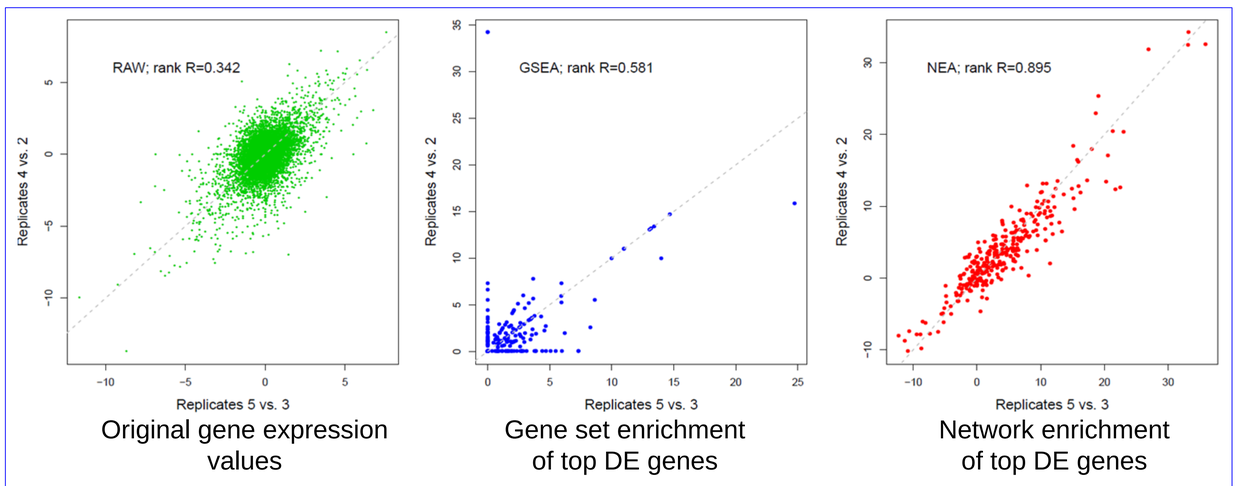
Network enrichment analysis of high-throughput data is both sensitive and robust

We developed a method for finding sensitive and robust biomarkers at the pathway level. Samples (patients etc.) are described with scores from network enrichment analysis, which transforms the original space of altered genes into a lower-dimensional space of pathways.
The network-based data interpretation has the following strengths:
1) It naturally combines all major types of molecular interactions,
2) individual alterations of genomic sequence, gene methylation, transcription, and protein abundance are generalized at the pathway level, and
3) the pathway view enables low-dimensional statistical analysis and is transparent for biological interpretation.
These dimensions are then correlated with clinical or other phenotypes. The method was tested using *in vitro* drug screen data and then on clinical data of The Cancer Genome Atlas. It proved superior to the original single-gene analysis in terms of 1) level of correlation with drug sensitivity in cancer cell lines, 2) consistency of the discovered correlates when applied to an independent drug screen, 3) ability to explain differential survival of patients, and 4) relevance of the *in vitro* correlates to survival of patients who received the same drug.

Consistency in differential expression analysis

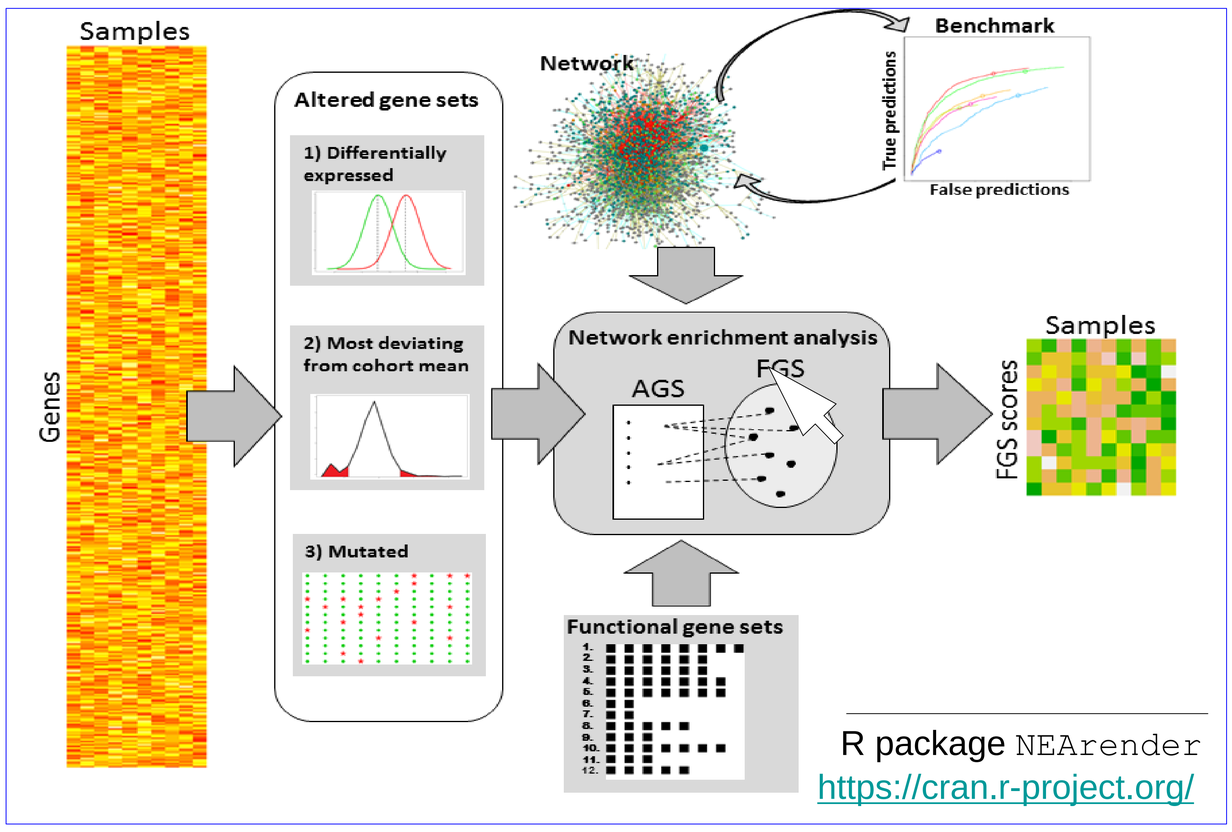


Original gene expression values | Gene set enrichment of top DE genes | Network enrichment of top DE genes

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)

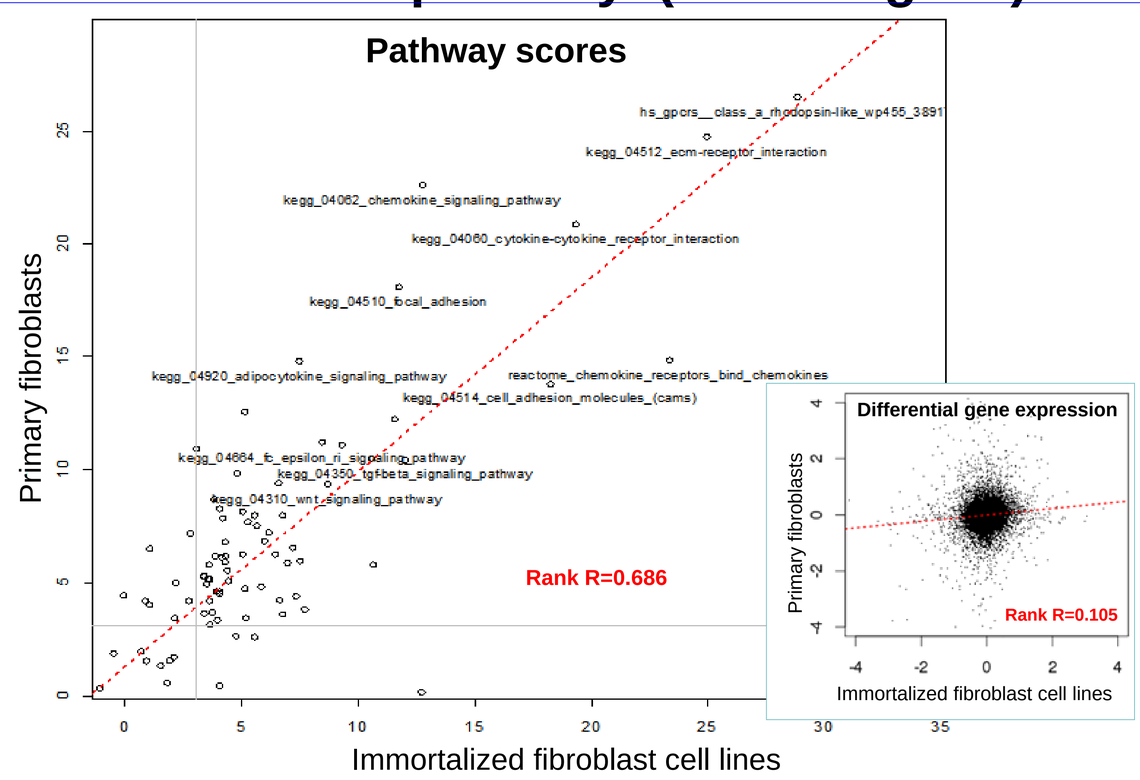
From: Jeggari A. and Alexeyenko A.

Analysis pipeline



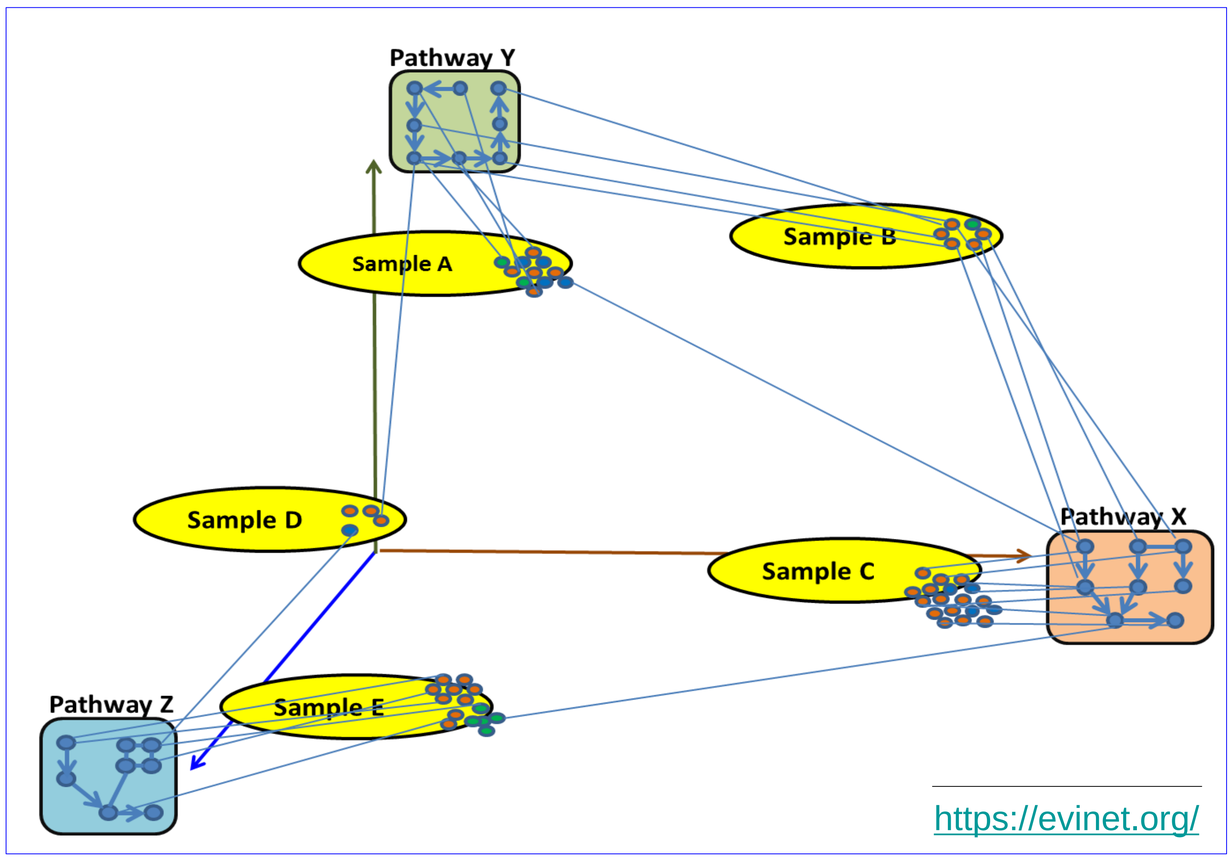
R package `NEArender`
https://cran.r-project.org/

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



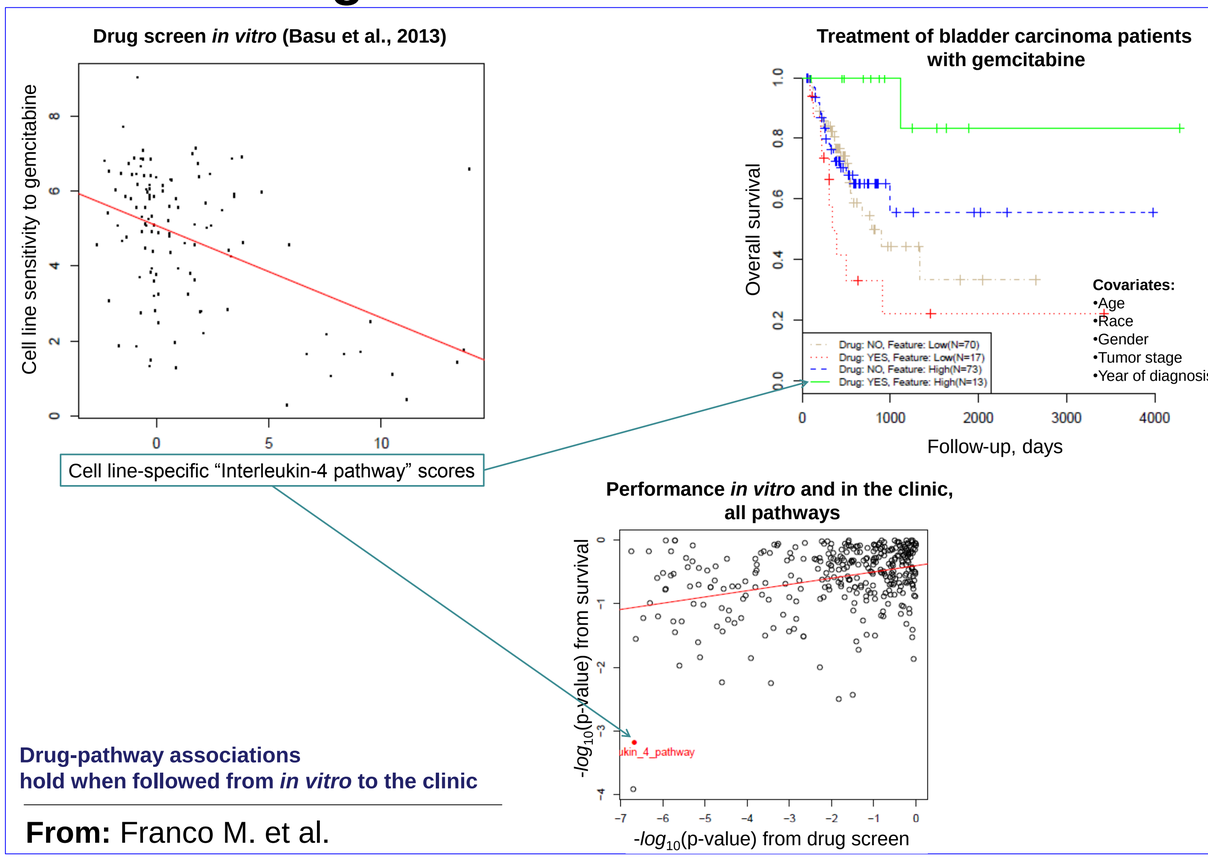
From: Alexeyenko A., Alkasalias T., … and Klein G. Confrontation of fibroblasts with cancer cells in vitro: gene network analysis of transcriptome... J Exp Clin Cancer Res. 2015

Samples in the pathway space



https://evinet.org/

Agreement between sensitivity to anti-cancer drugs *in vitro* and in the clinic



From: Franco M. et al.

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