

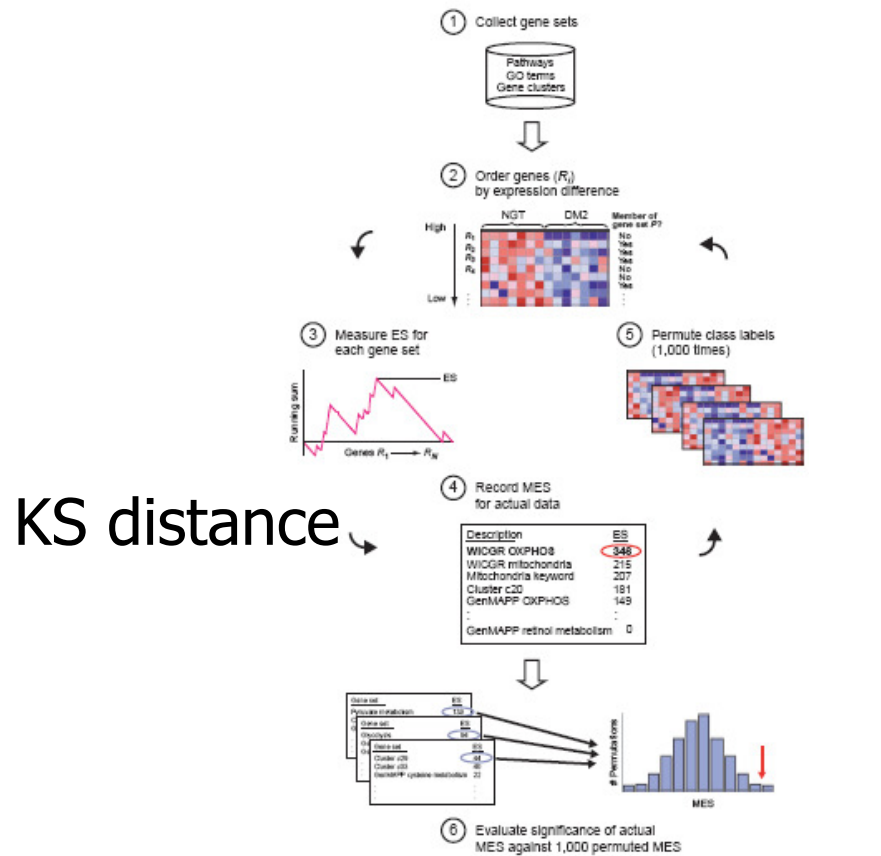
Oncogenic pathway signatures in human cancers as guide to targeted therapies

Perry Moerland

Bioinformatics Lab, KEBB, AMC

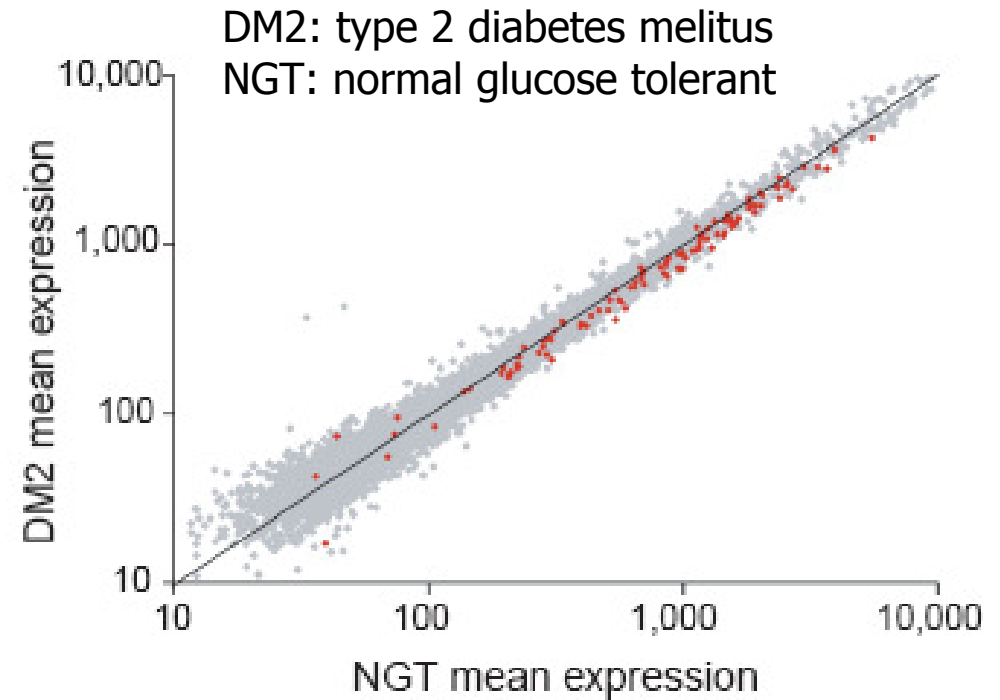
`p.d.moerland@amc.uva.nl`

Gene set enrichment analysis (GSEA)



KS distance

Null hypothesis estimated by permutation of either genes or class labels

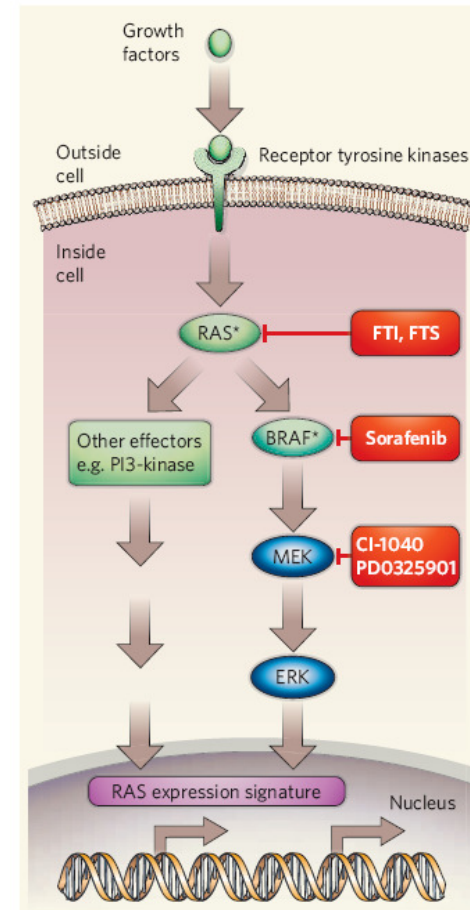


Red points are OXPHOS genes: modestly but coordinately down-regulated

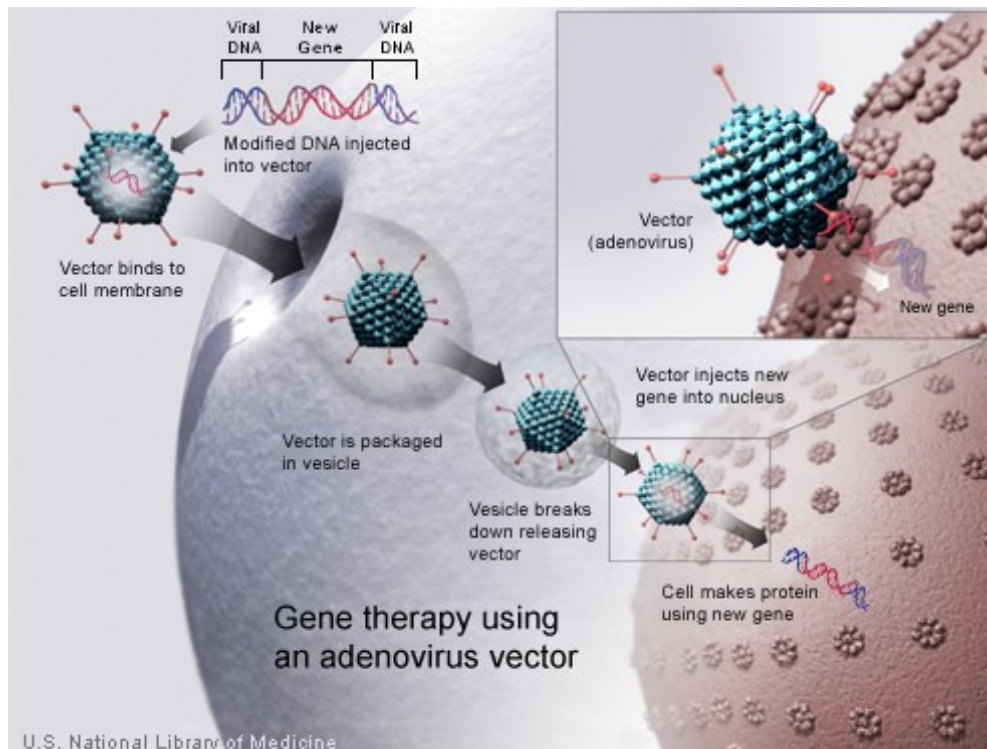
Mootha et al., Nat. Genetics, 34, 267-273 (2003)

Tumor biology

- Pathway activation
- Oncogenes: RAS, SRC, MYC
- Single mutations
- Drug sensitivity
- Multiple mutations
- Multiple pathways

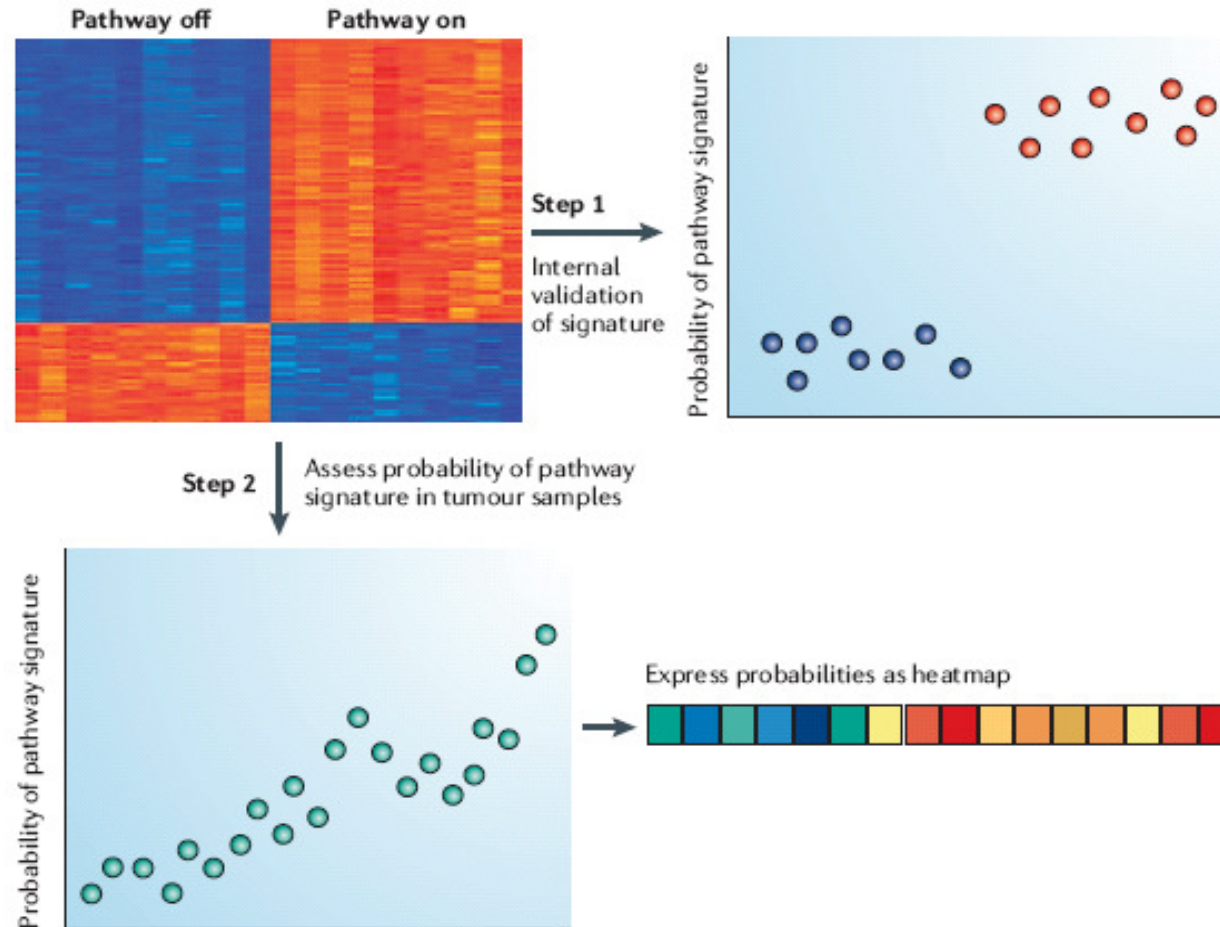


Experimental approach



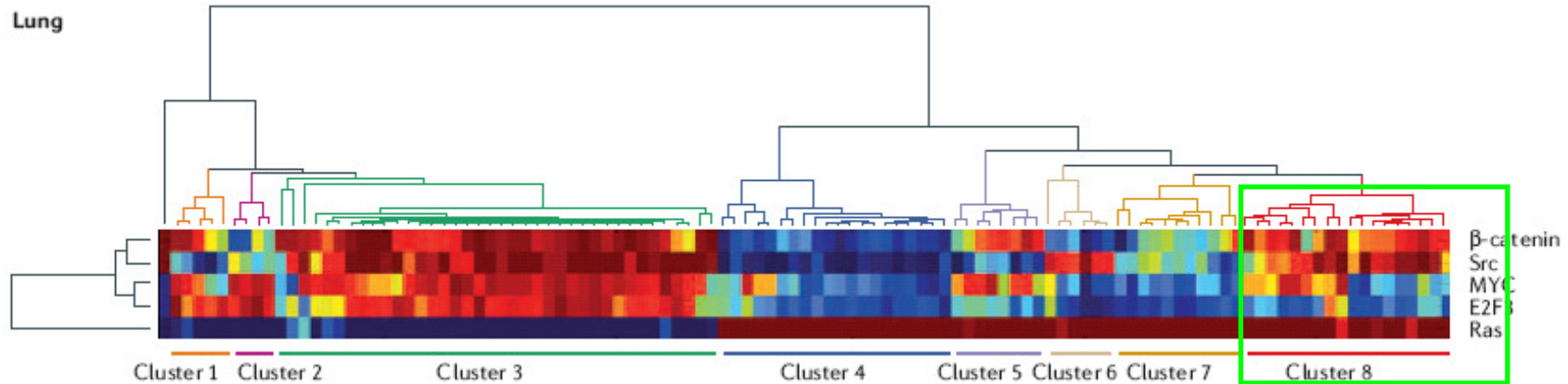
Activation of a specific pathway in quiescent (non-dividing) cells with adenovirus

Expression signature



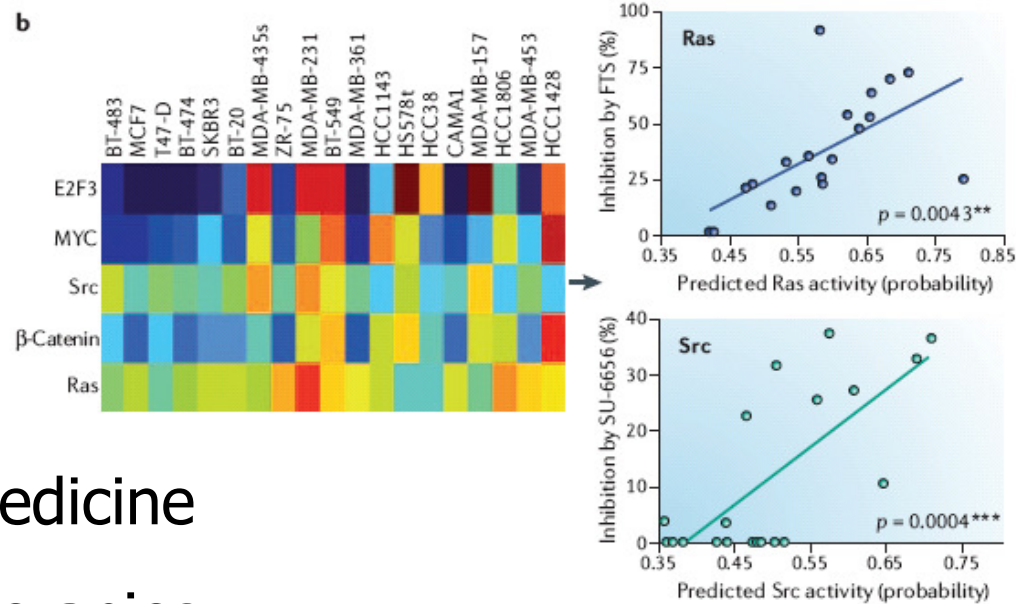
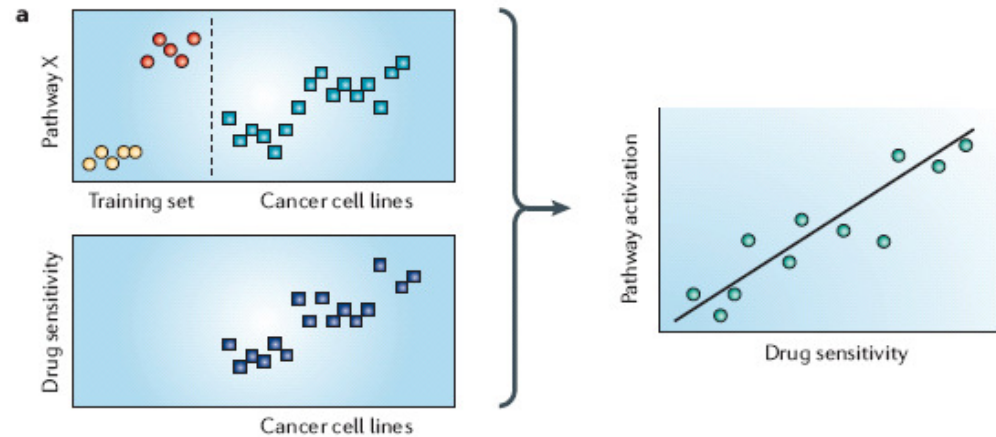
Assess status of pathway in a tumor sample

Patterns of pathway deregulation



Cluster 8: patients with poor survival – concerted deregulation of BCAT, SRC, MYC, and RAS

Linking pathways with therapies



- Personalized medicine
- Combination therapies

Oncogenic pathway signatures in human cancers (2010)