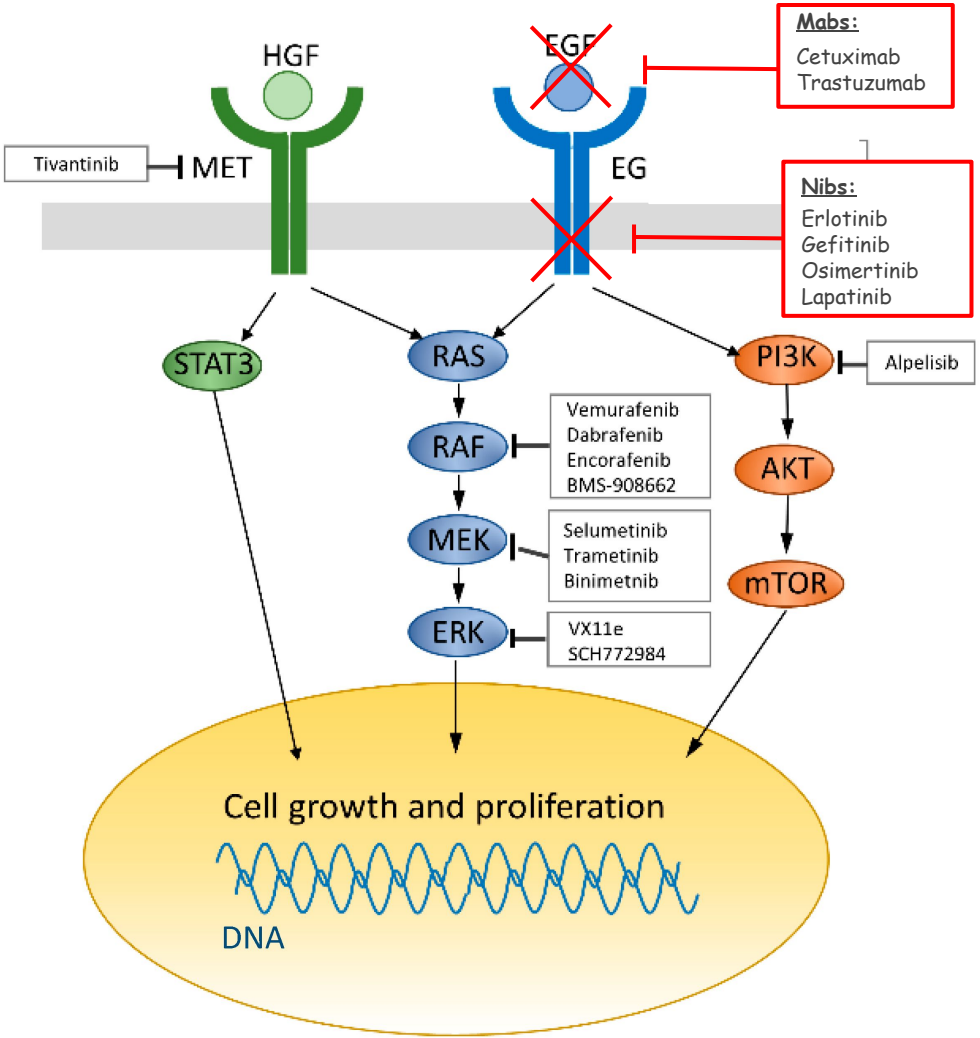
Biomarkers discovery in silico

команда Re:treat



Mutations in EGFR signalling pathway lead to resistance

Resistant cells have distinct expression and mutational profiles

We want to predict patients response to the therapy.

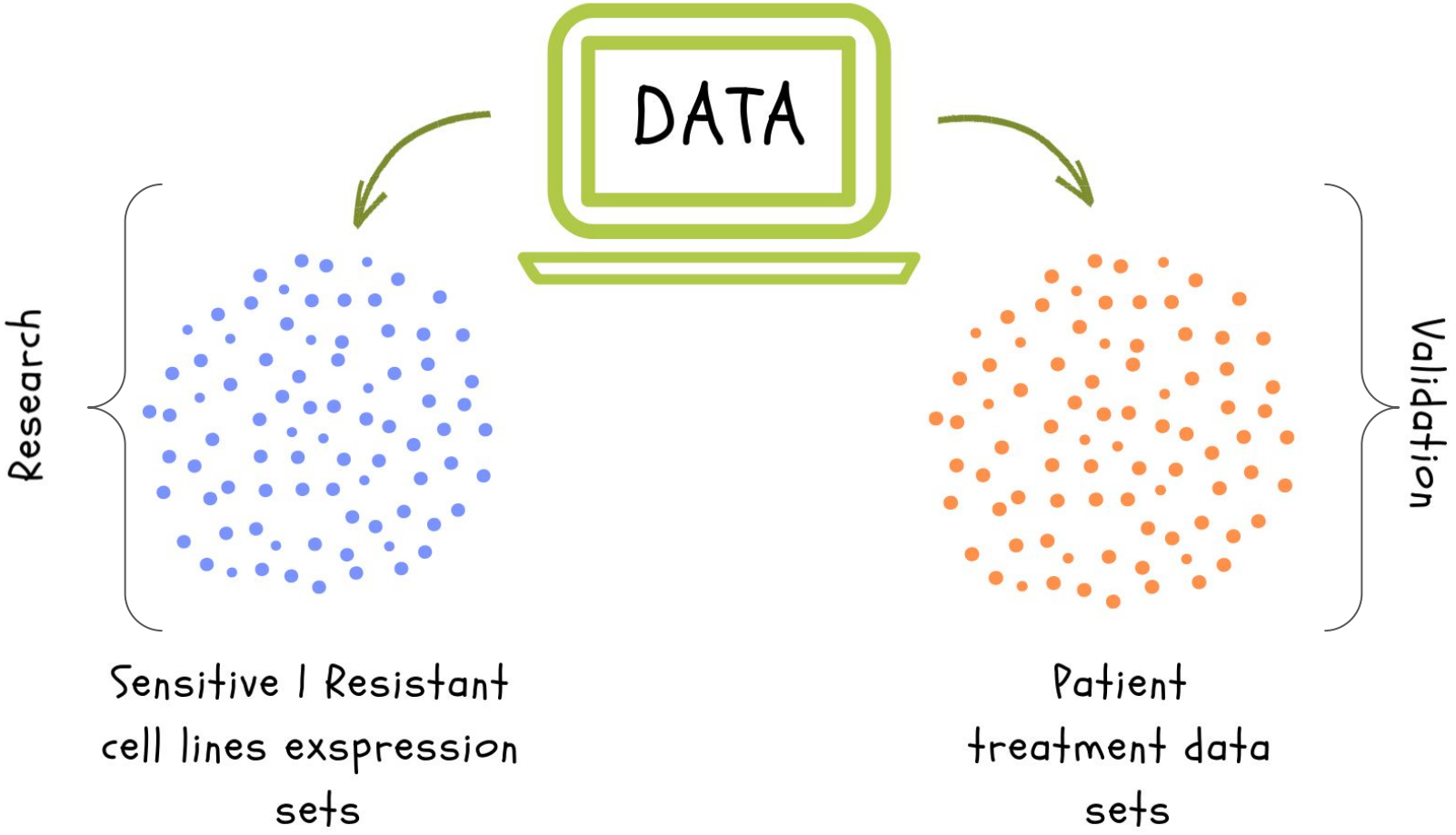
Project goal: find biomarkers of anti-EGFR therapy response

Objectives:

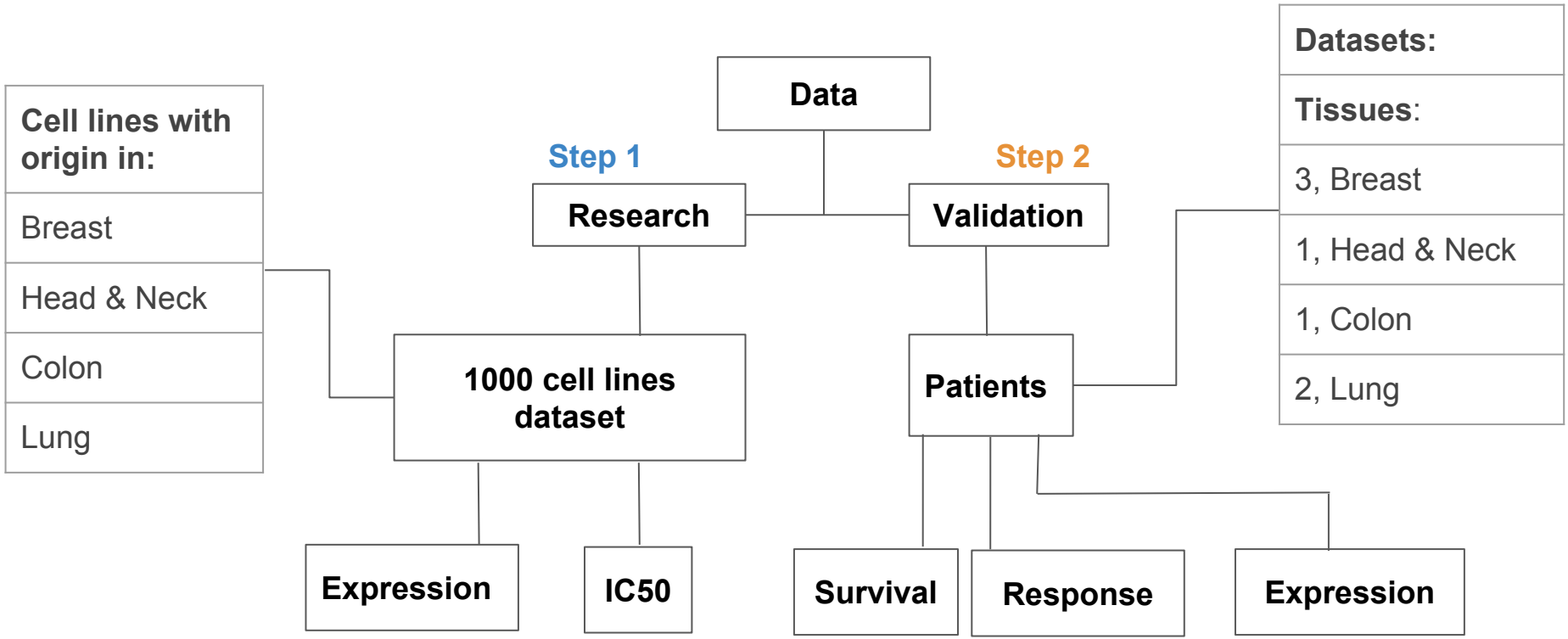
- Find possible biomarkers of response to EGFR inhibitors therapy among cell lines.
- Validate the model with patient transcriptomic data sets
- Asses the biological interpretation of discovered signatures

Methods:

- Differential expression analysis
- PROGENy


DATA
Research
Validation
Sensitive I Resistant cell lines exspression sets
Patient treatment data sets

Workflow

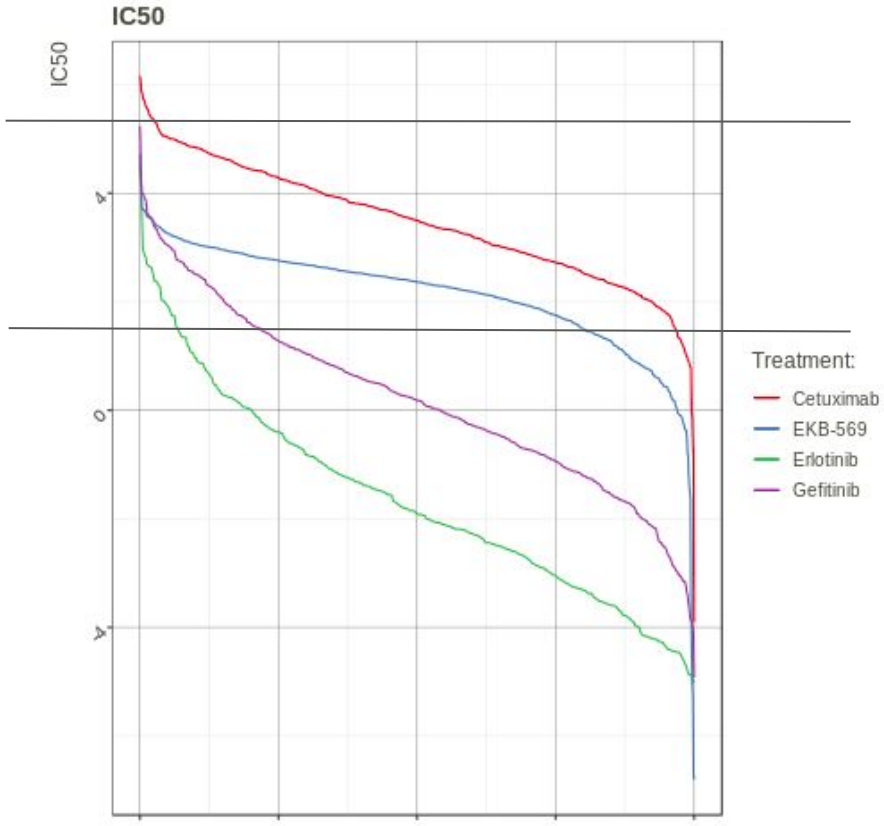

Data
Step 1
Step 2
Research
Validation
Cell lines with origin in:
Breast
Head & Neck
Colon
Lung
1000 cell lines dataset
Patients
Datasets:
Tissues:
3, Breast
1, Head & Neck
1, Colon
2, Lung
Expression
IC50
Survival
Response
Expression

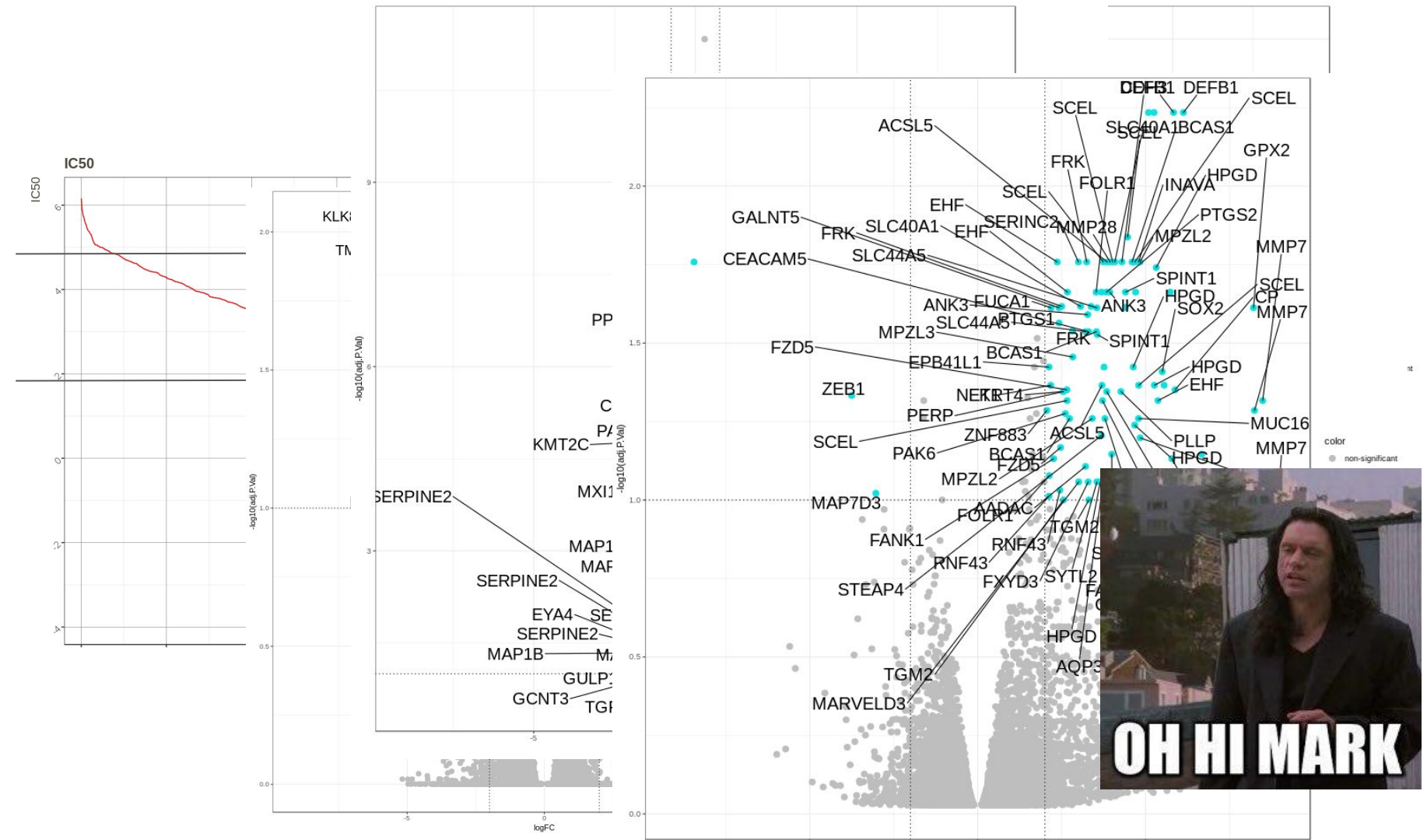
Framework for drug response analysis

Erlotinib
Cetuximab
Gefitinib
EKB-569

anti **EGFR**

IC50 across Cancer Cell Lines



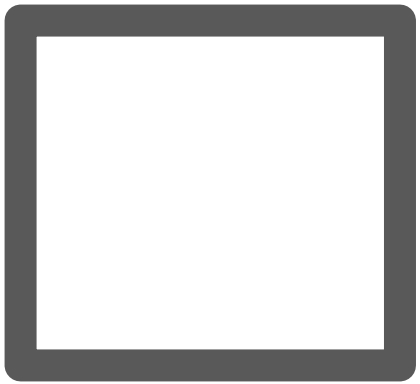

IC50
-log10(adj.P.Val)
logFC
color
non-significant
ACSL5
SCEL
DEFB1
SLC40A1
BCAS1
GPX2
FRK
HPGD
FOLR1
INAVA
EHF
SERINC2
PTGS2
GALNT5
MMP28
MPZL2
SLC40A1
SLC44A5
CEACAM5
MMP7
SPINT1
ANK3
FUCA1
SOX2
PTGS1
MPZL3
FZD5
EPB41L1
BCAS1
ZEB1
KRT4
PERP
MUC16
ZNF883
PLLP
PAK6
FZD5
MPZL2
MAP7D3
AADAC
FOLR1
TGM2
FANK1
RNF43
FXYD3
SYTL2
STEAP4
AQP3
MARVELD3
KMT2C
SERPINE2
MAP1B
EYA4
GCNT3
OH HI MARK

Framework for drug response analysis - Results

Biomarkers for Resistance and
Responsiveness to EGFR therapy

Tissue	Erlotinib	Gefitinib	Cetuximab	EKB569
Breast	-	-	+	+
Colon	+	+	-	-
Head&Neck	-	+	-	-
NSCLC	+	+	+	-

Differential expression signatures reflect public biomarkers



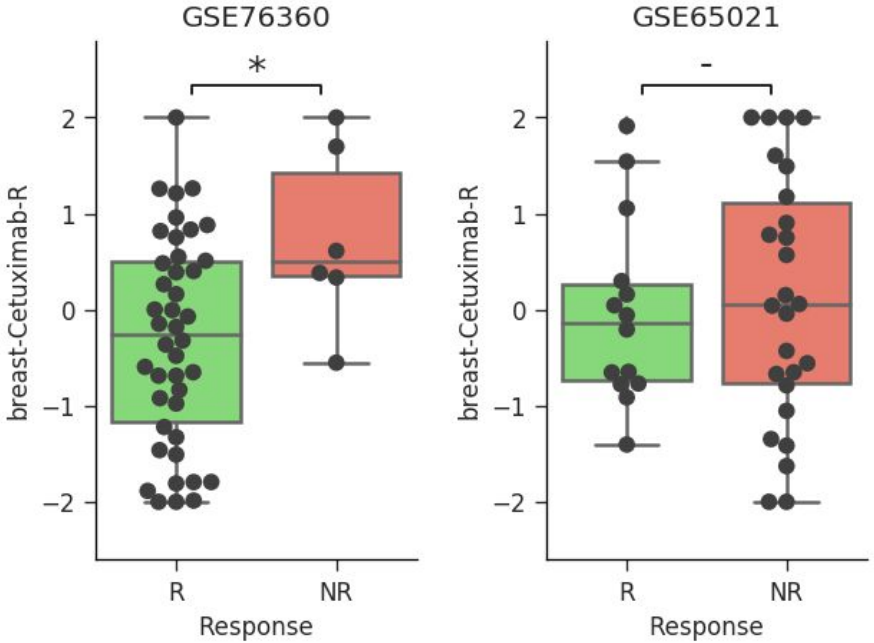
JAK/STAT/NF-kB

EMT

EGFR signaling

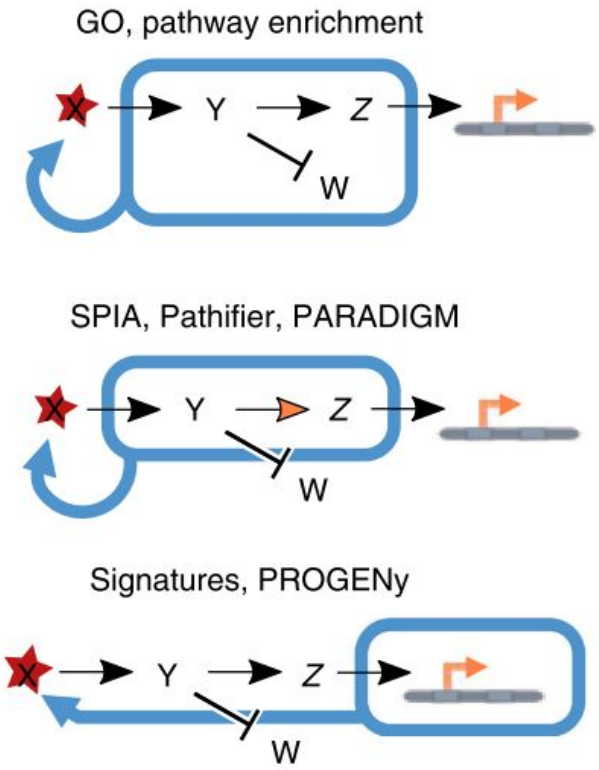
PI3K/MTOR signaling

Differential expression -> pathway scores



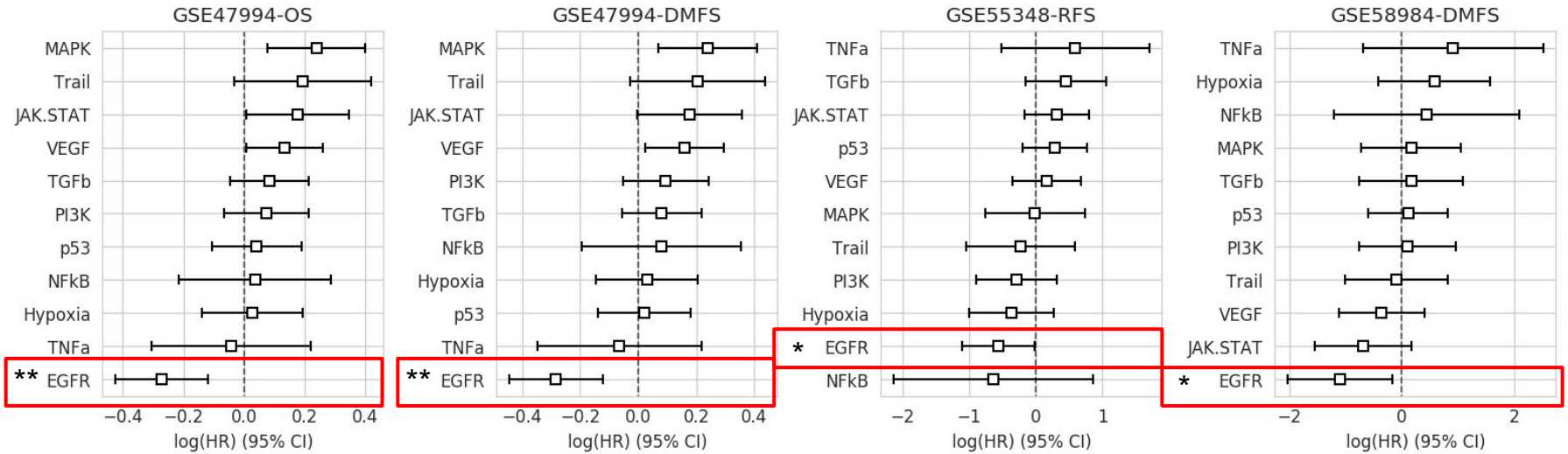
Obtained signatures

PROGENy



Schubert et al., Perturbation-response genes reveal signaling footprints in cancer gene expression. *Nature Communications* 2018

HER2+ Breast cancer



Biomarker:
Low EGFR signalling

Bad prognosis

Thank you for your attention!

GitHub: https://github.com/retreatBIOHACK/EGFR_biomarkers