

KIDNEY RENAL CLEAR CELL CARCINOMA: EXPRESSION ANALYSIS

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KIDNEY RENAL CLEAR CELL CARCINOMA

- KIRC is one of the most common Kidney cancer (95%).
- Resistant to Chemotherapy/Radiotherapy.
Nephrectomy, primary treatment.

Objectives:

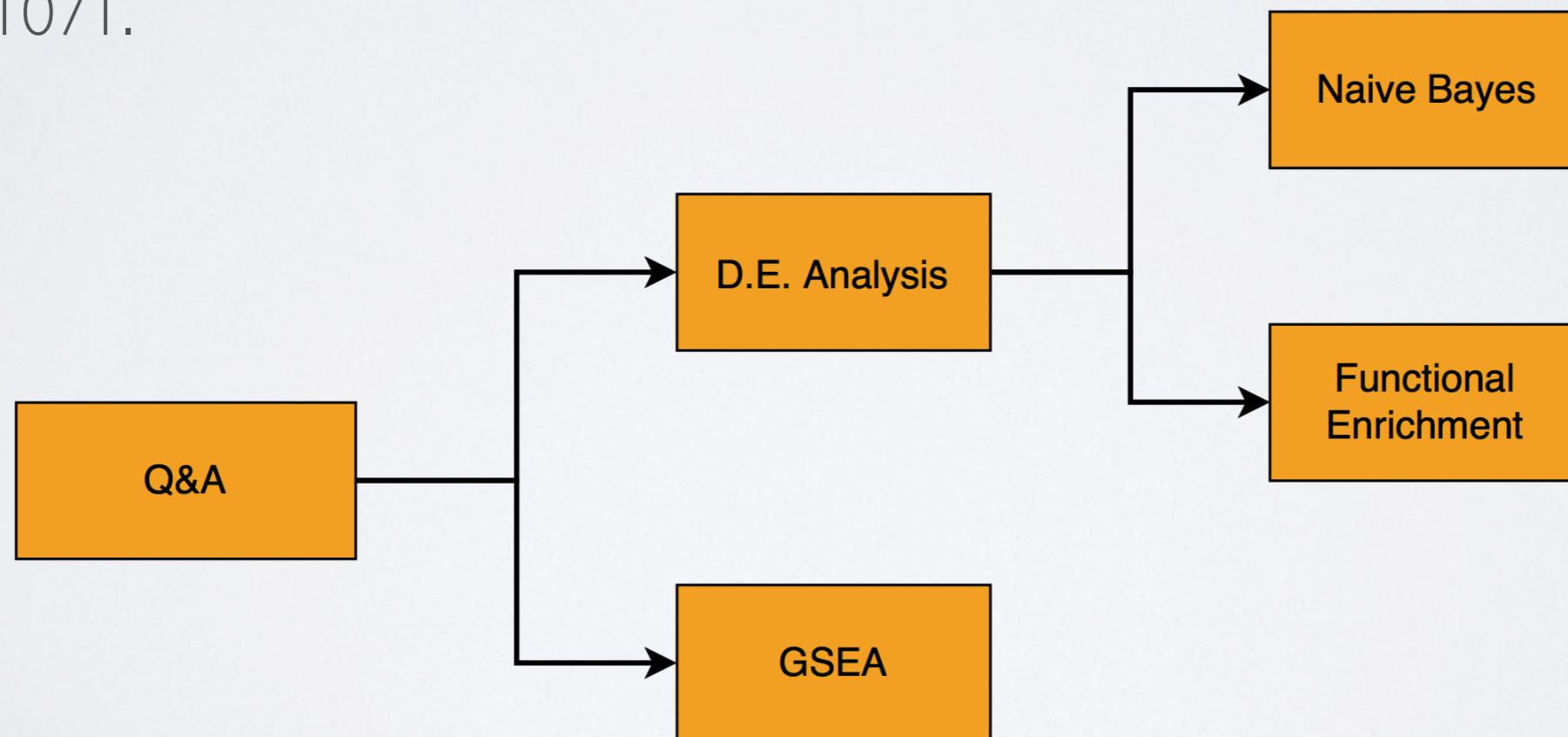
- Search for gene expression differences.
- Look for the causes of the variability between normal/tumor
- Provide the biological characterization of this tumour.

WORKFLOW

The KIRC RNA-seq data has been extracted from The Cancer Genome Atlas.

Most relevant R-packages:

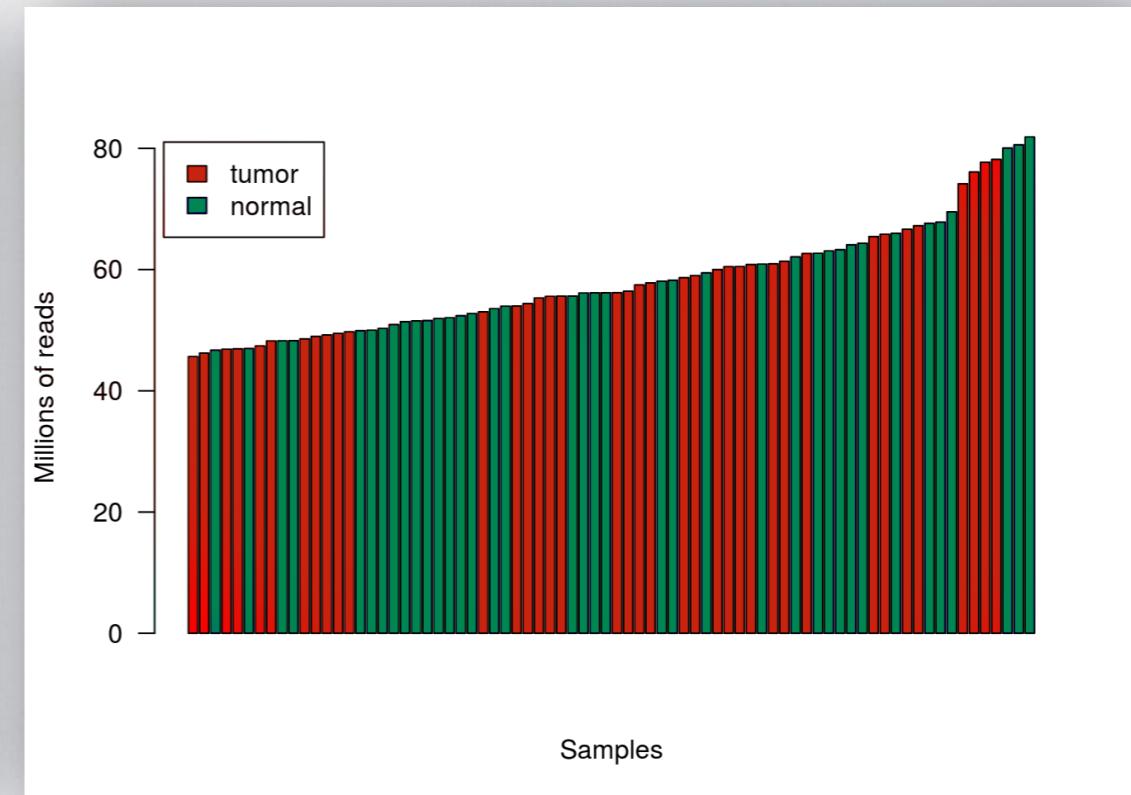
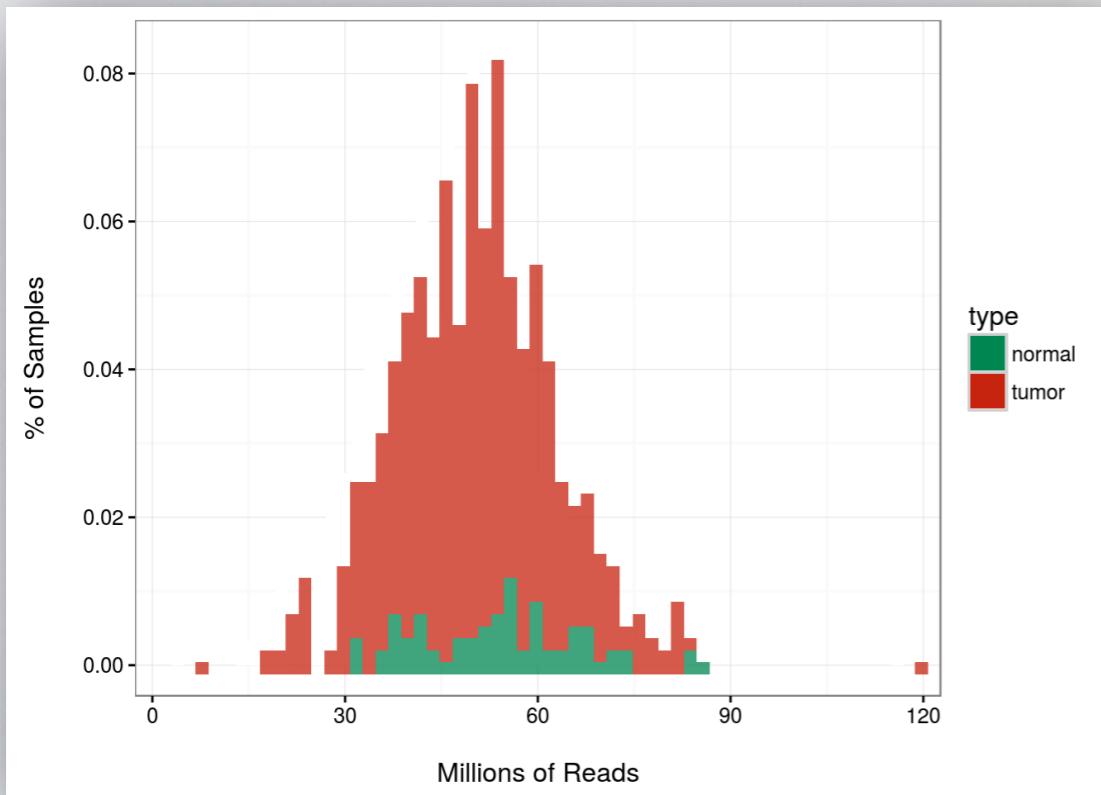
- BioConductor: edgeR, limma.
- e1071.



QUALITY ASSESSMENT

SAMPLE FILTERING

Initial dataset		Library size filter		Paired Data filter	
Tumour	Normal	Tumour	Normal	Tumour	Normal
542	72	298	48	38	38



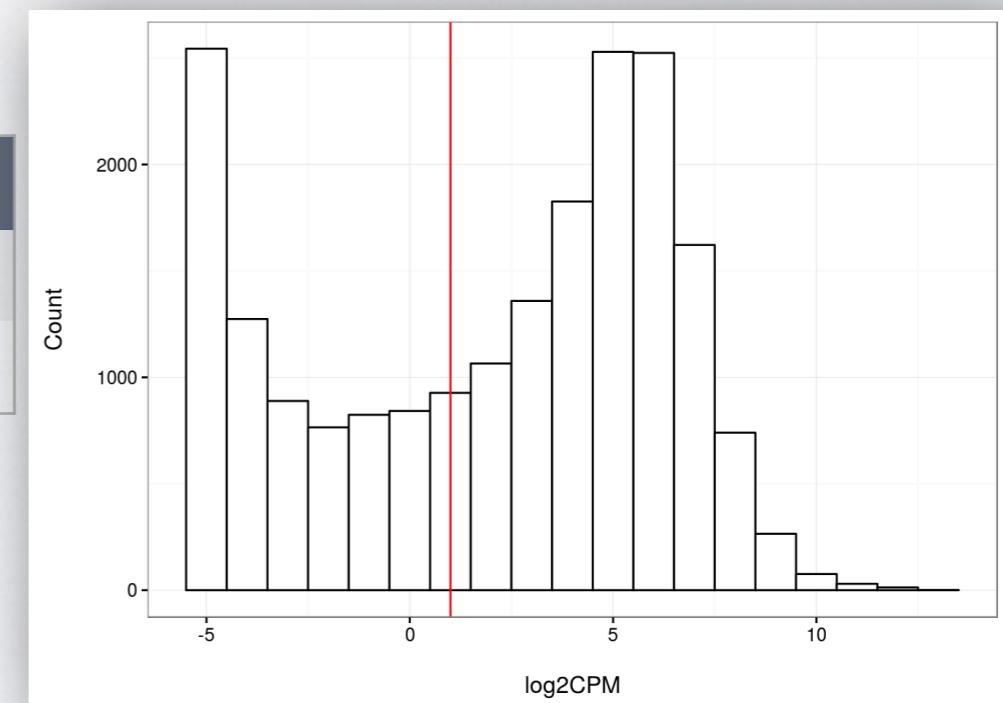
QUALITY ASSESSMENT

SAMPLE FILTERING

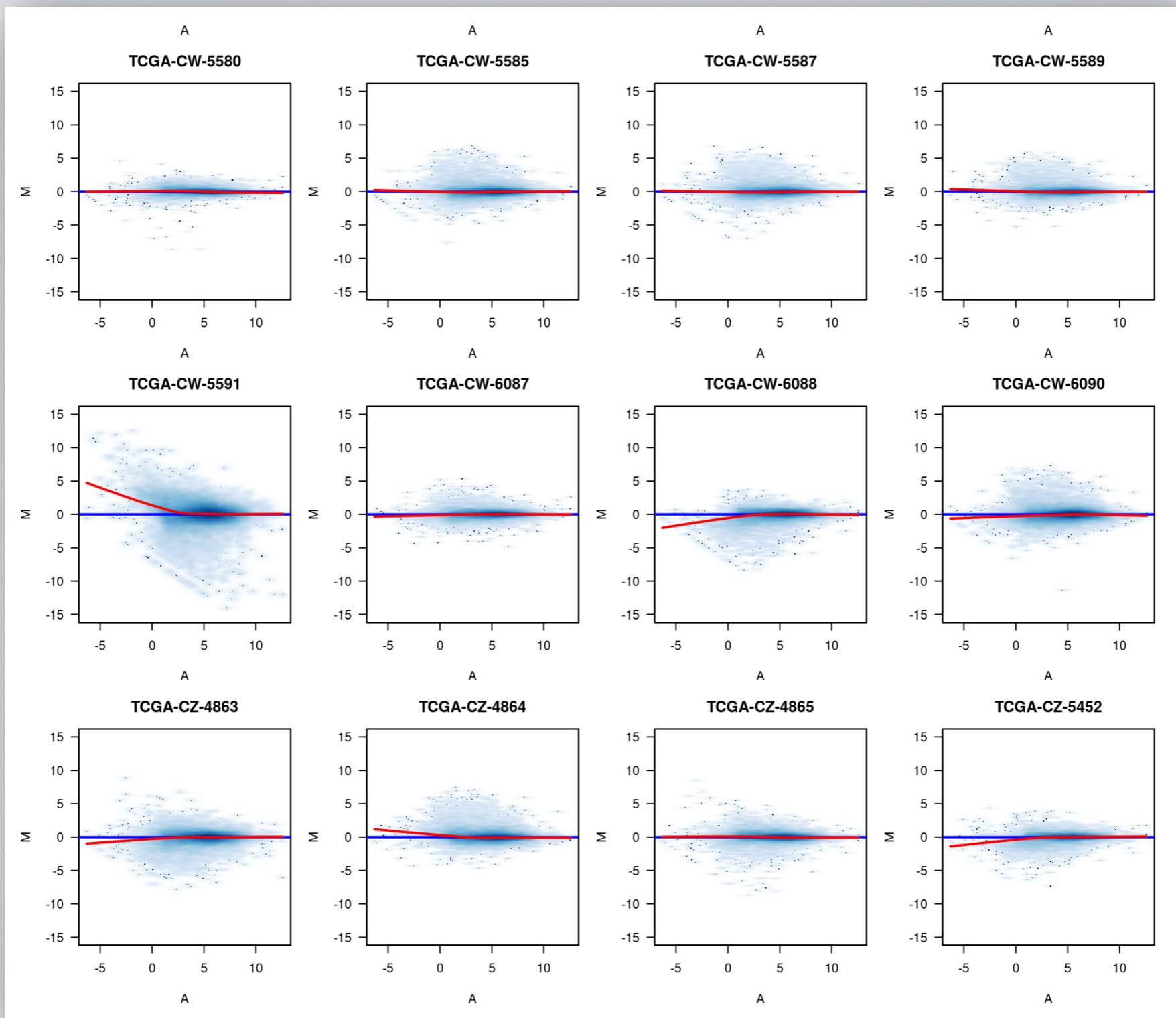
Initial dataset		Library size filter		Paired Data filter	
Tumour	Normal	Tumour	Normal	Tumour	Normal
542	72	298	48	38	38

GENE FILTERING

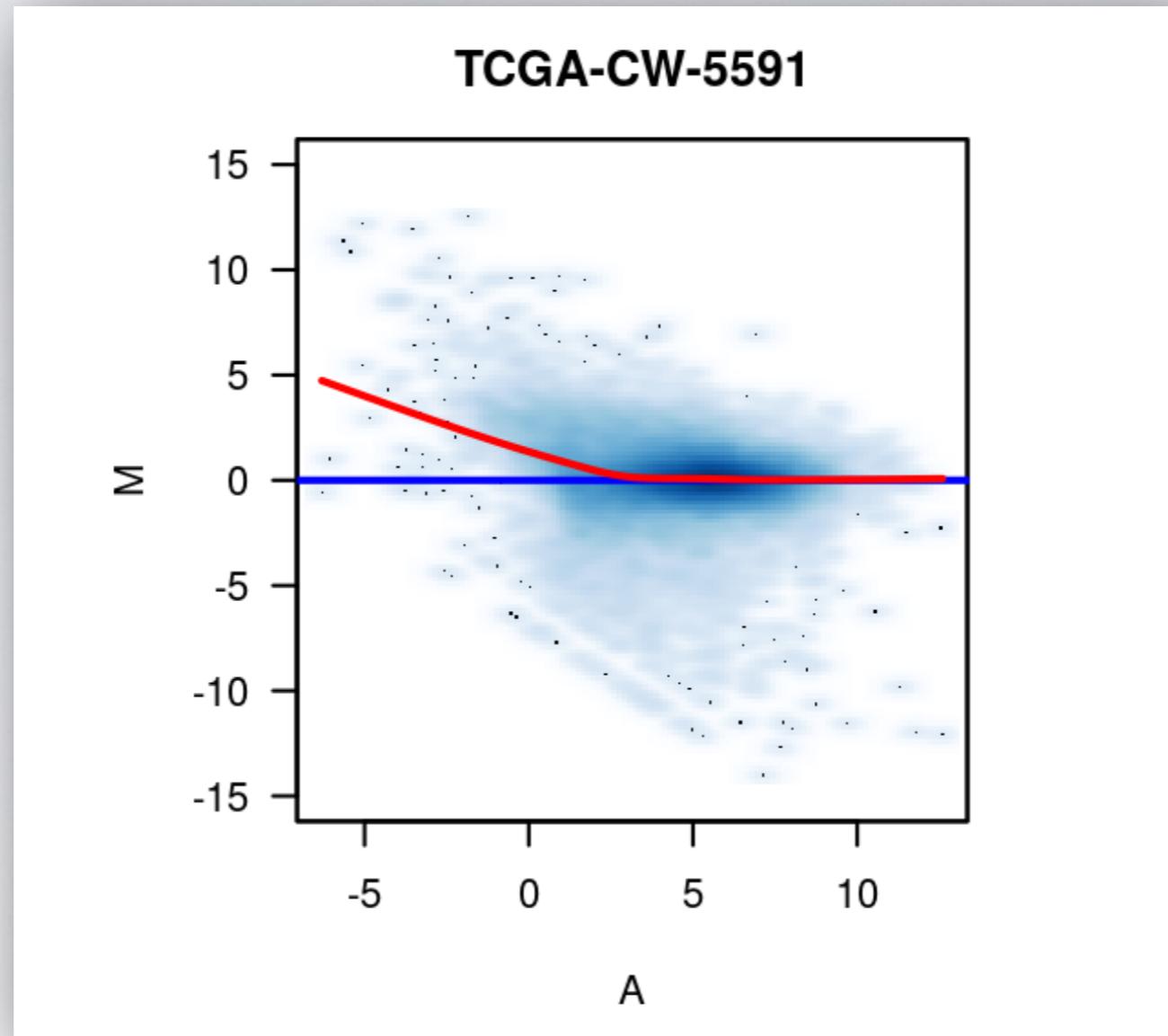
Paired dataset		Paired dataset	
Nº genes		Nº genes	
20,115		12,495	



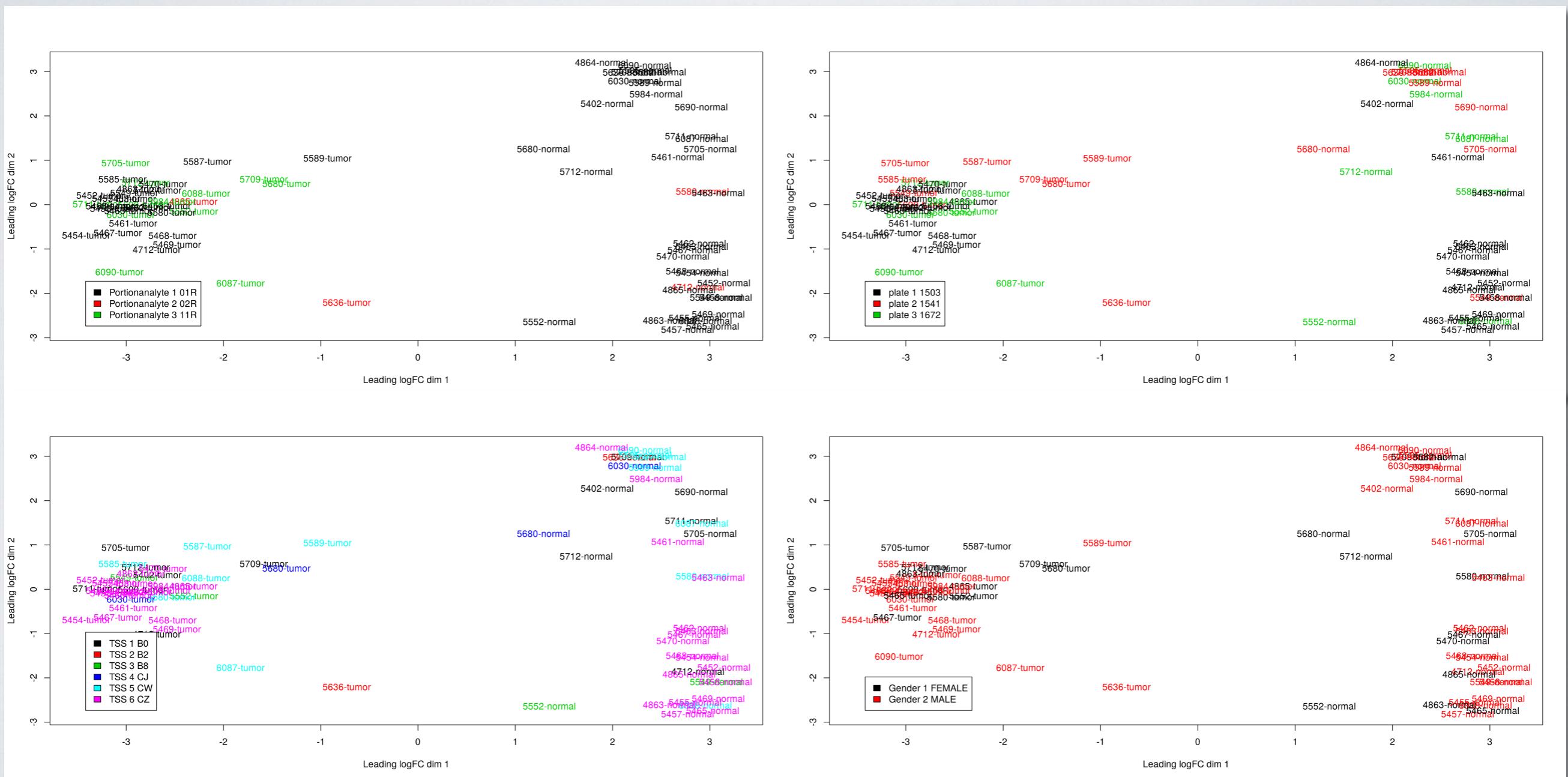
QUALITY ASSESSMENT



QUALITY ASSESSMENT



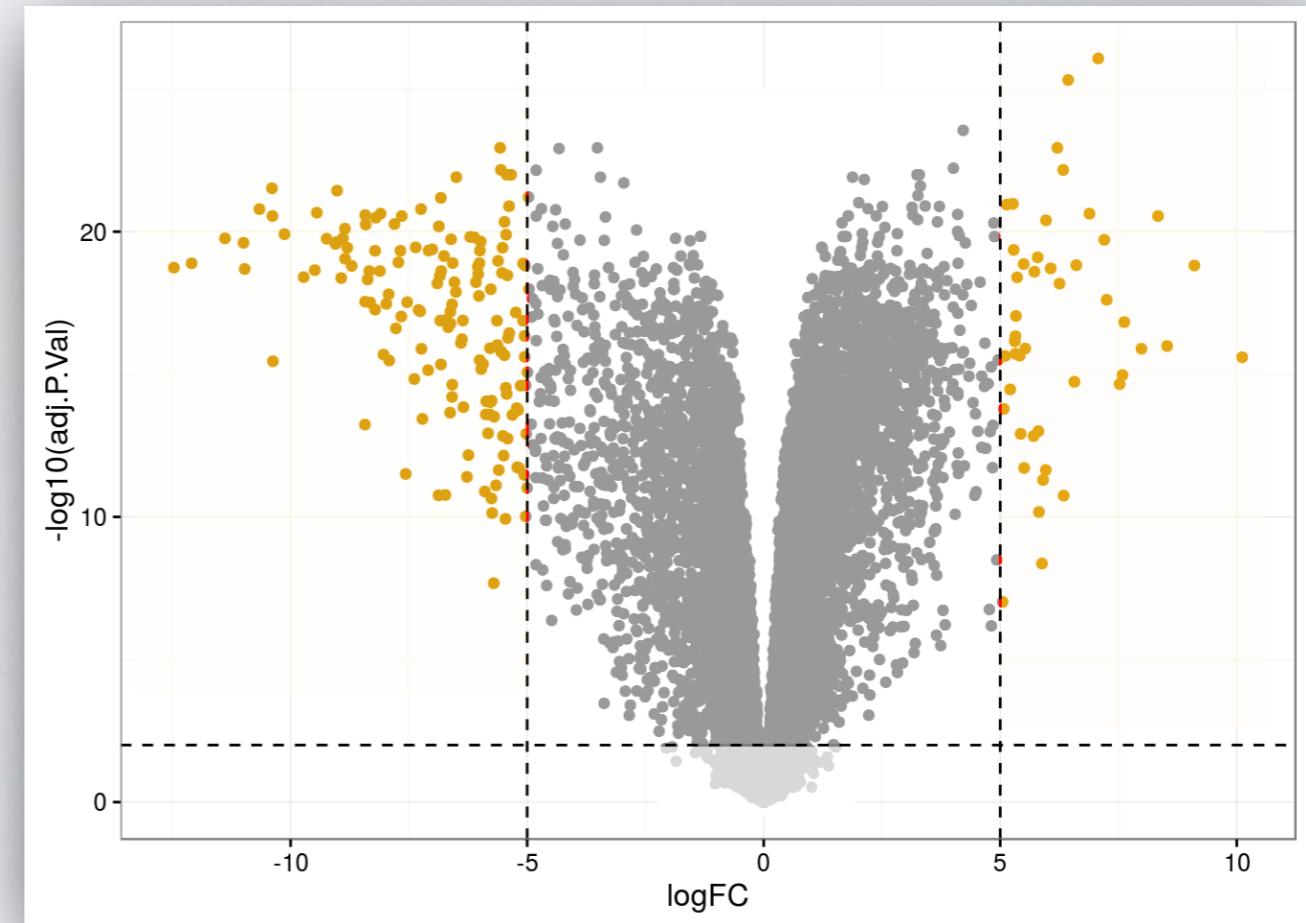
BATCH EFFECT



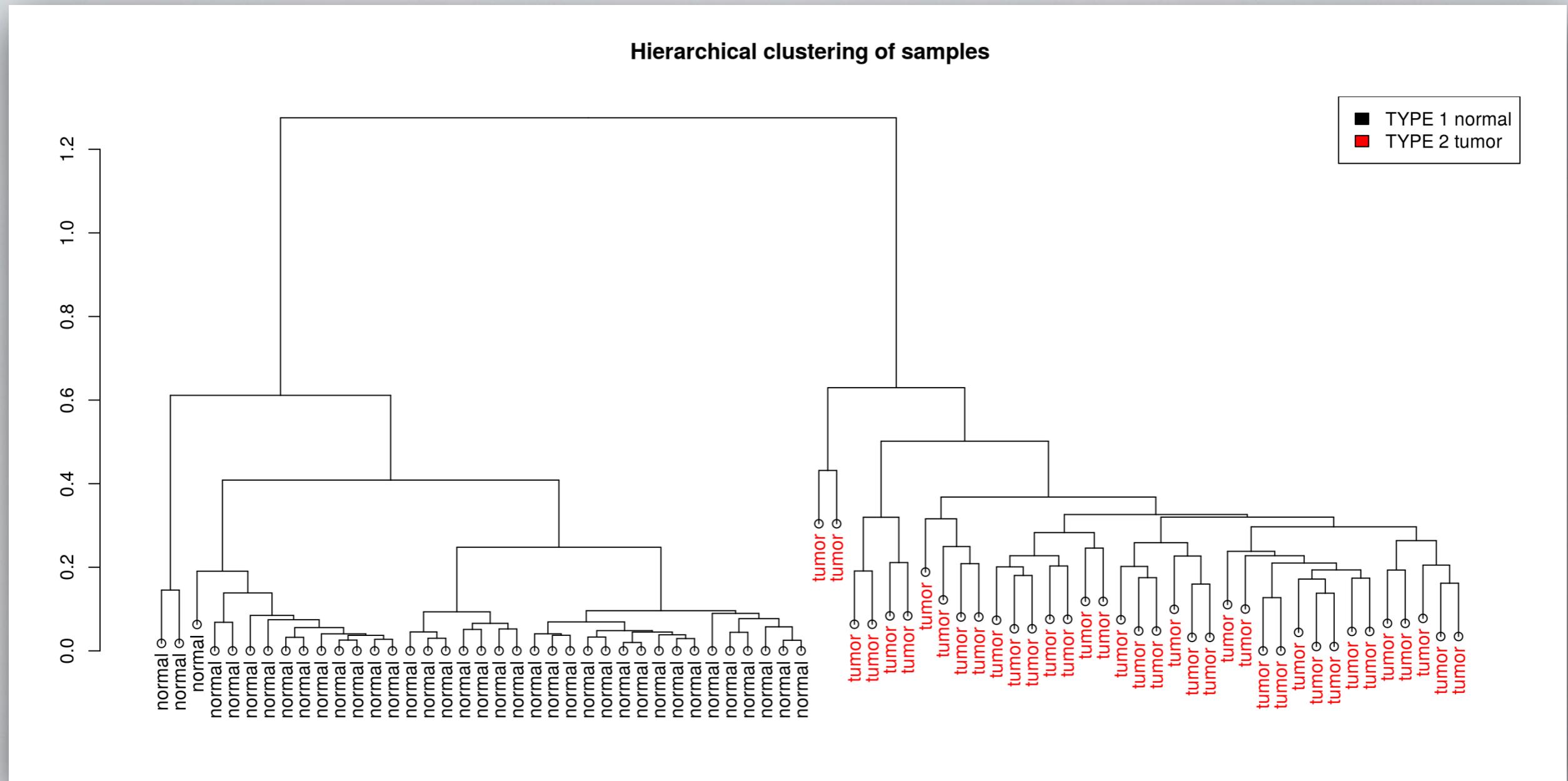
DIFFERENTIAL EXPRESSION ANALYSIS

Paired dataset	
Nº genes	
12,495	
↓	
DE genes	
Over	Under
5,094	4,014
↓	
Strongly DE genes	
Over	Under
46	153

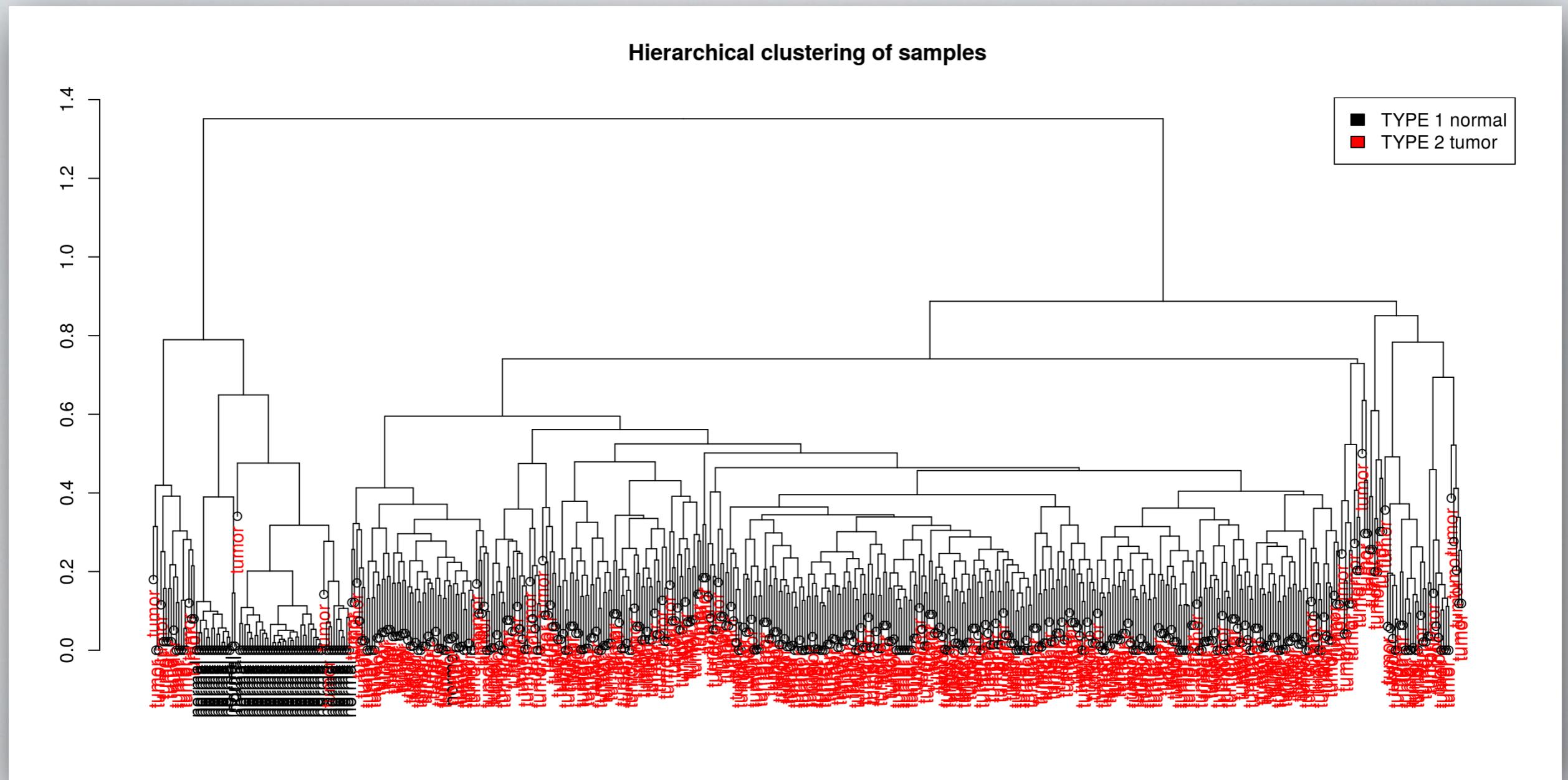
$$Y_{ijk} = \mu_0 + \alpha_i + \beta_j + e_{ijk}$$



HIERARCHICAL CLUSTERING



HIERARCHICAL CLUSTERING



NAIVE BAYES CLASSIFIER

- 448 samples testing
- 74 samples training

		Observed	
		normal	tumor
Prediction	normal	28	33
	tumor	1	386

PRECISION	SPECIFICITY	SENSITIVITY
0.9974	0.9655	0.9212

Yang, W., K. Yoshigoe, X. Qin, J. S. Liu, J. Y. Yang, A. Niemierko, Y. Deng, Y. Liu, A. Dunker, Z. Chen, L. Wang, D. Xu, H. R. Arabnia, W. Tong, and M. Yang, 2014 Identification of genes and pathways involved in kidney renal clear cell carcinoma. BMC bioinformatics **15 Suppl 1:** S2.

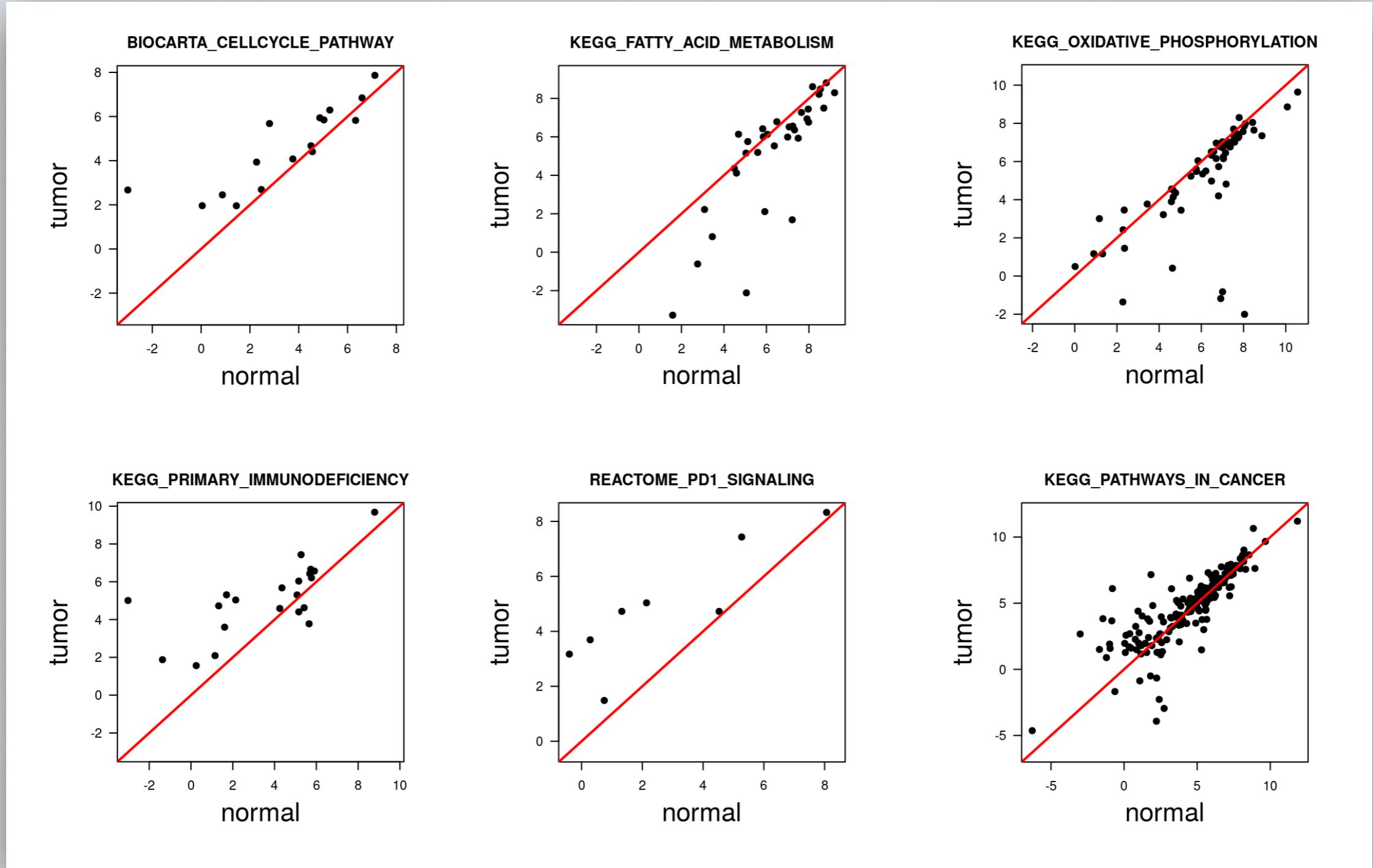
FUNCTIONAL ENRICHMENT ANALYSIS

- Gene Ontology Analysis: Fisher's Exact Test ($P < 0.01$).
- 96 over-represented & 59 under-represented GO terms.

Table 1 Five most over-represented Biological Process GO terms in over-expressed genes in KIRC.

GOBPID	Pvalue	OddsRatio	ExpCount	Count	Size	Term
GO:0051301	0.000	1.534	165	206	402	cell division
GO:0051251	0.000	2.064	54	77	131	positive regulation of lymphocyte activation
GO:0007156	0.000	2.469	35	53	84	homophilic cell adhesion via plasma membrane adhesion molecules
GO:0008283	0.000	1.275	459	518	1117	cell proliferation
GO:0032946	0.000	2.634	27	42	65	positive regulation of mononuclear cell proliferation

GENE SET ENRICHMENT ANALYSIS



BIOLOGICAL CHARACTERIZATION

Metabolic shift:

Under-expressed fatty acid degradation and oxidative phosphorylation.

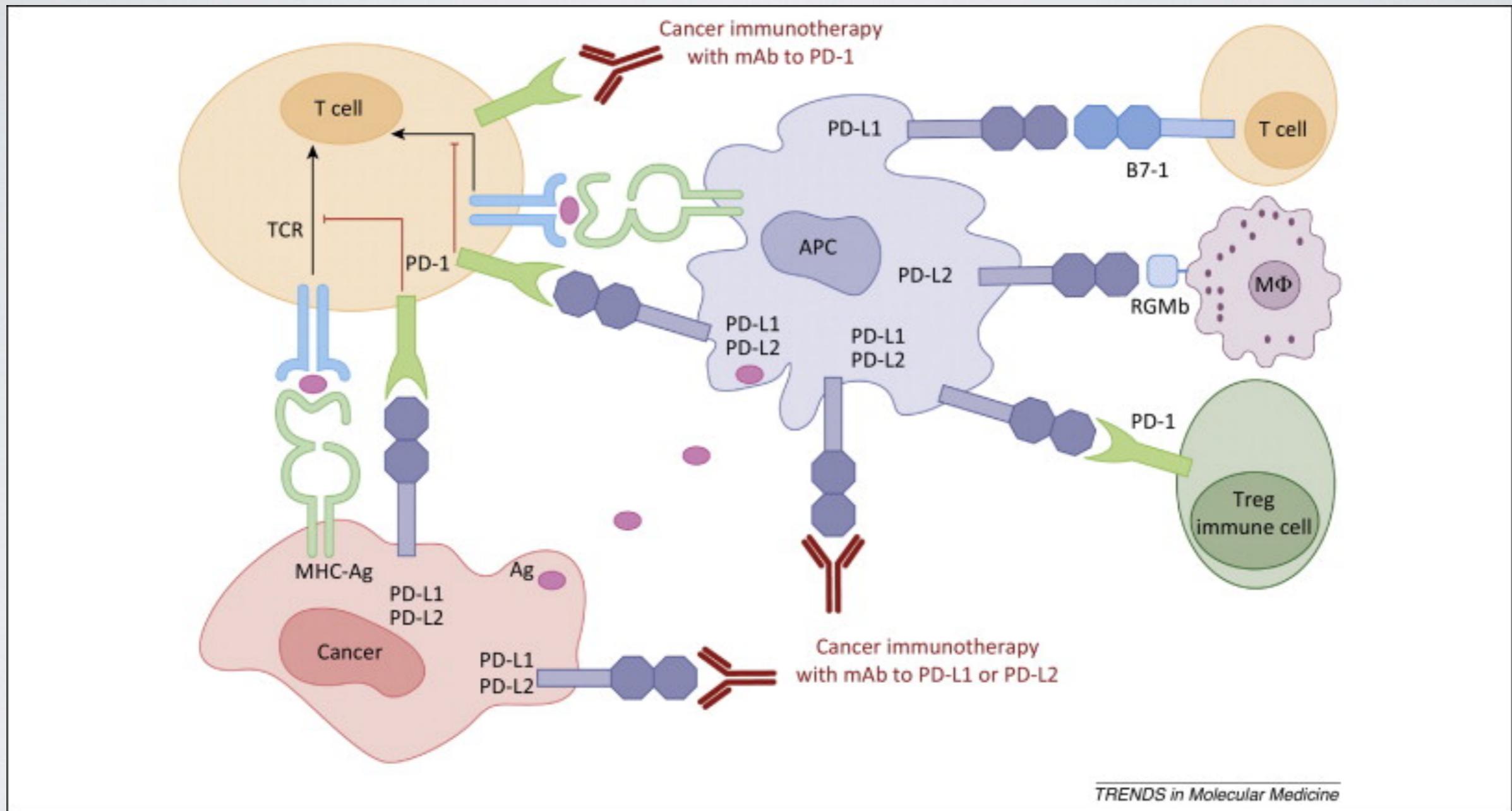
Loss of function:

Less small-molecule/cation transport.

Immune evasion:

PD-1 signalling and T-cell apoptosis.

BIOLOGICAL CHARACTERIZATION



PD-1 signalling and T-cell apoptosis.

CONCLUSION

- The most differentially expressed genes have been identified.
- KIRC tumour has been biologically characterized.
- The Naive Bayes classifier is a good tool to differentiate samples by cell-type using 199 genes.
- PD-1 has been identified as a possible target for cancer therapy.