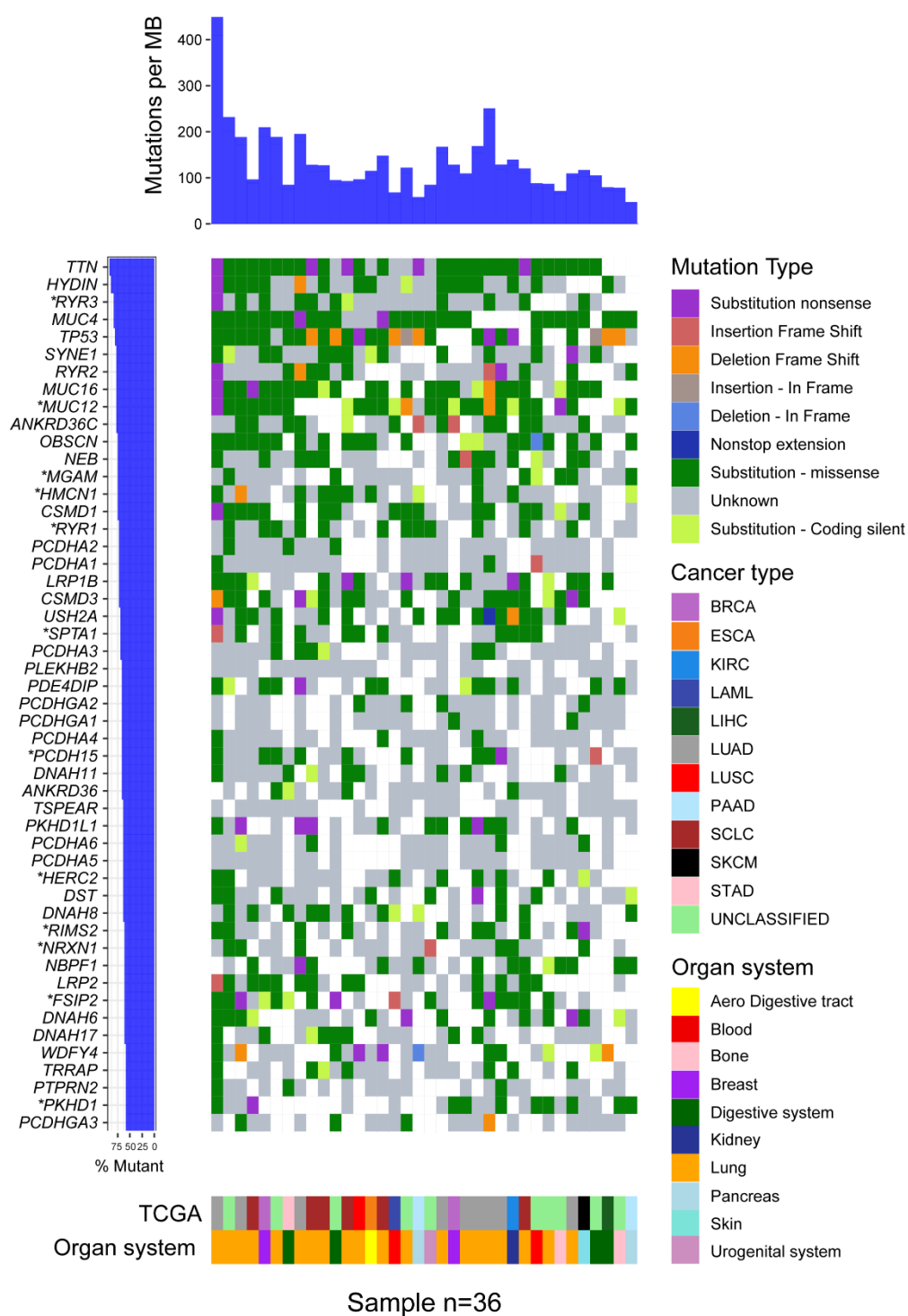


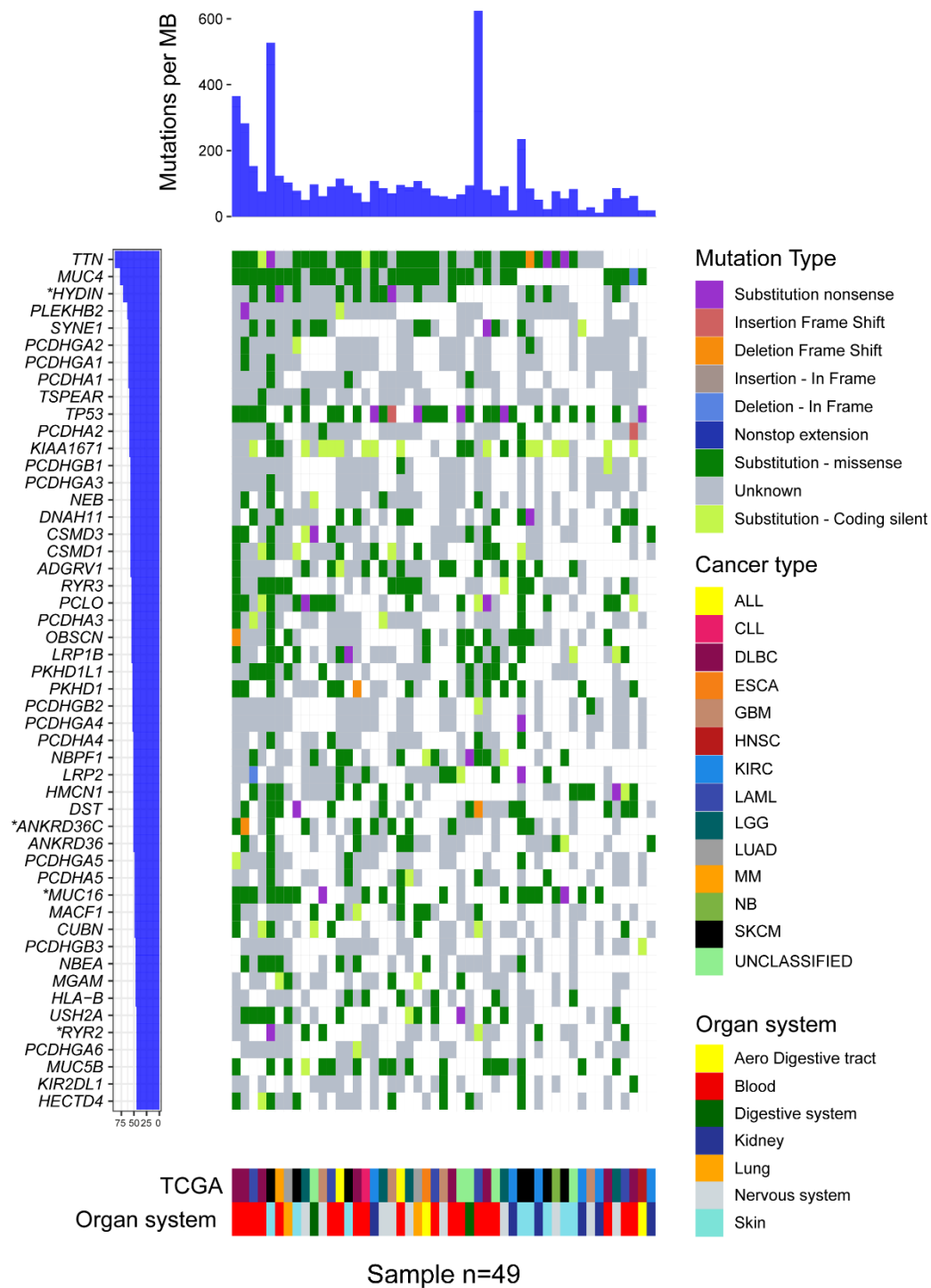
Supplementary Figures

Supplementary Fig. 1

a



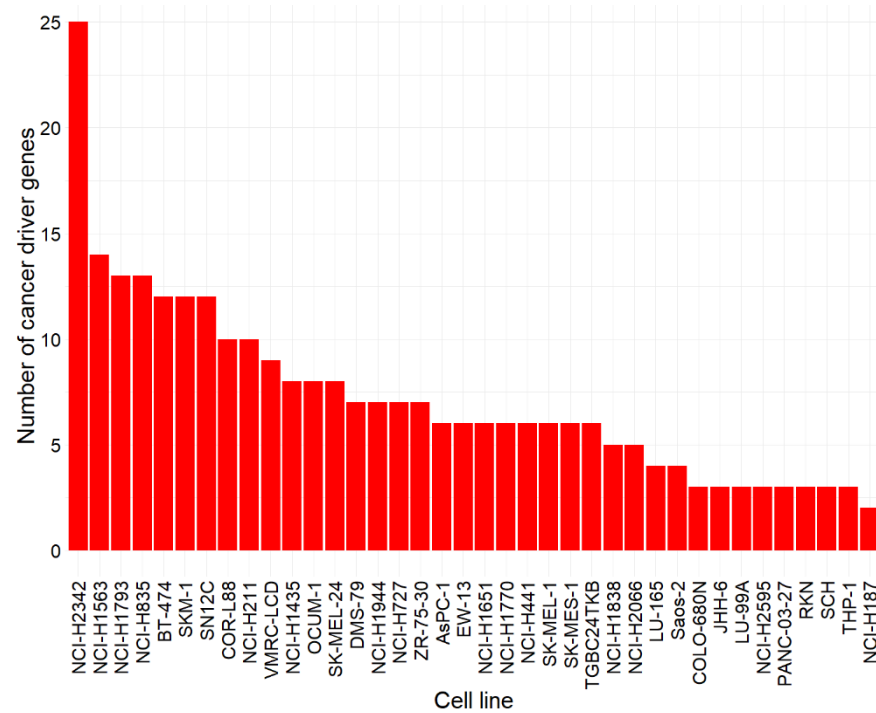
b



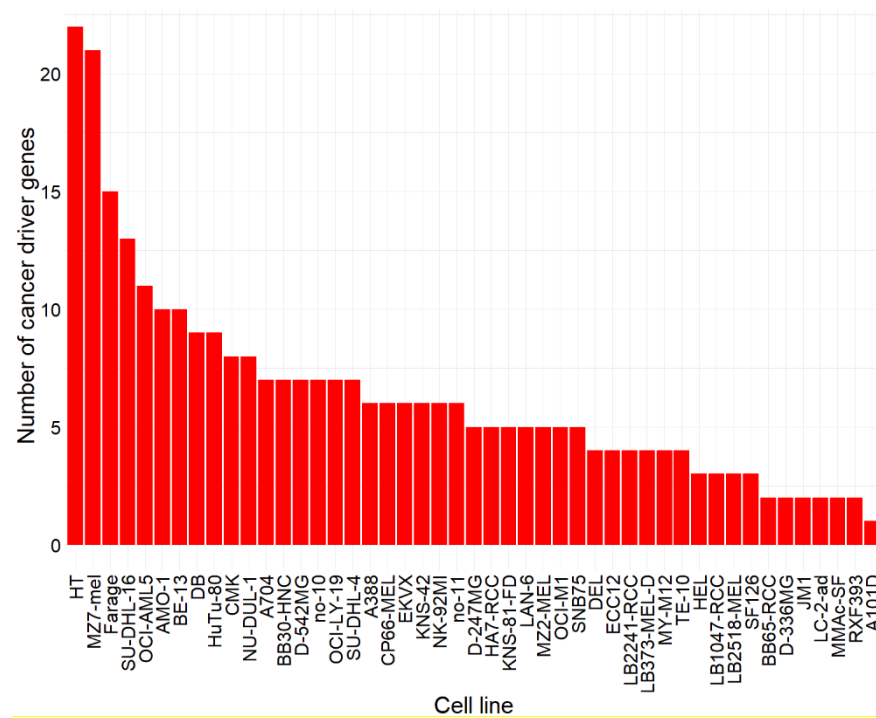
Supplementary Fig. 1. Waterfall plots depicting the 50 most mutated genes in (a) bortezomib-insensitive and (b) sensitive cancer cell lines.

Supplementary Fig. 2

a



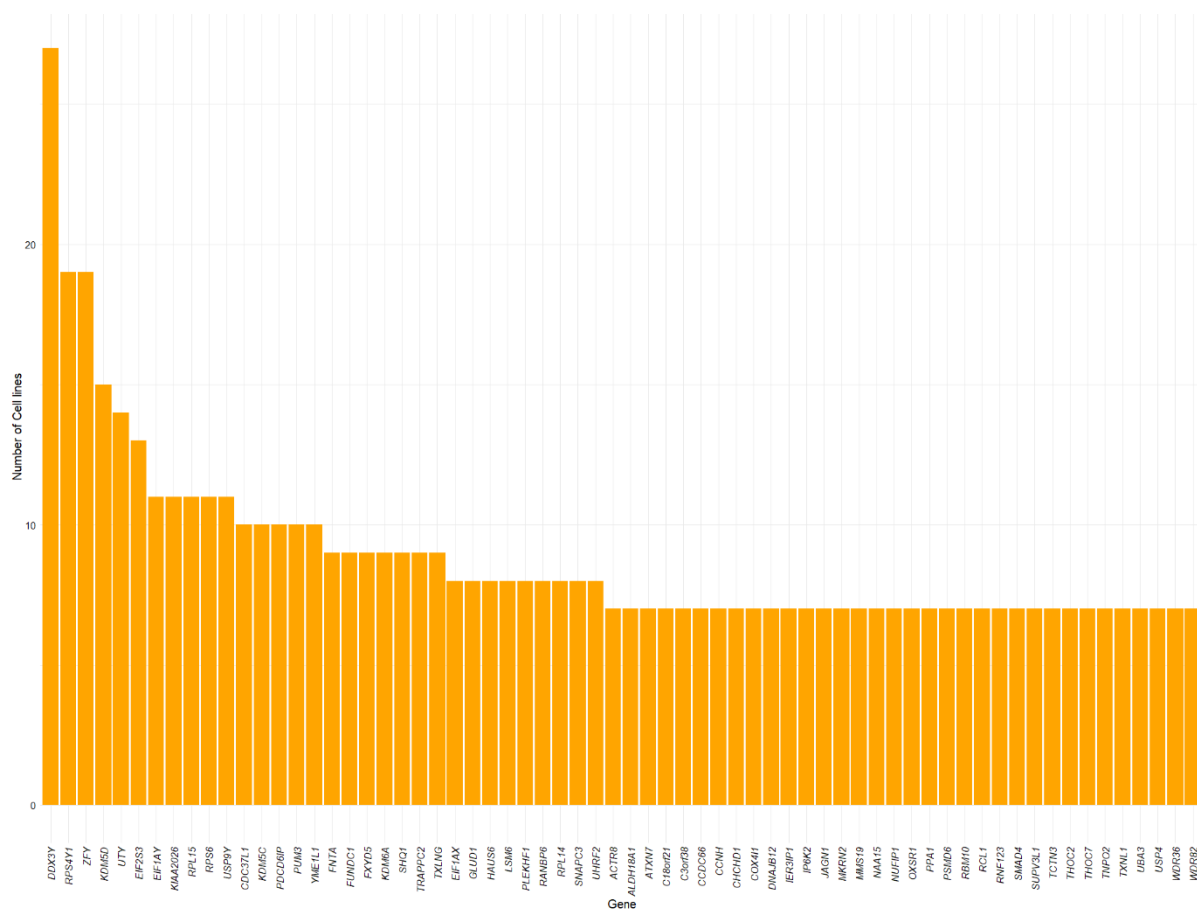
b



Supplementary Fig. 2. Bar charts showing the number of mutated cancer driver genes in (a) bortezomib-insensitive and (b) sensitive cancer cell lines.

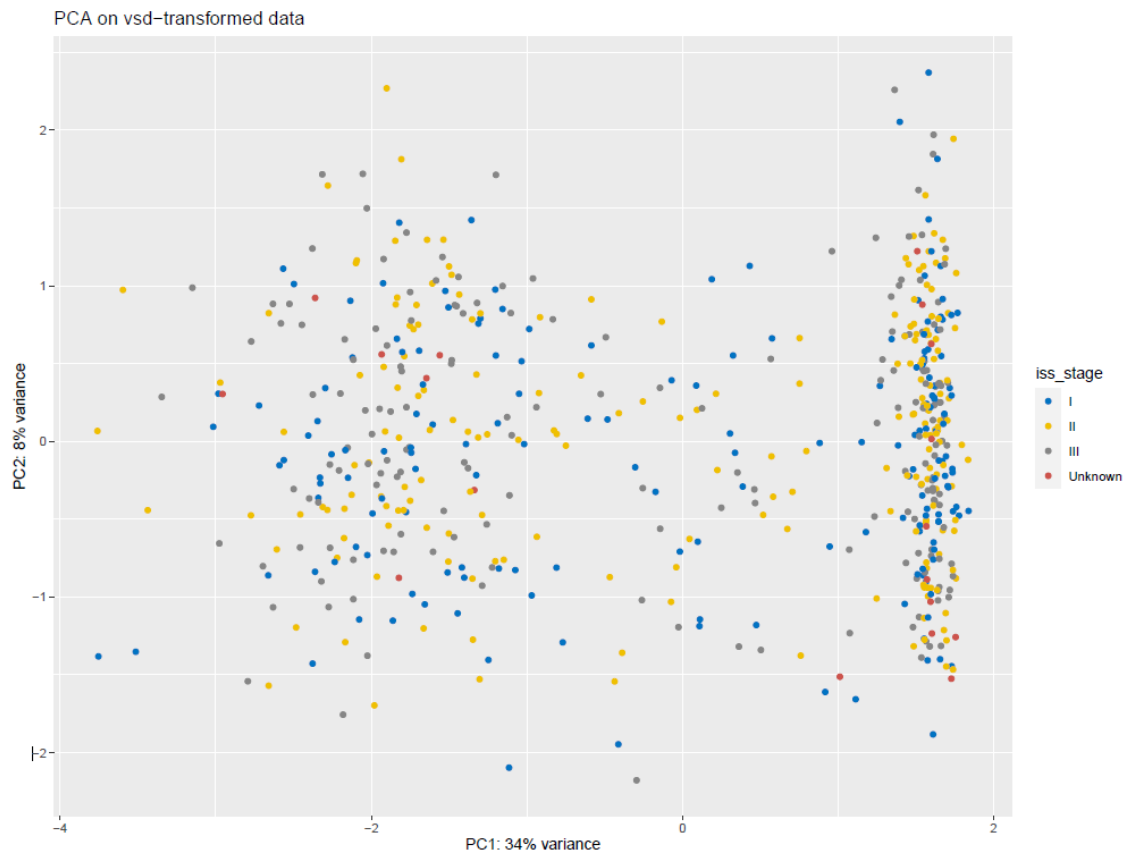
a



b

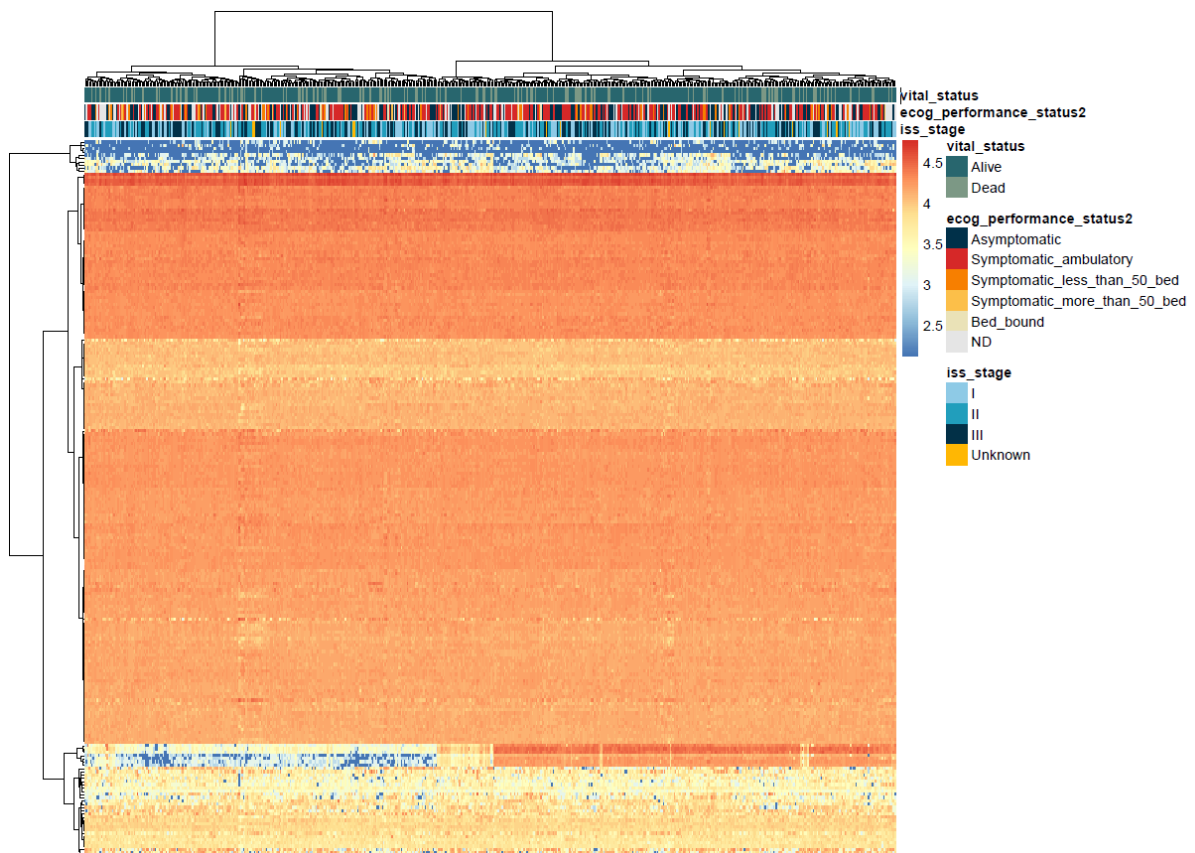
Supplementary Fig. 3. The number of (a) overexpressed and (b) underexpressed genes in bortezomib-insensitive cancer cell lines.

Supplementary Fig. 4



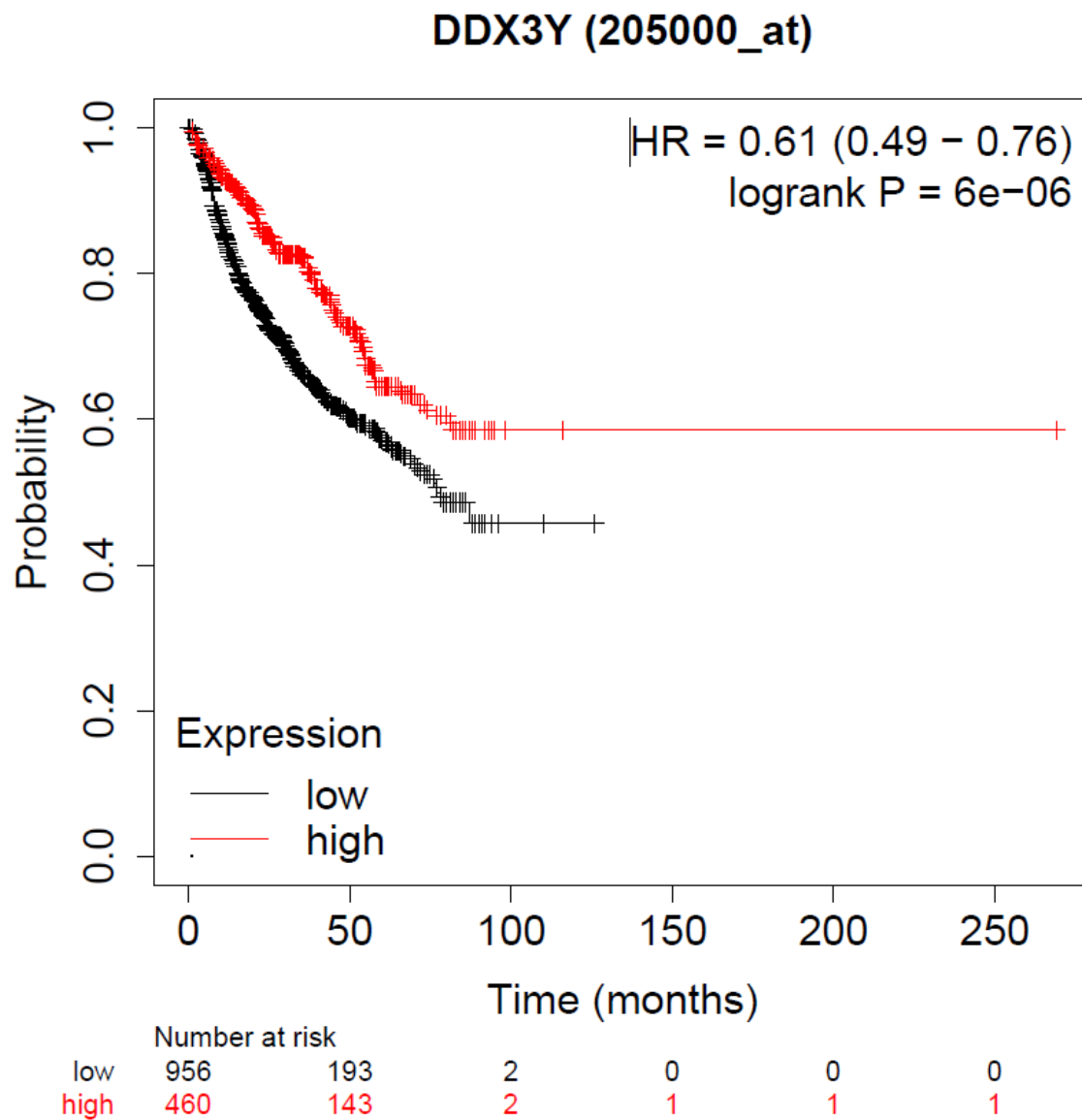
Supplementary Fig. 4. Principal component analysis using the gene expression patterns of 220 genes associated with bortezomib sensitivity stratified 589 patients (treated with bortezomib; classified by the International Staging System [ISS stage]) from the MMRF-COMMPASS into two clusters.

Supplementary Fig. 5

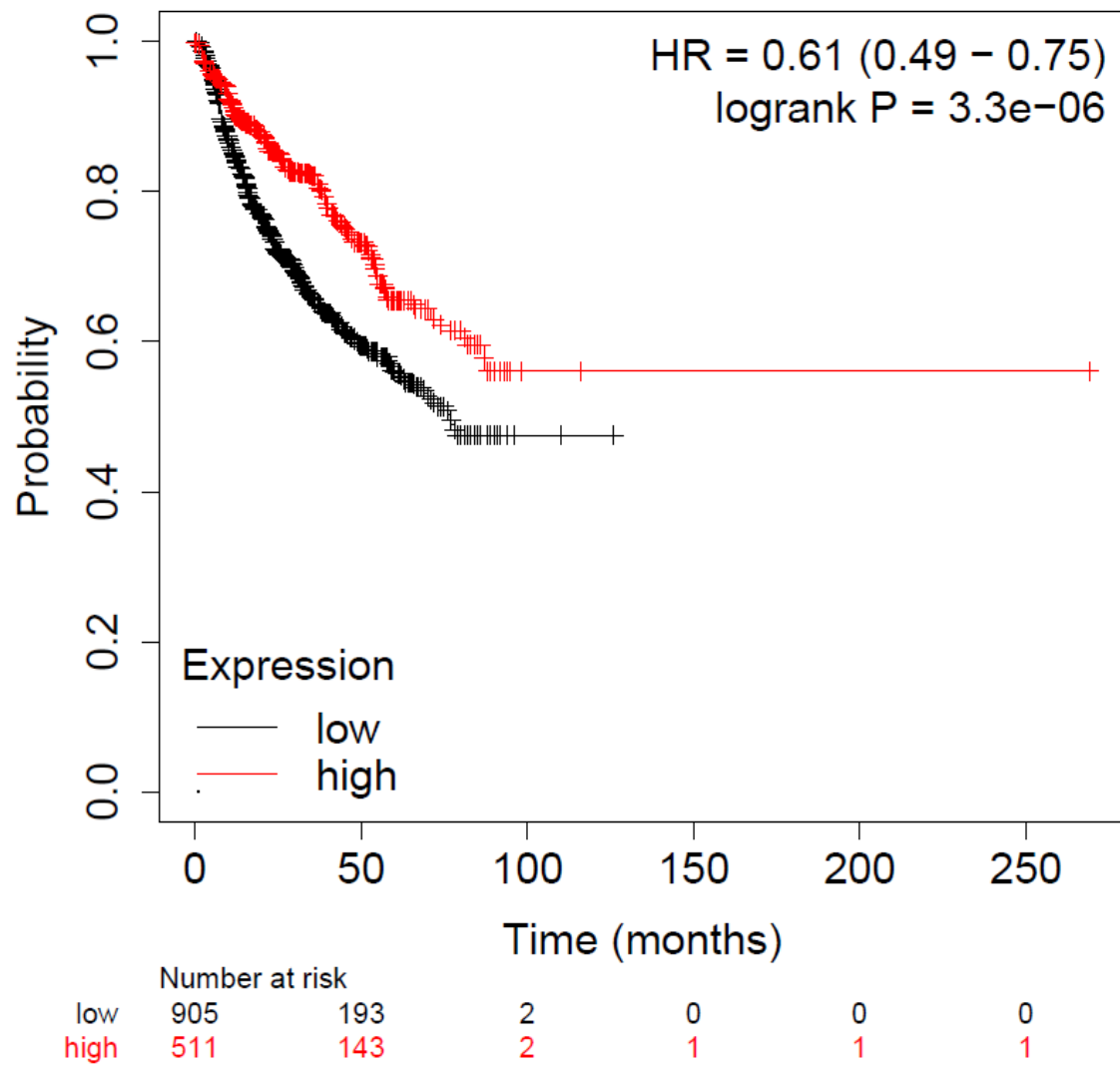


Supplementary Fig. 5. Hierarchical clustering of gene expression patterns for 220/234 genes associated with response to bortezomib treatment and their association with vital status, ECOG performance status, and cancer stage in 589 multiple myeloma patients. Aberrant expression for seven genes was found for the two patient clusters.

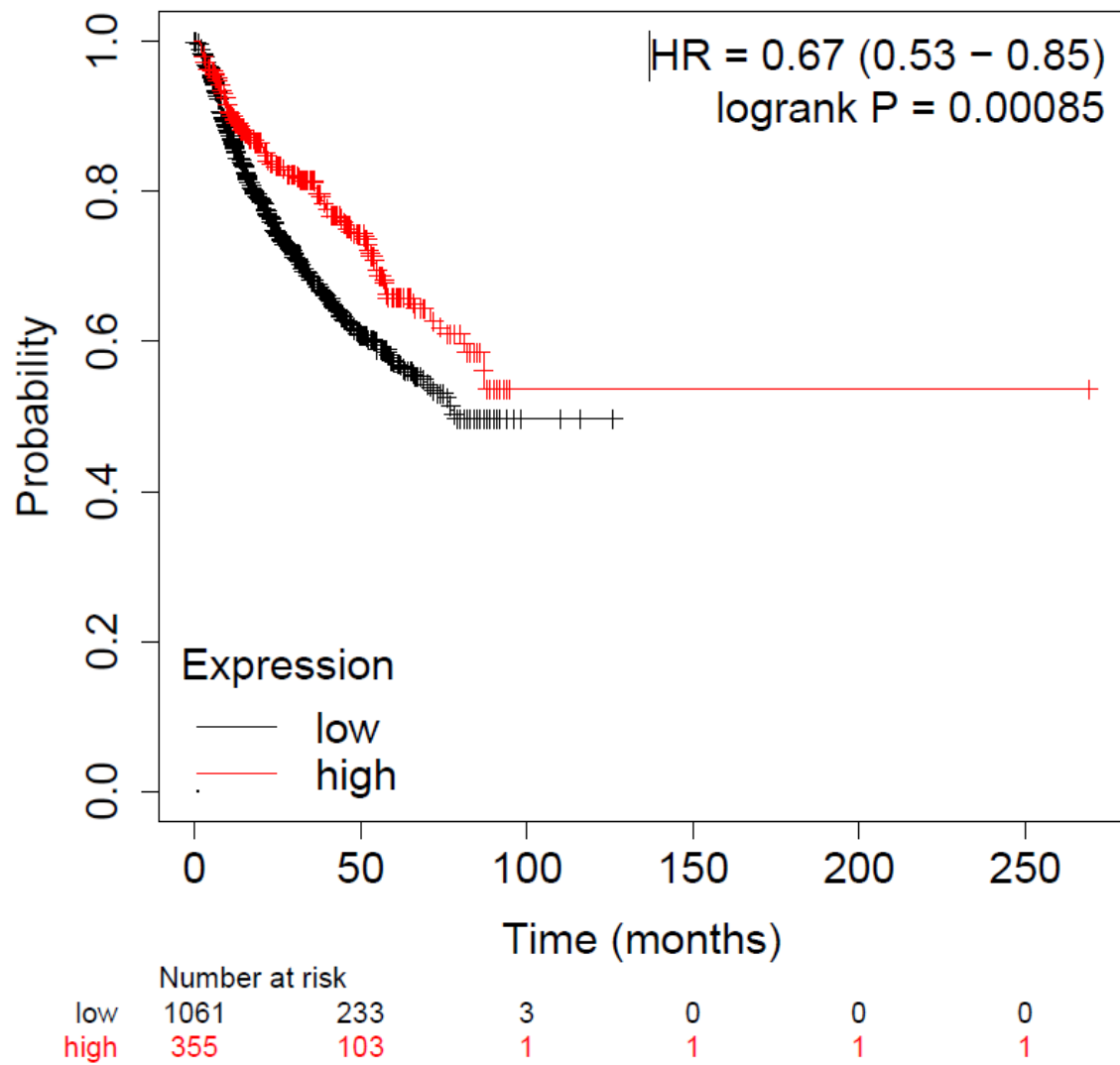
Supplementary Fig. 6



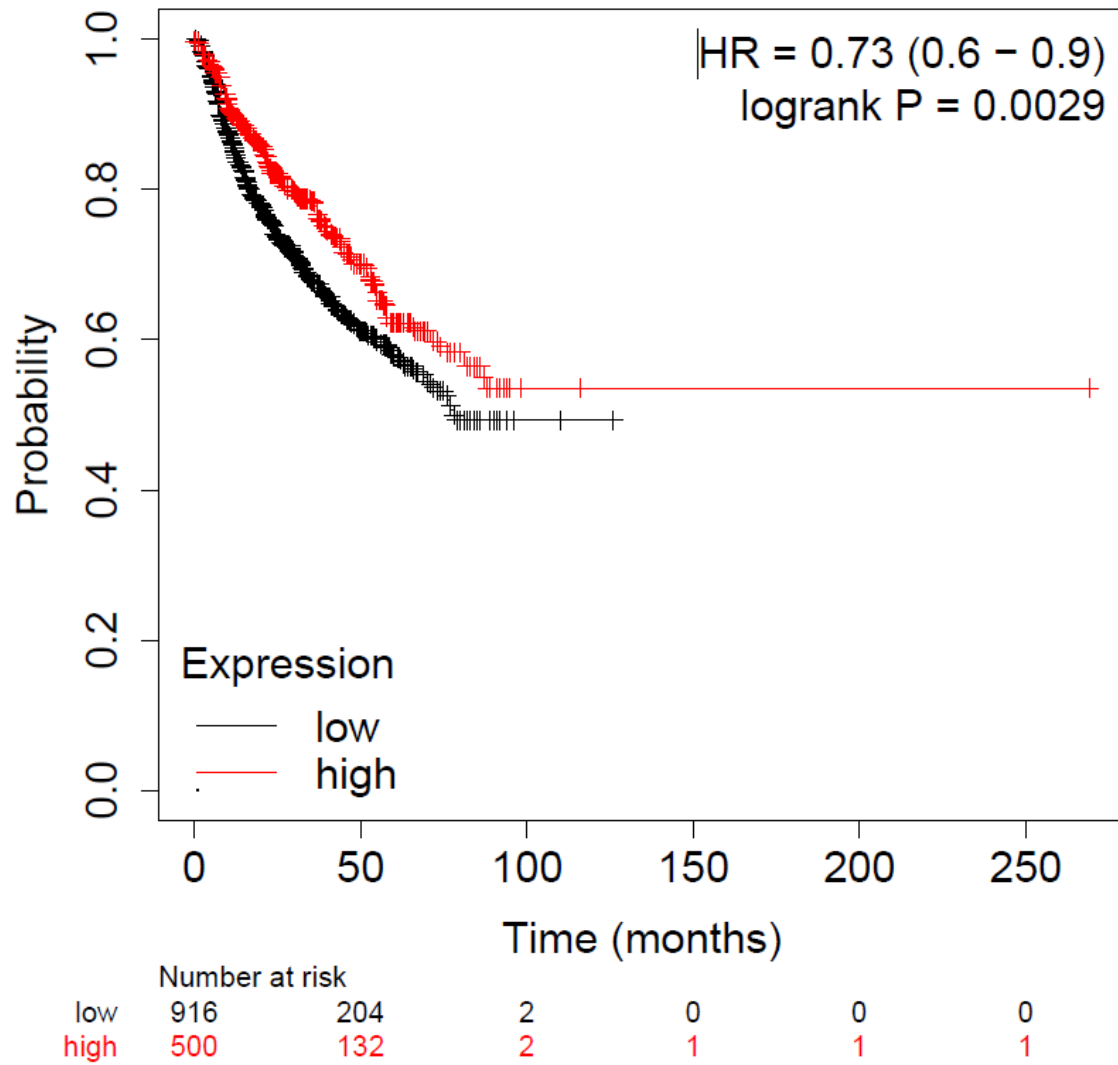
EIF1AY (204410_at)



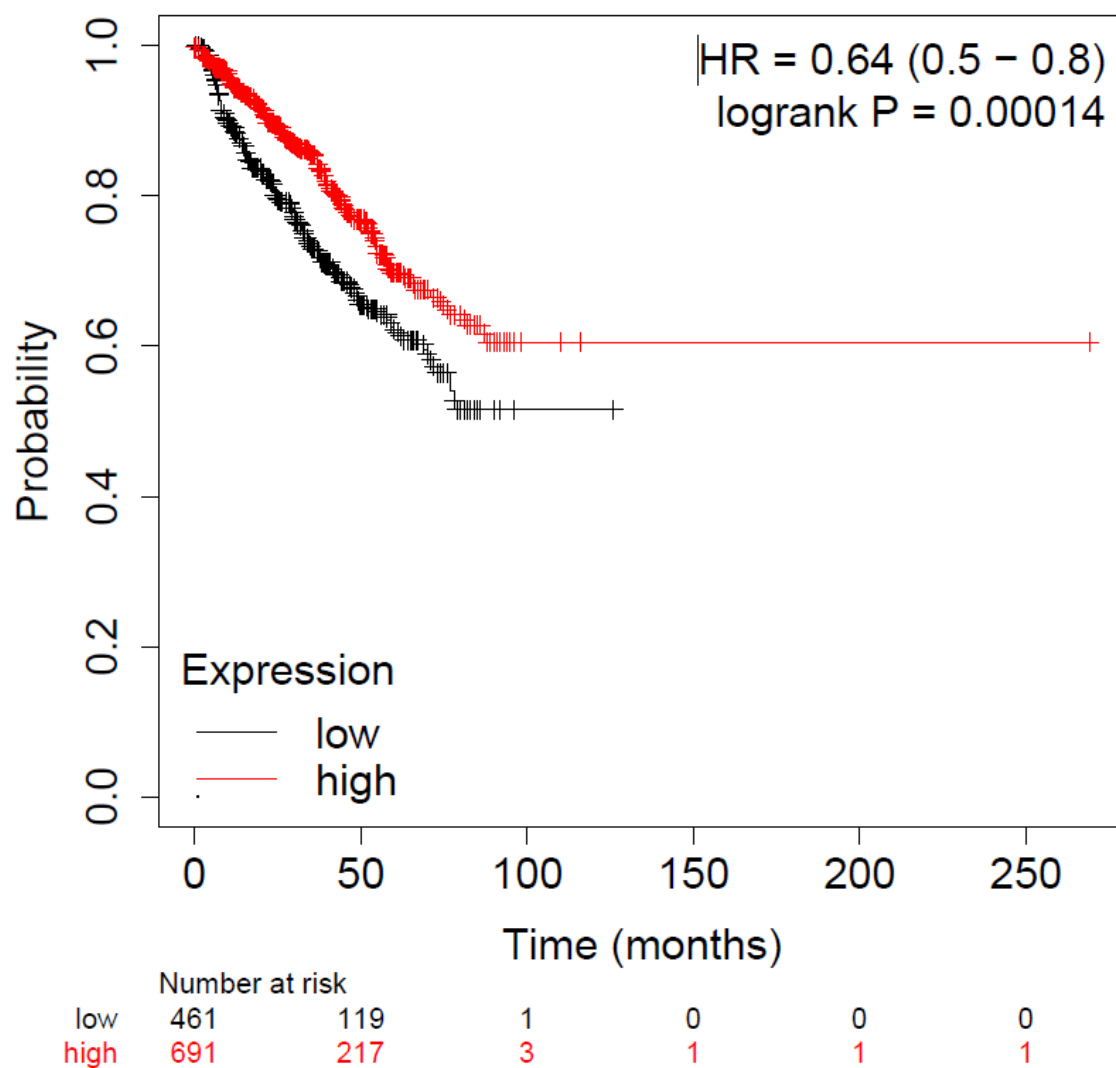
RPS4Y1 (201909_at)



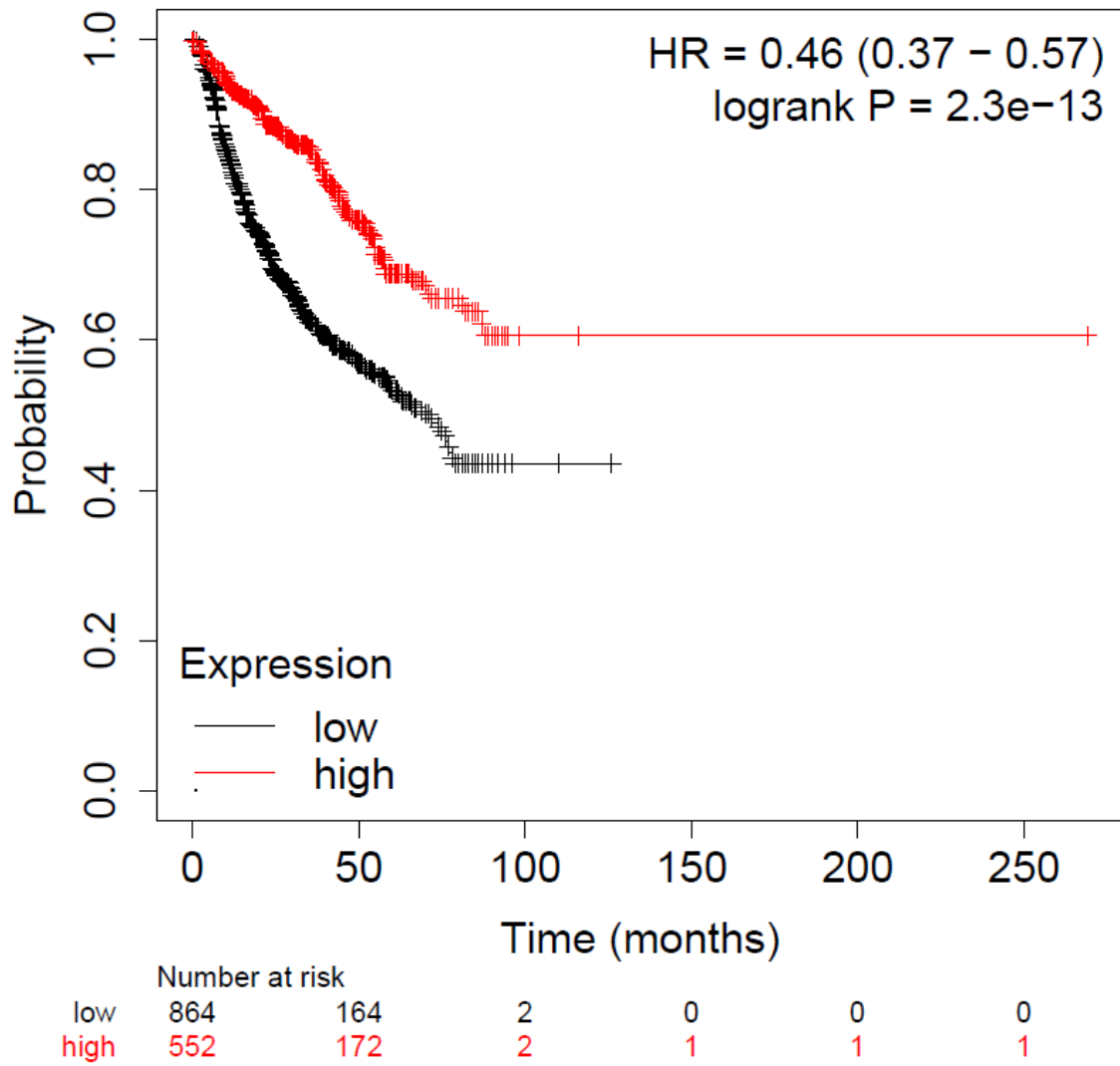
SMCY (206700_s_at)

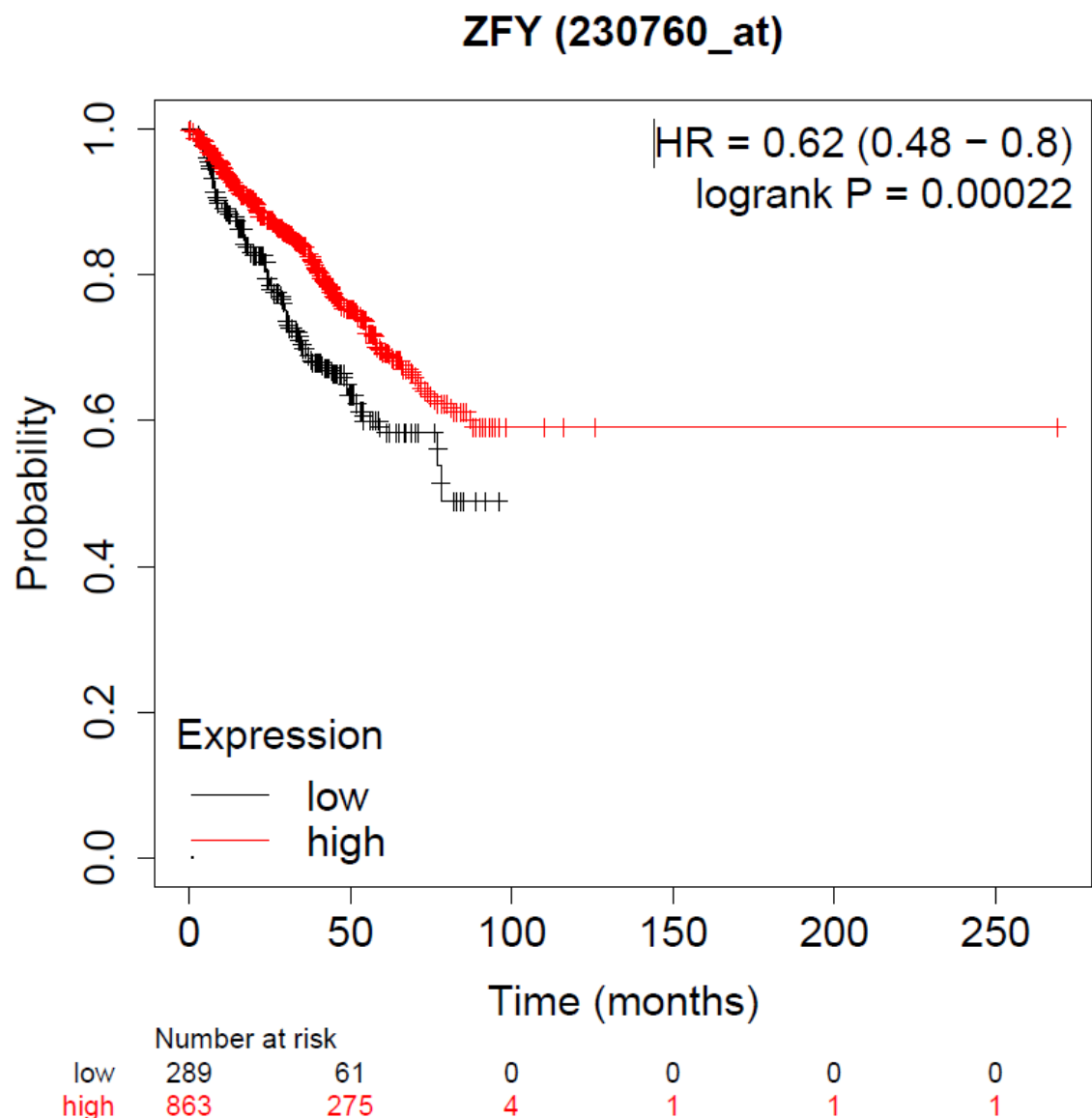


USP9Y (228492_at)



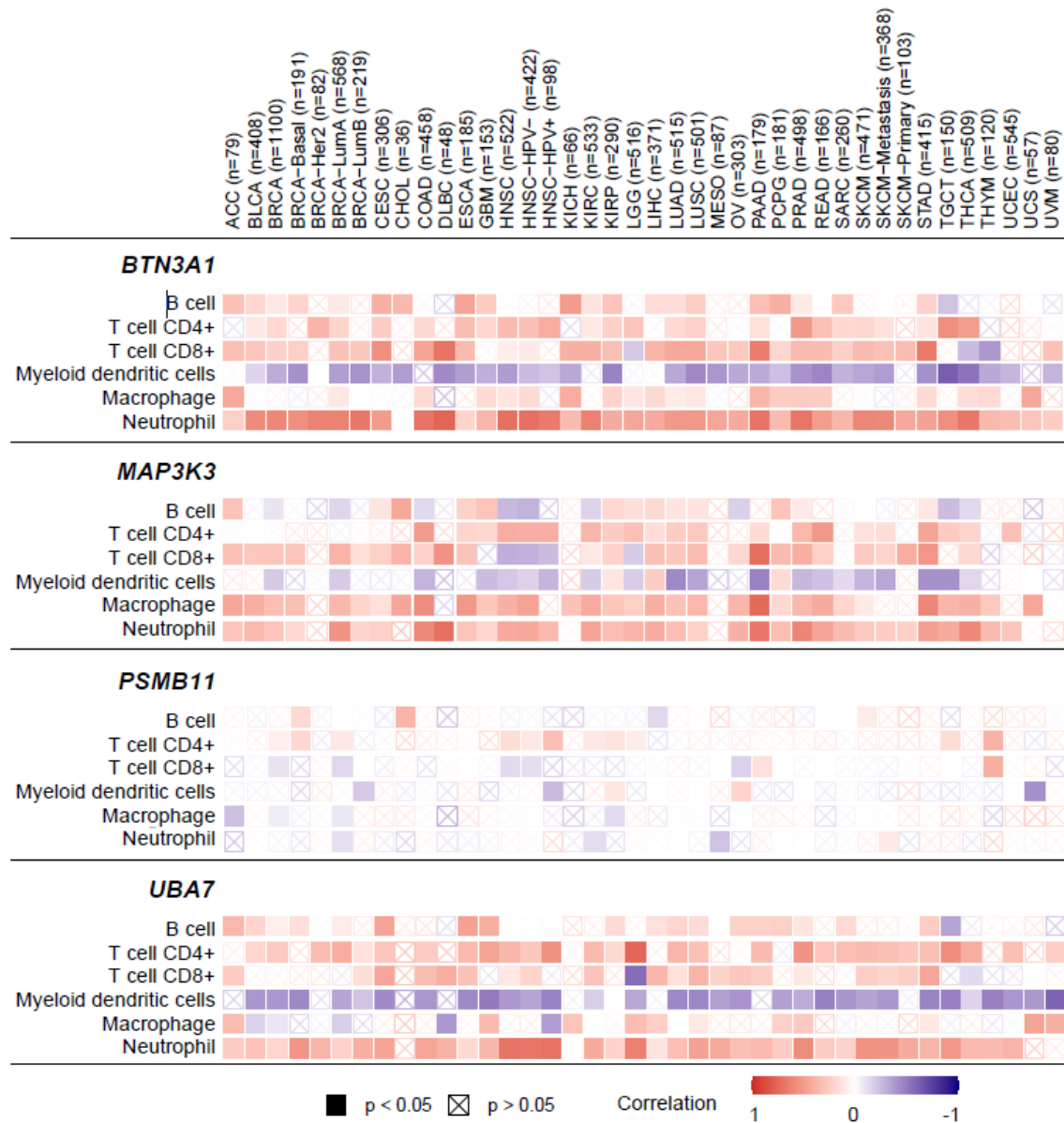
UTY (211149_at)





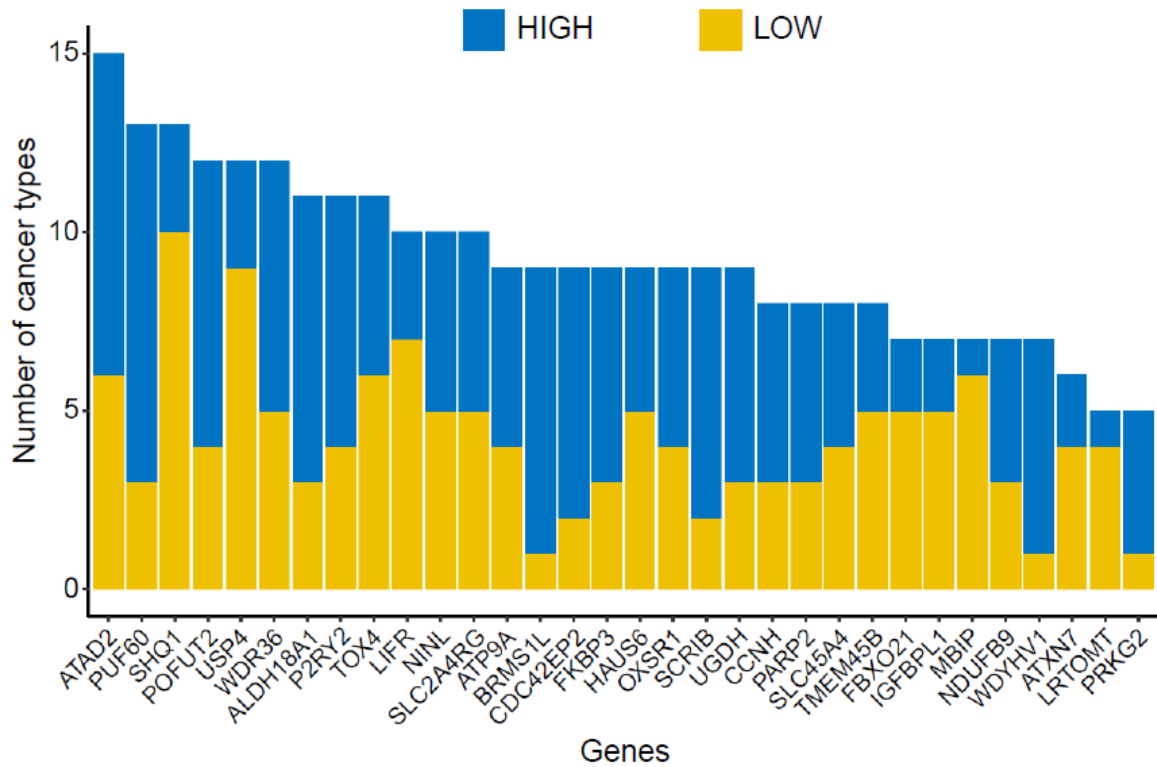
Supplementary Fig. 6. Analysis of overall survival with KM plotter depicting the clinical significance of 7 of 220 (*DDX3Y*, *EIF1AY*, *RPS4Y1*, *SMCY*, *USP9Y*, *UTY*, and *ZFY*; missing data for 14 genes) genes associated with immune response. Low expression of the seven genes was associated with significantly decreased overall survival in multiple myeloma patients.

Supplementary Fig. 7



Supplementary Fig. 7. Analyses of gene expression relationship between genes involved in bortezomib-sensitivity and immune cells in different cancer types using TIMER2.0. Genes *BTN3A1*, *MAP3K3*, and *UBA7* had positive expression relationships with the majority of immune infiltrates (B cells, CD4+ T cells, CD8+ T cells, macrophages, and neutrophils) in most cancer types.

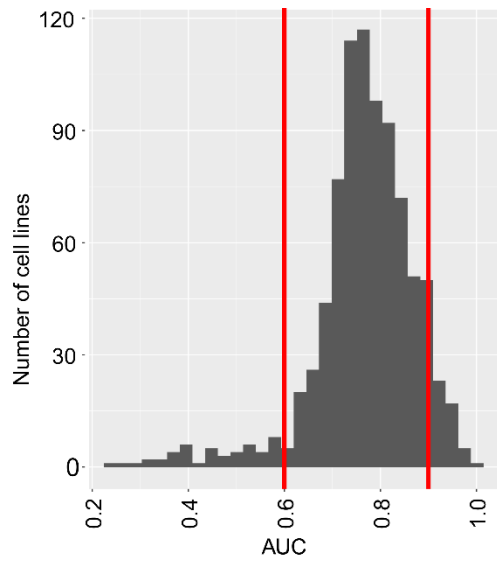
Supplementary Fig. 8



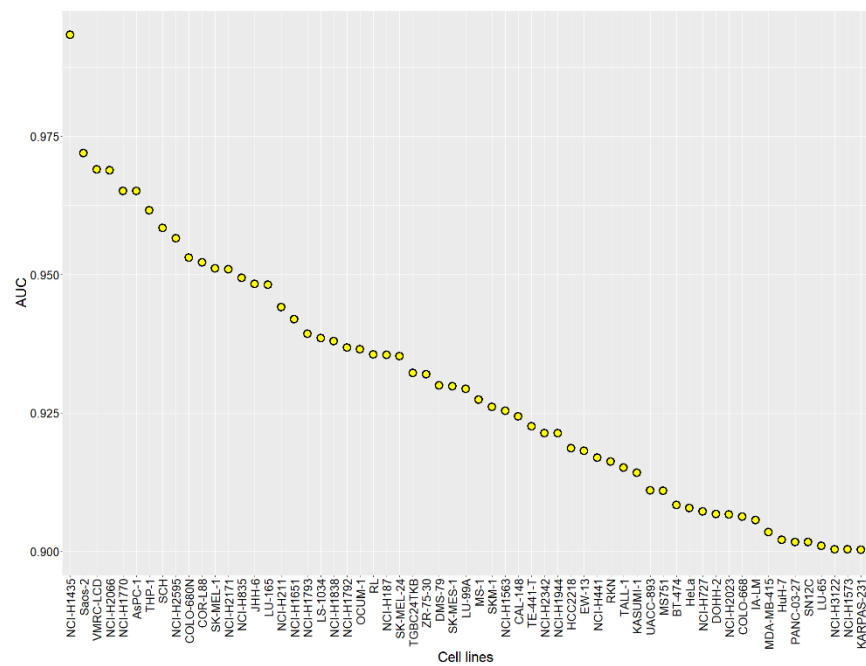
Supplementary Fig. 8. Bar chart depicting the clinical significance of 32 of 33 dysregulated genes on overall survival in 21 different cancer types (pan-cancer study; KM-plotter)

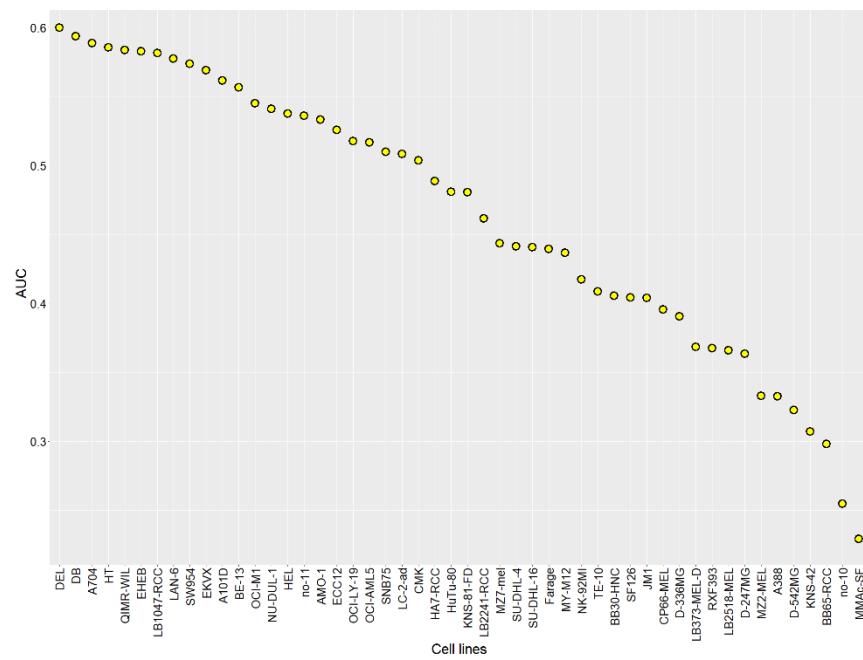
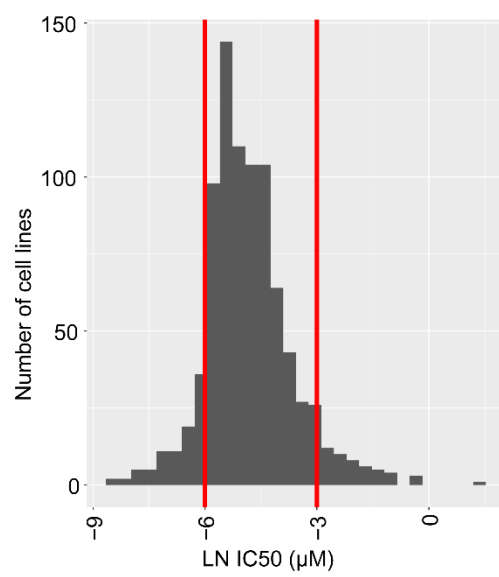
Supplementary Fig. 9

a

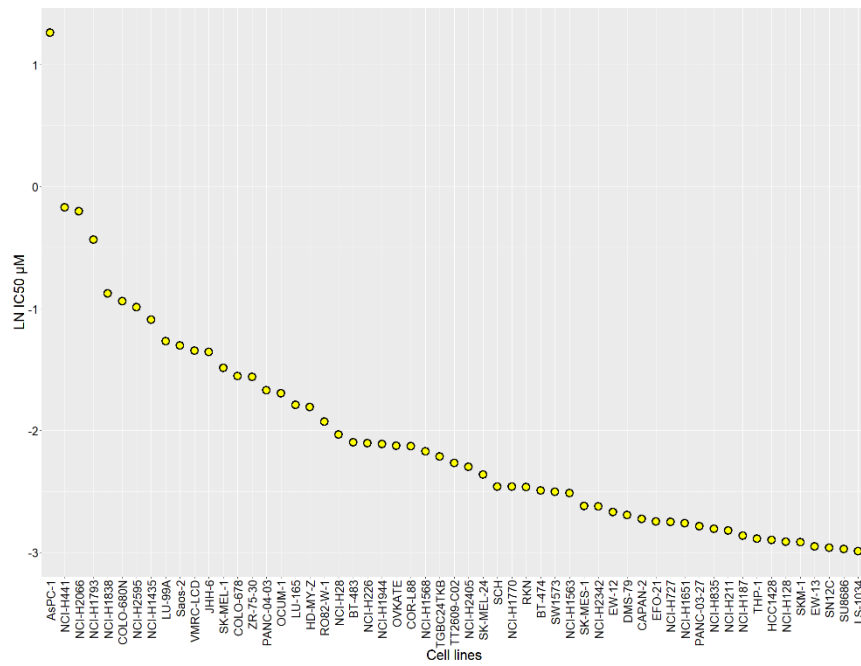


b

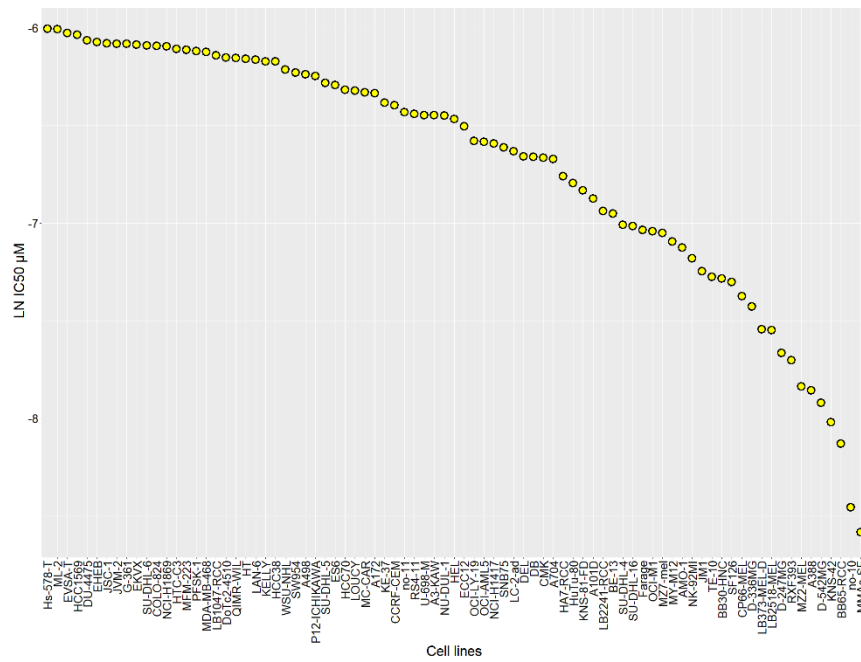


c**d**

e



f



Supplementary Fig. 9. Stratification of cancer cell lines according to bortezomib sensitivity using (a-c) area under the curve (AUC) and (d-f) natural logarithmic IC₅₀ (LNIC₅₀) values.