

Molecular and transcriptional changes in tumor endothelial cells after irradiation in mice

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Background

Radiotherapy (RT) does not only affect tumor cells but also the tumor microenvironment, including endothelial cells (ECs), which can be activated or damaged depending on the dose received. After activation with doses higher than 2 Gy, ECs switch into a pro-inflammatory state, which leads to increase the expression of chemokines, cytokines and adhesion molecules, therefore augmenting infiltration of immune cells into tumors and tumor shrinkage. In contrast, irradiation (IR) doses higher than 15 Gy have been reported to kill tumor ECs. However, the response of ECs on IR is poorly understood.

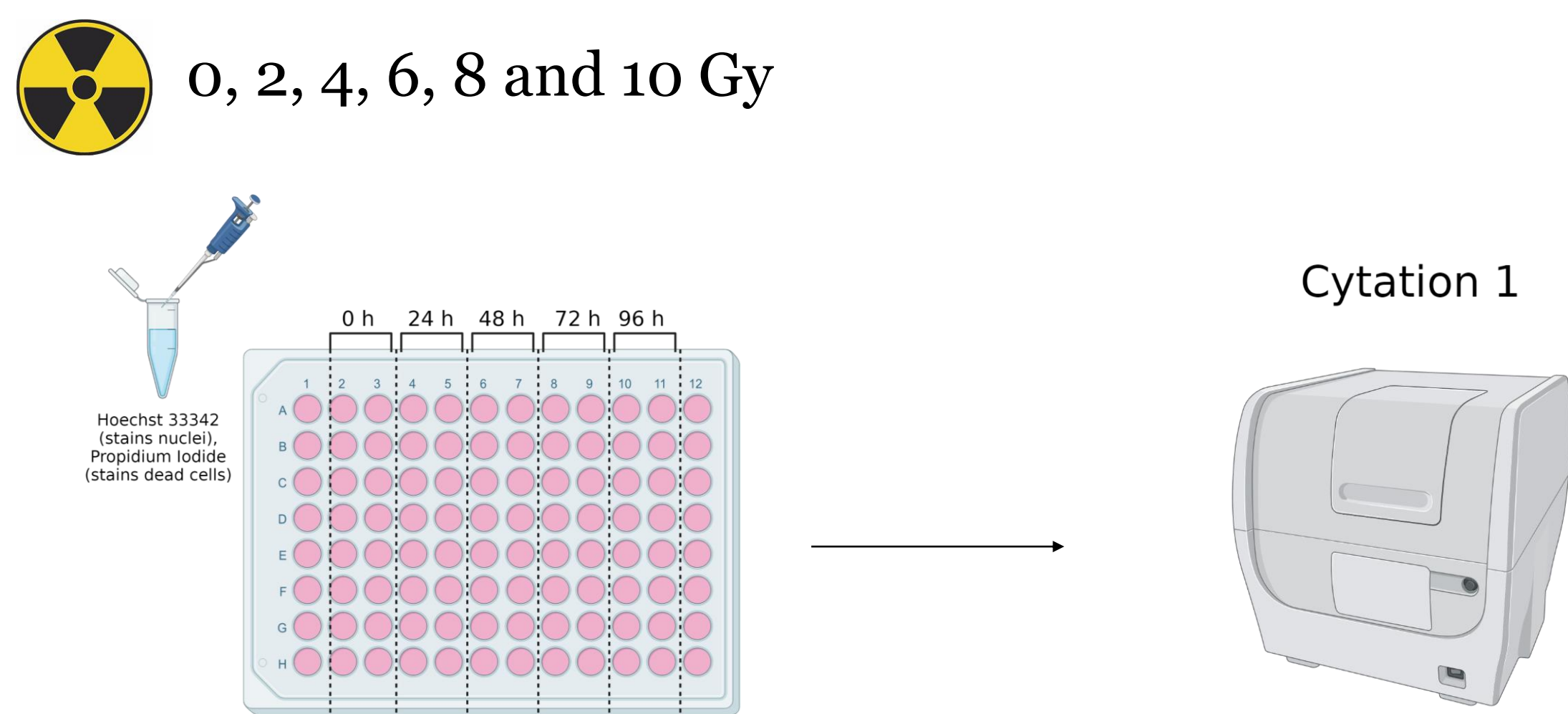
Conclusions

- 1) *In vitro* IR of ECs causes decrease in cell proliferation in a dose-dependent manner.
- 2) IR of murine tumors with a 15 Gy or 5 x 5 Gy leads to tumor reduction.
- 3) *In vivo* 15 Gy IR results in changes of ECs transcriptome.

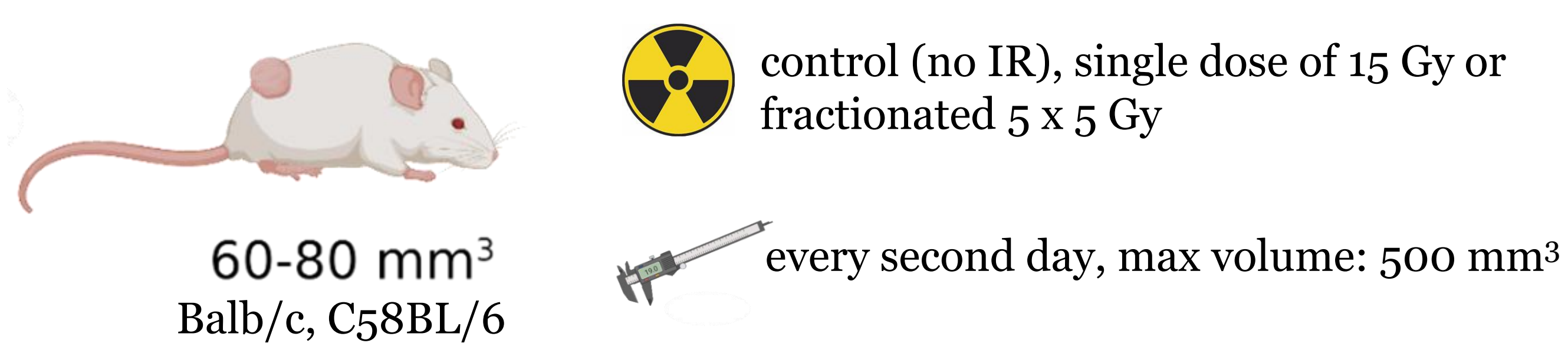
Results

Methods

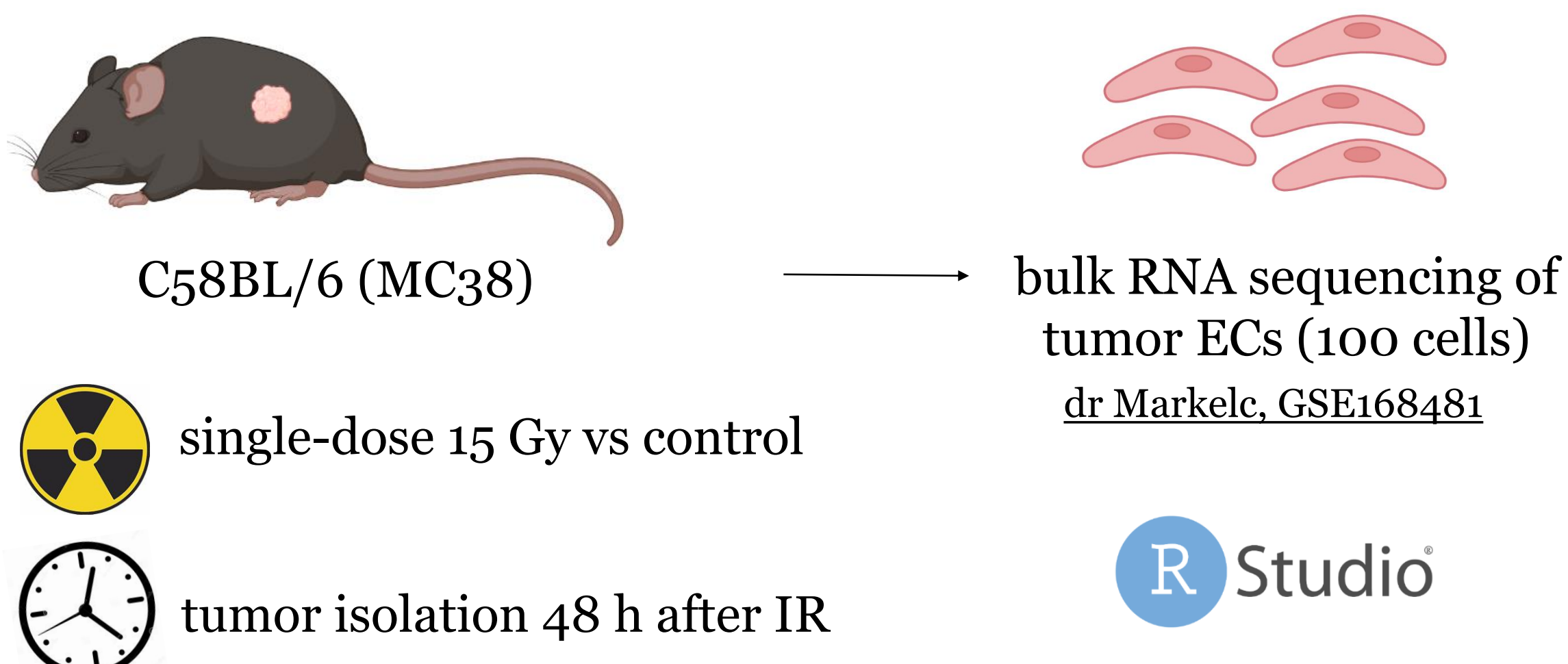
1) *In vitro* irradiation of ECs



2) Tumor IR



3) Tumor ECs transcriptomic analysis



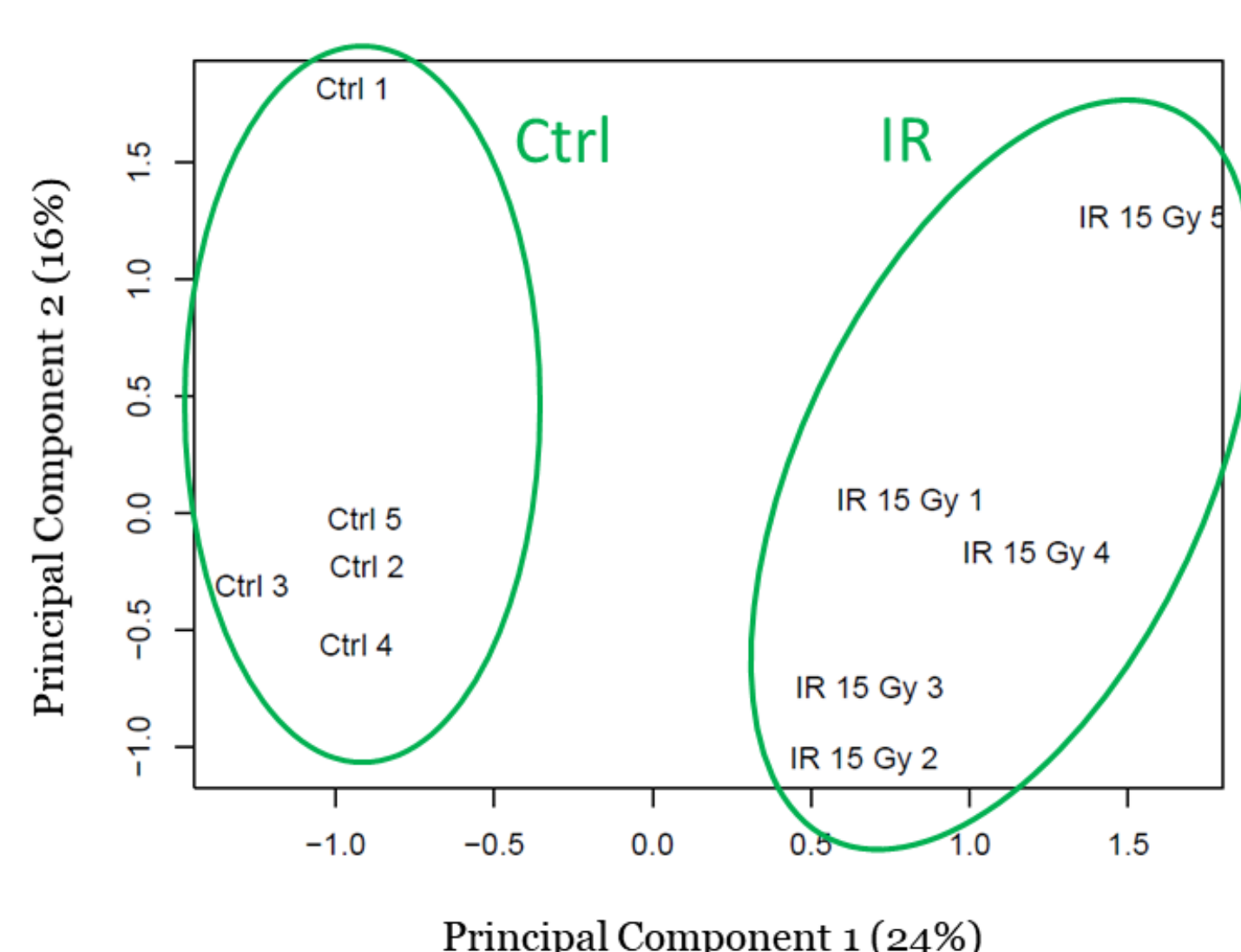
Aims

To determine:

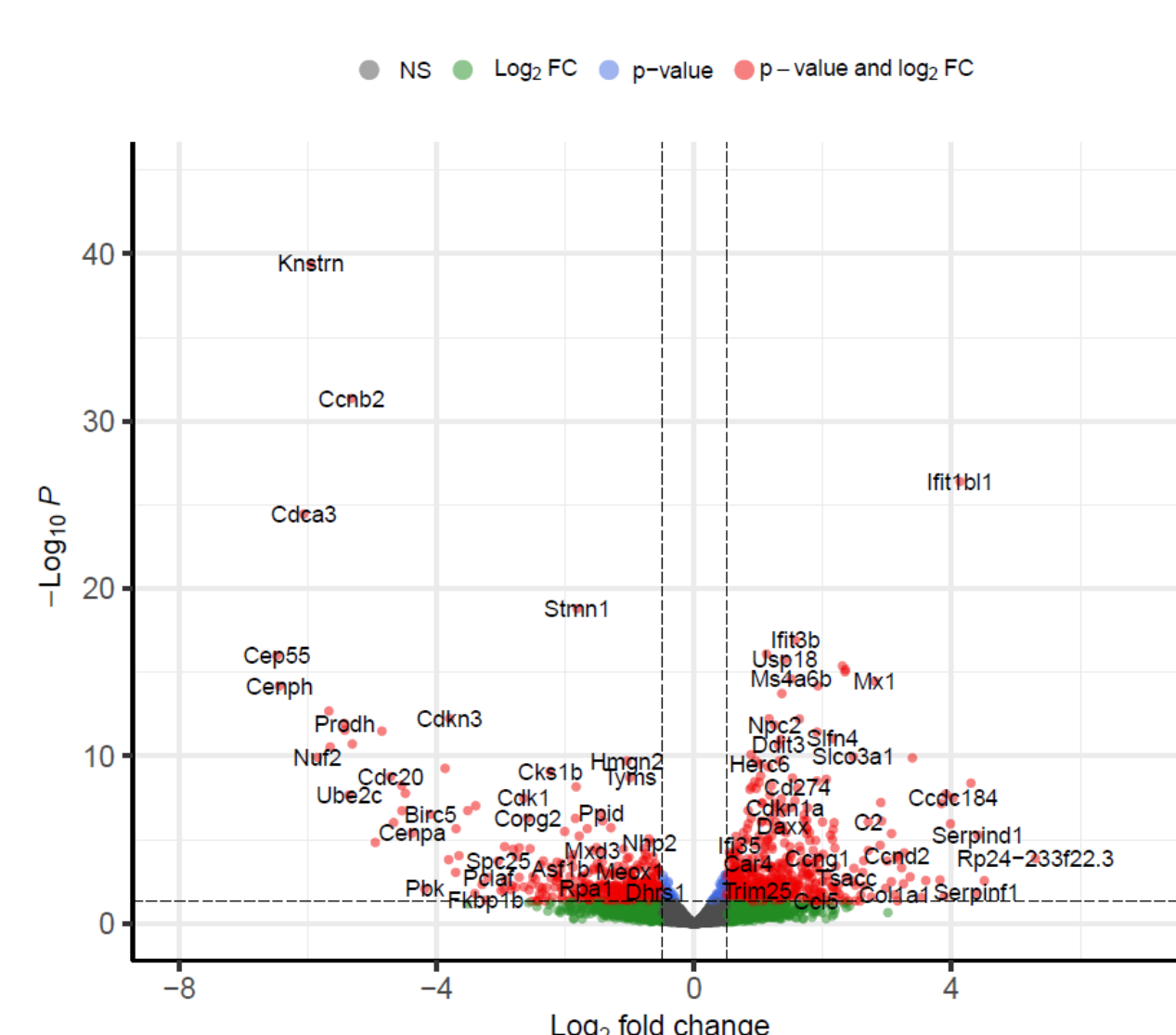
- 1) the effects of IR on ECs *in vitro*.
- 2) the response of tumors after IR *in vivo* level.
- 3) the IR-induced transcriptomic changes *in vivo*.

3) Tumor ECs transcriptomic analysis

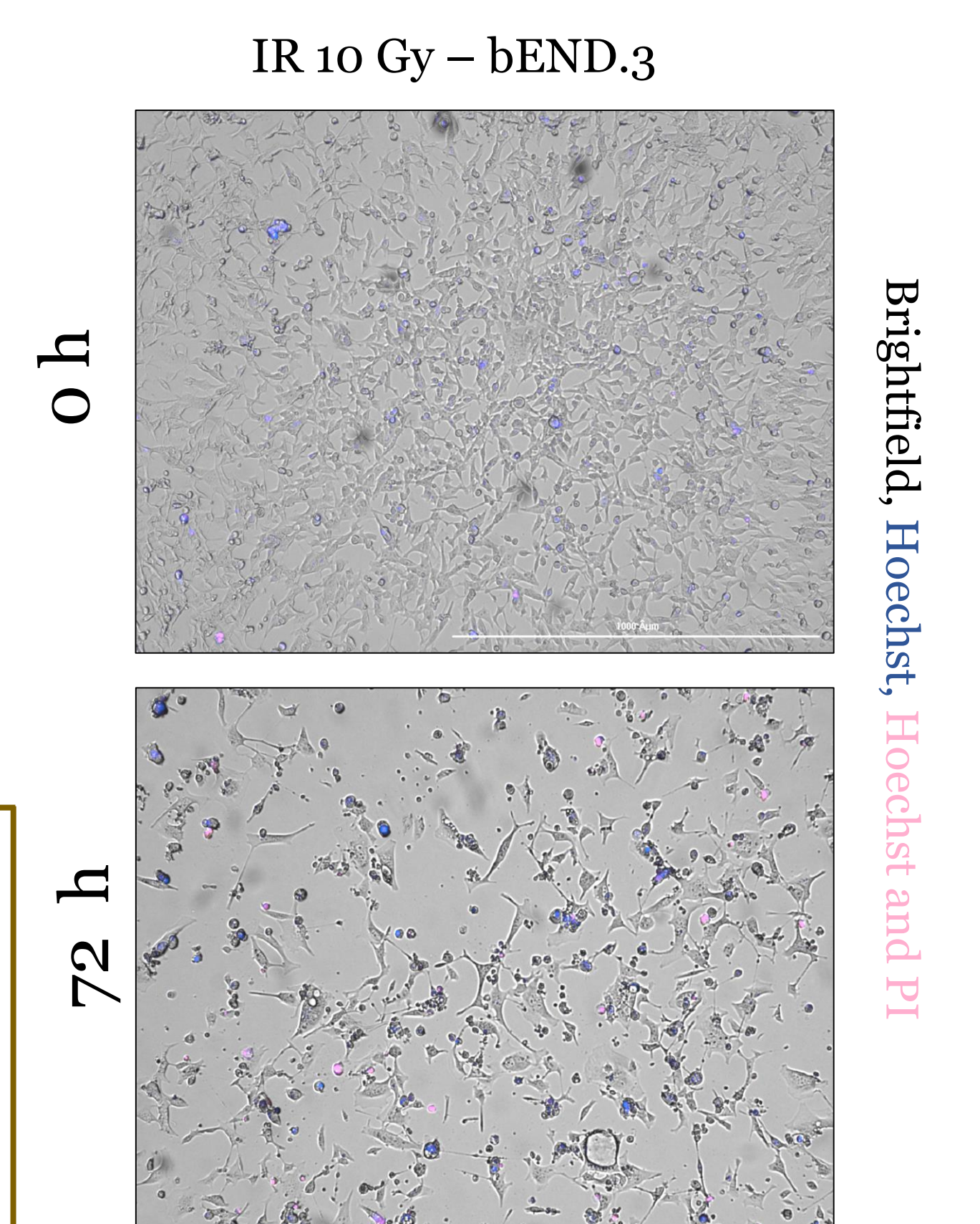
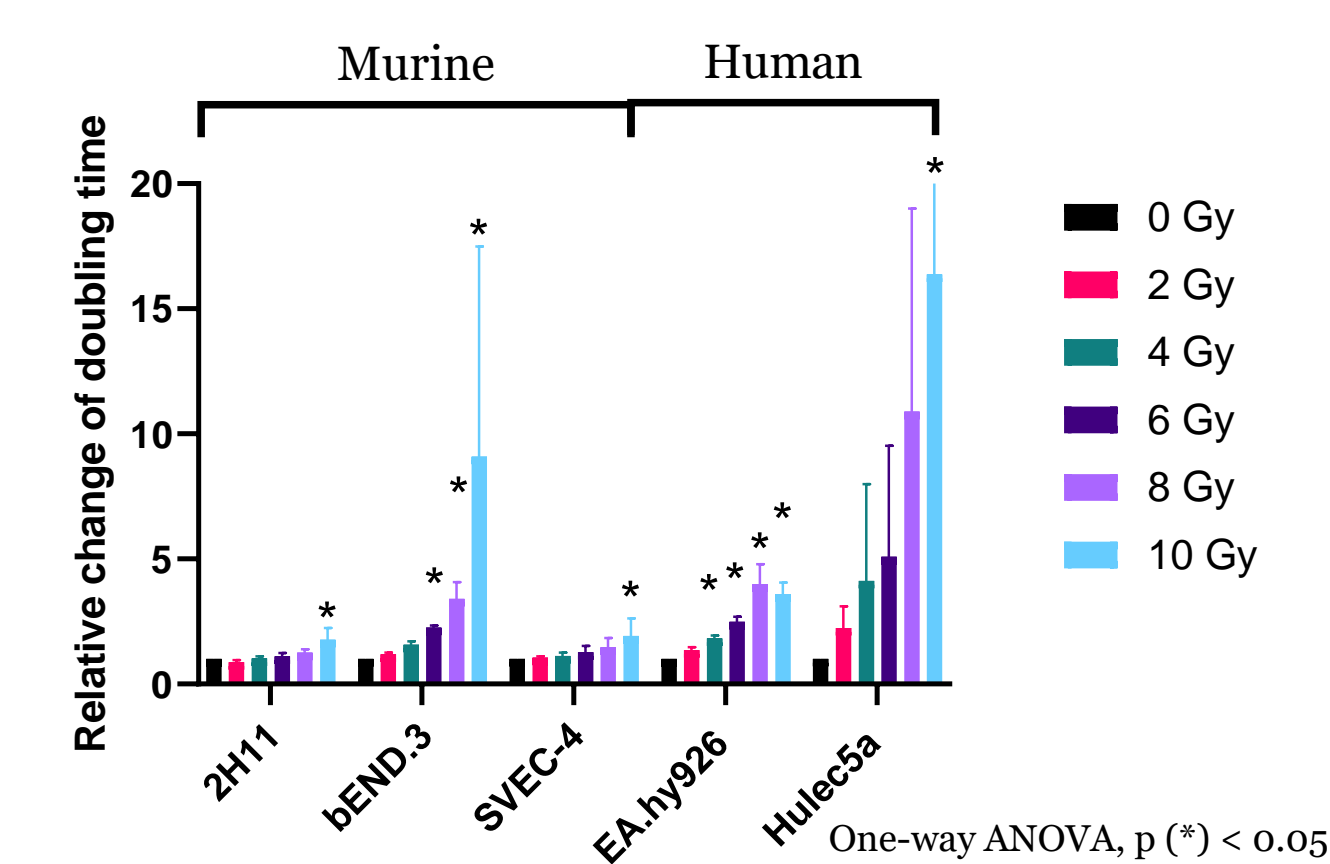
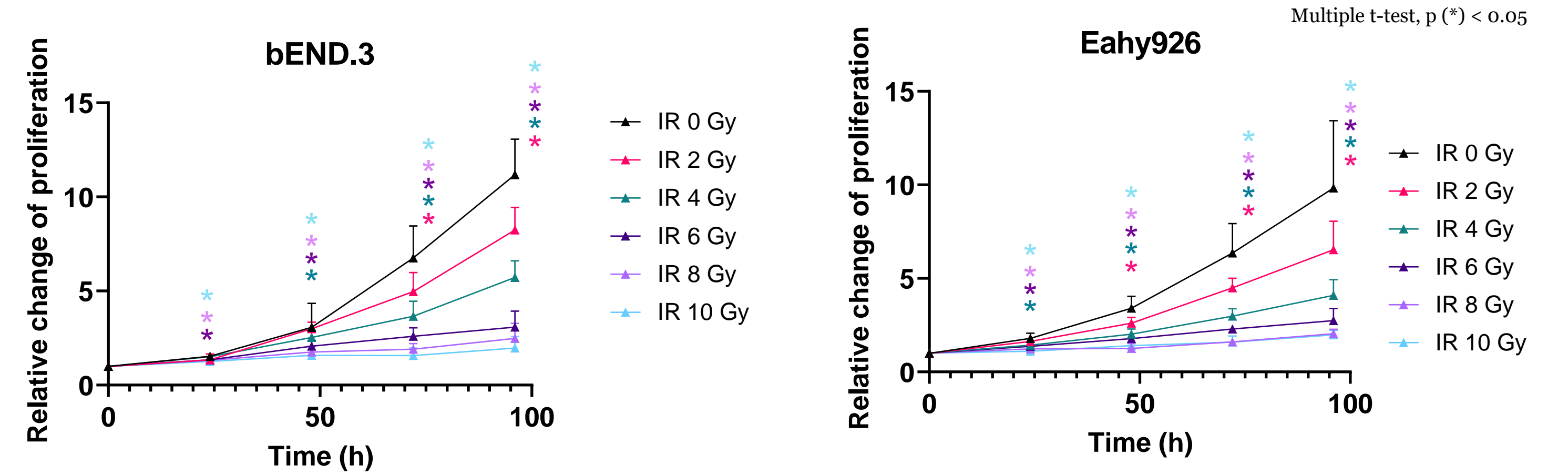
Principal component analysis (PCA)



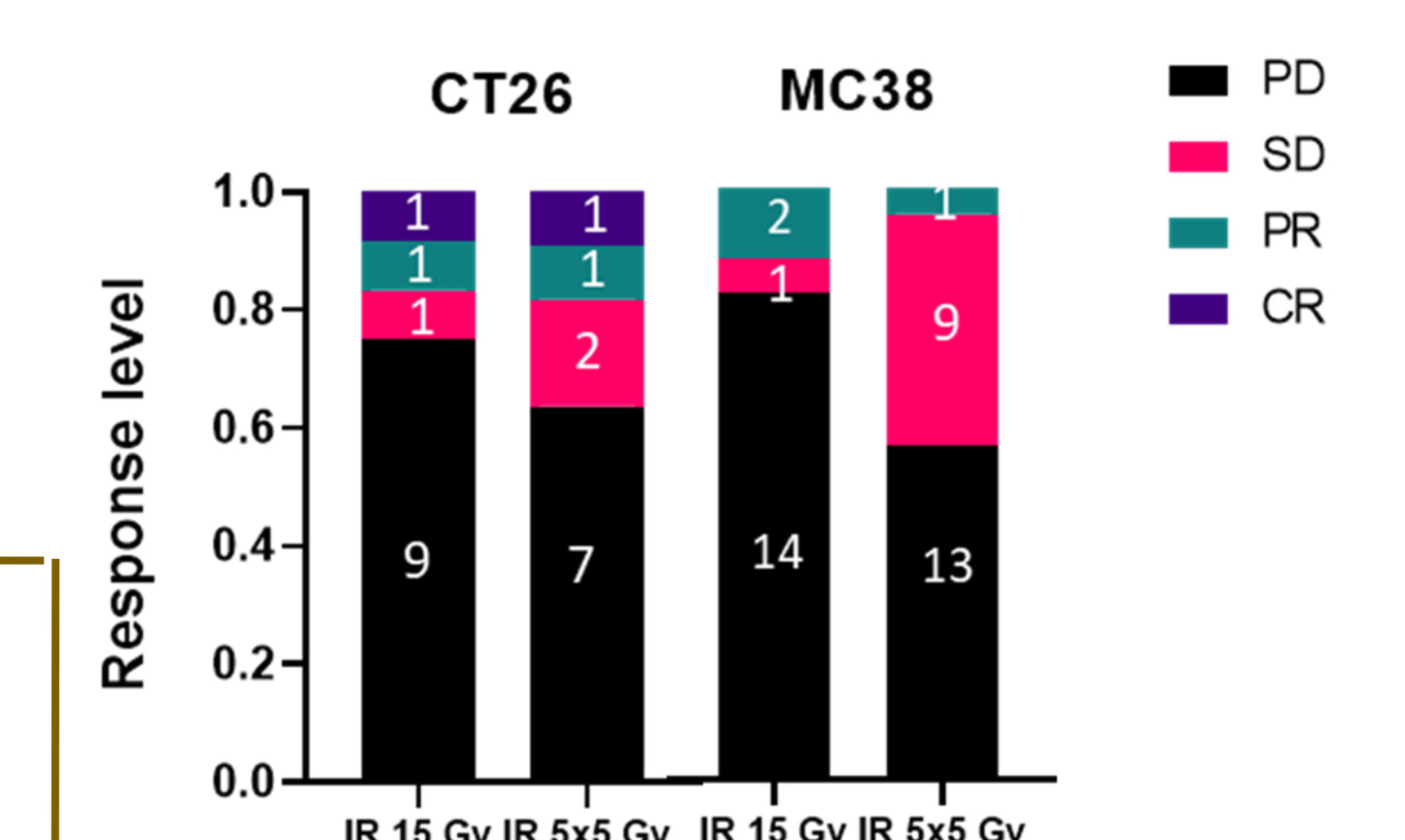
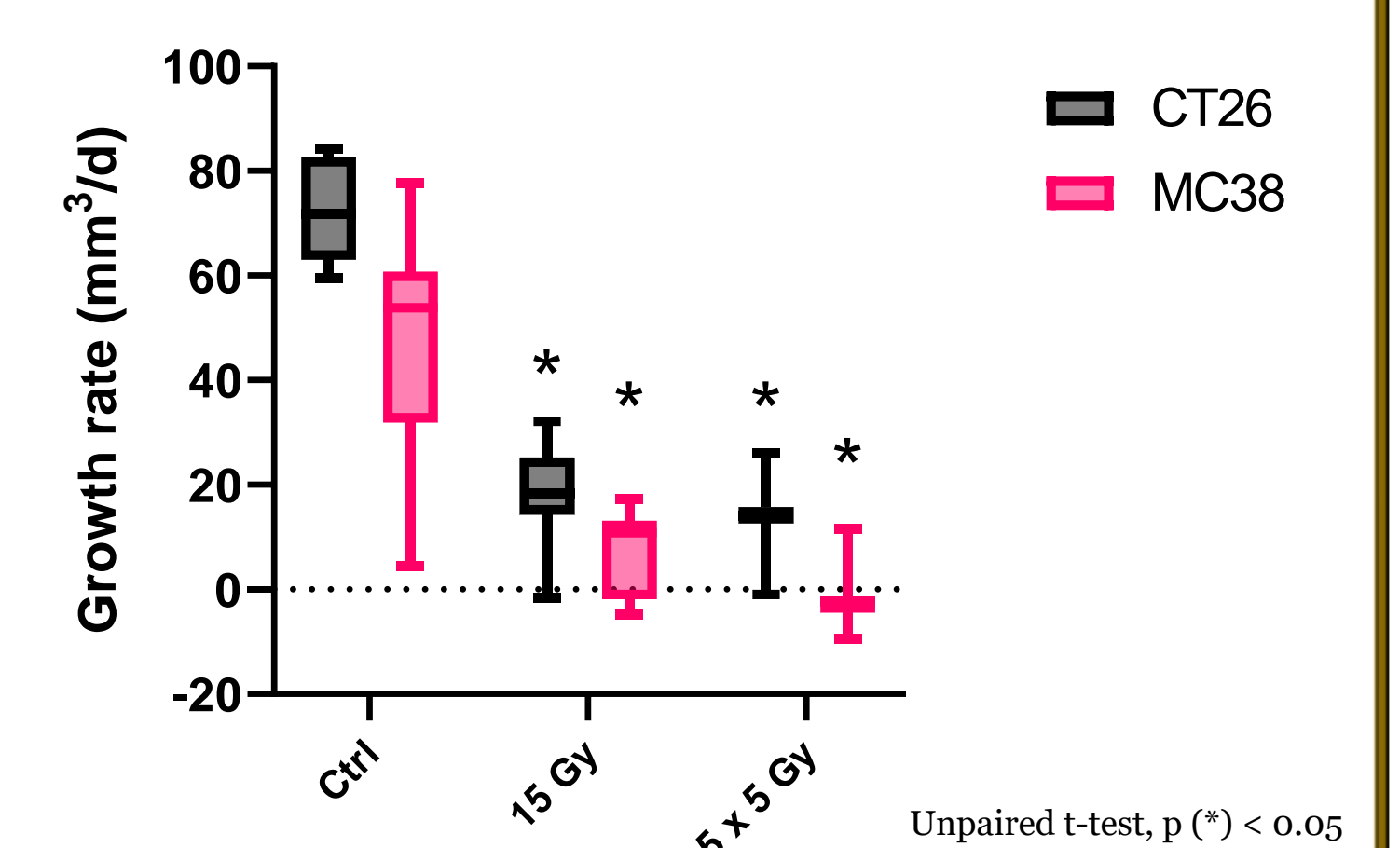
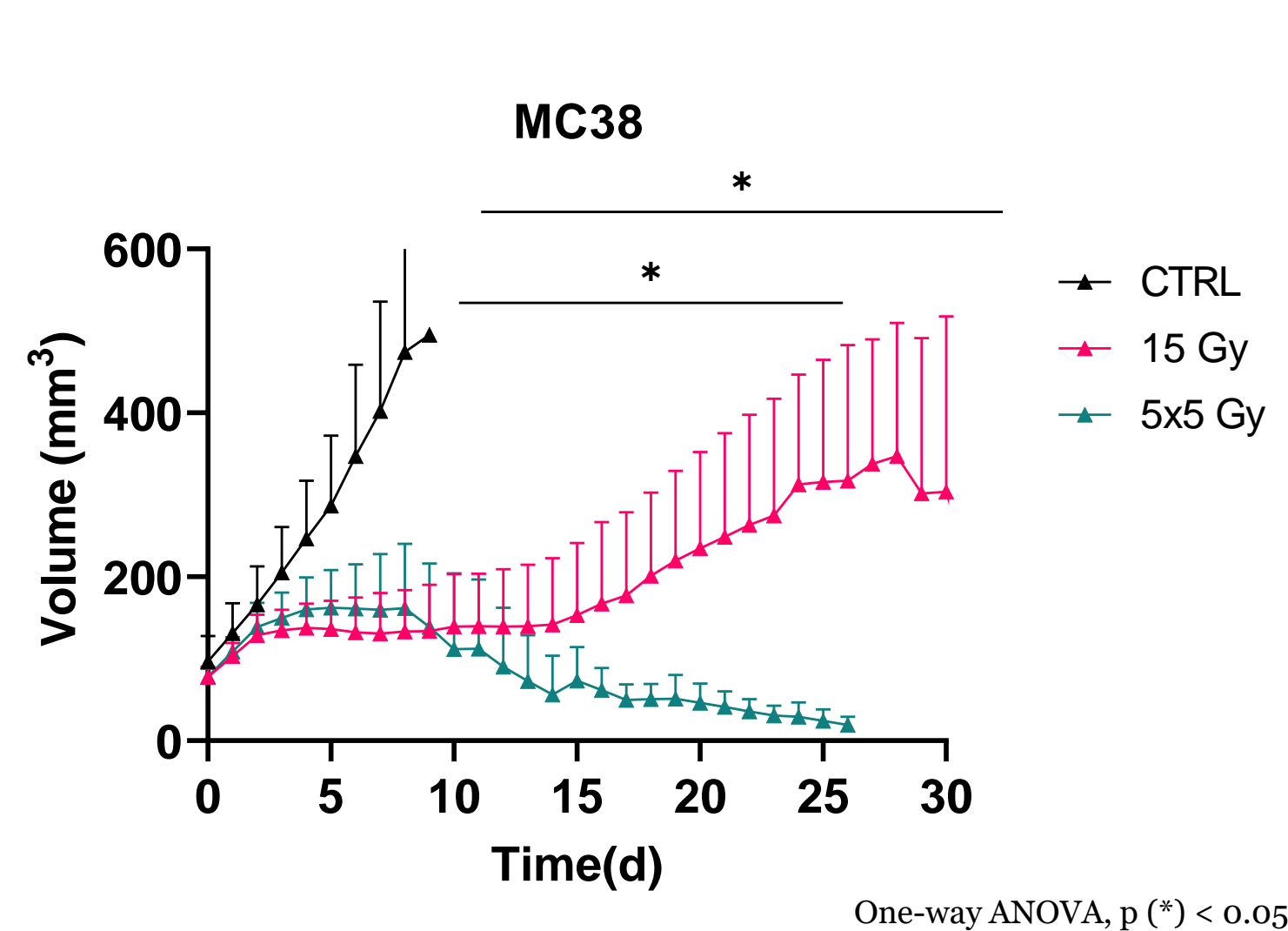
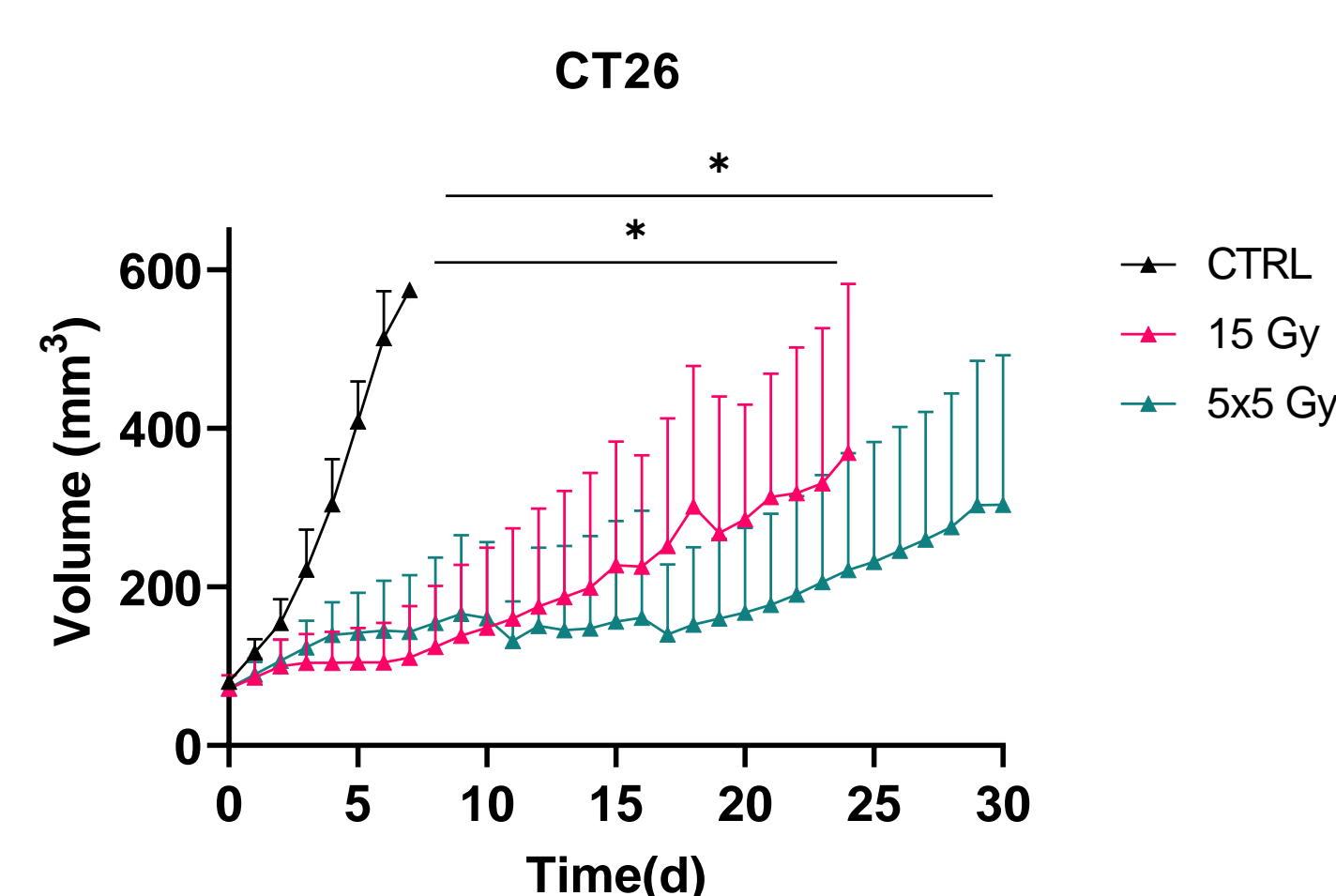
Differential gene expression analysis (DGE)



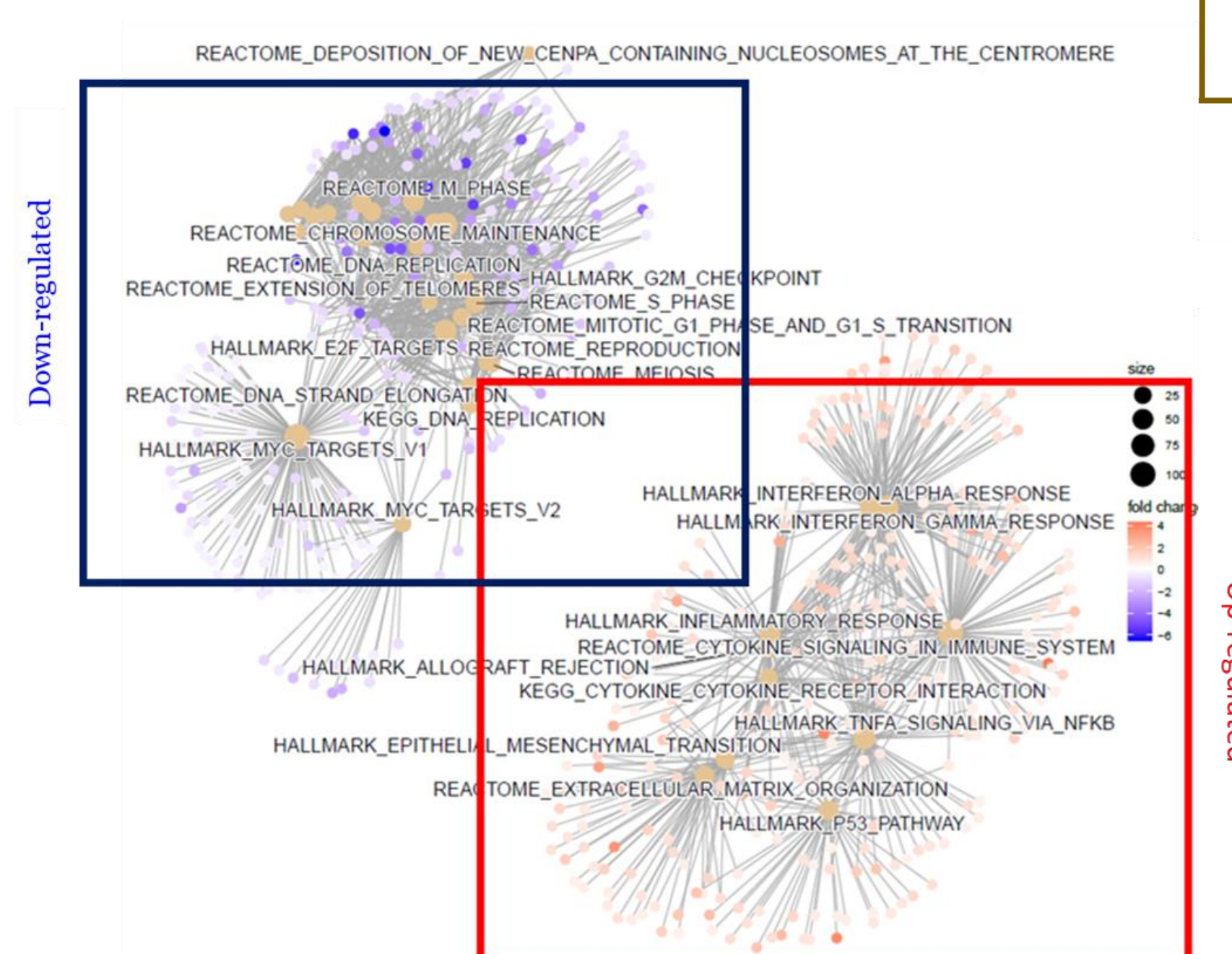
1) *In vitro* IR of ECs



2) Tumor IR



Gene set enrichment analysis (GSEA)



Total number of genes	7025
Up-regulated (P.value < 0.05)	533
Down-regulated (P.value < 0.05)	236
Total number of genes	7025

Positively enriched pathways (P.Adjusted < 0.05)	44
Negatively enriched pathways (P.Adjusted < 0.05)	101