Variability in radiotherapy outcomes across cancer types: A comparative study of glioblastoma multiforme and low-grade gliomas

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Overview of the data used in the study



Number of samples for each cancer type is shown, sorted by the total number of samples. Stacked bars are colored according to the sample category, including non-irradiated control samples, irradiated control samples, irradiated case samples, non-irradiated case samples, control samples without information about radiotherapy and case samples without information about radiotherapy.

## Survival analysis across 32 TCGA cancers



Survival curves for patients who received radiotherapy and those who didn't presented on a Kaplan-Meier plot for 32 TCGA cancers. The significance of survival results is plotted on a heatmap and colored red if radiotherapy increased survival outcomes and blue if the application of radiotherapy decreased survival outcomes. Non-significant results were colored white (p-value > 0.05). The log-rank test was used to calculate statistical significance.

## Survival analysis across 32 TCGA cancers: GBM and LGG



Survival analysis for IR treatment is presented on a Kaplan–Meier plot for TCGA-GBM (Glioblastoma, left figure) and TCGA-LGG (Brain Lower Grade Glioma, right figure) cancers. The log-rank test was used to calculate statistical significance.

## Signaling pathway enrichment analysis



Signaling pathways enriched with genes significantly down-regulated in the comparison of IR-treated and untreated GBM patients and simultaneously significantly up-regulated in the comparison of IR-treated and untreated LGG patients (left figure). Signaling pathways enriched with genes significantly up-regulated in the comparison of IR-treated and untreated GBM patients and simultaneously significantly down-regulated in the comparison of IR-treated and untreated LGG patients and simultaneously significantly down-regulated in the comparison of IR-treated and untreated LGG patients and simultaneously significantly down-regulated in the comparison of IR-treated and untreated LGG patients (right figure).

## Sub-stratification of GBM and LGG patients who were exposed to IR and signaling pathway enrichment analysis



Gain of function of KIT and loss of function of SPTBN5 genes compared with corresponding neutral CNV statuses of KIT and SPTBN5 genes respectively are associated with worse prognosis of IR-treated GBM patients. Survival analysis of IR-treated LGG patients revealed that there is only one gene whose gain of function significantly worsens survival outcome - EGFR. At the same time, loss of function of 30 genes, including CDKN2B, CDKN2A, MTAP, ELAVL2, IZUMO3, DMRTA1, IFNA8, IFNE, IFNA1, IFNA2, KLHL9, IFNA13, IFNA5, IFNA6, IFNW1, IFNA21, IFNA14, IFNA4, IFNA17, IFNA10, IFNA7, IFNA16, FOCAD, IFNB1, HACD4, MLLT3, NGEF, GBX2, ASB18, and AGAP, is associated with worse prognosis in IR-treated LGG patients.

Venn diagram describing the intersection of genes whose loss/gain status significantly stratifies IR-treated patients (left figure). Signaling pathways enriched with genes whose loss status in TCGA-LGG IR-treated patients is associated with worse prognosis (right figure).

Mutation profile of low-grade glioma cancer tissues in patients receiving radiotherapy



The top 15 genes with the highest number of mutations across radiotherapy-received LGG patients are plotted on a heatmap. Among the top 15 genes, IDH1 and TP53 stand out due to their well-known roles in glioma biology. ATRX was found to be the gene with the highest number of disruptive protein-coding mutations. EGFR was also observed in the list of the top 15 most mutated genes across IR-treated LGG patients.