

### **TCGA Dataset Analysis**

Bioinformatic analyses were done in R software v. 4.2.1. (R Core Team, 2020). Data from The Cancer Genome Atlas Liver Hepatocellular Carcinoma project (TCGA-LIHC) cohort comprising 374 HCC and 50 non-tumor liver samples were retrieved through FirebrowseR (Deng et al., 2017). Tumoral samples were divided based on miR-22 expression levels into high and low expressing groups. Differential expression analysis was performed using the DeSeq2 package (Love et al., 2014) with the low expressing group set as a reference. The Benjamini-Hochberg method was used to adjust the p-value for multiple comparisons. Gene set enrichment analysis (GSEA) was done to further explore the roles of the resulting deregulated genes using the fgsea R package (Korotkevich et al., 2021), run with a list of gene sets compiled from the Human Molecular Signatures Databases (MSigDB) Collections: hallmark gene sets, Gene Ontology, and KEGG (Subramanian et al., 2005; Mootha et al., 2003). Genes of interest were plotted using boxplots. Survival outcomes were obtained from TCGA-CCR (Liu et al., 2019).

## References

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