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Exploring L-asparaginase treatment response in an Acute Lymphoblastic Leukemia cell model: bioinformatics analysis of single-cell transcriptomics data and experimental validation

Acute Lymphoblastic Leukemia (ALL) is commonly treated with L-Asparaginase (L-ASNase), a chemotherapy agent that exploits metabolic vulnerability in leukemic cells by depleting asparagine/glutamine, aminoacids required for their proliferation and survival. Single-cell-RNA sequencing (scRNAseq) is a high-throughput technique providing unprecedented insights into treatment response. In this study, we applied bioinformatics analysis to investigate the transcriptional response to L-ASNase in RS4;11 (ALL cell line model). ScRNAseq was performed at the Italian National Facility Human-Technopole. RS4;11 cells (ATCC) were cultured in suspension and treated for 72h with L-ASNase (0.001U/ml).
Beside canonical genes involved in L-ASNase response (AKT1, E2F1, MYBL2, CCNE1, CDC6, FOXM1), we identified a strong transcriptional signature of ferroptosis. To validate these findings, western-blot and flow-cytometry experiments are currently being conducted, assessing cell-cycle progression (Ki67, CyB1, p21), cell viability (AnnexinV, 7-AAD), and reactive-oxygen-species accumulation. This study has a promising translational potential, identifying new possible vulnerabilities to be exploited to optimize L-ASNase treatments.

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