Synergy of Treatment: Therapeutic Vulnerabilities in Small Cell Lung Cancer

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Small cell lung cancer (SCLC) is the most aggressive form of cancer with a 5-year survival rate of <7%. SCLC's high mortality rate is attributed to early metastasis and treatment resistance. After decades without marked improvement in prognosis, immunotherapy has emerged as a potential milestone in the standard of care, yet clinical trials have had limited success due to low response rates and relapse and need further elucidation. The aim of the present study was to identify target genes that promote tumor survival and treatment resistance following targeted talazoparib and prexasertib treatment, which may be exploited in combination with immunotherapeutic treatment modalities. Ten single-cell RNA-seq datasets were obtained from the NCBI GEO study series, GSE138474. The samples were characterized as talazoparib treated resistant (n = 9,914), prexasertib treated resistant (n = 7,617), or untreated (n = 16,181) to complete a Gene Set Enrichment Analysis (GSEA). GSEA demonstrated that 2 genes, AKR1C2 and PRDX1 were upregulated post talazoparib and prexasertib treatment. A bulk RNA-seq dataset containing 80 individuals was analyzed and showed non-significant associations between AKR1C2 and PRDX1 expression on mutational burden, PD-L1 expression, and immune cell proportions. CIBERSORT analysis revealed that increased M2 macrophage proportions ($p > 0.05$) correlated with higher PRDX1 expression, further indicating that the synergistic treatment of talazoparib or prexasertib in synergy with immunotherapy may decrease SCLC prognosis. Future studies are needed to identify subtypes that influence synergistic treatment response and investigate the role of intratumoral heterogeneity in differential response, which may be applied to personalized medicine.