

Predicting Patient Response to CAR-T Cell Therapy Using Computational Methods for Biomarker Identification

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B-cell acute lymphoblastic leukemia (B-ALL), the most common pediatric cancer, is characterized by the proliferation of immature, leukemic B-lymphocytes in the bone marrow. CAR-T cell therapy, a targeted T-cell immunotherapy, provides an alternative to conventional cancer treatments. However, the risk of life-threatening or fatal response to CAR-T cell therapy warrants a method to effectively predict patient response. This study seeks to identify candidate genetic biomarkers associated with patient responses of complete remission (> 54 months) and relapse through the analysis of CAR-T cell infusion product transcriptomes of B-ALL patients. A differential gene expression analysis pipeline with FDR corrections on the Galaxy Project was used to determine the statistical significance of genes with differentiation between two groups of CAR-T cell products (unstimulated and stimulated by human CD19-expressing antigen presenting cells), and pathway enrichment analysis was performed to determine significantly enriched biological pathways in B-ALL patients who experienced relapse. The study revealed 65 highly differentially expressed genes (DEGs) with adjusted p-values < 0.05, of which 29 were candidate biomarkers for complete remission and 36 were candidate biomarkers for relapse. Pathway enrichment analysis validated results for DEGs associated with relapse. The identified genes are candidate biomarkers that will provide a tool to predict and monitor B-ALL patient response to CAR-T cell therapy, providing valuable insight into cancer progression and treatment methods necessary to prevent life-threatening side effects. This removes a significant obstacle in patient treatment using CAR-T cell therapy, allowing it to become a safer alternative to conventional cancer treatment.