In a study using single-cell V(D)J sequencing to extract T cells and then perform single-cell sequencing to capture the diversity of TCRs, T cell TCRs from 12 COVID-19 patients were analyzed and compared with 6 healthy controls and other viral infection samples. Particular attention was paid to the analysis of V and J gene combinations, which play a key role in TCR diversity [1]. A mathematical framework was proposed in one study to explain how TCRs bind to pMHC. This finding is crucial for understanding how T cells recognize and efficiently bind to pMHC complexes through TCRs [2]. With the help of a new tool "SPAN-TCR," a TCR library for multiple known antigens was analyzed, comparing and analyzing the amino acid composition of the CDR3 region of TCRs and revealing similarities and differences in amino acid usage and structure between different TCRs through entropy analysis [3]. A new computational method, SETE, uses the effects of adjacent amino acids in the CDR3β sequence, focusing on the influence of neighboring amino acids, and employs gradient boosting decision-making and feature learning to predict the binding of TCRs to epitopes [4]. The issue of TCR specificity in structural and biophysical studies explored the interactions between TCRs, MHC, and peptides [5]. A new deep learning model, EPIC-TRACE, uses the sequences of CDR3, V, and J gene regions of TCR's alpha and beta chains, along with the sequences of epitopes and MHC, to predict TCR binding to unseen epitopes [6]. The deep learning model TCR-ESM uses large-scale protein language models (ESM) to predict the binding of TCRs to peptides and MHC [7]. In an experiment comparing TCRs from COVID-19 patients with those from healthy controls using V(D)J sequencing technology, TCRs from PBMCs and BALF were analyzed. By comparing different TCR characteristics such as CDR3 amino acid length distribution, specific VJ gene segments, and their pairing, the dynamic changes in immune response were reflected [8]. A study employing deep learning and transfer learning techniques to predict the binding specificity between TCRs and epitopes used a pre-trained encoder to convert TCR and epitope sequences into numerical vectors, which were then input into a fully connected neural network. The effects of four main strategies: reference TCRs, random TCRs, random epitopes, and uniform epitopes, were systematically compared [9]. A new mathematical framework, "GIANA," can efficiently cluster TCR sequences and classify multi-disease immune libraries. It transforms the TCR sequence alignment and clustering problem into a nearest neighbor search in high-dimensional Euclidean space, significantly enhancing computational efficiency to handle up to millions of sequences [10]. By comparing the similarity between TCR sequences, clustering of TCRs was performed using sequence alignment and scoring matrices [11]. A study using "metaclonotypes" for TCR analysis identified them using tcrdist3, thereby enhancing the use of TCRs as biomarkers [12].

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