

A microfluidics-free approach for simultaneously profiling the whole transcriptome and TCR repertoire of 1 million cells in a single experiment

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T cells recognize and eliminate a wide variety of immunologic threats while maintaining self-tolerance. This pathogen recognition and clearance activity is managed through a process called V(D)J recombination, during which a T cell obtains a unique set of V, D and J gene segments for all the chains (α and β or γ and δ) that make up its T cell receptor (TCR). Each recombined TCR detects a specific disease-associated antigen peptide, which triggers the appropriate adaptive immune response.

The diversity of possible TCRs in the immune repertoire is enormous, yet the low throughput of existing tools have limited the ability to capture this complexity at high resolution. To overcome these limitations, we have extended Parse Biosciences' combinatorial barcoding technology (originally based on Split Pool Ligation-based Transcriptome sequencing or SPLiT-seq) to simultaneously characterize the TCRs alongside the full transcriptomes of up to 1 million T cells.

Using this approach, we fixed and prepared 1 million isolated Pan T cells from the PBMCs of 8 donors. Evercode TCR enabled detection of at least one TCR chain in 88% of all T cells together with their corresponding transcriptome. We found that clonotype detections were highly accurate as a cell cluster with known semi-invariant TCR alpha chains matched the TCR assignments in our analysis. We identified nearly half a million unique beta chain clonotypes across multiple samples with the Evercode TCR kit resulting in the most comprehensive immune repertoire detection from a single experiment to date.