DNA-barcoded pMHC Tetramer for Systems Immunology Based Immune Engineering

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Identification of correlated antigens recognized by T cell and its T cell receptor (TCR) sequences at single cell level is extremely useful to the understanding and treating immune-related diseases, but challenging. Here we describe a new technology, TetTCR-Seq for Tetramer associated TCR sequencing, that is capable of de novo generating a large amount of peptides and mapping antigen recognition with single cell TCR sequences by DNA barcoded tetramers. Using a published set of cancer neo-antigen sequences, we showed that these peptides and their wildtype counterparts can be quickly generated. Resulted tetramers can be used to clearly identify a population of neo-antigen only or wild type antigen only or double positive T cells. Simultaneous tetramer DNA barcode sequencing showed that many T cells are found to cross-reactive to both neo-antigen and its wild type counterpart, suggesting the necessity of strict screening for neo-antigen only TCR in adoptive cell transfer therapy.

In summary, TetTCR-seq enables one to quickly survey antigen repertoire again TCR repertoire at single cell level for a large number of peptides. It is a useful technology to screen for T cell cross-reactivity and select neo-antigen specific TCR for cancer immunotherapy.