Abstract

The immune system leverages the immense molecular diversity of the T cell receptor repertoire to distinguish between normal cells and cells altered by infection or cancer. This diversity can make determining exactly what is recognized during the course of a response extremely challenging. Furthermore, the mechanism by which the immune response balances specificity and the need to ensure coverage of all possible antigens has remained elusive. We combined protein engineering, combinatorial biology, structural biology, and next generation sequencing to develop a technique that allows us to unbiasedly and sensitively find peptide-MHC antigens for T cell receptors. Armed with this technique and a better understanding of T cell receptor cross-reactivity, we aim to find what peptides are recognized during the course of cancer, what antigens should be targeted in treatments, and how to determine why immunotherapy works and why it fails.

Recommended readings


Tuning up T-cell receptors. Rappazzo CG and Birnbaum ME. Nat Biotechnology 35 1145-1146 (2017).