Designer T cells by T cell receptor replacement.

Abstract:
T cell receptor (TCR) gene transfer is a convenient method to produce antigen-specific T cells for adoptive therapy. However, the expression of two TCR in T cells could impair their function or cause unwanted effects by mixed TCR heterodimers. With five different TCR and four different T cells, either mouse or human, we show that some TCR are strong—in terms of cell surface expression—and replace weak TCR on the cell surface, resulting in exchange of antigen specificity. Two strong TCR are co-expressed. A mouse TCR replaces human TCR on human T cells. Even though it is still poorly understood why some TCRalpha/beta combinations are preferentially expressed on T cells, our data suggest that, in the future, designer T cells with exclusive tumor reactivity can be generated by T cell engineering.