ABSTRACT

ENGINEERING T-CELL RECEPTORS

The use of model T cell receptors (TCRs) as scaffolds for *in vitro* engineering of novel specificities is provided. TCRs with de novo binding to a specific peptide-major histocompatibility complex (MHC) product can be isolated by: 1) mutagenizing a T cell receptor protein coding sequence to generate a variegated population of mutants (a library), 2) selection of the library of TCR mutants with the specific peptide-MHC, using a process of directed evolution and a "display" methodology (*e.g.,* yeast, phage, mammalian cell) and the peptide-MHC ligand. The process can be repeated to identify TCR variants with improved affinity for the selecting peptide-MHC ligand.

FIG. 1