Affinity Maturated T-Cell Receptor (Yeda)

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Summary

However, a more efficacious and less toxic T cells based treatment is required. Effective therapy depends on the functional avidity between T cell receptors (TCRs) and peptide-MHC complex (pMHC). However the natural affinity of TCR is low and they do not naturally undergo the processes that improve antibody affinity, such as somatic hypermutation (SHM). Currently there is no method of increasing the affinity of a TCR to its ligand. Moreover there is no knowledge on how use affinity maturated TCRs for creating anti-tumor reactive cellsThis technology presents a method of increasing the affinity of a TCR to its ligand. This is done by subjecting TCR genes to SHM via the enzyme Activation Induced cytidine Deaminase (AID). The technology further provides affinity maturated TCRs (in cell- bound or in soluble form) and their pharmaceutical potential for immunotherapy.

Applications

Generating anti-tumor T cells
Generating T cells reactive against selected antigen

Advantages

Rapid
Effective

echnology's Essence

rst a nucleic acid construct encoding a TCR gene is expressed in a host cell. Next SHM is used to introduce utations to the TCR gene. Last, the the cells will be analyzed for affinity maturation by tetramer staining and ubsequently sorted by FACS. There are three parallel approaches to perform affinity maturation for the TCR: 1) Ex-vivo affinity maturation system, using Tet-regulated expression of AID (2) Ex-vivo affinity maturation ystem, using controlled expression of AID by mRNA electrophoresis (3) In-vitro affinity maturation system, sing extracts from cells that are in SHM and recombinant AID.

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