Activated T cell

T-cell activation is a key event in the adaptive immune response and is vital to the generation of both cellular and humoral immunity. Activation is required not only for effective CD4 T cell responses but also to provide help for B cells and the generation of cytotoxic T cell responses.

Activated T cells must still traffic to, infiltrate, and persist within the tumor in order to mediate tumor lysis. These requirements for efficacy pose unique challenges for brain tumor immunotherapy, due to specific anatomical barriers and populations of specialized immune cells within the central nervous system that function to constrain immunity. Both autoimmune and infectious diseases of the central nervous system provide a wealth of information on how T cells can successfully migrate to the central nervous system and then engender sustained immune responses [1].

An activated T cell (ATC) protocol including cytokine activation and expansion in culture to target glioma stem cell (GSC) were generated and optimized for a planned phase I clinical trial. Miyaguchi et al compared three different antigen-loading methods on dendritic cells (DCs) to effectively activate T cells, which were GBM patient-derived glioma stem cell (GSC)-lysate, acid-eluate of GSCs, and synthetic peptides derived from proteins expressed in GSCs. DCs derived from HLA-A2 positive blood samples were loaded with tumor-associated antigens (TAAs). Autologous T cells were activated by co-culturing with loaded DCs. The efficiency and cytotoxicity of ATCs were evaluated by targeting TAA-pulsed DCs or T2 cells, GSCs, or autologous PHA blasts. Characteristics of ATCs were evaluated by Flow Cytometry and ELISpot assay, which showed an increased number of ATCs secreting IFN-γ targeting GSCs as compared with non-activated T cells and unloaded target cells. Neither GSC-lysate nor acid-eluate loading showed enhancement in response to ATCs but the synthetic peptide pool showed significantly increased IFN-γ secretion and increased cytotoxicity towards target cells. These results demonstrate that ATCs activated using a TAA synthetic peptide pool efficiently enhance cytotoxicity specifically to target cells including GSC [2].

Data indicate that the leptomeninges represent a checkpoint at which activated T cells are licensed to enter the CNS parenchyma and non-activated T cells are preferentially released into the CSF, from where they can reach areas of antigen availability and tissue damage [3].

Global T cell deficiency exacerbates motor behavioral defects in a rat model of Parkinson's disease [4].

1)
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