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Cell biology and possible therapeutic applications of anti-CD3-activated killer-T cells (review).

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Abstract

Polyclonal T lymphocyte populations can be stimulated with anti-CD3 antibody to proliferate, secrete cytokines, and mediate MHC-unrestricted cytotoxic activity against a wide range of tumor target cells. Because anti-CD3-activated killer-T (AK-T) cells may be useful in the immunotherapy of human cancers, it is important to understand the signaling pathways and cell-surface structures involved in the induction and tumoricidal effector function of AK-T cells. Studies in the mouse model system have characterized the cytokines, signal transduction pathways, and costimulatory molecules involved in AK-T cell development. The recognition/adhesion and subsequent signaling events which lead to tumoricidal activity by mouse AK-T cells have also been defined. These findings, providing they translate accurately to the human system, may allow for the design of effective strategies to use AK-T cells for the treatment of human cancers. However, to date, the encouraging results obtained with anti-CD3 antibody/AK-T cell-based immunotherapies in mouse models of cancer have not been duplicated in clinical trials. The most likely explanation for this dis-appointing result is that tumor-reactive T lymphocytes in long term tumor-bearers fail to function correctly in the tumor microenvironment due to tumor-induced immune suppression and defects in key signal transduction molecules. It is clear that a detailed understanding of the inhibitory effect of established tumors on host T cells and the means to overcome tumor-induced immunosuppression are needed before anti-CD3 antibody/AK-T cell-based immunotherapies can be expected to succeed in the clinical setting.

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