

LYMPHOTOXIN-BETA AND LYMPHOTOXIN-BETA COMPLEXES

BACKGROUND: The initiation of the immune response involves a complex array of intercellular signals that occur in lymphoid organs between lymphocytes and surrounding antigen presenting cells and stromal cells. Modulation of these complex interactions can be accomplished by blocking key cytokines that control lymphoid tissue organization. Lymphotoxins (LT) constitute a subfamily of cytokines that are expressed on the surface of activated T and B lymphocytes. LT are essential for regulating the organization of lymphocytes with other tissue cells, in part by activating a specific cell surface receptor present on antigen presenting cells and stromal cells. The binding of LT to the receptor controls the expression of other proteins on the antigen presenting cells such as chemokines that recruit lymphocytes to the site of inflammation, and integrins, required for lymphocytes to become organized at sites of immune and inflammatory reactions. This appears to be very important to establish chronic inflammation. Blockade of LT have been shown to attenuate unwanted inflammatory reactions in in vivo models of inflammation and autoimmune diseases.

DESCRIPTION: Researchers at the University of California have identified a novel protein, called lymphotoxin-beta (LT-beta), found on the surface of several types of lymphocytes. LT-beta is a 31-35kD type II transmembrane protein with regions of homology in its extracellular domain to members of the TNF family of cytokines, particularly LT-alpha. LT-beta forms a novel complex with LT-alpha and forms complexes with other LT-beta subunits. Importantly, the researchers found that LT-beta, as a cell membrane protein, binds the LT-beta receptor, which is responsible for inducing organization of lymphocytes. As such, the LT-beta/LT-alpha complexes may be important in T cell activation events, cellular immunotherapies, and in mediating autoimmune diseases. Cell lines expressing whole and partial LT-beta, methods for producing LT-beta protein, as well as antibodies to LT-beta and the LT-beta/LT-alpha complex are available.

ADVANTAGES: The identification of LT-beta allows for the development of novel research tools and therapeutics designed to modulate inflammation and immune responses.

APPLICATIONS:

- Compositions and methods for T cell activation or T cell suppression.
- Therapeutic agents in the treatment of inflammation.

- Therapeutic agents for applications requiring cytolytic activities, such as inhibition of tumor cell or neoplasia growth.
- Cellular immunotherapies, including enhancing the tumoricidal properties of tumor infiltrating lymphocytes in Tumor Infiltrating Lymphocyte ("TIL") therapy.

PATENT STATUS: US Patent No. [5,661,004](#) issued August 26, 1997; US Patent No. [5,670,149](#) issued September 23, 1997; US Patent No. [5,795,964](#) issued August 18, 1998; US Patent No. [7,030,080](#) issued April 18, 2006

