

ANTHRAX LETHAL TOXIN INHIBITS PROLIFERATION OF HUMAN CD4+ T CELLS IN RESPONSE TO T CELL RECEPTOR STIMULATION AND MITOGEN STIMULATION

Technology Summary

Bacillus anthracis is a deadly disease that can be used as an efficient bioterrorism agent. Efforts are underway to develop and stockpile therapeutics for the treatment of anthrax infections. Currently, *in vitro* assays are available for measuring anthrax lethal toxin (LT) activity, but such assays are based on the species- and strain-specific actions of the toxin on murine macrophage cell lines. *In vitro* assays are needed that reflect the *in vivo* effects of the toxin during human infections. There is a need for bioassays based on human cell parameters.

To address this need, FDA researchers have developed a method using a human tumor CD4 T cell line to screen and determine the efficacy of anti-anthrax therapeutics. Using this method, the effects of anthrax LT were demonstrated to inhibit the proliferation of human CD4+ T cells in response to T cell receptor and mitogen stimulation. Specifically, anthrax LT was discovered to be a potent inhibitor of the MAPKK-dependent upregulation of cytokines (IL-2, IL-4 and IFN- γ) and IL-2-dependent proliferation by primary human CD4 T cells following T-cell receptor (TCR) stimulation.

Potential Commercial Applications

- Human bioassay development for anthrax lethal toxin activity, diagnosis, and treatment

Competitive Advantages

- Determination of anthrax lethal toxin activity in human cells.

Development Stage: Early proof-of-concept

Inventors: David Frucht, Hui Fang

Intellectual Property:

- United States Patent: [7,803,565](#) issued 9/28/2010
- United States Patent: [8,383,359](#) issued 2/26/2013

Publications:

- Fang, H. et. al. Anthrax lethal toxin has direct and potent inhibitory effects on B cell proliferation and immunoglobulin production. *J Immunol.* 2006 May 15;176(10):6155-61. PMID: [16670324](#)
- Fang, H. et al. Anthrax lethal toxin blocks MAPK kinase-dependent IL-2 production in CD4+ T cells. *J Immunol.* 2005 Apr 15;174(8):4966-71. PMID: [15814725](#)
- Cordoba-Rodriguez, R. et. al. Anthrax lethal toxin rapidly activates caspase-1/ICE and induces extracellular release of interleukin (IL)-1 β and IL-18. *J Biol Chem.* 2004 May 14;279(20):20563-6. PMID: [15010463](#)

Product Area: anthrax bioassay, diagnostic, bioterrorism

FDA Reference No: E-2004-039

Licensing Contact:

Ken Millburne, J.D.

FDA Technology Transfer Program

Email: FDALicensing@fda.hhs.gov

Phone: 240-402-2245