

Christopher L. Karp, MD

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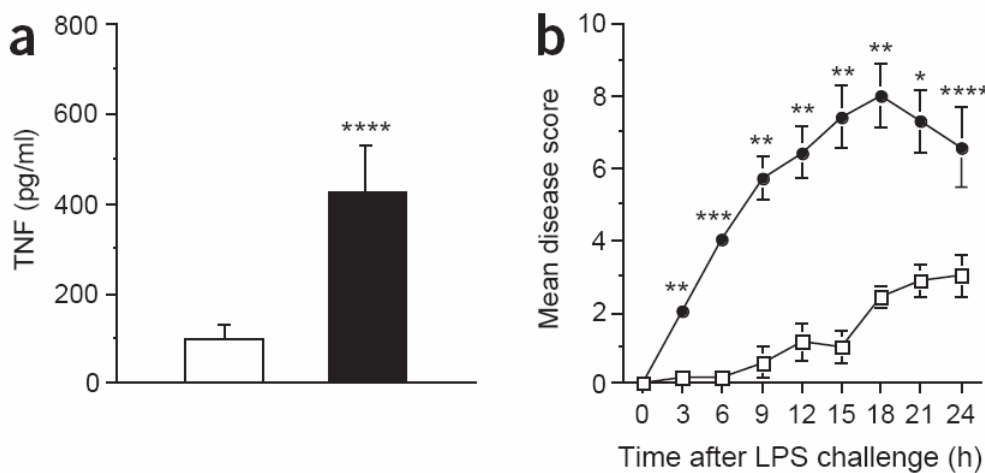
Description of Research:

Dr. Karp's research focuses on understanding the molecular mechanisms underlying cytokine-mediated dysregulation of cell mediated immune responses in human infectious and autoimmune diseases. Interrelated, ongoing areas of study include: molecular mechanisms of measles-induced immunosuppression (both in vivo and in vitro) and molecular mechanisms underlying IL-12 regulation and dysregulation in measles, multiple sclerosis, hepatitis C, and HIV infection. Other areas of research include: (a) the mechanisms underlying dysregulation of pulmonary inflammatory responses in cystic fibrosis; (b) Ebola virus pathogenesis and therapy; (c) molecular mechanisms underlying endotoxin tolerance; (d) molecular mechanisms of control of Toll-like receptor-driven signaling pathways; and (e) the role of regulatory T cell in modulating innate immune responses. Dr. Karp uses both an animal model system and human samples in his research. Dr. Karp has been able to show that RP105, a toll-like receptor (TLR) homolog, is a physiological negative regulator of TLR4 signaling. Recently he has been able to demonstrate that the cytotoxic T-lymphocyte antigen which is an inhibitory T-cell receptor expressed by activated and regulatory T cells, influences the recovery from hepatitis C virus infection.

Collaborations:

Drs. Karp and Aronow have established a collaboration using Bioinformatics and Affymetrix GeneChip experiments to study the genetic profiles in IL-12 regulation and dysregulation in infectious and autoimmune diseases. He also collaborates with Dr. Denson to define the identity and function of the gut IL-10 expressing cells in inflammatory bowel disease and murine colitis. Dr. Karp is co-mentoring a GI fellow, Brad Pasternak, with Dr. Denson on a Pediatric Scientist Development Program grant. Dr. Karp uses Dr. Montrose's 2-photon microscope to analyze IL-10 transcriptional knockout mice.

Representative Figure:



Exaggerated in vivo responses to LPS in RP105-deficient mice. A. Wild-type mice (n = 17; open bar) or RP105-deficient mice (n = 18; filled bar) were challenged intraperitoneally with 25 μ g of purified *E. coli* K235 LPS. Serum was collected 60 min later. B. Wild-type mice (open symbols) and RP105-deficient mice (filled symbols) were challenged with 8 mg/kg of purified *E. coli* K235 LPS (n = 7 per group). Data represent means + s.e.m. *, P < 0.0005; **, P < 0.00005; ***, P < 0.00000001; and ****, P < 0.01. Figure 10 from *Nat Immunol*, 2005; 6:571-578.