

Welcome to the Herbert Lab



RESEARCH OVERVIEW

The UCSF Division of Experimental Medicine is primarily focused upon understanding the cellular and molecular immunology of chronic infectious disease. The Herbert laboratory investigates parasitic helminth(worm) infections to better understand the mechanisms of protective immunity and resolution of mucosal inflammation.

Specifically, we pose three central questions:

How are tissue macrophages involved in mucosal repair following infection-induced injury?

Tissue macrophages are key constituents of homeostasis, inflammation, and repair. We previously found that the interleukin 4/13-driven alternative pathway of macrophage activation

prevents lethal intestinal immunopathology caused by the human blood fluke *Schistosoma mansoni* (Herbert et al. 2004). Also, we demonstrated that Arginase I, which is a catabolic enzyme of L-arginine, is an important effector molecule derived from alternatively activated macrophages that limits infection-induced tissue injury (Herbert et al. 2010). Ongoing studies will determine whether Arginase I regulates inflammation via influencing extracellular matrix turn-over and/or inflammatory cytokine production. Furthermore, we are interested in whether human alternatively activated macrophages also serve a critical role in the regulation of tissue repair or resistance to helminth infection.

How is Type 2 inflammation initiated and executed?

We postulate that Type 2 immunity is selectively initiated by mechanisms that drive tissue repair within the mucosa. A major project in the laboratory focuses upon mammalian Trefoil factors, which are mucus proteins that drive epithelial cell restitution. Trefoil factor 2 regulates interleukin 33, which induces of Type 2 immunity in the context of hookworm infection and allergy (Wills-Karp et al. 2012). Furthermore, the lack of TFF2 in mice results in enhanced development of Type 1 immunity against *Toxoplasma gondii* (McBerry et al. 2012). Ongoing studies will explore the immunological role for each of the TFF members in homeostasis and host protection against pathogens.

How do helminths maintain chronic infection of their hosts?

Transforming growth factor beta (TGF-beta) is a key cytokine that regulates the balance between tolerance and immunity, but surprisingly little is known regarding how it regulates macrophage biology. Our lab has demonstrated that TGF-beta specifically acts on macrophages to suppress helminth immunity, but promote the resolution of colitis and pulmonary tissue damage (Herbert et al. 2008, Rani et al 2011, Heitmann et al. 2012). Ongoing studies will further dissect the molecular mechanisms of TGF-beta-dependent regulation of macrophage activation and investigate whether this cytokine promotes chronic worm infection in humans.

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