

THE HARTWELL FOUNDATION

2008 Individual Biomedical Research Award

Review of Proposed Research

Investigator: **Laura J. Knoll, Ph.D.**
Associate Professor
Department of Medical Microbiology

Institution: **University of Wisconsin Madison**

Proposal: **Using a Mutant Microbe to Help Us
Understand the Relationship Between
Inflammation and Obesity**



Based on a serendipitous discovery in an unusual animal test system, Dr. Knoll proposes a unique relationship must exist between obesity and inflammation. Stimulation of an immune response in the brain of mice with a particular mutant strain of the parasite *Toxoplasma* unexpectedly produces rapid and dramatic weight gain in treated animals, independent of food intake. Everyone accepts that weight is not a simple function of caloric intake; how the body uses or stores the calories is why exercise is so important. Dr. Knoll's observation however, suggests stimulation of the immune system may be an independent trigger for obesity; a transformative idea not only for interpretation of the multiple disease states influenced and exacerbated by obesity, such as diabetes and heart disease, but also for the definition of "normal and healthy" living. Dr. Knoll offers a disruptive paradigm, which brings new meaning to the socially threatening and often-heard declaration of an obesity epidemic. For example, while it is widely accepted that adipose tissue is a place where the body stores fat, recent studies suggest fat is a complex organ that produces many hormones responsible for regulating appetite and altering how calories are either stored or used for expending energy. Remarkably, adipose cells and the immune system can both produce and be regulated by the some of the same signaling proteins: adipokines when produced by adipose cells and cytokines when produced by immune cells. Dr. Knoll proposes to dissect the mechanism of the *Toxoplasma* mutant-induced obesity to understand how specific stimulators of the immune system are able to trigger weight gain by altering adipose tissue metabolism and proliferation. If Dr. Knoll is successful, understanding how stimulation of the immune system triggers obesity will lead to valuable diagnostic tests that could distinguish between mechanisms of obesity, as well as therapeutic target drugs useful for stimulating or suppressing specific branches of the immune system to control or prevent obesity.