

THE HARTWELL FOUNDATION

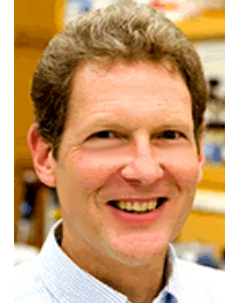
2009 Individual Biomedical Research Award

Review of Proposed Research

Investigator: Michael P. Timko, PhD
Professor
Department of Biology

Institution: University of Virginia

Proposal: Tailored Probiotic Delivery of Therapeutic Peptides for Prevention of and Recovery from Necrotizing Enterocolitis (NEC)



Dr. Timko proposes the novel use of probiotic bacteria to deliver therapeutic glutamine containing peptides to the gastrointestinal tract to promote tissue repair in necrotizing enterocolitis (NEC). The most common life-threatening inflammatory bowel disease observed in premature and low-birth weight infants, NEC afflicts an estimated 25,000 infants yearly in the U.S. each year. While its cause remains unknown, the disorder presents as a decrease in blood flow to the intestine, resulting in tissue death and cessation of normal mucus production, which then leaves the intestine susceptible to infection from adventitious bacteria. Patients often develop severe complications, including systemic infection, sepsis, and consequent multi-system organ failure. Despite advancements in perinatal care, mortality rates following the onset of NEC have not changed significantly in recent decades and remain unacceptably high. There are currently no effective means to counteract NEC except to offer antibiotics and surgically remove the necrotic intestine, which are frequently ineffective. Accumulating evidence however, indicates that the use of certain strains of probiotics (defined as nonpathogenic microbes of human origin) may assist in preventing, treating and attenuating the severity of intestinal inflammatory conditions. Probiotics have been consumed safely by humans in various fermented food and dairy products for thousands of years. On this basis, Dr. Timko and his collaborators have pioneered the use of alanyl-glutamine dipeptides as potential therapeutics, useful in promoting intestinal injury repair. Dr. Timko now intends to explore the potential synergistic effects of targeted delivery using probiotic supplementation as an effective strategy for preventing and treating NEC. He will create a set of genetically-tailored probiotic bacteria capable of expressing novel glutamine-rich peptides in the gastrointestinal tract and evaluate their effects on NEC in animal models. The long term goal is to transfer the knowledge gained from the proposed research into the development of food grade probiotic bacteria, which can be the basis of therapeutic infant formula for universal low-cost prevention and treatment of NEC in preterm infants. If his innovative approach is successful, it could lead to new strategies not only for managing NEC, but serve as a template for the probiotic delivery of therapeutic agents for other gastrointestinal diseases.