

James & Esther King Biomedical Research Program

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*2008 Program
New Investigator (3-year project)*

Project Title: Role of MCP1P1 in Nicotine-Induced Repression of Macrophage Inflammation

Project Summary: Cigarette smoking is an established risk factor for cardiovascular disease, lung cancer, chronic obstructive pulmonary disease, respiratory infections, and the leading cause of avoidable mortality in industrialized countries. Its effects are largely due to cigarette smoke-induced impairment of the immune system.

Nicotine is a major immunosuppressive component in cigarette smoke. However, how nicotine impairs the immune system is not clear. Previously we have found that a novel protein MCP1P1 can suppress macrophage inflammation through targeting an important signal pathway NF- κ B signaling in macrophages. Our preliminary studies suggest that MCP1P1 may be an important mediator in nicotine-induced repression of macrophage inflammation. Our long-term goal is to identify molecular signals mediated by cigarette smoke action on macrophage inflammation and study their contribution to human diseases such as atherosclerosis. In this grant, we will use MCP1P1 knockout mice as a tool to further define the mediator role of MCP1P1 in nicotine-induced repression of macrophage inflammation. We will also carry out a series of in vitro experiments to define how MCP1P1 inhibits NF- κ B activation and how nicotine induces MCP1P1 transcription. Understanding the molecular mechanisms involved in the inflammatory processes in tobacco/nicotine-treated macrophages is essential for development of novel drug therapies against tobacco-related inflammatory diseases.