NIH Award from the National Institute Of General Medical Sciences

Principal investigator: Christian Stehlik, rheumatology
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- Project: Pyrin Proteins as Regulators of Innate Immune Pathways
- Start Date: September 30, 2009
- Total Award Amount: $388,306

How the results of this project will benefit society:
Excessive production of IL-1β and IL-18 are directly responsible for the symptoms of an increasing number of inflammatory diseases with destructive pathogenesis, including some of the most common diseases of industrialized nations, such as arthritis, asthma, inflammatory bowel disease, ulcerative colitis, atherosclerosis, periodontitis, type 2 Diabetes, lung fibrosis, multiple sclerosis, Alzheimer’s disease, stroke and cancer. Currently there are no effective treatments available, causing life-long symptoms in patients and a huge economical and financial impact on our social and medical systems. Therefore, this study on novel mechanisms that regulate production of IL-1β and IL-18 is expected to positively affect human health by providing the basis for the development of novel and improved treatment options for preventing uncontrolled release of IL-1β and IL-18 in patients suffering from inflammatory diseases.

The problem the project is trying to solve:
We are seeking funds in response to NOT-OD-09-058 “NIH American Recovery Act Funds for Competitive Revision Applications” to allow us to expand specific aim 3 of our approved parent award. All three specific aims of our parent award are based on molecular, cellular, and biochemical studies to elucidate three novel steps in the regulation of inflammasome assembly and activity in macrophages. With this revision, we are proposing to include a novel sub aim to our approved aim 3 to translate our in vitro studies into in vivo animal models.

How this project will work:
Based on our progress with specific aim 3, we propose to generate a macrophage-specific conditional knockout mouse to study inflammasome activity in knock-out macrophages in vitro, and in inflammasome-dependent disease models in vivo. We request funds to cover the generation of this mouse model and that of technical support for the animal work. This revision will increase the scope of our approved parent award and enable our laboratory to establish mouse-disease models.

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