

2012 Abstracts



Eileen Bauer, PhD

University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

*Complement Activation as a Novel
Mechanism of Endothelial Activation in PH*

Recent data from our laboratory demonstrate a role for the complement system, a major humoral component of innate immunity, in the pathogenesis of pulmonary hypertension (PH). However, the mechanisms by which complement promotes PH are poorly understood. This proposal aims to test the novel hypothesis that genetic deletion of complement components C3 or C5, or inhibition of activated complement, prevents and/or halts the progression of PH by inhibiting endothelial activation. To test this hypothesis I have proposed two specific aims. Aim 1 will explore if activated complement directly causes activation of pulmonary artery endothelial cells *in vitro*, and will establish a timeline of endothelial activation *in vivo* in our animal model of hypoxic exposure. Genetic deletion of complement components C3 or C5 will establish a role for complement in mediating endothelial activation *in vivo*. Aim 2 will focus on determining the therapeutic potential of the complement inhibitor CR2-crry in PH. Preliminary data show promising results when CR2-crry is administered to mice at the beginning of the disease course suggesting that complement inhibition can attenuate chronic hypoxia-induced PH. The first component of this aim will focus on further refinement of the dosage and timing interval to optimize CR2-crry delivery. Based on these results, inhibitor studies will be performed using mice with established PH to test the inhibitor's therapeutic potential. Completion of the proposed research will give us a stronger foundation upon which to 1) further investigate the role of innate immunity in PH and 2) further explore the therapeutic potential of drugs targeting the complement system.