Zharikov, Sergey

Department of Medicine, Pulmonary Division — *2004 Program*
University of Florida College of Medicine — *New Investigator (3-year project)*

Project Title: Effects of Cigarette Smoke on the CAT-1 L-arginine Transporter and Nitric Oxide Production in Pulmonary Endothelial Cells

Project Summary: Although the underlying mechanisms are not completely understood, Substantial evidence indicates that cigarette smoking causes injury to vascular endothelium, leading to endothelial cell dysfunction. Cigarette smoking-induced endothelial dysfunction includes deterioration in production of nitric oxide (one of the main regulators of blood pressure and other cellular functions) by endothelial cells. Nitric oxide (NO) production in endothelial cells depends on the activity of nitric oxide synthase (NOS) and on the availability of the amino acid L-arginine – the only substrate for synthesis of NO. At present, the main focus of studies on the tobacco-induced deterioration of NO production is concentrated on the role and changes in endothelial NOS. This project will clarify effects of cigarette smoke on L-arginine transport from blood to lung endothelial cells and mechanisms of these effects as well as clarify how cigarette smoke-induced changes in activity of the CAT-1 L-arginine transporter contribute to NO production by lung endothelial cells. Potentially, research in this direction may lead to new and improved treatment strategies for tobacco-related diseases, such as chronic obstructive pulmonary disease, pulmonary hypertension, and arteriosclerosis.