Other Grant Support for Dr. Ira Tabas

**Ongoing Research Support:**

5 R01 HL075662 (Tabas, PI) 3/1/13-2/28/18
NIH/NHLBI $245,000
Mechanisms and Consequences of Stress-Induced Macrophage Death in Atherosclerosis
Goals: to investigate the mechanisms and consequences of mitochondrial oxidative stress and caspase activation in atherosclerosis
Aims: (1) To test the hypothesis, and mechanisms therein, that mitochondrial oxidative stress is a key inducer of advanced lesional macrophage death and plaque necrosis; (2) To explore the hypothesis that a novel Bax/Bak-casp8 pathway is a key effector arm of macrophage death in the setting of ER/oxidative stress and advanced atherosclerosis.
No overlap

8/13/10-8/12/15
N01 BAA-HV-10-08 (Fayad, PI; Tabas, co-RI Project 2)
NIH/NHLBI $159,145
NHLBI Programs of Excellence in Nanotechnology
Translational Nanomedical Therapies for Cardiac and Vascular Diseases
Goals: to test whether delivery of IL-10 to mouse models of advanced atherosclerosis using nanoparticles improves defective inflammation resolution
Aims: (1) Combinatorial development and pharmaceutical optimization of targeted NPs for atherosclerosis plaque targeting; (2) Screening of targeted NPs for safe and effective atherosclerosis plaque localization after systemic delivery; (3) In vivo efficacy of targeted NPs for atherosclerosis disease retardation and lesion resolution.
No overlap

P01 HL087123 (Tabas, PI; Tabas, RI Project 1) 2/1/13-1/31/18
NIH/NHLBI $333,182
Mechanisms of Atherogenesis in Insulin Resistance 2.4 Cal Mnth (20%)
Goals: to determine how insulin resistance in macrophages resulting from systemic insulin resistance affects macrophage processes relevant to atherosclerosis
Aims: (1) To test the hypothesis that macrophage CaMKIIγ deficiency will lessen advanced lesional macrophage apoptosis and plaque necrosis in insulin-resistant mice; (2) To further characterize and explore the mechanisms whereby liver CaMKIIγ deficiency improves the metabolic disturbances of obesity and to test the hypothesis that liver-specific CaMKIIγ deficiency will suppress atherosclerosis in obese mice.
No overlap

1 R01 HL106019 (Tabas, PI) 1/1/11-11/30/14
NIH/NHLBI $283,091
Autophagy in Advanced Atherosclerosis 2.4 Cal Mnth (20%)
Goals: to investigate the role of autophagy in the progression of advanced atherosclerotic plaques

Aims: (1) To explore the hypotheses that NOX2 links autophagy inhibition to ER stress-induced apoptosis and that failure of autophagy with prolonged ER stress triggers apoptosis; (2) To test the hypothesis that inhibition of autophagy in apoptotic macrophages inhibits their clearance by efferocytosis; (3) To explore autophagy as a function of lesion stage in murine aortic root and human coronary plaques and to test the hypothesis that inhibition of autophagy will promote, and enhancement of autophagy will suppress, the progression of atherosclerosis.

No overlap

1 R01 HL107497 (Tabas, PI) 12/1/11-11/30/15
NIH/NHLBI $245,000
Mechanisms of Defective Efferocytosis in Advanced Atherosclerosis 2.4 Cal Mnth (20%)

Goals: To explore mechanisms of defective efferocytosis in advanced atherosclerosis

Aims: (1) To explore the hypothesis that MerTK cleavage in advanced lesional macrophages promotes defective efferocytosis and plaque necrosis; (2) To explore the hypothesis that enrichment of atheromata with mature dendritic-like cells during plaque progression promotes defective efferocytosis and plaque necrosis.

No overlap

Pending Support:

1 R01 HL127464-01 (Tabas, PI) 4/1/15-3/31/20
NIH/NHLBI $250,000
2.4 Cal Mnth (20%)

Enhancing Inflammation Resolution in Atherosclerosis via Targeted Nanoparticle-Mediated Delivery of Biologics

Goals: To explore mechanisms of defective efferocytosis in advanced atherosclerosis

Aims: (1) To elucidate athero-protective, pro-resolving mechanisms of Col IV-Ac2-26 NPs; (2) To develop and test mechanisms and efficacy of IL-10 NPs in advanced atherosclerosis; (3) To develop and test mechanisms and efficacy of a pro-resolving microRNA NP in atherosclerosis.

No overlap

Recently Completed Research Support:

5 P01 HL054591 (Tabas, RI Project 2 [Tall, overall PPG PI]) 4/7/06-3/31/11
NIH/NHLBI
Macrophage Death in Plaque Vulnerability

Goals: To explore new pathways of inflammation and efferocytosis in atherosclerosis

Aims: (1) To elucidate the roles of p38 and Bcl2 in macrophage apoptosis and inflammation; (2) To explore the roles and mechanisms of MerTK in the phagocytic clearance of apoptotic macrophages.

No overlap
Interaction of Atherogenic Lipoproteins with Macrophages.

Goals: to investigate intracellular lipoprotein-cholesterol endocytosis and trafficking in macrophages
Aims: (1) To use a proteomics approach to identify novel molecules involved in lipoprotein-cholesterol trafficking and to further explore the role of P5 in this process; (2) Genomics-based strategy to identify genes involved in the trafficking of LP-Cho; (3) To examine the trafficking of lipoprotein-derived sterol and methyl-β-cyclodextrin-derived sterol using fluorescence microscopy.
No overlap

Mechanisms of Atherogenesis in Insulin Resistance
Molecular Links between Insulin Resistance and Macrophage Death in Atherosclerosis (PJ1)

Goals: To elucidate the roles of the type A scavenger receptor and toll-like receptor 4 in macrophage apoptosis and to investigate how these pathways are influenced by insulin resistance in macrophages per se and systemically, with the latter focused on the role of adiponectin.
Aims: (1) To investigate the role of SRA and TLR4 in apoptosis of ER-stressed macrophages in insulin-sensitive and insulin-resistant states; (2) To investigate the cellular mechanisms and in-vivo consequences of adiponectin-mediated suppression of the Unfolded Protein Response and apoptosis in macrophages.
No overlap