

CCAR Investigators Present Findings at the 2014 Annual Society of Toxicology (SOT) Meeting

**Matthew Campen of the University of New Mexico** co-chaired a SOT Symposium entitled: Role of Circulating Factors in Mediating Systemic Toxicity of Inhaled Substances. As part of this symposium, Matthew Campen presented the following talk: *Endothelial Cell Pattern Recognition Receptors, CD36 and LOX-1, Contribute to Responses to Pollution-Induced Circulating Factors.*

Abstract: Our laboratory initially discovered that the serum from health human volunteers contains a bioactive component following controlled exposures to diesel or nitrogen dioxide that can activate inflammatory endothelial cell responses. While we have eliminated the possibility that common cytokines are the driving factor(s) in this response, the identity of the biochemical ligands that drive such responses remains unknown. However, we have considered the possibility that multiligand pattern recognition receptors (PRRs), as mediators of response to extracellular damage, could play a specific role in endothelial cell responses to pollution induced circulating factors. Two specific receptors have been investigated: cluster of differentiation 36 (CD36) and the lectin-like oxidized low density lipoprotein receptor-1 (LOX-1). These observations help explain systemic vascular inflammatory effects of diverse inhaled pollutants such as ozone and PM, along with complex mixtures from combustion sources. Ongoing translational work enables cumulative response patterns in controlled settings to improve assessment of relative toxicity of individual components and mixtures of pollutants.

**J.B. Brower of Lovelace Respiratory Research Institute** presented a poster entitled: Acute Inhalation Exposure to Mixed Vehicle Emissions Induces Serum Metabolite Changes Related to Oxidative Stress, Lipid Peroxidation, and Energy Metabolism

Abstract: The adverse health effects of environmental exposure to gaseous and particulate components of vehicular emissions are a major concern among urban populations. A link has been established between respiratory exposure to vehicular emissions and the development of cardiovascular disease (CVD), but the mechanisms driving this interaction remain unknown. Chronic inhalation exposure to mixed vehicle emissions has been linked to CVD in animal models. This study evaluated the temporal effects of acute exposure to mixed vehicle emissions (MVE; mixed gasoline and diesel emissions) on potentially active metabolites in the serum of exposed mice. C57Bl/6 mice were exposed to a single 6 hour exposure to filtered air (FA) or MVE (100 or 300  $\mu\text{g}/\text{m}^3$ ) by whole body inhalation. Immediately after and 18 hours after the end of the exposure period, animals were sacrificed for serum and tissue collection. Serum was analyzed for metabolites that were differentially present between treatment groups and time points. Changes in metabolite levels representative of increased oxidative stress (oxidized glutathione, cysteine disulfide, taurine), lipid peroxidation (13-HODE, 9-HODE), energy metabolism (lactate, glycerate, branched chain amino acid catabolites, butyrcarnitine, fatty acids), and inflammation (DiHOME, palmitoyl ethanolamide) were observed immediately after the end of exposure in the serum of animals exposed to MVE relative to those exposed to FA. By 18 hours post exposure, serum metabolite differences between animals exposed to MVE versus those exposed to FA were less pronounced. Experiments are underway to investigate the potential bioactivity of these metabolites in an ex vivo model of vascular reactivity.