Transcriptional Endothelial Biosensor Response to Diesel-Induced Plasma Compositional Changes

Matthew Campen[1], Michael Madden[2], Jonathan Schisler[3], and Monte Willis[3]

[1]University of New Mexico, Albuquerque, NM; [2]United States Environmental Protection Agency, Human Studies Division, Chapel Hill, NC; [3]University of North Carolina, Chapel Hill, NC

Air pollution, especially emissions derived from traffic sources, is associated with adverse cardiovascular outcomes. However, it remains unclear how inhaled factors drive an extrapulmonary pathology, as the lung is an effective barrier for solid particulates and many gases. Previously, using plasma from healthy human subjects exposed to diesel exhaust under controlled conditions, we found that canonical inflammatory response transcripts of interleukin-8 (IL-8), intracellular adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-1 (VCAM-1) were elevated in endothelial cells treated wih plasma obtained after exposure compared with pre-exposure samples or filtered air (sham) exposures. While the findings confirmed the presence of bioactive factor(s) in the plasma after diesel inhalation, we wanted to better examine the complete genomic response to investigate 1) major responsive transcripts and 2) collected response pathways and ontogeny that may help to refine this method. Thus, we assayed previousy collected RNA with microarray chips, examining the responses of cultured endothelial cells to plasma obtained from 6 healthy human subjects exposed to 100 $\mu g/m^3$ diesel exhaust or filtered air for 2 h on separate occasions. In addition to pre-exposure baseline samples, we investigated samples obtained immediately post and 24h post exposure. Primary human coronary artery endothelial cells were grown to confluence and treated with 10% plasma for 24 h, followed by isolation of RNA for microarrays. Microarray analysis of the coronary artery endothelial cells challenged with plasma identified 320 genes significantly altered when challenged with plasma from 1 and 24 hours post-diesel exhaust exposure, compared to baseline matched plasma. Transfac analysis of the differentially expressed genes identified 168 transcripts with E2F transcription factor promoter regions and 50 with NFκB transcription promoter regions (p values=0.0003 and 0.004, respectively). These outcomes are consistent with our recent findings that plasma contains bioactive and inflammatory factors following pollutant inhalation and provide a novel pathway to explain the well-reported extrapulmonary toxicity of ambient air pollutants. [This is an abstract of a proposed presentation and may not reflect official US EPA policy.]

Meeting: American Thoracic Society; May 16-21, 2014; San Diego, CA