

“Role of S-nitrosylation in asthma pathophysiology”

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Project Summary/Abstract

We propose to optimize current proteomic technologies to enable comprehensive quantitative evaluation of global protein expression and site-specific mapping of post-translational modifications within the proteome as well as the mitochondrial proteome in response to environmental stressors. We have selected to focus on site-specific identification of protein cysteine residues that undergo selective oxidative modifications to form S-sulfenylated, S-glutathionylated, and S-nitrosylated proteins. These site-specific cysteine modifications in addition to protein phosphorylation and lysine acetylation represent critical signaling mechanisms that are dependent on the redox environment of the cell and the mitochondria. Using established models of exposure to polyhalogenated (mostly chlorinated) biphenyl hydrocarbons (PCBs), which are chemically stable pollutants that impact human health we will explore and quantify changes in the mouse brain and liver proteome, phosphoproteome, lysine acetylome and cysteine post-translational modifications. Beyond the utility as markers of redox changes the cysteine post-translational modifications will provide mechanistic insights on the adapted metabolic responses and signaling changes that follow alterations in mitochondrial redox state after PCB exposure. We will continue the distribution of material and expertise of these technologies to other laboratories as well as distribute the data generated in this application to the research community through a web-based application. Dissemination of these technologies and data will remove significant barriers in the field and will allow researchers in any discipline of mitochondrial biology and metabolism to generate novel hypotheses regarding the biological and molecular mechanisms of mitochondrial and cellular signaling that coordinates responses to environmental stresses.