

PAGE MORTON HUNTER DISTINGUISHED SEMINAR SERIES



Cigarette Smoke Induced Lung Injury

Cigarette smoke (CS) is a major risk factor for chronic obstructive pulmonary disease (COPD). Free radical damage to proteins following CS exposure induces endoplasmic reticulum (ER) stress. High levels of S-glutathionylated protein disulfide isomerase (PDI) were found in the lungs of murine smokers compared with non-smokers. To decipher if S-glutathionylated PDI contributes to pro-apoptotic redox signaling, we investigated the causality between PDI S-glutathionylation, changes in its cellular localization and apoptosis. PDI spatially linked to mitochondria increased upon exposure to lethal doses of CSE, where it causes cytochrome c (Cyt c) release through the mitochondrial permeability transition pore, which in turn leads to caspase-3 mediated apoptosis. Rescue of mitochondrial function in lung cells can be achieved either by over-expressing PDIFLFL, a S-glutathionylation refractory mutant of PDI, or with pharmacological inhibition of glutathione transferase P, an enzyme that mediates S-glutathionylation, and both in turn could reduce the cytotoxicity caused by CS. We conclude that CS exposure induces PDI S-glutathionylation, and its proximity to mitochondria, where it causes Cyt c release from mitochondria, leading to intrinsic apoptosis.

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Danyelle Townsend is a Professor and Interim Department Chair of Drug Discovery and Biomedical Sciences at the Medical University of South Carolina. Her lab utilizes proteomics and analytical biochemistry to identify molecular targets affected by oxidative and nitrosative stress, exploring the impact of redox signaling on cellular responses. Her research on the redox proteome and associated pathways has established a foundation for drug discovery and redox biomarker development, leading to multiple clinical trials. Dr. Townsend brings expertise in drug metabolism and pharmacokinetics and is the Director of the Analytical Redox Biochemistry Core Facility and Editor in Chief of Biomedicine and Pharmacotherapy.

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Location:

Basic Science Building 435 at MUSC

or

<https://clemsun.zoom.us/j/98859080650>



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