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Lung cellular senescence atlas, senescence biomarkers, and senolytic therapy in COPD

Abstract:

Environmental airborne pollutants and inhaled toxicants including climate change associated increased particulates, environmental tobacco smoke exposures, and wildfire/biomass smoke along with heat stress are involved in pathogenesis of several debilitating diseases and their exacerbations including Chronic Obstructive Pulmonary Disease (COPD). These exposures can cause oxidant/antioxidant imbalance and epithelial barrier junction dysfunction, leading to inflammatory responses and DNA damage, which are associated with cascades of cellular signaling and damaging effects. We have shown accelerated aging due to increased cellular senescence occurs in the pathogenesis of COPD using both SA- -Gal staining and C12FdG staining in lung tissues. Interestingly, we observed highest cellular senescence in the parenchymal region from the lower lobes of COPD patients, thus proving that maximum damage is caused in the lower lung lobes during the disease progression. Initial analyses of scRNA seq data identified 19 distinct cell types in each of our experimental groups. We are further analyzing the scRNA seq data to identify specific markers for senescence that are correlated with COPD disease development and progression based on phenotypes. We further provided the insights into the cellular phenotypes during pulmonary conditions, and how polyphenolic compounds alters senescence (immunosenescence) mechanisms, and provide rationale for therapeutic targets (via senolytics/senotherapeutics/senomorphics) in this chronic lung diseases of aging. We will further discuss the involvement of CAR T cells, which are synthetic receptors that are capable of readdressing the specificity and other functions of T cells; which have been shown to be lost in many lung diseases, and possibly regulated by nutraceuticals impacting cellular senescence in COPD pathogenesis. Overall, we identified markers and single cell atlas of cellular senescence that are unique for patients with COPD, which could help in early diagnosis and efficient localized therapy based on cellular senescence using senolytics/senomorphics for this debilitating disease.

Biography

Irfan Rahman, PhD is the Dean's Professor of Environmental Medicine, Medicine (Pulmonary), and Public Health Sciences at the University of Rochester Medical Center (URMC) in Rochester, NY. He also serves as the Director of the Center for Flavoring Inhalation Toxicology. Dr. Rahman is renowned for his research in the field of environmental medicine, particularly in understanding the effects of inhaled toxicants, including e-cigarettes and flavoring agents, on lung health. His work has significantly contributed to public health knowledge and policy regarding inhalation toxicology and respiratory diseases.