

Award Recipient:
Jessica Chia, MD
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Project:
**“Role of Aging and Endoplasmic Reticulum
Stress in the Pathogenesis of Pulmonary
Fibrosis”**

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive condition of unknown origin in which lung tissue becomes thickened, scarred, and stiff. The epidemiology of IPF demonstrates that this condition disproportionately affects the elderly population, with increasing incidence in older age, and with a majority of patients in their mid to upper 60s at the time of diagnosis. The resultant progressive dyspnea and hypoxemia from IPF often leads to a global functional decline. In an already vulnerable population of older, frail seniors, the functional limitations and disability due to pulmonary fibrosis can swiftly result in loss of independence and are often rapidly devastating. As a result, IPF inevitably ends in respiratory failure, usually within three to five years of diagnosis.

As such, IPF carries the unfortunate distinction of being the most common, devastating, and fatal of the various interstitial lung diseases. This is in large part due to the challenging management of IPF, as there are no established effective medical therapies. Our current limited understanding of the pathogenesis of IPF precludes the ability to provide effective treatment options.

Recent evidence suggests that the endoplasmic reticulum (ER) stress response may represent an important mechanism of the altered repair process following lung injury that leads to fibrosis. ER stress describes the condition in which various cellular insults result in aberrant protein folding and the accumulation of misfolded proteins within the cell. If this cannot be resolved, cell death occurs. Several genes known to be involved in the ER stress response are significantly upregulated in elderly patients with IPF, and increased expressions of ER stress markers have been seen in lung tissue from patients with IPF. These observations lead to our hypothesis that the aging lung epithelium may be more susceptible to ER stress. We propose that the aging alveolar epithelium's response to ER stress represents a mechanism in the pathogenesis of pulmonary fibrosis.

The broad objective of this research project is to identify whether aged alveolar epithelium demonstrates cellular defects in its ability to handle ER stress and injury. The three aims include: (1) characterization of the pulmonary ER stress response in young and aged mice in response to various ER stress-inducing agents; (2) determination of the role of ER stress in regulating pulmonary fibrosis during non-infectious lung injury in young and aged mice; and, (3) determination if alveolar epithelial cells from elderly IPF patients have increased susceptibility to ER stress.

With the support of the ASP-CHEST Foundation of the American College of Chest Physicians Geriatric Development Research Award, I endeavor to develop skills in conducting independent investigation relevant to the etiology, basic mechanisms, and treatment of pulmonary fibrosis, and to translate emerging knowledge in lung biology into clinically relevant concepts. This award will allow me to advance my research team's understanding of the role of aging and ER stress in pulmonary fibrosis, and treatment of pulmonary fibrosis, and will help lay the foundation for an academic career as a physician-scientist with expertise in geriatric aspects of pulmonary disease. With enhanced understanding of the molecular and cellular aspects of pulmonary aging, the ultimate goal is to reduce disability and frailty from IPF in older adults, thereby ensuring their well-being, vitality, and quality of life.

**ASP-CHEST Foundation of
the American College of
Chest Physicians Geriatric
Development Research
Award**



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