Glutathione-induced protein oxidation in tissue fibrosis: New avenues for redox-based therapeutics?

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Abstract:
Pulmonary fibrosis is a disease that claims the lives of 3 million people worldwide. Each year in the USA about 50,000 people succumb to this disease. Despite recent FDA-approved therapeutics that slow lung function decline, survival has not improved. Over 30 years ago is was demonstrated that the glutathione redox homeostasis was affected in lungs from patients with fibrosis. However the details whereby glutathione regulates the pathophysiology of pulmonary fibrosis remain unknown. Similarly, it is not clear whether disruptions in glutathione redox homeostasis can be targeted therapeutically. I will be discussing the cellular and molecular pathways that are critical in the pathogenesis of fibrosis. I will describe the pathways of glutathione-mediated protein oxidation (S-glutathionylation) an its reversal (de-glutathionylation). I will also describe approaches to unravel the S-glutathionylated proteome in the lung, and describe one S-glutathionylation target. Lastly, I will describe the steps taken thus far towards commercialization of this focus area, and current challenges.

Bio:
Dr. Janssen-Heininger is an internationally recognized leader in the field of epithelial biology and on the role of epithelial cells in the orchestration of chronic inflammatory processes, fibrotic remodeling and lung cancer. Specifically, she is interested in understanding how changes in the redox environment regulate the aforementioned processes. The concept that oxidants act as regulatory molecules (redox biology) and not merely induce damage (oxidative stress) is just emerging and has potential diagnostic but also therapeutic relevance. Within that context, her laboratory has been working to elucidate the impact of S-glutathionylation chemistry in regulating epithelial cell plasticity, metabolic control, and pro-inflammatory responses, and its role in airways remodeling. Her laboratory is also investigating the impact of glutathione S transferase P (GSTP)-catalyzed S-glutathionyation and glutaredoxin (GLRX)-mediated deglutathionylation for endoplasmic reticulum redox stress, oxidative processing of the death receptor Fas, and redox-based post translational modification of extracellular matrix proteins in fibrosis.