

Wnt signaling and pulmonary fibrosis in mouse and man

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Pulmonary fibrosis is a chronic, progressive and poorly understood disease that may be idiopathic or associated with systemic sclerosis. While lung fibrosis may be attributable to a variety of causes, it is generally thought that the initiating injury activates repair processes that aim to restore the original tissue architecture, but a failure to finely tune the repair process leads to persistent fibroblast activation. Recent studies employing genome-wide expression profiling indicate that signaling pathways required for normal embryonic development are abnormally up-regulated in end-stage lung fibrosis. These observations raise the possibility that an inability to limit the activation of core developmental pathways during repair may drive the pathological process. My lab is interested in how activation of one particular developmental pathway, the Wnt/ β -catenin signaling pathway, contributes to the cellular changes associated with fibrosis. Using the 21-day, bleomycin murine model of fibrosis, we find that the Wnt co-receptor, Lrp5, is necessary for the development of fibrosis. Microarray and cell-targeting approaches suggest that Wnt-signaling in the lung parenchyma drives disease progression, through controlling the expression collagen processing enzymes and components that mediate cell/matrix interactions. In collaboration with Naftali Kaminski's group at the University of Pittsburgh, expression changes in Wnt signaling components in peripheral blood mononuclear cells (PBMCs) from a cohort of patients with idiopathic fibrosis correlate strongly with disease progression, suggesting that the extent of Wnt signaling in PBMCs may serve as a biomarker for outcome.

Biography

Gottardi completed her Ph.D from Yale University and postdoctoral studies from the Pasteur (France) and Sloan-Kettering (New York City) Institutes. She is an Assistant Professor of Pulmonary Medicine at Northwestern University Feinberg School of Medicine. She has published 44 papers in reputed journals and currently serves on the Faculty of 1000, and is an Academic Editor of PLoS ONE.

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