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Quantitative proteome analysis of alveolar type-II cells reveals a connection of integrin receptor subunits beta 2/6 and WNT signaling

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Abstract

Alveolar type-II cells (ATII cells) are lung progenitor cells responsible for regeneration of alveolar epithelium during homeostatic turnover and in response to injury. Characterization of ATII cells will have a profound impact on our understanding and treatment of lung disease. The identification of novel ATII cell-surface proteins can be used for sorting and enrichment of these cells for further characterization. Here we combined a high-resolution mass spectrometry-based membrane proteomic approach using lungs of the SILAC mice with an Affymetrix microarray-based transcriptome analysis of ATII cells. We identified 16 proteins that are enriched in the membrane fraction of ATII cells and whose genes are highly expressed in these cells. Interestingly, we confirmed our data for two of these genes, integrin beta 2 and 6 (Itgb2 and Itgb6), by qRT-PCR expression analysis and Western blot analysis of protein extracts. Moreover, flow cytometry and immunohistochemistry in adult lung revealed that ITGB2 and ITGB6 are present in subpopulations of surfactant-associated-protein- C-positive cells, suggesting the existence of different types of ATII cells. Furthermore, analysis of the Itgb2-/- mice showed that Itgb2 is required for proper WNT signaling regulation in the lung. © 2013 American Chemical Society.

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Keywords

ATII cells, integrin, lung, SILAC mice, WNT signaling