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Systemic analysis of human lung metabolites in pulmonary arterial hypertension

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Multiple, complex molecular studies have been done for understanding the development and progression of pulmonary hypertension. Analyzing the molecular networks that distinguish this organ-confined disease may re-scope the investigation and the identification of critical biomarkers for pulmonary hypertension. Although multiple gene and protein expression have been extensively profiled in human PAH, little is known about the global metabolomic alterations that characterize the interaction between the lung and other organs and between the pulmonary vascular system and the airway cell system. Using a combination of high-throughput liquid-and-gas-chromatography-based mass spectrometry, we profiled 376 metabolites, of which 93 were significantly changed in eight metabolized systems across 8 clinical lung samples related to PAH compare with that of the normal control. Applying microarray and real-time RT-PCR techniques, we identified significantly up/down regulated genes that encoded key enzymes for these metabolic pathways. We further identified and localized the protein enzymes that changed significantly in the PAH lung. These unbiased metabolomic profiles were able to distinguish unrecognized metabolic pathways, which will explore the interaction between the lung and other organs and between pulmonary vascular cells. By profiling the metabolomic alterations of the PAH lung, we reveal newly discovered pathogenesis mechanism of PAH, which is not limited to pulmonary vascular system itself but also related to other organs. The interaction between pulmonary and other organs could serve as coordinate components that potentially regulate important metabolic intermediary of PAH.

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