Qualitative Metabolic Flux Study Reveals the Metabolism Change in Pulmonary Arterial Smooth Muscle Cells From Patient and Donor Control

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BACKGROUND

Pulmonary arterial hypertension (PAH) is the most common form of primary pulmonary hypertension, characterized by increased resistance to pulmonary blood flow that culminates in heart failure. Except for lung transplant, there is no cure for PAH. This study aimed to investigate the metabolomic differences between PAH and patient control, and to identify the abnormal cell metabolism in the pathogenesis of PAH.

METHODOLOGY

Cell culture: Patients and Controls through the Pulmonary Hypertension Breakthrough Initiative (PHBI). Lung Tissue (pulmonary arterial smooth muscle cells): Cells were cultured from patients with hereditary or idiopathic (H/I) PAH and donor control to identify the abnormal cell metabolism in the pathogenesis of PAH.

RESULTS

The metabolite profiling of human PASMCs was performed by proton nuclear magnetic resonance (1H NMR). The results revealed that after 8 hours the majority of glucose tracers were being derived from the [U-13C 6] glucose. The incorporation rates were faster in PASMC of donor control, PAH and PAH with siALDH.

CONCLUSION

The metabolic flux study in PASMCs showed that the histone acetylation, the incorporation of the stable isotope tracer, and the glycolytic function of PAH PASMC has lower TCA cycle turnover rate compared to donor control, which resulted in a decrease of the histone acetylation. siALDH in PAH PASMC decreases the glycolytic function resulted in a decrease of the histone acetylation. This study also revealed a novel mechanism that may help us understand the higher energy production from glycolysis in PAH PASMC.

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