

Session/Poster#

Presenter

B03

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Use of extracellular substrates by alveolar type 2 pneumocytes for surfactant lipid synthesis.

Pulmonary surfactant is a lipoprotein complex essential for lung function. It reduces surface tension during inspiration and avoids alveolar collapse during expiration. It is synthesized by alveolar type 2 pneumocytes (T2C) and it is composed of phospholipids (~90%), mainly phosphatidylcholine (PC), and specific proteins. Decreased surfactant and altered composition are associated with multiple adult lung diseases. However, T2C lipid metabolism and their use of extracellular glucose and lipid for surfactant synthesis has not been studied. Our prior results showed that the low density lipoprotein receptor related 1 (LRP1) is needed for surfactant synthesis.

We hypothesized that nutritional conditions and LRP1 function impact the pathways used by T2C to synthesize surfactant. Control and LRP1 knockdown T2C-derived A549 cells were cultured in DMEM with 10% FBS and maintained at the air-liquid. Then, cells were cultured in DMEM with delipidated FBS and BSAcomplexed palmitic acid (PA) at different concentrations (0-0.25 mM) for 2 hours and mRNA of surfactant synthetic enzymes was analyzed.

mRNA expression of Fatty acid synthase (FASN) and Choline kinase (CK) decreased and respectively when at least 0.05 mM PA was present. FASN and CK expression was downregulated in the absence of LRP1. mRNA expression of genes involved in cholesterol metabolism were assessed too. HMG-CoA reductase decreased only at the highest concentration of PA, while expression of HMG-CoA synthase and lipid exporters ABCA1 and ABCG1 was not affected. ABCG1 expression was compromised in LRP1 knockdown cells.

Extracellular availability of glucose and fatty acids affects mRNA expression of genes involved in surfactant lipid synthesis in T2C, suggesting metabolic pathway flexibility during different nutritional conditions. In the absence of extracellular lipid sources, glucose can be used by T2C for fatty acid synthesis. Furthermore, LRP1 expression affects the metabolic pathways used by T2C.