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Use of plasma free fatty acids by alveolar epithelial type 2 cell for surfactant lipid synthesis.

Surfactant is a lipoprotein complex that reduces surface tension during inspiration and prevents alveolar collapse during expiration. It is produced by alveolar epithelial type 2 cells (AT2) and is composed of phospholipids, proteins, and cholesterol. AT2 must tightly regulate lipid metabolism to ensure surfactant homeostasis. Disruptions in surfactant lipid levels are linked to adult lung diseases, but the pathways and extracellular substrates used for AT2 to maintain precise lipid metabolism are not understood. Prior research in the lab showed that expression of the low-density-lipoprotein receptor-related protein 1 (LRP1) is needed in AT2 for surfactant availability, and its loss compromises pulmonary function in vivo. In humans, SNPs in LRP1 are associated with multiple diseases, including chronic obstructive pulmonary disease. Understanding AT2 lipid metabolism will provide a foundation for future therapeutic strategies to improve lung function.

We studied the use of plasma free fatty acids (FFA) as a substrate for AT2 surfactant lipid production. Primary AT2 isolated from wild type (WT) and AT2-specific LRP1 inducible knockout mice (LRP1-/-) were incubated with [3H]-FFA and intracellular radioactivity was detected after 5 minutes. No differences were attributable to LRP1. In vivo, mice were intravenously injected with radiolabeled FFA. Blood was collected at 0.5, 5, 15 minutes and 4 h, and liver, heart, lung and surfactant were harvested at 4h. Most FFA was taken by tissues within 5 minutes equally for both genotypes. However, LRP1-/- showed lower radiolabel in lungs than WT mice 4h post-injection. No tracer was detected in surfactant for either genotype. In WT mice, there was a decrease of label detected from 15 minutes to 4h in hearts and lungs, without increased detection in blood.

These data show that lungs can take plasma FFA and suggest that they are consumed and not used as a source for surfactant lipid synthesis. LRP1 in AT2 is needed for this process.