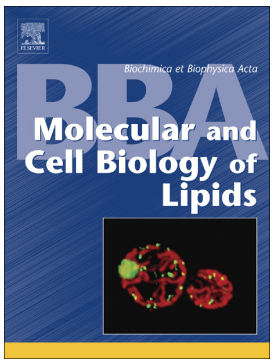

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Lysophosphatidylcholine Acyltransferase 3 Deficiency Impairs 3T3L1 Cell Adipogenesis through Activating Wnt/β-catenin Pathway

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Running title: LPCAT3 and adipogenesis

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Keywords: lysophosphatidylcholine acyltransferase3 gene knockdown,phosphatidylcholine remodeling, 3T3L1 adipocytes, Wnt/β-catenin pathway, adipogenesis, lipogenesis

ABSTRACT

Levels of polyunsaturated phosphatidylcholine (PC) influence plasma membrane structure and function.Phosphatidylcholine (PC) is synthesized de novo in the Kennedy pathway and then undergoes extensive deacylation/reacylation remodeling via Lands' cycle (non-Kennedy pathway). The reacylation is catalyzed by lysophosphatidylcholine acyltransferase (LPCAT), which adds a polyunsaturated fatty acid at the sn-2 position. Four LPCAT isoforms have been described to date, among which we found LPCAT3 to be the major isoform in adipose tissue, but its exact role in adipogenesis is unclear. In this study, we aimed to investigate whether LPCAT3 activity affects 3T3L1 cell adipogenic differentiation potential and its underline mechanism. Lentivirus-mediated LPCAT3 shRNA expression stably knocked down LPCAT3 in 3T3L1 preadipocytes and LPCAT3 deficiency dramatically reduced the levels of cellular polyunsaturated PCs. Importantly, we found that this deficiency activated the β-catenin dependent Wnt signaling pathway, which suppressed the expression of adipogenesis-related genes, thereby inhibiting 3T3L1 preadipocyte differentiation and lipid accumulation. Moreover, three different Wnt/β-catenin pathway inhibitors reversed the effect of LPCAP3 deficiency, suggesting that Wnt/β-catenin pathway activation is one of the causes for the observed phenotypes. To the best of our knowledge, we show here for the first time that PC remodeling is an important regulator of adipocyte differentiation.

Introduction