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Johannes Breithofer

Phospholipase A2 group IVD mediates the acyl-CoA independent synthesis of di- and triacylglycerol in mammalian cells

Johannes Breithofer[1], Dominik Bulfon[1], Gernot F. Grabner[1], Nermeen Fawzy[1], Anita Pirchheim[2], Lennart Hartig[1], Ulrike Taschler[1], Achim Lass[1,3], Dagmar Kratky[2,3], and Robert Zimmermann[1,3].

[1]Institute of Molecular Biosciences, University of Graz, Austria
[2]Gottfried Schatz Research Center, Molecular Biology and Biochemistry, Medical University of Graz, Austria
[3]BioTechMed-Graz, Austria

Mammalian acyltransferases, which catalyze the synthesis of triacylglycerol (TAG), use acyl-CoA as acyl donor and diacylglycerol (DAG) as acceptor. Plants and yeasts have evolved an additional mechanism of TAG synthesis using phospholipids as acyl donors and DAG as acceptor. Recent studies have shown that mammalian cells lacking the major acyl-CoA-dependent DAG acyltransferases (DGATs) are still capable of synthesizing TAG, indicating alternative synthetic pathways. Here, we show that an enzyme of the mammalian cytosolic phospholipase A2 family (PLA2G4D) catalyzes the transacylation of monoacylglycerol (MAG) and DAG, generating DAG and TAG, respectively. In this transacylation reaction, PLA2G4D uses phospholipids and acylglycerols as acyl donors. Overexpression of PLA2G4D in mammalian cells increased acylglycerol synthesis in the absence and presence of DGAT inhibitors and the incorporation of polyunsaturated fatty acids into TAG stores. Overall, our observations demonstrate that acyl-CoA-independent pathways can promote the synthesis of acylglycerols in mammalian cells.