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Novel roles of iPLA$_2\alpha$ in hepatic lipid metabolism

The group VIA phospholipase A$_2$ (iPLA$_2\alpha$) is highly expressed in metabolically active tissues and recent studies have connected the enzyme to a variety of metabolic diseases. Our studies are focused on the role of the enzyme in fatty liver disease. Exogenous unsaturated fatty acids (UFA) suppress expression and processing of sterol regulatory element binding protein-1 (SREBP-1), a transcription factor that regulates lipogenic gene expression in the liver. We compared hepatic lipid metabolism in iPLA$_2\alpha^{-/-}$ and wild type mice, to test the hypothesis that the iPLA$_2\alpha$ might be a source of endogenous UFA that regulate SREBP-1 and thereby modulate fatty liver. As expected, iPLA$_2\alpha^{-/-}$ livers contained more SREBP-1c and exhibited increased processing of this protein, compared to wild type livers. The changes in SREBP-1 expression/processing correlated with increased lipogenic gene expression, synthesis of fatty acids and triacylglycerols (TAG), and TAG mass in iPLA$_2\alpha^{-/-}$ livers. We also observed evidence of reduced secretion of TAG, cholesterol, and cholesterol ester in iPLA$_2\alpha^{-/-}$ hepatocytes, suggesting that TAG accumulation in iPLA$_2\alpha^{-/-}$ livers is the result of both increased synthesis and reduced secretion. Our studies indicated that iPLA$_2\alpha$-derived lipids contribute to pathogenesis of at least two metabolic diseases. Identification of the bioactive lipids and their mechanisms of action may uncover novel ways to treat diabetes mellitus and fatty liver disease.

Biography

Suzanne E Barbour has a BS (Chemistry) from Rutgers University, a PhD (Molecular Biology and Genetics) from The Johns Hopkins University, and Post-doctoral training from the University of California San Diego. From 1993-2015, she was in the faculty at the Virginia Commonwealth University School of Medicine. In 2013, she became a Program Director of Molecular and Cellular Biosciences at the National Science Foundation, where she ran a program in Cellular Dynamics and Function. She moved to the University of Georgia in July 2015 where currently she is the Dean of the Graduate School and Professor of Biochemistry and Molecular Biology.

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