Perilipin 5 regulates hepatic lipid metabolism and systemic glucose tolerance in mice

S.N. Keenan, J. Lo, R.C.R. Meex and M.J. Watt , Department of Physiology, Monash University, Clayton, VIC 3800, Australia.

The perilipin (Plin) family of proteins are abundant lipid droplet associated proteins, providing stabilization of intracellular lipid droplets and control of triglyceride lipolysis. Plin5 is an important regulator of cardiac lipid metabolism and is highly expressed in other oxidative tissues, such as the liver and muscle.

The aims of this study were to investigate the role of Plin5 in regulating lipid metabolism in hepatocytes and systemic glucose metabolism. Plin5−/− and Plin5+/+ mice were anaesthetized with 2% isoflurane gas and hepatocytes were isolated from their livers by collagenase digestion. Hepatocytes were cultured for one day prior to the assessment of lipid metabolism by radiometric methods.

Fatty acid uptake and storage into intracellular acylglycerols was not significantly different between Plin5−/− and Plin5+/+ hepatocytes. Plin5 ablation decreased free fatty acid oxidation by 35% and intrahepatic triglyceride-derived fatty acid oxidation by 69% compared with Plin5+/+ hepatocytes. The decrease in fatty acid oxidation was not due to defects in mitochondrial respiration. Treatment of hepatocytes with glucose resulted in increased lipogenesis (76%) in Plin5−/− compared with Plin5+/+ hepatocytes. Triglyceride secretion from hepatocytes was increased nearly 4-fold with Plin5 deletion. Studies in mice with liver specific deletion of Plin5 (Plin5-LKO) indicate that Plin5 in hepatocytes is essential for controlling triglyceride secretion from the liver and whole-body glucose tolerance.

Thus, we conclude that Plin5 is essential for maintaining lipid homeostasis, by facilitating fatty acid oxidation and inhibiting excessive triglyceride secretion, and that the absence of Plin5 causes glucose intolerance in mice.