



Insulin Regulation of Lipolysis in Adipocytes

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Abstract

Insulin suppresses adipose tissue lipolysis after a meal, playing a key role in metabolic homeostasis. This is mediated via the kinase Akt and its substrate phosphodiesterase 3B (PDE3B). Once phosphorylated and activated, PDE3B hydrolyses cAMP leading to the inactivation of cAMP-dependent protein kinase (PKA) and suppression of lipolysis. Here we identify that the PDE3B-interacting protein, a/b-hydrolase ABHD15 is a key regulator of adipocyte lipolysis. Deletion of ABHD15 in adipocytes resulted in a significant defect in insulin-mediated suppression of lipolysis with no effect on insulin-mediated glucose uptake. ABHD15 plays a role in suppressing PKA signalling as phosphorylation of the PKA substrate Perilipin-1 remained elevated in response to insulin upon ABHD15 deletion. ABHD15^{-/-} mice had normal glucose metabolism but defective fatty acid metabolism: plasma fatty acids were elevated upon fasting and in response to insulin and this was accompanied by elevated liver triglycerides upon b-adrenergic receptor activation. This is likely due to unrestrained lipolysis as evident by the larger triglyceride depletion in brown adipose tissue in these mice. Finally, ABHD15 protein levels were reduced in adipocytes from mice fed a Western diet, further implicating this protein in metabolic homeostasis. Collectively, ABHD15 regulates adipocyte lipolysis and liver lipid accumulation, providing novel therapeutic opportunities for modulating lipid homeostasis in disease.

Bio

Jacqueline Stöckli obtained her PhD from the University of Basel in Switzerland where she studied intracellular protein trafficking and trafficking signals. She then joined Prof David James' group when he was at the Garvan Institute in Sydney and she initially focused on insulin regulated protein trafficking with a particular interest in GLUT4 and vesicle trafficking proteins, such as Rabs and RabGAPs. In the James Lab she learned about Insulin Signalling, Glucose Metabolism and Mouse Physiology. She is currently a Senior Research Fellow at the Charles Perkins Centre and the School of Life and Environmental Sciences at the University of Sydney. Her group "Molecular Cell Biology" focuses on the insulin regulation of lipolysis.

Please note the new Friday afternoon seminar time of 3pm, drinks to follow

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