

## Adipocyte ATP-binding cassette G1 promotes triglyceride storage, fat mass growth, and human obesity

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Résumé en anglais	The role of ATP-binding Cassette G1 (ABCG1) transporter in human pathophysiology is still largely unknown. Indeed, beyond its role in mediating free cholesterol efflux to HDL, ABCG1 transporter equally promotes lipid accumulation in a triglyceride (TG)-rich environment through regulation of the bioavailability of Lipoprotein Lipase (LPL). As both ABCG1 and LPL are expressed in adipose tissue, we hypothesize that ABCG1 is implicated in adipocyte TG storage and could be then a major actor in adipose tissue fat accumulation. Silencing of Abcg1 expression by RNAi in 3T3-L1 preadipocytes compromised LPL-dependent TG accumulation during initial phase of differentiation. Generation of stable Abcg1 Knockdown 3T3-L1 adipocytes revealed that Abcg1 deficiency reduces TG storage and diminishes lipid droplet size through inhibition of Pparγ expression. Strikingly, local inhibition of adipocyte Abcg1 in adipose tissue from mice fed a high fat diet led to a rapid decrease of adiposity and weight gain. Analysis of two frequent ABCG1 SNPs (rs1893590 (A/C) and rs1378577 (T/G)) in morbidly obese individuals indicated that elevated ABCG1 expression in adipose tissue was associated with an increased PPARγ expression and adiposity concomitant to an increased fat mass and BMI (haplotype AT>GC). The critical role of ABCG1 regarding obesity was further confirmed in independent populations of severe obese and diabetic obese individuals. For the first time, this study identifies a major role of adipocyte ABCG1 in adiposity and fat mass growth and suggests that adipose ABCG1 might represent a potential therapeutic target in obesity.
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