Seipin promotes adipose tissue fat storage through the ER Ca^{2+}-ATPase SERCA

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Fats are the major forms of energy storage for organisms. Fat storage in adipose tissue and non-adipose tissue is tightly associated with human health. The disruption of fat storage homeostasis leads to severe human diseases including obesity, lipodystrophy, diabetes, and fatty liver. Berardinelli-Seip congenital lipodystrophy type 2 (BSCL2), one of the most severe lipodystrophy diseases in humans, is caused by mutations of the *Seipin* gene. Previous studies by Dr. Huang's laboratory, published in *PLoS Genetics* in 2011, have suggested that Seipin may tissue-autonomously participate in phosphatidic acid metabolism and subsequently prevent ectopic lipid droplet formation. Despite Seipin plays an important role in adipocyte differentiation and lipid homeostasis, its molecular functions are still unclear. Recent studies by Dr. Huang's team have showed that Seipin physically interacts with the sarco/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) in both *Drosophila* and humans. SERCA, an endoplasmic reticulum (ER) calcium pump, is solely responsible for transporting cytosolic calcium into the ER lumen. Like Seipin, SERCA cell-autonomously promotes lipid storage in *Drosophila* fat cells. Seipin modulates ER calcium homeostasis and acts genetically upstream of SERCA. These results reveal that Seipin promotes adipose tissue fat storage by regulating intracellular calcium homeostasis. This finding may lead to an effective therapy for BSCL2.

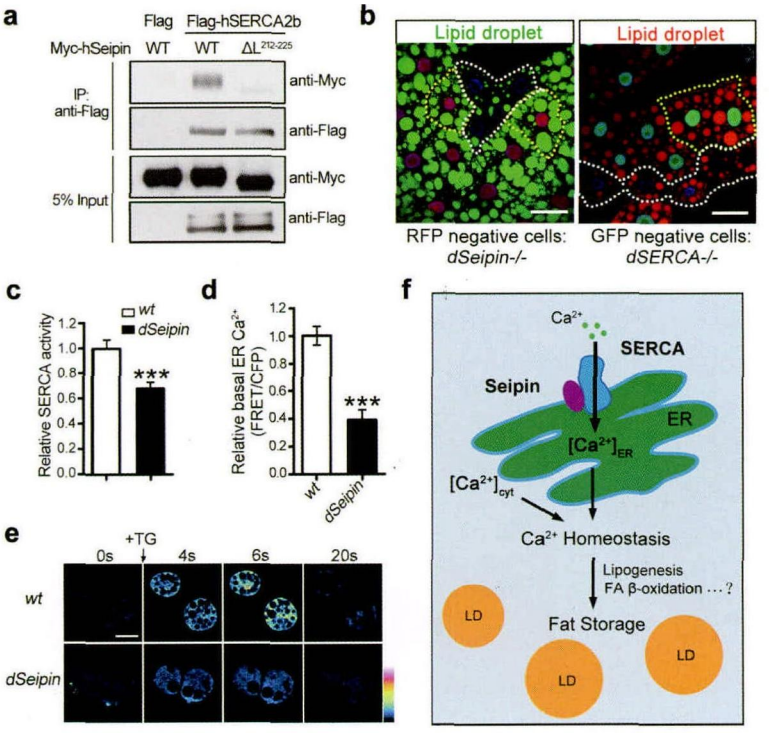

Figure Seipin promotes adipocytes fat storage by modulating Ca^{2+} homeostasis through SERCA. a, Seipin directly binds with SERCA. b, Seipin and SERCA cell-autonomously promote fat storage in *Drosophila* adipocytes. c-e, Seipin regulates Ca^{2+} homeostasis of adipocytes through SERCA. f, Model for the molecular function of Seipin in adipocytes fat storage.