Special Lecture Tokuron

基盤医学特論

日時：4 月 20 日(金) 17:00～18:30

場所：３号館６階 ライブラリー

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Understanding the biogenesis of lipid droplets and the development of adipose tissue through congenital generalized lipodystrophy

先天性全身型リポジストロフィーを通して脂肪滴形成と脂肪組織の発生を理解する

Obesity is characterized by accumulation of adipocytes loaded with lipid droplets (LDs). By genetic screening in yeast, we demonstrated that the deletion of a previously uncharacterized gene, *FLD1*, results in the formation of “super-sized” LDs (>50 times the volume of normal ones). Interestingly, null mutations of the mammalian orthologue of *FLD1*, *SEIPIN*, are associated with human Berardinelli-Seip Congenital Lipodystrophy 2 (BSCL2) which is characterized by the most severe form of insulin resistance and hepatic steatosis. We use mouse and fly models to confirm an essential role of SEIPIN in adipogenesis. Therefore, SEIPIN regulates two important aspects of lipid storage: adipocyte differentiation (systemic lipid storage) and lipid droplet formation (cellular lipid storage). Our recent results suggest that SEIPIN functions to regulate the activity of glycerol-3-phosphate acyl transferase (GPAT): SEIPIN deficiency leads to increased GPAT activity and the accumulation of certain lipid species, such as phosphatidic acid (PA). The accumulated PA may interfere with PPARgamma function during adipocyte differentiation, causing severe lipodystrophy. PA accumulation may also result in morphological changes of LDs, e.g. the formation of “supersized” LDs, in other cell types. These findings highlight the critical role of phospholipids in mammalian lipid storage, and also suggest that GPAT inhibitors may be used to treat human congenital generalized lipodystrophies.

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事前連絡不要