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Septin 11, Cytoskeletal Protein Involved in the Regulation of Lipid Metabolism in Adipocytes

Authors : Natalia Moreno-Castellanos, Amaia Rodriguez, Gema Frühbeck

Abstract : Introduction: In adipocytes, the cytoskeleton undergoes important expression and distribution in adipocytes rearrangements during adipogenesis and in obesity. Indeed, a role for these proteins in the regulation of adipocyte differentiation and response to insulin has been demonstrated. Recently, septins have been considered as new components of the cytoskeletal network that interact with other cytoskeletal elements (actin and tubulin) profoundly modifying their dynamics. However, these proteins have not been characterized as yet in adipose tissue. In this work, were examined the cellular, molecular and functional features of a member of this family, septin 11 (SEPT11), in adipocytes and evaluated the impact of obesity on the expression of this protein in human adipose tissue. Methods: Adipose gene and protein expression levels of SEPT11 were analysed in human samples. SEPT11 distribution was evaluated by immunocytochemistry, electronic microscopy, and subcellular fractionation techniques. GST-pull down, immunoprecipitation and a Yeast-Two Hybrid (Y2H) screening were used to identify the SEPT11 interactome. Gene silencing was employed to assess the role of SEPT11 in the regulation of insulin signaling and lipid metabolism in adipocytes. Results: SEPT11 is expressed in human adipocytes, and its levels increased in both omental and subcutaneous adipose tissue in obesity, with SEPT11 mRNA content positively correlating with parameters of insulin resistance in subcutaneous fat. In non-stimulated adipocytes, SEPT11 immunoreactivity showed a ring-like distribution at the cell surface and associated to caveolae. Biochemical analyses showed that SEPT11 interacted with the main component of caveolae, caveolin-1 (CAV1) as well as with the fatty acid-binding protein, FABP5. Notably, the three proteins redistributed and co-localized at the surface of lipid droplets upon exposure of adipocytes to oleate. In this line, SEPT11 silencing in 3T3-L1 adipocytes impaired insulin signaling and decreased insulin-induced lipogenesis. Conclusions: Those findings demonstrate that SEPT11 is a novel component of the adipocyte cytoskeleton that plays an important role in the regulation of lipid traffic, metabolism and can thus represent a potential biomarker of insulin resistance in obesity in adipocytes through its interaction with both CAV1 and FABP5.

Keywords : caveolae, lipid metabolism, obesity, septins
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