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The importance of heparan sulfate in 3T3-L1 cells and white adipose tissues

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Heparan sulfate (HS) is a highly sulfated glycosaminoglycan distributed on the cell surface and in the extracellular matrix. HS is involved in diverse biological events including embryonic development, angiogenesis and tumor metastasis. Recent studies revealed the pathophysiological involvement of HS in diabetes and we showed HS had a great impact on pancreatic β -cell function. However, the roles of HS in adipose tissue, an important tissue for glucose metabolism, remained to be elucidated.

First, we evaluated the roles HS in 3T3-L1, a cell line of mouse adipocytes. Biochemical assays indicated that HS promoted differentiation of 3T3-L1 possibly via enhancement of FGF signaling. Next, we generated and phenotyped white adipocyte-specific HS-deleted mice (cKO). Several differentiation markers in cKO adipocytes were decreased, emphasizing the important role of HS in adipocyte differentiation. We also confirmed the reduction in gene expression of essential factors for insulin-dependent glucose transport in cKO adipocytes. Indeed, glucose tolerance test revealed glucose intolerance due to insulin resistance in cKO mice. These results demonstrated that HS played an important role in adipocyte differentiation, leading to normal insulin sensitivity and glucose homeostasis.