Activin B: A potential target to cure diabetes

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Activins, members of transforming growth factor β (TGF β ; superfamily proteins, are known to play pivotal roles in the reproductive and developmental processes and their variety of functions have recently been explored in many cell types, while the role in glucose metabolism is poorly understood. Here we show that administration or overexpression of Activin B, which is endogenously produced in liver in the fasted state, markedly reduces blood glucose levels in both obese diabetic mice and insulin deficient diabetic mice. Activin B exerts glucose lowering effects via induction of FGF21 through the canonical pathway, suppression of gluconeogenesis and increased insulin secretion through the non-canonical pathway. Although expression of Activin B is not altered by obesity, expression of FSTL3, known as an inhibitory molecule for TGF β superfamily proteins, in adipocytes is increased by obesity and strongly correlates with BMI and insulin resistance in mice and humans. Indeed, metabolically beneficial effects of Activin B is completely canceled by co-administration of FSTL3, while suppression of FSTL3 improves glucose homeostasis in obese mice. Thus, increasing expression or action of Activin B may be a novel therapeutic strategy to cure diabetes.