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Target FoxO1 to prevent metabolic disorders

Zhiyong Cheng
Virginia Tech University, USA

Metabolic disease has been a globally growing epidemic. Increasing evidence suggests that the aberrant glucose and lipid metabolism in diabetic and obese individuals may arise from defective insulin secretion and action. We and others have established that the transcription factor forkhead box O1 (FoxO1) is hyperactive due to impaired insulin signaling, and regulates an array of genes relevant to mitochondrial and metabolic regulation. In addition, FoxO1 controls the expression and activity of peroxisome proliferator-activated receptor gamma (PPAR- γ), a key regulator of adipogenesis. The multiple roles of FoxO1 in metabolism have prompted us to target FoxO1 and explore new therapeutic options for diabetes and obesity. We found manipulation of FoxO1 activity with genetic approaches or small molecule antagonist potently suppresses gluconeogenesis and adipogenesis. Consistent with this, supplement of FoxO1 antagonist prevents hyperglycemia in mice. In this seminar, I will present the compelling evidence and prospect the future studies that may promote FoxO1 as the target for diabetes and obesity treatment.

zcheng@vt.edu