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Targeting IKKβ signaling for treatment of obesity and Diabetes

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Obesity is associated with a state of chronic low-grade inflammation that is a major contributor to insulin resistance and Diabetes. IκB kinase β (IKKβ), a central coordinator of inflammation through activation of NF-κB, has been implicated in the pathogenesis of obesity-associated metabolic disorders. However, the role of IKKβ in adipose tissue development and metabolism remains elusive. We have recently revealed an important role of IKKβ in the regulation of adipocyte differentiation and adipose tissue development in response to high-fat feeding. Deficiency of IKKβ in adipocyte precursor cells diminished the ability of these cells to differentiate into adipocytes. By analyzing mice that selectively lack IKKβ in the white adipose lineage, we found that deficiency of IKKβ protected mice from high-fat diet-induced obesity. Moreover, IKKβ deficient mice had decreased plasma proinflammatory cytokine levels and enhanced insulin sensitivity. Pharmacological inhibition of IKKβ also efficiently inhibited both murine and human adipocyte differentiation. Further, chronic treatment of mice with a potent IKKβ inhibitor ameliorated diet-induced obesity and insulin resistance. Our findings demonstrate a pivotal role of IKKβ in linking overnutrition to adipose tissue development and insulin resistance, and provide strong evidence for using appropriate IKKβ inhibitors in the treatment of obesity and metabolic disorders.

Biography

Changcheng Zhou received his PhD in 2004 from the University of California, Irvine. He performed Postdoctoral work at the University of Washington and the Rockefeller University. In 2010, he joined the faculty of the University of Kentucky and is currently an Assistant Professor in the Department of Pharmacology and Nutritional Sciences. He also holds an Adjunct Faculty position at the Rockefeller University. He has published more than 25 papers in reputed journals including *Journal of Experimental Medicine and Journal of Clinical Investigation* and has been serving as an editorial board member of several journals.

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