FoxO proteins in insulin action and metabolism.

Barthel A, Schmoll D, Unterman TG.

Source

Department of Endocrinology, Diabetes and Rheumatology, University Hospital Düsseldorf, Moorenstrasse 5, D-40225 Düsseldorf, Germany.

Erratum in


Abstract

There is increasing evidence that Forkhead box 'Other' (FoxO) proteins, a subgroup of the Forkhead transcription factor family, have an important role in mediating the effects of insulin and growth factors on diverse physiological functions, including cell proliferation, apoptosis and metabolism. Genetic studies in Caenorhabditis (Caenorhabditis elegans) and Drosophila demonstrate that FoxO proteins are ancient targets of insulin-like signaling involved in the regulation of metabolism and longevity. Studies in mammalian cells reveal that FoxO proteins regulate cell cycle progression and promote resistance to oxidative stress; both in vivo and cell culture studies support the concept that FoxO proteins have an important role in mediating the effects of insulin on metabolism, including its effects on hepatic glucose production. Phosphorylation and acetylation modulate FoxO function and control nuclear-cytoplasmic shuttling, DNA binding and protein-protein interactions. FoxO transcription factors exert positive and negative effects on gene expression, through direct binding to DNA target sites and protein-protein interactions with other transcription factors and coactivators. This paper provides an overview of studies leading to the identification of FoxO proteins as targets of insulin action and the mechanisms mediating the effects of insulin-like signaling on FoxO function, emphasizing the role of FoxO proteins in mediating the effects of insulin on metabolism.