

SIRT1 in metabolism and metabolic diseases

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SIRT1 is a highly-conserved NAD⁺-dependent protein deacetylase that plays essential roles in the regulation of energy metabolism, genomic stability, and stress response. Recent studies in a number of transgenic and tissue-specific knockout mouse models have revealed essential roles of this enzyme in the modulation of gene expression and metabolic activities in response to changes in cellular energy status. We have reported that upon high-fat diet feeding, mice lacking SIRT1 in hepatocytes develop hepatomegaly/steatosis due to decreased PPAR α /PGC-1 α signaling and fatty acid oxidation and ketogenesis. Metabolomic analyses confirmed that the SIRT1 liver specific knockout mice are defective in ketone bodies production as well as other lipid and amino acid metabolism. On the other hand, loss of a single-copy of SIRT1 gene systemically in mice results in enhanced insulin resistance, elevated hepatic gluconeogenesis and oxidative stress, and accumulation of lysolipids, yet surprisingly depletes hepatic glycerolipid metabolites and free fatty acids. Taken together, our studies indicate that SIRT1 not only is an essential metabolic sensor for many aspects of energy metabolism in central metabolic organs such as liver, but also plays a vital role in coordination of metabolic processes in these metabolic tissues and modulates whole-body energy homeostasis in response to nutrient signals.

Biography

Xiaoling Li received her Ph.D. in Biological Chemistry from the Johns Hopkins School of Medicine in 2002. She currently heads the Mammalian Aging Group within the Laboratory of Signal Transduction at the National Institutes of Health, National Institute of Environmental Health Sciences. She has published a number of peer-reviewed articles in leading biomedical journals, which reveal the essential function of SIRT1, a vital metabolic sensor and chromatin modification enzyme, in metabolic homeostasis in response to environmental signals.