25. SIRT1 enhances lipid storage and utilization in adipose tissues by promoting mitophagy: role of adiponectin

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Objective: SIRT1, as a NAD^+-dependent protein deacetylase, is a key energy sensor controlling cellular responses to nutrient availability and in turn protecting against ageing-related metabolic diseases. Previous study demonstrated mice overexpressing SIRT1 selectively in adipose tissues (Adipo-SIRT1) exhibit increased capacity of lipid storage and utilization, which contributes to their enhanced systemic insulin sensitivity. The present study aims to assess whether the beneficial effect of SIRT1 is dependent on adiponectin, an adipocyte-derived and insulin-sensitizing hormone.
Methods: In light of this, Adipo-SIRT1 mice have been crossed with adiponectin-knockout mice (AKO) to produce mice with both genetic modifications (Adipo-SIRT1/AKO).
Results: Compared to Adipo-SIRT1 mice, adiponectin deficiency prevents SIRT1-mediated lipid storage in adipose tissues, but enhances ectopic lipid accumulation in liver. Compared to wild type mice, Adipo-SIRT1/AKO mice are less insulin sensitive and show impaired glucose tolerance. Mechanistically, mitophagy is enhanced by SIRT1 overexpression in adipose tissues, accompanied by decreased activity of mitochondrial complex-I.
Conclusions: Adiponectin is involved in the regulation of mitochondria functions by SIRT1, through modulating lipid constituents in adipose tissues.
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