Succinate dehydrogenase is a direct target of sirtuin 3 deacetylase activity

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Résumé en anglais	BACKGROUND: Sirtuins (SIRT1-7) are a family of NAD-dependent deacetylases and/or ADP-ribosyltransferases that are involved in metabolism, stress responses and longevity. SIRT3 is localized to mitochondria, where it deacetylates and activates a number of enzymes involved in fuel oxidation and energy production. METHODOLOGY/PRINCIPAL FINDINGS: In this study, we performed a proteomic screen to identify SIRT3 interacting proteins and identified several subunits of complex II and V of the electron transport chain. Two subunits of complex II (also known as succinate dehydrogenase, or SDH), SDHA and SDHB, interacted specifically with SIRT3. Using mass spectrometry, we identified 13 acetylation sites on SDHA, including six novel acetylated residues. SDHA is hyperacetylated in SIRT3 KO mice and SIRT3 directly deacetylates SDHA in a NAD-dependent manner. Finally, we found that SIRT3 regulates SDH activity both in cells and in murine brown adipose tissue. CONCLUSIONS/SIGNIFICANCE: Our study identifies SDHA as a binding partner and substrate for SIRT3 deacetylase activity. SIRT3 loss results in decreased SDH enzyme activity, suggesting that SIRT3 may be an important physiological regulator of SDH activity.

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