

SUPPRESSOR OF CYTOKINE SIGNALING 6 (SOCS6) INDUCES CHANGES IN MITOCHONDRIAL MORPHOLOGY AND FUNCTION IN MAMMALIAN CELLS

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Mitochondria are highly motile organelles that constantly undergo fission and fusion. Impairment of mitochondrial dynamics is frequently associated with mitochondrial dysfunction and linked to the pathogenesis of neurodegenerative diseases and cancer. In this study, we identified human suppressor of cytokine signaling 6 (SOCS6) as a novel mitochondrial protein that interferes with mitochondrial dynamics. By confocal microscopy, ectopically expressed SOCS6 is predominantly localized in mitochondria, and the carboxyl-terminal SOCS box is important for the mitochondrial localization. We further showed that localization of SOCS6 in mitochondria is accompanied with increased mitochondrial fragmentation, which can be reversed by coexpression of mitochondrial fusion proteins Mfn1 or Mfn2 but not the dominant negative version of the fission protein Drp1, Drp1K38A. Our data suggest that SOCS6 interferes with mitochondrial dynamics by interrupting the fusion process. Firstly, SOCS6 expression severely impairs the dynamics and mobility of mitochondria in live cells by fluorescence recovery after photobleaching (FRAP) experiments. Secondly, SOCS6 expression significantly hampers intermitochondrial transfer and fusion in the somatic hybrid produced by PEG-induced fusion. As a consequence, SOCS6 expression attenuated mitochondrial membrane potential and mitochondrial function as evidenced by increased oxygen consumption and lactate production, leading to increased cellular ATP levels.

Keywords:

SOCS6, mitochondrial dynamic.