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Autor(en) des Beitrags:

Um, Sung Hee; Sticker-Jantscheff, Melanie; Chau, Gia Cac; Vintersten, Kristina; Mueller, Matthias; Gangloff, Yann-Gael; Adams, Ralf H; Spetz, Jean-Francois; Elghazi, Lynda; Pfluger, Paul T; Pende, Mario; Bernal-Mizrachi, Ernesto; Tauler, Albert; Tschöp, Matthias H; Thomas, George; Kozma, Sara C

Titel des Beitrags:

S6K1 controls pancreatic ? cell size independently of intrauterine growth restriction.

Abstract:

Type 2 diabetes mellitus (T2DM) is a worldwide heath problem that is characterized by insulin resistance and the eventual loss of ? cell function. As recent studies have shown that loss of ribosomal protein (RP) S6 kinase 1 (S6K1) increases systemic insulin sensitivity, S6K1 inhibitors are being pursued as potential agents for improving insulin resistance. Here we found that S6K1 deficiency in mice also leads to decreased ? cell growth, intrauterine growth restriction (IUGR), and impaired placental development. IUGR is a common complication of human pregnancy that limits the supply of oxygen and nutrients to the developing fetus, leading to diminished embryonic ? cell growth and the onset of T2DM later in life. However, restoration of placental development and the rescue of IUGR by tetraploid embryo complementation did not restore ? cell size or insulin levels in S6K1-/- embryos, suggesting that loss of S6K1 leads to an intrinsic ? cell lesion. Consistent with this hypothesis, reexpression of S6K1 in ? cellsof S6K1-/- mice restored embryonic ? cell size, insulin levels, glucose tolerance, and RPS6 phosphorylation, without rescuing IUGR. Together, these data suggest

that a nutrient-mediated reduction in intrinsic ? cell S6K1 signaling, rather than IUGR, during fetal development may underlie reduced ? cell growth and eventual development of T2DM later in life.

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