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Title: Upstream Signalling of mTORC1 and Its Hyperactivation in Type 2 Diabetes (T2D)

Article Type: Mini Review

Keywords: mTORC1 restriction; insulin resistance; hypertriglyceridemia; diabetes; Diabetes

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Running Title: Restriction of Hyperactive mTORC1 in Diabetes.

Keywords: mTORC1 restriction, insulin resistance, hypertriglyceridemia, diabetes

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ABSTRACT

Mammalian target of rapamycin complex 1 (mTORC1) is known to play a major role in cell growth, proliferation, polarity, differentiation, development, and controls transitioning between anabolic and catabolic states of the cell. It collects almost all extracellular and intracellular signals from growth factors, nutrients, and maintains cellular homeostasis, and is involved in a number of pathological conditions including, neurodegeneration, type 2 diabetes (T2D), obesity, and cancer. In this review, we summarize current knowledge of upstream signaling of mTORC1 to explain etiology of T2D and hypertriglyceridemia, in which state, a role of telomere attrition is explained. We also discuss if the chronic inhibition of mTORC1 can reverse adverse effects resulting from its hyperactivation. In conclusion, we suggest the regulatory role of telomerase (TERT) and hexokinase II (HKII) on mTORC1 as a possible remedy to treat its hyperactivation. The former inhibits mTORC1 under nutrient-rich while the latter under starved condition. We also provide an idea of TOS (TOR signaling) motifs that can be utilized for the regulation of mTORC1.