Metformin combats adipose tissue expansion via AMPK

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(HealthDay)—AMPK activation by metformin is associated with

inhibition of interstitial fibrosis and suppression of transforming growth factor β-1 (TGF-β1), according to a study published online May 13 in *Diabetes*.

Ting Luo, from the Boston University School of Medicine, and colleagues explored the initiation of aberrant extracellular matrix (ECM) remodeling of white adipose tissue (WAT) during obesity development.

The researchers found that metformin treatment inhibited excessive ECM deposition in WAT of ob/ob mice and diet-induced obese mice, with reduction in collagen deposition surrounding adipocytes and expression of fibrotic genes, including the regulator of collagen cross-linking, LOX. Metformin-induced inhibition of interstitial fibrosis may be due to activation of AMPK and suppression of TGF-β1/Smad3 signaling, which leads to enhanced systemic insulin sensitivity. In primary cells from the stromal vascular fraction, the dominant negative AMPK abolished the ability of metformin to suppress TGF-β1-induced fibrogenesis. AMPK agonists and the constitutively active AMPK suppressed TGF-β1-induced insulin resistance in 3T3L1 adipocytes. There was also a correlation for interstitial fibrosis with AMPK inactivation, TGF-β1/Smad3 induction, aberrant ECM production, myofibroblast activation, and adipocyte apoptosis in omental fat depots of obese humans.

"Collectively, integrated AMPK activation and TGF-β1/Smad3 inhibition may provide a potential therapeutic approach to maintain ECM flexibility and combat chronically uncontrolled adipose tissue expansion in obesity," the authors write.

More information: Full Text (subscription or payment may be required)