Metformin's potential role in atherosclerosis explored

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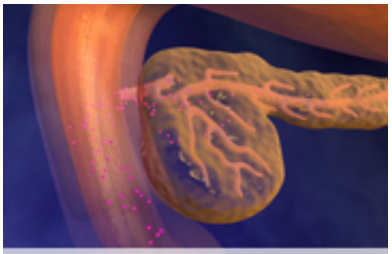
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(HealthDay)—Metformin's role in atherosclerosis may be inhibition of monocyte-to-macrophage differentiation via AMPK-mediated inhibition of STAT3 activation, according to research published online Dec. 31 in *Diabetes*.

Sathish Babu Vasamsetti, from the Indian Institute of Chemical Technology in Hyderabad, and colleagues examined the molecular mechanisms responsible for monocyte-to-macrophage differentiation. They also examined the effect of metformin in regressing Angiotensin-II-mediated atheromatous plaque formation in ApoE$^{-/-}$ mice.

The researchers observed a dose- and time-dependent downregulation in AMPK activity during PMA-induced monocyte-to-macrophage differentiation; this was accompanied by upregulation of production of

pro-inflammatory cytokines. These were significantly attenuated with AMPK activators metformin and AICAR. In the absence of PMA, compound C-induced inhibition of AMPK activity alone was not effective for promoting monocyte-to-macrophage differentiation. JNK activity inhibited the inflammation induced by PMA, but not differentiation. Both inflammation and monocyte-to-macrophage differentiation were inhibited with inhibition of STAT3 activity. Increased AMPK activation with metformin and AICAR decreased STAT3 phosphorylation, causing inhibition of the differentiation of monocytes to macrophages. In $ApoE^{-/-}$ mice, metformin attenuated Ang-II-induced atheromatous plaque formation and aortic aneurysm, partly by decreasing infiltration of monocytes.

"We conclude that AMPK-STAT3 axis plays a pivotal role in regulating monocyte-to-macrophage differentiation and that AMPK activators by decreasing STAT3 phosphorylation through increased AMPK activity inhibit monocyte-to-macrophage differentiation," the authors write.

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