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Metformin inhibits the senescence-associated secretory phenotype by interfering with IKK/NF-κB activation.

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Abstract

We show that the antidiabetic drug metformin inhibits the expression of genes coding for multiple inflammatory cytokines seen during cellular senescence. Conditioned medium (CM) from senescent cells stimulates the growth of prostate cancer cells but treatment of senescent cells with metfomin inhibited this effect**. Bioinformatic analysis of genes downregulated by metformin suggests that the drug blocks the activity of the transcription factor NF-κB**. In agreement, metformin prevented the translocation of NF-κB to the nucleus and inhibited the phosphorylation of IκB and IKKα/β, events required for activation of the NF-κB pathway. These effects were not dependent on AMPK activation or on the context of cellular senescence, as metformin inhibited the NF-κB pathway stimulated by LPS in ampk null fibroblasts and in macrophages. **Taken together, our results provide a novel mechanism for the anti-aging and anti-neoplastic effects of metformin reported in animal models and in diabetic patients taking this drug.**