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Methylsulfonylmethane suppresses breast cancer growth by down-regulating STAT3 and STAT5b pathways.

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Source

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Abstract

Breast cancer is the most aggressive form of all cancers, with high incidence and mortality rates. The purpose of the present study was to investigate the molecular mechanism by which methylsulfonylmethane (MSM) inhibits breast cancer growth in mice xenografts. MSM is an organic sulfur-containing natural compound without any toxicity. In this study, we demonstrated that MSM substantially decreased the viability of human breast cancer cells in a dose-dependent manner. MSM also suppressed the phosphorylation of STAT3, STAT5b, expression of IGF-1R, HIF-1α, VEGF, BrK, and p-IGF-1R and inhibited triple-negative receptor expression in receptor-positive cell lines. Moreover, MSM decreased the DNA-binding activities of STAT5b and STAT3, to the target gene promoters in MDA-MB 231 or co-transfected COS-7 cells. We confirmed that MSM significantly decreased the relative luciferase activities indicating crosstalk between STAT5b/IGF-1R, STAT5b/HSP90α, and STAT3/VEGF. To confirm these findings in vivo, xenografts were established in Balb/c athymic nude mice with MDA-MB 231 cells and MSM was administered for 30 days. Concurring to our in vitro analysis, these xenografts showed decreased expression of STAT3, STAT5b, IGF-1R and VEGF. Through in vitro and in vivo analysis, we confirmed that MSM can effectively regulate multiple targets including STAT3/VEGF and STAT5b/IGF-1R. These are the major molecules involved in tumor development, progression, and metastasis. Thus, we strongly recommend the use of MSM as a trial drug for treating all types of breast cancers including triple-negative cancers.

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