PPAR-g agonists have potential therapeutic role in gastric carcinoma?

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Recently, the potential of PPAR-γ as a target for the prevention and treatment of cancer has been widely studied. However, the potential therapeutic role of PPAR-γ agonists has been questioned, based on contradictory results. Studies using animal models of colon cancer found that PPAR-γ agonists increased the development of colon tumors.

This contradictory result was supplemented by a recent report using transgenic mice expressing a constitutive active form of PPAR-γ in mammary glands which showed that PPAR-γ signaling accelerated tumor development in mammary glands. The actual role of PPAR-γ in cancer has been complicated by recent findings that PPAR-γ agonists affect cancer cells independently of PPAR-γ, and silencing of PPAR-γ and a PPAR-γ antagonist inhibit cancer cell growth. To date, the role of PPAR-γ in gastric carcinogenesis remains unclear.

A research article to be published on August 21, 2009 in the World Journal of Gastroenterology addresses this question. A study from China found that PPAR-γ may be involved in gastric carcinogenesis, and that the PPAR-γ agonist 15d-PGJ2 may inhibit the growth of human gastric carcinoma MGC803 cell by inducing apoptosis and G1/G0 arrest, involving survivin, Skp2 and p27, but via a PPAR-γ-independent pathway.

The study showed that the PPAR-γ agonist 15d-PGJ2 inhibited growth of cultured gastric cancer MGC803 cells, and demonstrated that the PPAR-γ antagonist GW9662 did not block this effect of 15d-PGJ2 and

that 2.5 μM GW9662 inhibited growth of MGC803 cells. Furthermore, PPAR-γ siRNA remarkably inhibited the growth of MGC803 cells.

These results indicated that 15d-PGJ2 inhibited growth of cultured gastric carcinoma MGC803 cells by a PPAR-γ-independent pathway. These results also suggest that PPAR-γ agonists could be useful in the chemoprevention or chemotherapy of gastric malignancies.

More information: Ma XM, Yu H, Huai N. Peroxisome proliferator-activated receptor-g is essential in the pathogenesis of gastric carcinoma. *World J Gastroenterol* 2009; 15(31): 3874-3883; www.wjgnet.com/1007-9327/15/3874.asp

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