

Nature Medicine **4**, 1046 - 1052 (1998)

doi:10.1038/2030

Differentiation and reversal of malignant changes in colon cancer through PPAR γ

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Abstract

PPAR γ is a nuclear receptor that has a dominant regulatory role in differentiation of cells of the adipose lineage, and has recently been shown to be expressed in the colon. We show here that PPAR γ is expressed at high levels in both well- and poorly-differentiated adenocarcinomas, in normal colonic mucosa and in human colon cancer cell lines. Ligand activation of this receptor in colon cancer cells causes a considerable reduction in linear and clonogenic growth, increased expression of carcinoembryonic antigen and the reversal of many gene expression events specifically associated with colon cancer. Transplantable tumors derived from human colon cancer cells show a significant reduction of growth when mice are treated with troglitazone, a PPAR γ ligand. These results indicate that the growth and differentiation of colon cancer cells can be modulated through PPAR γ .