

## **Inhibitory Effects of n-3 Polyunsaturated Fatty Acids on Sigmoid Colon Cancer Transformants.**

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Various types of polyunsaturated fatty acids (PUFAs) have been suggested to exert different effects on the colon in terms of promotion or inhibition of tumor development. Results of in vitro and in vivo studies are, however, inconsistent and it remains unclear whether or not the cellular effects of PUFAs change along with the malignant transformation of colonic cells.

In this study, we used the NIH3T3 cell line and its SIC (sigmoid colon cancer) oncogene transformants to compare the effects of PUFAs on the proliferation of non-malignant and malignant cells. We also determined the cellular utilization of fatty acids in media by a high-performance liquid chromatography method. The addition of exogenous arachidonic acid (ARA, an n-6 fatty acid), eicosapentaenoic acid (EPA, n-3), and docosahexaenoic acid (DHA, n-3) exerted different effects on NIH3T3 cells, and on SIC transformants, in which selective inhibitory effects were observed at media concentrations ranging from 10 to 20 microg/ml.

In cells cultured in media supplemented with EPA or DHA at a concentration of 2 microg/ml, which had no effect on cell proliferation, the cellular utilization of linoleic acid (n-6), a precursor of n-3 fatty acids, was inhibited. This inhibition was stronger in SIC transformants than in NIH3T3 cells ( $P < 0.05$ ). There was no difference in the utilization of fatty acids between the two cell lines cultured in media supplemented with ARA.

We conclude that the cellular response to exogenous long-chain PUFAs is modified during the course of malignant transformation, and that EPA and DHA (n-3 PUFAs) appear to have specific inhibitory effects on cancer cells and may thus enhance the host defense against colon cancer.

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