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Omega 3 but not omega 6 fatty acids inhibit AP-1 activity and cell transformation in JB6 cells.

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Abstract

Epidemiological and animal-based investigations have indicated that the development of skin cancer is in part associated with poor dietary practices. Lipid content and subsequently the derived fatty acid composition of the diet are believed to play a major role in the development of tumorigenesis. Omega 3 (omega3) fatty acids, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), can effectively reduce the risk of skin cancer whereas omega 6 (omega6) fatty acids such as arachidonic acid (AA) reportedly promote risk. To investigate the effects of fatty acids on tumorigenesis, we performed experiments to examine the effects of the omega3 fatty acids EPA and DHA and of the omega6 fatty acid AA on phorbol 12tetradecanoate 13-acetate (TPA)-induced or epidermal growth factor (EGF)-induced transcription activator protein 1 (AP-1) transactivation and on the subsequent cellular transformation in a mouse epidermal JB6 cell model. DHA treatment resulted in marked inhibition of TPA- and EGF-induced cell transformation by inhibiting AP-1 transactivation. EPA treatment also inhibited TPA-induced AP-1 transactivation and cell transformation but had no effect on EGF-induced transformation. AA treatment had no effect on either TPA- or EGFinduced AP-1 transactivation or transformation, but did abrogate the inhibitory effects of DHA on TPA- or EGF-induced AP-1 transactivation and cell transformation in a dose-dependent manner. The results of this study demonstrate that the inhibitory effects of omega3 fatty acids on tumorigenesis are more significant for DHA than for EPA and are related to an inhibition of AP-1. Similarly, because AA abrogates the beneficial effects of DHA, the dietary ratio of omega6 to omega3 fatty acids may be a significant factor in mediating tumor development.

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