Are Omega-3 Fatty Acids Effective in Enhancing Tumoricidal Cell Activity?1

Kevin L. Fritsche2

Department of Animal Sciences, University of Missouri, Columbia, MO

EXPANDED ABSTRACT

KEY WORDS: • eicosanoid • anti-inflammatory • IL-12

Evidence from epidemiological and animal experiments suggests that consumption of a diet rich in omega-3 fatty acids may diminish the incidence and/or severity of cancers of the prostate, breast, and colon (1–4). Several mechanisms have been proposed to explain the putative effect of these nutrients on cancer, including direct cytotoxic action on tumor cells, alteration of carcinogen metabolism, reduction in eicosanoid biosynthesis, alteration of gene expression, and improvement in one or more components of the host immune response against the tumor cells (5–7). Several different types of immune cells are thought to play a role in immunosurveillance [e.g., natural killer (NK), NKT, and γδ T cells], while CD8+ T cells and cytolytic macrophages are central to immunotherapeutic treatment of existing tumors in cancer patients. The impact of omega-3 fatty acids on the immune system is generally characterized as anti-inflammatory (8). Reduced biosynthesis of various pro-inflammatory eicosanoids (e.g., prostaglandin E2 and leukotriene B4) and cytokines (e.g., TNF-α, IL-1β, and IL-6) are well documented in humans and various animal models of cancer. Such changes may help explain the beneficial impact of omega-3 fatty acids on the tissue wasting and weight loss of cancer (i.e., cancer cachexia) (9). Elevated intake of omega-3 fatty acids is associated with reduced IL-12 and IFN-γ biosynthesis (10). These cytokines play a critical role in promoting Th1-type immune responses that are essential for the generation of cytolytic CD8+ T-cells and macrophages. That omega-3 fatty acids diminish in vivo host responsiveness to IFN-γ and diminish in vitro signal transducers and activators of transcription phosphorylation may undermine the usefulness of omega-3 fatty acids in adjunctive immunotherapy protocols (11). Furthermore, studies with animals, and a recent human supplementation study, suggest that omega-3 fatty acids may reduce basal NK cell activity (12–14). So it appears that alterations in various components of the immune system by omega-3 fatty acids may reduce host tumor immunity (15). However, little is known about the impact of these fatty acids on the function of NKT or γδ T cells. Recent advances now make it possible to assess NK-cell activity in human blood samples, even though they only make up ~0.1% of the leukocytes present (16). In summary, it appears that whatever beneficial effects omega-3 fatty acids may have on cancer development or treatment, enhanced antitumor immunity is not playing a significant role in this activity.

Research needs

1. At present, there is nothing known about the impact of omega-3 fatty acids on the function of NKT or γδ T cells in animals or humans.
2. Evaluation of IL-12 and IFN-γ production during tumor development and immunotherapy should be conducted, since the existing data were collected in an infectious disease model.

LITERATURE CITED

acids and docosahexaenoic acid impair murine interleukin-12 and interferon-
11. Irons R, Fritsche KL. Omega-3 polyunsaturated fatty acids impair in vivo
12. Purasiri P, McKechnie A, Heys SD, Eremin O. Modulation in vitro of
human natural cytotoxicity, lymphocyte proliferative response to mitogens and
13. Almallah YZ, El-Tahir A, Heys SD, Richardson S, Eremin O. Distal procto-
colitis and n-3 polyunsaturated fatty acids: the mechanism(s) of natural cytotox-
Calder PC. Dietary supplementation with eicosapentaenoic acid, but not with
other long-chain n-3 or n-6 polyunsaturated fatty acids, decreases natural
539–48.
15. Salem ML, Kishihara K, Abe K, Matsuzaki G, Nomoto K. N-3 polyunsat-
urated fatty acids accentuate B16 melanoma growth and metastasis through
suppression of tumoricidal function of T cells and macrophages. Anticancer Res.