Omega-3 fatty acids:

Burns, C. P., S. Halabi, et al. (2004). "Phase II study of high-dose fish oil capsules for patients with cancer-related cachexia." Cancer **101**(2): 370-8.

BACKGROUND: The authors undertook a multiinstitutional Phase II cooperative group study to examine the potential of oral fish oil fatty acid supplements administered at high doses to slow weight loss and to improve quality of life in patients with malignancy-related cachexia. METHODS: Patients with advanced malignancy and weight loss > or = 2% of body weight in the preceding month took concentrated, high-dose omega-3 fatty acid capsules (7.5 g eicosapentaenoic acid plus docosahexaenoic acid for a 70 kg individual) that were supplied by the National Institutes of Health. RESULTS: Forty-three patients with moderate or severe malnutrition were enrolled. The median time receiving treatment was 1.2 months. For the 36 patients who took at least 1 capsule and did not have edema, there was a weight change ranging from -6.2 kg to +3.5 kg and an overall median weight loss of 0.8 kg. Twenty-four patients had weight stabilization (a gain of < or = 5% or a loss of < 5%), 6 patients gained > 5% of their body weight, and 6 patients lost > or = 5% of their body weight. There was marked variability in the tolerability of the capsules, and many patients had gastrointestinal side effects. There was a correlation between time receiving treatment and weight gain for the 22 patients who were able to tolerate the capsules for at least 1 month. Quality-of-life scores were superior for patients who gained weight. CONCLUSIONS: **A majority of patients did not gain weight, and in that sense, the results of the study were unfavorable. However, a small but definite subset of patients had weight stabilization or weight gain. This suggests that omega-3 fatty acids have potential utility at the study doses, which were more than twice the doses used in published Phase III studies.**

Rhodes, L. E., H. Shahbakhti, et al. (2003). "Effect of eicosapentaenoic acid, an omega-3 polyunsaturated fatty acid, on UVR-related cancer risk in humans. An assessment of early genotoxic markers." Carcinogenesis **24**(5): 919-25.

Dietary omega-3 polyunsaturated fatty acids (omega-3 PUFAs) protect against photocarcinogenesis in animals, but prospective human studies are scarce. The mechanism(s) underlying the photoprotection are uncertain, although omega-3 PUFAs may influence oxidative stress. We examined the effect of supplementation on a range of indicators of ultraviolet radiation (UVR)-induced DNA damage in humans, and assessed effect on basal and post-UVR oxidative status. In a double-blind randomized study, 42 healthy subjects took 4 g daily of purified omega-3 PUFA, eicosapentaenoic acid (EPA), or monounsaturated, oleic acid (OA), for 3 months. EPA was bioavailable; the skin content at 3 months showing

an 8-fold rise from baseline, P < 0.01. No consistent pattern of alteration in basal and UVR-exposed skin content of the antioxidants glutathione, vitamins E and C or lipid peroxidation, was seen on supplementation. Sunburn sensitivity was reduced on EPA, the UVR-induced erythemal threshold rising from a mean of 36 (SD 10) mJ/cm(2) at baseline to 49 (16) mJ/cm(2) after supplementation, P < 0.01. Moreover, UVR-induced skin p53 expression, assessed immunohistochemically at 24 h post-UVR exposure, fell from a mean of 16 (SD 5) positive cells/100 epidermal cells at baseline to 8 (4) after EPA supplementation, P < 0.01. Peripheral blood lymphocytes (PBL) sampled on 3 successive days both pre- and post-supplementation, showed no change with respect to basal DNA single-strand breaks or oxidative base modification (8-oxo-dG). However, when susceptibility of PBL to ex vivo UVR was examined using the comet assay, this revealed a reduction in tail moment from 84.4 (SD 3.4) at baseline to 69.4 (3.1) after EPA, P = 0.03. No significant changes were seen in any of the above parameters following OA supplementation. Reduction in this range of early markers, i.e. sunburn, **UVR-induced p53 in skin and strand breaks in PBL, indicate protection by dietary EPA against acute UVR-induced genotoxicity; longer-term supplementation might reduce skin cancer in humans.**

Gogos, C. A., P. Ginopoulos, et al. (1998). "Dietary omega-3 polyunsaturated fatty acids plus vitamin E restore immunodeficiency and prolong survival for severely ill patients with generalized malignancy: a randomized control trial." Cancer **82**(2): 395-402.

BACKGROUND. The aim of the current prospective, randomized control study **was to investigate the effect of dietary omega-3 polyunsaturated fatty acids plus vitamin E on the immune status and survival of well-nourished and malnourished patients with generalized malignancy.** METHODS. Sixty patients with generalized solid tumors were randomized to receive dietary supplementation with either fish oil (18 g of omega-3 polyunsaturated fatty acids, PUFA) or placebo daily until death. Each group included 15 well-nourished and 15 malnourished patients. The authors measured total T cells, T-helper cells, T-suppressor cells, natural killer cells, and the synthesis of interleukin-1, interleukin-6, and tumor necrosis factor by peripheral blood mononuclear cells before and on Day 40 of fish oil supplementation. Karnofsky performance status, nutritional state, and survival were also estimated. RESULTS. The ratio of T-helper cells to T-suppressor cells was significantly lower in malnourished patients. **Omega-3 PUFA had a considerable immunomodulating effect by increasing this ratio in the subgroup of malnourished patients.** There were no significant differences in cytokine production among the various groups, except for a decrease in tumor necrosis factor production in malnourished cancer

patients, which was restored by omega-3 fatty acids. The mean survival was significantly higher for the subgroup of well-nourished patients in both groups, whereas omega-3 fatty acids prolonged the survival of all the patients. CONCLUSIONS. **Malnutrition appears to be an important predictor of survival for patients with end stage malignant disease. Omega-3 polyunsaturated fatty acids had a significant immunomodulating effect and seemed to prolong the survival of malnourished patients with generalized malignancy.**

Gogos, C. A., P. Ginopoulos, et al. (1995). "The effect of dietary omega-3 polyunsaturated fatty acids on T-lymphocyte subsets of patients with solid tumors." Cancer Detect Prev **19**(5): 415-7.

The effect of omega-3 polyunsaturated fatty acids (PUFA) on the immune system seems to be beneficial. There has been a number of studies concerning the effect of dietary omega-3 PUFA on different immune parameters. **The aim of our present study was to investigate the effect of dietary omega-3 PUFA on T-cell subsets and natural killer (NK) cells of patients with solid tumors.** We studied 20 patients with solid tumors who received 18 g fish oil/day for 40 consecutive days. We detected a significant increase in T-helper/T-suppressor cell ratio 40 days into omega-3 supplementation, due mainly to a decrease in the number of suppressor T cells. **We concluded that dietary omega-3 fatty acids may have a beneficial effect on the already compromised immune system of patients suffering from solid tumors.**

Yam, D., A. Peled, et al. (2001). "Suppression of tumor growth and metastasis by dietary fish oil combined with vitamins E and C and cisplatin." Cancer Chemother Pharmacol **47**(1): 34-40.

PURPOSE: **The anticancer activity of omega-3 polyunsaturated fatty acids (omega-3 PUFA) has been shown in a large number of studies. This study was undertaken to analyze the combined effect of omega-3 PUFA and antioxidative vitamins on the level of spontaneous metastatic dissemination.** The supportive effect of this dietary combination on chemotherapy with cisplatin (CP) was determined in parallel. METHODS: C57BL/6J mice bearing the Lewis lung carcinoma 3LL were fed ad libitum one of three isocaloric diets containing 5% soybean oil supplemented with 40 mg/kg alpha-tocopherol acetate (SO diet), or 4% fish oil plus 1% corn oil, and basal amounts of vitamin E (FO diet) or FO diet supplemented with vitamins E and C (FO+E+C diet). These diets were tested in combination with the conventional cytotoxic agent CP in a series of regimens. Tumor growth, feed consumption, body weight, lung metastasis and lung histology were followed. RESULTS: Both the FO dietary groups showed significantly lower tumor development than the SO group in all examined parameters, indicating that omega-3 PUFA

have anticancer activity. However, the FO diet, in comparison with the FO+E+C diet induced a significantly slower rate of tumor growth, and lower metastatic load, as reflected in lung weight. The decrease in the anticancer activity of FO by the addition of vitamins E and C suggests that in situ oxidation of omega-3 PUFA underlies their anticancer action. **It is thus proposed that oxidized omega-3 PUFA accumulates in the membranes and the cytosol of tumor cells, reducing their vitality and eventually leading to their death.** No signs of anorexia or cachexia were observed in either FO group, in contrast to the SO group. CP treatment with the SO diet had no apparent therapeutic effect, while with the FO diets it reduced the metastatic load. The best regimen of this combined treatment was FO diet followed by CP treatment with FO diet supplemented with vitamins E and C after resection of the primary growth. This regimen could be translated to a combined therapy for human cancer. CONCLUSIONS: Diets enriched with omega-3 PUFA may have beneficial anticancer effects in particular when containing only basal amounts of antioxidants such as vitamin E or C. Furthermore, the addition of drugs which promote oxidation of omega-3 PUFA, such as ferrous salts (e.g. as prescribed for the treatment of anemia), may further increase these effects. **However, the supportive effect of omega-3 PUFA in chemotherapy (e.g. with CP) increases when vitamins E and C are also included.**