

Letters to the Editor

Marine *n*-3 Fatty Acids and Colorectal Cancer: Is There a Real Link?

To the Editor: Oh et al. (1) investigated the possible inverse association between consumption of fish/*n*-3 highly unsaturated fatty acids (HUFAs, marine omega-3 fatty acids mainly consisting of icosapentaenoic acid and docosahexaenoic acid) and the risk of colorectal cancer in the Nurses' Health Study, but failed to observe any link. However, we have documented elevated apoptosis in normal colonic membranes in Japanese patients, in the Dietary Intervention in Polypectomized Patients Study, who adhered to our regimen of high fish consumption along with fish oil and perilla oil (rich in α -linolenic acid; ref. 2), suggesting a reduced risk of colorectal adenomas/tumors.

n-3 PUFAs (or *n*-3 HUFAs) compete with *n*-6 PUFAs (or arachidonic acid) in various enzymatic processes and the absolute consumption of *n*-3 PUFAs (or *n*-3 HUFAs) may be crucial for colorectal carcinogenesis (3). The median energy percentages from fish/*n*-3 HUFAs in the study group of Oh et al. were distributed from 0.03 to 0.18, according to quintile categorization (1), while our Japanese Dietitians' Epidemiologic Study noted a distribution of 0.26 to 0.53 (4), indicating that the quantity of fish/*n*-3 HUFAs consumed by Americans is only approximately one-tenth of the Japanese level. Indeed, there is no overlap with each other, the amount of the highest quintile for Americans being less than the lowest quintile for Japanese, as also discussed by the authors. Therefore, the findings in Americans, with an intake possibly insufficient to exert pharmacologic influence, may at least not be applicable to Japanese.

Furthermore, the ratio of *n*-6 PUFAs/*n*-3 PUFAs (or *n*-3 HUFAs) may also be critical for colorectal carcinogenesis. The intake of *n*-6 PUFAs by Americans is exceedingly high and their median ratios of *n*-3 HUFAs/*n*-6 PUFAs appear to be distributed from 0.006 to 0.04 (or *n*-6 PUFAs/*n*-3 HUFAs: 25.0-166.7; ref. 1), whereas those for Japanese are 0.05 to 0.11 (or *n*-6 PUFAs/*n*-3 HUFAs: 9.2-21.1; ref. 4), again with no overlap between the two populations. Plasma phospholipids in Americans would be expected to be highly saturated with *n*-6 PUFAs and the concentrations of *n*-3 HUFAs, even in the highest quintile group, might not effectively compete (5). Accordingly, we would like to stress that *n*-3 PUFAs and/or fish/*n*-3 HUFAs may indeed be favorable for the prevention of colorectal adenomas/tumors in populations, including Japanese, who consume appreciable amounts of fish and other marine foods.

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