Correspondence

Effect of Dietary Fat on Human Breast Cancer Growth and Lung Metastasis in Nude Mice

Rose et al. (1) recently published an experimental study examining the effects of dietary fat on the growth and metastasis of human lung cancer in a nude mouse xenograft model. The conclusion reached was that the high-fat diet shortened the latency before tumor development, increased the growth rate of the tumor, increased the fraction of animals developing primary tumors, and increased the fraction of animals developing metastases. What is not clear is whether there were differences in the caloric intake of the two groups. This important study is made somewhat more difficult to interpret in the absence of such information because credible data implicate calories (or more properly, total energy intake) with tumor development and progression. In light of the acknowledged difficulty of separating the influence of total calories and fat in human studies, it would be of particular value to control these two variables in the experimental models. Once strong data implicating a role for high dietary fat among animals consuming isocaloric diets that differ only in fat content are available in animal models, one might have more faith that the proposed human studies are aiming at the correct target.

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Reference


Response

Longo expresses concern that our study did not distinguish between the potential effects of fat and energy intake on the growth and metastasis of MDA-MB-435 cells in nude mice. While it is true that the high-fat diet is calorically more dense than the low-fat diet, it is clear that there was an “adjustment for calories” in the eating patterns, as has been well described previously for rats. Cohen et al. (1), for example, found that the body weight gain curves for rats fed diets containing 5%, 10%, and 20% fat (as corn oil) were statistically indistinguishable despite significant differences in tumorigenesis; moreover, the deposition of fat in adipose tissues, as a percentage of body fat, was not significantly different in the three groups. Cohen et al. also found that the animals fed high-fat diets consumed less feed than those fed low-fat diets, all of which speak against a caloric effect. In our study, and noted in our report, the body weight gains for the two dietary groups were virtually identical until 11 weeks into the 16-week study, when the greater weight gain in the high-fat-fed animals was entirely accounted for by the difference in the tumor weights between groups. Similar results have been reported by others (1,2).

Biological plausibility for a direct effect of fat per se, specifically the omega-6 fatty acids, is provided by our previous demonstration (3) that the growth of human breast cancer cell lines in vitro is stimulated when linoleic acid is incorporated into the serum-free medium, an effect which is negated by pharmacologically blocking eicosanoid biosynthesis. In unpublished experiments, we showed that these effects hold for MDA-MB-435 cells.

Moreover, in the experiments performed by Hubbard and Erickson (2) with the metastatic 4526 mouse mammary tumor cell line, a high-fat, linoleic acid-rich diet, compared with an isocaloric high-fat, linoleic acid-poor diet, enhanced metastasis. We are about to perform the same experiment with MDA-MB-435 cells, the results of which will address directly the issue raised by Longo.

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References


Human Genetics, Bioethics, and the Law

The “human genome project” is potentially a prolific source of data concerning the architecture of the human genome. The detailed mapping of the human cell’s estimated 100,000 genes may possibly result in the identification of genes associated with various types of cancer, Alzheimer’s disease, alcoholism, and coronary artery disease (1). Benefits are already accumulating. Recently, genes responsible for Marfan’s syndrome and familial adenomatous polyposis coli have been cloned (2). The human genome project generally should result in an improved ability to isolate and characterize genes involved with disease and normal human biology and further provide a powerful tool for diagnosing defects at the DNA level (3).

Although construction of the human gene map is a promising undertaking for...