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## Chapter 27

# Effect of Varying Dietary Omega-3:Omega-6 Fatty Acid Ratio on L-azaserine Induced Preneoplastic Development in Rat Pancreas

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Recently several studies have indicated that dietary intake of a specific class of fats, marine lipids, may inhibit cancer in some animal models (1, 2, 3). These studies used diets containing large amounts of either fish oil or vegetable oil. In this report, we describe the effect of varying the relative amounts of dietary menhaden oil and corn oil (i.e. varying dietary omega-3:omega-6 fatty acid ratio) on the development of L-azaserine-induced preneoplastic lesions in rat pancreas.

### Method

At age 14 days, male Wistar rats were given an i.p. dose of 30mg L-azaserine/kg body weight. At age 21 days the rats were weaned and 15 were assigned to each dietary regimen. The diets contained 20% by weight of freeze-dried cod, 54.8% glucose monohydrate, 0.5% DL-

methionine, 0.2% choline chloride, 3.5% American Institute of Nutrition (AIN) mineral mix and 1% AIN vitamin mix. All diets contained 20% by weight of lipid, but the relative proportions of corn oil/menhaden oil (CO/MO) in the different regimens were 20%CO + 0%MO (20/0), 19%CO + 1%MO (19/1), 17%CO + 3%MO (17/3), 15%CO + 5%MO (15/5), 10%CO + 10%MO (10/10), 5%CO + 15%MO (5/15), 3%CO + 17%MO (3/17), 1%CO + 19%MO (1/19) and 0%CO + 20%MO (0/20). The dietary omega-3:omega-6 fatty acid ratio of these regimens was 0.01, 0.03, 0.09, 0.16, 0.41, 1.2, 1.9, 3.9 and 7.0 respectively.

After 120 days on the dietary regimens, the rats were killed, H&E slides of the pancreata were prepared and examined for the presence of preneoplastic atypical acinar cell nodules (AACN) as described previously (1).

TABLE 1.  
Effect of dietary treatment on preneoplastic development

CO/MO	Number AACN/cm <sup>3</sup>	Mean AACN diameter (um)	% vol of pancreas occupied by AACN
0/20	318 ± 39*	479 ± 18*	2.42 ± 0.45*
1/19	389 ± 45	431 ± 24	2.22 ± 0.43
3/17	401 ± 37	439 ± 17	2.37 ± 0.39
5/15	344 ± 47	441 ± 23	2.30 ± 0.46
10/10	431 ± 50	515 ± 22	4.25 ± 0.88
15/5	440 ± 35	553 ± 27	5.62 ± 1.41
17/3	498 ± 47	546 ± 23	6.28 ± 1.20
19/1	522 ± 48	483 ± 28	5.06 ± 1.04
20/0	632 ± 63	496 ± 24	6.01 ± 1.13

\*Mean ± SEM

## Results and Discussion

No significant effect of dietary treatment was observed on terminal body weight or pancreas weight. As seen in Table 1, an increase in dietary MO content (i.e. increased omega-3:omega-6 ratio) significantly decreased the number of AACN/cm<sup>3</sup> and the % volume of pancreas occupied by AACN. It is apparent that the % volume of pancreas occupied by preneoplastic lesions increased greatly as the % dietary CO increased to between 5% and 10% (i.e. 5/15 and 10/10 regimens). This corresponds to an intake of between 3% and 6% linoleic acid. A similar

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threshold for increased neoplastic response has been reported previously in this model and a mammary tumor model (4, 5). Once this threshold level of linoleic acid is consumed, further increase in neoplastic response is a function of total fat intake. In summary, our data suggest that an increase in dietary omega-3:omega-6 ratio inhibits preneoplastic response in this model.

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