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Effect of Dietary Fat on Fatty Acid Composition of Mouse and Rat Mammary Adenocarcinomas[1] (40781)

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Studies by Wood and co-workers (1) have shown that the fatty acid composition of Morris hepatoma 7288CTC was not altered by changes in dietary fat. In previous studies from this laboratory, we have shown that a mouse mammary adenocarcinoma (tumor C) did respond to dietary fat in that its tissue fatty acid patterns reflected those of the dietary fatty acids (2, 3). In addition, we showed that linoleate-rich diets greatly increased the growth of this mammary tumor in C3H mice (3, 4). The polyunsaturated fatty acids, linoleic, 8,11,14-eicosatrienoic, and arachidonic acids, are precursors for prostaglandins, thromboxanes, prostacyclins, and noncyclic hydroxy fatty acids (5). Such enhanced tumor growth could be prevented by 5, 8,-11,14-eicosatetraynoic acid (TYA) (6), an acetylenic analog of arachidonic acid, which inhibits the conversion of linoleate to arachidonate (6, 7) and arachidonate to prostaglandins (8). Subsequently, we could show that indomethacin, an inhibitor of prostaglandin synthetase, is also effective in retarding tumor growth (9). In view of the possible relationship among dietary fat, tissue content of fatty acids, and tumor growth, we report here on the fatty acid composition of four additional mammary adenocarcinomas, three of which were implanted into mice and one into rats fed different dietary fats. These mammary tumors were selected to include those which metastasize, contain the murine mammary tumor virus, and are hormone responsive. The growth rate of all of these neoplasms was shown to be affected by polyunsaturated dietary fat (9).

Materials and methods. The C3H mice were bred and maintained in our laboratory. The BALB/c mice and the Fischer rats were purchased from Simonsen Laboratories, Gilroy, California. Standard stock diets which are nutritionally complete were used to maintain rats (Green Diet) and mice (Berkeley Diet Mouse Breeder Food), both obtained from Feedstuffs Processing Company, San Francisco, California. The rat stock diet contained 4.5% fat and the mouse stock diet contained 9% fat.

Mammary adenocarcinomas 3910-30 and CfZ No. 3 developed spontaneously in female mice in our colony and are maintained by serial subcutaneous transplantation. Tumor 3910-30 arose in a BALB/c mouse (a strain which is free of the mammary tumor virus) and is maintained in the same strain. Tumor CfZ No. 3 developed in a BALB/cfC3H mouse and is now maintained in BALB/c mice. Tumors 3910-30 and CfZ No. 3 were obtained from Dr. R. L. Ceriani of this laboratory. Tumor C arose in a C3H mouse (which contains the mammary tumor virus) as a result of the surgical implantation of a hyperplastic alveolar nodule into the cleared fat pads of the mouse when it was 3 weeks old (10, 11) and is carried in the same strain. Tumor 16/C originated as a spontaneous mammary adenocarcinoma in a C3H/He mouse and was obtained from Dr. T. H. Corbett of the Southern Research Institute, Birmingham, Alabama. It metastasizes to the lungs in over 75% of the host mice (12). Tumor 16/C can be maintained by implanting lung frag-

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ments subcutaneously into recipient C3H mice. The hormone-responsive mammary adenocarcinoma R3230AC (13), maintained by serial transplantation into female Fischer rats, was obtained from Dr. R. Hilf of the University of Rochester, Rochester, New York.

Immediately after subcutaneous tumor implantation (14), all animals were placed on the test diets and were kept in a temperature-controlled room (22–23°) with a 12-hr light–dark cycle. They were fed the appropriate diets and allowed water *ad libitum*. All test diets were based on a fat-free (FF) mixture which contained, by weight: 50% glucose; 22% vitamin-free casein; 6% salt mixture, U.S.P. XIV; 2% defatted liver; 1% vitamin mixture[4]; and 19% cellulose. When fat or fatty acid was included in the diet, a similar amount of cellulose was excluded. As determined by gas–liquid chromatography, the corn oil (CO) used contained the weight percentages of the following fatty acids: palmitic, 7.9%; stearic, 1.4%; oleic, 28.6%; linoleic, 59.9%; and linolenic, 2.2% (4). The safflower oil (SO) contained: palmitic, 5.6%; stearic, 2.6%; oleic, 11.7%; and linoleic, 80.1%.

Total fatty acids were isolated by refluxing small pieces of tissue (100–200 mg) with 1 ml of 30% KOH:methanol (1:1) overnight at 85°. Hydroquinone (0.01%) was added to retard the oxidation of unsaturated fatty acids. Sterols and unsaponifiable material were removed by extraction with petroleum ether (30–60°) and after acidification, fatty acids were extracted with hexane and the fatty acid methyl esters were prepared with diazomethane (15). Gas chromatography was carried out on a Varian aerograph (model 3700) equipped with a flame ionization detector and a stainless-steel column (6 ft × ⅛ in.) packed with 10% DEGS-PS on Supelcoport (Supelco, Bellefonte, Pa.). Fatty acid methyl esters were identified by their retention times and the percentage fatty acid composition was determined with a Varian model CDS111 data system. The heat program had an initial temperature of 110° and at 2 min after sample injection the temperature was increased at a rate of 10°/min to a final temperature of 185°. At 28 min, the temperature was elevated to 190° at a rate of 10°/min and stayed at that temperature for the remainder of the analysis.

Total lipids were extracted from the tissues with chloroform:methanol (2:1, v/v) and washed with Folch upper phase (16). Lipid classes were separated by thin-layer chromatography on 0.25-mm silica gel plates (LK5D, Whatman) with the solvent mixture of petroleum ether:diethyl ether:acetic acid (85:15:1.5). The phospholipid and triglyceride fractions were extracted from the silica gel and saponified, and then the fatty acids esterified in the same manner as given above.

Results. The growth rates of these five mammary tumors in rats and mice as they are affected by dietary fats have been the subject of a previous report from this laboratory (9). Briefly, although all tumors increased in size more rapidly when corn oil was added to the diet, their response to various levels of pure linoleic and arachidonic acids was somewhat variable. Thus, whereas it appears that dietary polyunsaturated fats are responsible for the increased growth rate of these tumors, the amounts required to produce the effect varies with species and strain of animal.

The total fat content of each of the mammary tumors studied here, whether in mice or rats, was unaffected by the presence of fat in the diets fed *ad libitum* (2, 9). Indeed, the ratio of phospholipid to neutral lipids in these same mammary neoplasms was also found to be unchanged (9) by such changes in diet. Thus, changes observed in the fatty acid composition of these tissues reflect absolute changes in the amount of fatty acids present. A comparison of the fatty acid compositions of the four mouse mammary tumors studied is given in Table I. The fatty acid compositions of all tumors were similar when host mice were fed the fat-free diet (Table I). When host mice were fed the 15% corn oil-containing diet, the tumors re-

[4] The vitamin mix provided the following milligrams of vitamin per kilogram diet: vitamin A palmitate, 55; vitamin D_2, 21; *d*-α-tocopheryl succinate, 463; menadione sodium sulfate, 1.4; thiamine–HCl, 8.6; riboflavin, 17.2; pyridoxine–HCl, 8.6; nicotinic acid amide, 103; calcium pantothenate, 55; vitamin B_{12} (in gelatin), 3.4; crystalline folic acid, 3.4; and choline bitartrate, 9260.

TABLE I. FATTY ACID COMPOSITION OF MAMMARY ADENOCARCINOMAS IN MICE RECEIVING FAT-FREE OR CORN OIL-CONTAINING DIETS[a]

Fatty acid chain length	Fat-free diet				15% Corn oil diet			
	C3H mice		BALB/c mice		C3H mice		BALB/c mice	
	Tumor C (4)[b]	Tumor 16/C (5)	Tumor 3910-30 (6)	Tumor CfZ No. 3 (6)	Tumor C (4)	Tumor 16/C (6)	Tumor 3910-30 (5)	Tumor CfZ No. 3 (5)
14:0	1.4 ± 0.1	1.3 ± 0.1	1.4 ± 0.1	1.4 ± 0.1	1.8 ± 0.6	1.1 ± 0.2	1.2 ± 0.1	1.0 ± 0.1
16:0	20.4 ± 2.9	22.8 ± 0.9	24.1 ± 1.1	20.2 ± 0.5	22.6 ± 2.8	17.3 ± 2.4	21.3 ± 0.6	20.1 ± 0.6
16:1	8.1 ± 0.8	6.1 ± 0.8	7.0 ± 1.2	5.7 ± 0.8	3.2 ± 0.1	3.8 ± 0.5	3.0 ± 0.4	2.7 ± 0.6
18:0	12.1 ± 1.5	9.4 ± 1.4	9.3 ± 1.1	9.3 ± 1.4	17.0 ± 0.5	8.0 ± 1.6	12.4 ± 2.2	12.2 ± 1.3
18:1	41.4 ± 4.7	39.4 ± 2.8	40.9 ± 2.5	39.5 ± 2.5	20.2 ± 0.2	33.2 ± 2.7	26.6 ± 2.6	26.8 ± 2.1
18:2	6.2 ± 1.3	6.3 ± 1.3	4.7 ± 0.9	7.6 ± 1.8	15.4 ± 2.0	21.5 ± 3.4	18.9 ± 4.5	16.2 ± 1.7
18:3	0.6 ± 0.1	0.1 ± 0	0.3 ± 0.2	0.3 ± 0.3	0	0.5 ± 0.2	0.2 ± 0.1	0.7 ± 0.7
20:3 ω9	0	1.2 ± 0.5	2.0 ± 0.6	0.6 ± 0.2	0	0	0.6 ± 0.2	0
20:4	10.0 ± 2.4	10.8 ± 1.9	9.9 ± 1.9	12.1 ± 2.5	20.1 ± 1.6	11.3 ± 2.9	14.4 ± 3.8	15.6 ± 2.6
22:4 ω6	n.d.[c]	2.4 ± 0.5	2.0 ± 0.4	2.1 ± 0.3	n.d.	3.3 ± 0.8	3.8 ± 1.0	3.8 ± 0.4

[a] Results are percentages of total fatty acids and reported as mean ± SEM. Hosts for tumor C were fed diets for 21 days; tumor 16/C, 17 days; tumor 3910-30, 13 days; and tumor CfZ No. 3, 19 days.

[b] Numbers in parentheses, number of animals used.

[c] Not determined.

sponded with an increase in 18:2 and 20:4 and a decrease in 16:1 and 18:1. However, the response to this CO diet for each adenocarcinoma was somewhat different. The percentage 20:4 in tumor C was twice that in the same tumor in mice fed the fat-free diet. The 20:4 level was only moderately increased (30–40%) in the two tumors of BALB/c mice and showed little or no increase in tumor 16/C in C3H mice. Thus, the 20:4 content of the rapidly growing, metastasizing tumor 16/C was altered very little by linoleate-rich diets whereas tumor C, which is slower growing and nonmetastasizing, showed the greatest change.

We next examined the rate at which linoleate-rich diets change the fatty acid composition of tumor C in female C3H mice (Fig. 1). Groups of mice were sequentially fed (a) a diet containing 15% safflower oil for 3 weeks, then (b) a fat-free diet for varying lengths of time up to 8 weeks, and finally (c) returned to the 15% safflower oil diet for 1 or 4 days. Three weeks after the SO diet was fed, tumor linoleate levels plateaued at about 15% and arachidonate at about 20% of the total tissue fatty acids. After the mice were placed on the fat-free diet, 18:2 levels dropped slowly, taking 6 weeks to reach their lowest point, whereas 20:4 levels took about 1 week to attain their nadir. In addition, when linoleate was reintroduced into the diet, arachidonate levels were restored more rapidly than those of linoleate.

In these same experiments (Fig. 1), about 4 weeks were required for 20:3 ω9 to appear in the adenocarcinoma lipids and maximum levels (11%) were attained after 8 weeks on the linoleate-free diet. This fatty acid, which is characteristic of the essential fatty acid deficiency syndrome, rapidly disappeared when linoleate was again added to the diet and took only 4 days to almost completely vanish.

As discussed previously (10, 14), it is difficult to select a normal tissue which can act as a proper control for the mammary adenocarcinoma in comparative studies between normal and tumor tissues. Although the liver is not a proper control tissue for this tumor, it is a convenient normal tissue for studies on alterations in fatty acid composition as they relate to dietary fatty

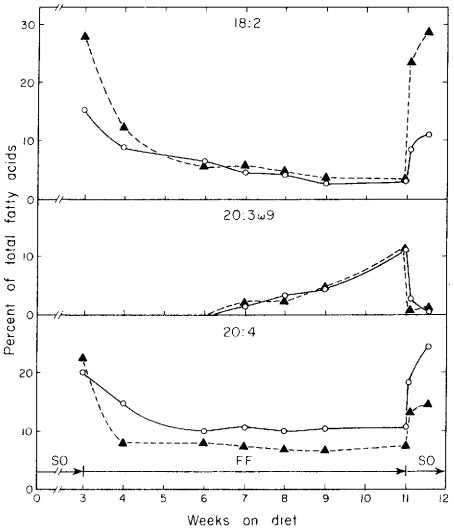

FIG. 1. After implantation with tumor C, C3H mice were fed sequentially the 15% safflower oil (SO) diet for 3 weeks, the fat-free diet (FF) for 8 weeks, and then returned to the SO diet. Three tumor-bearing mice were sacrificed at the times indicated and their livers (▲) and tumors (○) removed for fatty acid analysis as described in text. Only the values for 18:2, 20:3 ω9, and 20:4 are given and each point represents the mean value obtained.

acids in the host animals (4, 6). It is interesting to note that the liver responded to the changes in diet to a somewhat greater extent than did the neoplasm (Fig. 1). For example, when the diets were changed from linoleate rich to linoleate poor, the 18:2 and 20:4 contents of the liver were depleted at a rate not unlike those of the tumor. In addition, when dietary linoleate was restored, the liver accumulated this polyunsaturated fatty acid to a greater extent than did the tumor. On the other hand, under those same conditions, the tumor accumulated more 20:4 than did the liver. However, 20:3 ω9 in both tissues followed a similar course, namely, it accumulated and disappeared at about the same rate.

Since the mammary adenocarcinoma R3230AC both synthesizes (S. Abraham and R. Hilf, unpublished observations) and contains (17) medium-chain-length fatty acids (8:0 through 12:0), we compared the fatty acid compositions of triglycerides and phospholipids from liver and tumor in female Fischer rats receiving either fat-free or corn oil-containing diets (Table II). In

TABLE II. FATTY ACID COMPOSITION OF LIPID CLASSES IN LIVER AND TUMOR R3230AC OF FISCHER RATS FED DIFFERENT DIETS[a]

	Fat-free diet				15% Corn oil diet			
	Liver		Tumor		Liver		Tumor	
Fatty acid chain length	PL[b] (3)[c]	TG (3)	PL (5)	TG (5)	PL (3)	TG (3)	PL (5)	TG (5)
8:0	0	0.1 ± 0	2.1 ± 0.5	0.9 ± 0.4	0.1 ± 0	0	1.1 ± 0.3	0.4 ± 0.3
10:0	0	0.1 ± 0	0.3 ± 0.2	3.0 ± 0.9	0	tr	0.2 ± 0.1	4.1 ± 1.7
12:0	0.1 ± 0	0.1 ± 0	0.3 ± 0.1	8.4 ± 2.3	0	tr	0.2 ± 0.1	13.0 ± 2.8
14:0	0.3 ± 0.1	1.6 ± 0	2.2 ± 0.2	10.2 ± 1.7	0.1 ± 0	1.0 ± 0.2	2.3 ± 0.3	16.6 ± 1.1
16:0	15.3 ± 0.5	29.4 ± 1.7	21.9 ± 0.9	24.8 ± 1.5	14.4 ± 0.3	23.7 ± 0.8	24.3 ± 1.0	24.3 ± 1.5
16:1	5.1 ± 0.2	14.5 ± 1.3	5.3 ± 0.6	10.1 ± 1.0	0.1 ± 0	1.6 ± 0.2	3.6 ± 0.3	4.3 ± 0.6
18:0	29.9 ± 0.9	3.2 ± 0.7	14.3 ± 0.5	3.0 ± 0.4	38.3 ± 1.5	3.0 ± 0.4	16.4 ± 1.1	4.7 ± 0.6
18:1	18.5 ± 0.6	49.3 ± 1.3	36.7 ± 1.5	37.5 ± 4.6	5.7 ± 0.2	26.9 ± 1.5	26.8 ± 0.8	17.9 ± 2.1
18:2	2.2 ± 0.5	0	0.1 ± 0.1	0.5 ± 0.2	8.5 ± 1.7	33.3 ± 2.2	3.7 ± 0.5	3.0 ± 1.5
18:3	0	0	0.7 ± 0.3	0.3 ± 0.2	0.1 ± 0	1.2 ± 1.2	0.1 ± 0.1	0.1 ± 0
20:3 ω9	12.6 ± 0.7	0.7 ± 0.5	6.1 ± 0.4	0.7 ± 0.2	0.8 ± 0	0.8 ± 0.5	0.8 ± 0.2	0.5 ± 0.2
20:4	15.5 ± 0.5	0.8 ± 0.5	8.2 ± 1.5	0.2 ± 0.1	31.7 ± 2.5	7.9 ± 0.3	15.8 ± 2.0	3.7 ± 0.4
22:4 ω6	1.3 ± 0.6	0	1.8 ± 0.3	0.6 ± 0.2	0	0	4.6 ± 0.8	6.6 ± 0.3

[a] Results are percentages of total fatty acids and reported as mean ± SEM. Rats were fed diets for 21 days.
[b] Abbreviations: PL, phospholipids; TG, triglycerides; tr, trace.
[c] Number in parentheses, number of animals used.

liver triglycerides from rats fed the FF diet, 16:0, 16:1, and 18:1 accounted for over 90% of the total fatty acids. On the CO diet, 18:2 and 20:4 made up 30 to 40% of the fatty acids. Fatty acids with less than 16 carbons made up about 22% of the tumor triglycerides on the FF diet and about 34% on the CO diet. In tumor R3230AC, it would appear that almost all of the fatty acids with carbon chains of 16 or less are present in the triglycerides. This is not surprising since in the normal lactating gland, these fatty acids are also found almost exclusively in the triglycerides (18). The distribution of the long-chain fatty acids in the triglycerides of this neoplasm, discounting its content of the shorter-chain fatty acids, was very similar to that in the triglycerides of the liver with the single exception of 18:2 which is unusually low in this tumor even when the host rats were fed the CO diet.

A major portion of the 20:4 present in both liver and tumor lipids was found to reside in the phospholipid fraction (Table II). This finding is consistent with our previous observations made with tumor C and host liver in C3H mice (2). When found in tissue lipids, 20:3 ω9 was concentrated in the phospholipids of the liver and the tumor (Table II).

The results of experiments in which small amounts of pure fatty acids were added to the diet of BALB/c mice bearing mammary adenocarcinoma CfZ No. 3 are given in Table III. We could find no significant change in the fatty acid composition of the tumors in mice fed the 18:0 and 18:2 diets that could be related to tumor size. The response of tumor growth was as expected, namely, those in mice fed the 18:0 diet were only 60% of the size of tumors found in mice fed the 18:2 diet and addition of TYA to this 18:2 diet reversed the growth stimulating effect. TYA did inhibit the conversion of 18:2 to 20:4 and 18:1 to 20:3 ω9 since increased amounts of 18:2 and 20:3 ω6 and decreased amounts of 20:4 and 20:3 ω9 were observed in these tumors. This result with TYA in BALB/c mice is consistent with the observations made previously with C3H mice. One might infer that the tumor-enhancing effect of 18:2 is related to its conversion to 20:4. Unexpectedly, however, the 0.5% 20:4 diet did not enhance tumor growth significantly (9) although it did increase the percentage of 20:4 and 22:4 in the tumor tissue (Table III). This latter finding suggests that poor absorption of arachidonate does not account for its lack of tumor growth stimulation.

Discussion. Many aspects of lipid structure and metabolism have been examined in relation to tumorigenesis (19). Often, an apparent correlation between lipids and tumor incidence or promotion cannot be substantiated by further evidence. For example, we found a correlation between the arachidonate content of a mammary tumor in C3H mice and the rate of tumor growth (4). However, subsequently we found that the tissue level of 20:4, or its precursor 18:2, did not correlate with growth in other mammary tumors of BALB/c mice (9). If high levels of 20:4 in tumor lipids, or responsiveness of 20:4 to dietary linoleate, were related to enhanced tumor growth, one would expect the more rapidly growing metastasizing tumor 16/C to have higher levels of 20:4, or be more responsive to dietary 18:2, than the slower growing, nonmetastasizing tumor C. We have shown here that this is not the case. In addition, tumors taken from BALB/c mice ingesting diets which contain as little as 0.1% 18:0 or 0.1% 18:2 had essentially the same fatty acid compositions even though they grew more rapidly on this small amount of 18:2. Thus, the simple generalization that all tumors grow more rapidly when they contain high levels of arachidonate is not accurate.

The BALB/c mice fed diets containing 0.1% 18:2 were essential fatty acid deficient as their tumors and livers contained appreciable amounts of 20:3 ω9. Apparently, a continuous supply of dietary linoleate is needed to promote tumor growth in BALB/c mice. It is interesting that the lipids of tumors taken from mice receiving fat-free diets contain between 4 and 8% 18:2 and between 10 and 12% 20:4. Apparently, these polyunsaturated fatty acids are not available for the tumor-enhancing process, that is at least, in the absence of dietary linoleate.

A clear finding from our previous studies

TABLE III. EFFECT OF LOW LEVELS OF DIETARY POLYUNSATURATED FAT AND TYA ON FATTY ACID COMPOSITION AND WEIGHT OF TUMOR CfZ No. 3 IN FEMALE BALB/c MICE[a]

Fatty acid chain length	0.1% 18:0 Diet (3)[b]	0.1% 18:2 Diet (6)	0.1% 18:2 Diet plus TYA[c] (6)	0.5% 20:4 Diet (4)
14:0	1.2 ± 0	1.4 ± 0.1	1.6 ± 0.2	1.4 ± 0.2
16:0	19.4 ± 0.9	20.7 ± 0.9	19.7 ± 0.5	21.7 ± 0.3
16:1	6.1 ± 0.8	7.9 ± 0.9	8.2 ± 0.9	5.7 ± 0.3
18:0	11.3 ± 0.4	8.9 ± 0.8	8.1 ± 0.9	9.0 ± 0.4
18:1	41.4 ± 1.7	44.6 ± 1.3	47.0 ± 1.5	34.8 ± 1.6
18:2	4.0 ± 0.9	3.6 ± 0.5	7.0 ± 0.7	4.0 ± 1.0
20:3 ω9	1.5 ± 0.4	1.1 ± 0.3	0.1 ± 0	0.4 ± 0.1
20:3 ω6	0.4 ± 0.3	0.4 ± 0.1	0.9 ± 0.2	0.3 ± 0
20:4	12.0 ± 0.3	9.2 ± 1.1	5.8 ± 1.1	17.9 ± 1.8
22:4 ω6	2.4 ± 0.4	2.0 ± 0.6	1.5 ± 0.4	4.3 ± 0.3
Tumor wt (g wet wt)	0.8 ± 0.2 (8)	1.5 ± 0.2[d] (6)	0.7 ± 0.1 (6)	1.1 ± 0.2 (7)

[a] Results are percentages of total fatty acids and reported as mean ± SEM. Mice were fed the diets for 16 days.
[b] Numbers in parentheses, number of animals used.
[c] TYA, 0.56 mg, was added to each gram of diet.
[d] Significance determined by paired Student's *t* test in comparison to 0.1% 18:0 diet ($P < 0.02$).

is the ability of dietary linoleate to enhance the growth of transplantable mammary tumors (3, 6, 9). We have also confirmed the fact that TYA prevents the enhancement of tumor growth by pure *cis*-9-*cis*-12-octadecadienoic acid. The reduction of 20:4 and the increase of 18:2 in the tumors of TYA-treated mice suggest that one of the products of 18:2 metabolism related to arachidonate synthesis may be responsible for enhanced tumor growth. Nevertheless, dietary 20:4 at the 0.5% level was not sufficient to substitute for dietary linoleate at the 0.1% level (9).

From the present study, it would appear that mouse and rat mammary adenocarcinomas are not different from normal tissues in their ability to respond to changes in the fatty acid composition of the diet. Such dietary modifications of the fatty acid composition of tumor lipids has also been found with the L1210 murine leukemia ascites cells (20) and the Ehrlich ascites tumor cells (21). In the L1210 cells, these changes occurred in both the phospholipid and neutral lipid classes (20), a finding similar, in many respects, to that shown here with the R3230AC mammary adenocarcinoma in the Fischer rat.

When one looks at many kinds of transplantable mammary adenocarcinomas (virus containing, metastasizing, etc.), the specific relationship of one fatty acid to another in the tissue lipids is not related to the growth rate of the neoplasm. Although diets rich in linoleate appear to be most effective in enhancing neoplastic growth, those tumors which have the highest content of this polyunsaturated fatty acid are not necessarily the fastest growing.

Summary. The fatty acid composition of four mammary adenocarcinomas carried by C3H and BALB/c mice and one carried by the Fischer rat fed different dietary fats is presented. In general, the neoplastic tissue fatty acid profiles reflected those of the dietary fat in that those tumors taken from animals fed polyunsaturated fats contained greater amounts of linoleate and arachidonate than those fed a saturated fat or a fat-free diet. Mammary tumor fatty acid composition changed almost as rapidly as it did in host liver in response to alterations in the type of dietary fat. The rate of tumor growth could not be correlated with the levels of 20:4 found in all murine mammary adenocarcinomas.

Although low levels (0.1%) of pure 18:0

and 18:2 had little effect on the fatty acid composition of tumor lipids, this level of 18:2 was sufficient to enhance tumor growth in BALB/c mice.

The administration of 5,8,11,14-eicosatetraynoic acid (TYA) to BALB/c mice retarded the increased growth of transplanted mammary tumors in mice fed diets which contained pure *cis*-9-*cis*-12-octadecadienoic acid. This effect of TYA confirms previous observations made with mammary adenocarcinomas in C3H mice in that 18:2 levels increased while 20:4 and 20:3 ω9 levels decreased.

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