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Reduction of Synthetic Rate of Lipoprotein Lipase in Adipose Tissues of Patients with Carcinoma

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A CLINICAL FEATURE of cancer cachexia is loss of body fat, and a possible cause is reduction of lipoprotein lipase (LPL) activity in adipose tissue. LPL hydrolyses triacylglycerol (TG) in circulating chylomicrons and very low density lipoprotein to free fatty acid (FFA) and monoacylglycerol [1–3]. This FFA can then be re-esterified and accumulated in the TG pool of adipose tissues. We report here the activity and synthetic rate of LPL in adipose tissues of patients with carcinoma.

Adipose tissue was obtained from two different regions (the omentum and abdomen) in patients with gastric cancer (4 patients), rectal cancer (3 patients), bladder tumour (1 patient) and ovarian endometrial adenocarcinoma (1 patient) [mean age (S.D.) 61.1 (2.7) years]. Metastases and tumour infiltration was not present in the adipose tissue. Adipose tissue from 9 patients with non-neoplastic diseases [mean age 60.1 (4.0) years] was used as control. A 25% homogenate of the adipose tissue was used to make an acetone/ether powder as described previously [4]. LPL activity in extracts of acetone/ether powders of adipose tissues was measured with tri[9, 10 (n)-^{3}H]oleoylglycerol as substrate [4].

The LPL activities for adipose tissue of control and cancer patients are indicated in Table 1. The mean activity in subcutaneous adipose tissue from the abdomen of controls was 67% of that in control omental adipose tissues. The mean LPL activities in omental and subcutaneous adipose tissue of patients with carcinoma were lower than those in the corresponding tissues of control subjects: in omental adipose tissues the activity was 45% of that of controls, while in subcutaneous adipose tissues it was 36% of that of controls.

Synthesis of LPL was analysed by incubating the adipose tissues with [^{35}S]methionine for 2 h, immunoprecipitating ^{35}S-labelled LPL with chicken antisera to LPL, and resolving it by SDS–PAGE [5]. The amounts of ^{35}S incorporated into total protein in adipose tissues of patients with carcinoma were identical to those in adipose tissues of control subjects, indicating that carcinoma had no effect on synthesis of total protein in adipose tissues (data not shown).

Table 1. LPL activity in omental and subcutaneous adipose tissues of control subjects and patients with carcinoma

	LPL activity (mU/mg DNA)*		^{35}S in LPL (cpm)	
Subjects	Omental	Subcutaneous	Omental	Subcutaneous
Control	20.7 ± 0.5 (4)	13.9 ± 0.6 (5)	359 ± 94 (3)	380 ± 55 (4)
Carcinoma	9.3 ± 1.8 (5)	5.0 ± 1.0 (4)	80 ± 26 (2)	213 ± 66 (3)

Values are expressed as mean ± S.E. Numbers in parentheses are the numbers of samples. *One milliunit of LPL activity was defined as that releasing 1 nmole of fatty acid/min at 37°C.

All the adipose tissues examined synthesised LPL subunits with M_r = 57 000. Radioactivity zones corresponding to LPL were excised from the gels, and dissolved with 30% hydrogen peroxide. Radioactivity was then determined with a liquid scintillation counter. The amounts of radioactivities in LPL in omental and subcutaneous adipose tissue of patients with carcinoma were 22 and 56% of those in the corresponding tissues of control subjects, respectively (Table 1). The ratio of radioactivity in LPL to that in total protein at 2 h was 0.0029–0.0040% in adipose tissue of control subjects and 0.0007–0.0019% in those of patients with carcinoma. Thus, reduction of LPL activity in adipose tissue of patients with carcinoma could result from reduced synthetic rate of LPL.

LPL activities in adipose tissue correlated with their TG contents (r = 0.57, P<0.02). The amount of TG in omental adipose tissue of patients with carcinoma was 31% of that of control subjects (the former, 0.40 ± 0.07 g/mg DNA; the latter, 1.28 ± 0.18 g/mg DNA, P<0.01). The amount of TG in subcutaneous adipose tissue was also lower, but not significantly, in patients with carcinoma than in control subjects.

In conclusion, loss of body fat of patients with carcinoma was due, at least partly, to reduced LPL activity in their adipose tissues.

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