Hepatic regeneration induces changes in lipoprotein lipase activity in several tissues and its re-expression in the liver

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We examined the expression of lipoprotein lipase (LPL) gene and LPL activity following a two-thirds hepatectomy and during liver regeneration. In most of the tissues studied, LPL activity increased a few hours after partial hepatectomy, but soon returned to normal levels. The greatest increase was found in the adrenal glands, plasma and liver. This increase in LPL activity in the liver could be partially due to an increase in the influx of the enzyme from extrahepatic tissues. There is, however, also a re-expression of LPL mRNA in the liver after partial hepatectomy (during the first hours). It is well known that LPL is expressed in

the liver of neonatal animals, but progressively decreases during post-natal development, to reach adult levels around the time of weaning. Our results show by the first time that the remaining liver re-expresses LPL gene during the regeneration process and that the hepatocytes de-differentiate and acquire some of the neonatal characteristics. The increase in LPL mRNA will contribute to the rise in LPL activity after hepatectomy. This presence of LPL could enable the liver to take up fatty acids from the circulating triacylglycerols, which are needed as energetic and plastic substrates during the process of hepatic regeneration.

INTRODUCTION

After partial hepatectomy, consisting of the surgical removal of two-thirds of the liver, regeneration of the organ occurs [1]. Under these conditions the liver is usually regenerated in 6–8 days [2]. All the cell types in the liver participate in this process: not only hepatocytes, but also bile-duct epithelial cells, Ito cells, Kupffer cells, etc. However, since hepatocytes constitute most of the hepatic mass (80–90%), their contribution to the process of regeneration is greatest [2,3]. The molecular signals that control the process of regeneration include: serum factors, growth factors, hormones and nutrients (reviewed in [2,4–7]).

Among the various metabolic processes that take place during hepatic regeneration some parameters of lipid metabolism have been reported: the rate of esterification of fatty acids from adipose tissue is higher, lipogenesis is increased [8], capacity to take up circulating lipoproteins is reduced, and lecithin cholesterol acyltransferase (LCAT) activity is low. Liver regeneration is also associated with a reduction in plasma levels of very-low-density lipoprotein (VLDL) and an increase in the levels of low-density lipoprotein (LDL) [9]. In order for the liver to be able to regain its complete functionality and regenerate its mass, contributions of metabolic precursors from other tissues are required. In this respect the provision of fatty acids, phospholipids and cholesterol is essential for the maintenance of the rate of formation of the membranes of dividing liver cells.

Lipoprotein lipase (LPL; EC 3.1.1.34) is an enzyme that can be detected in a great variety of tissues (cardiac and skeletal muscle, white and brown adipose tissue, lung, lactating mammary gland). It hydrolyses the triacylglycerols in circulating lipoproteins such as in VLDL and chylomicrons. The resulting free fatty acids produced by this reaction are taken up by the subjacent tissue, for future re-esterification and storage, use as fuel for energy, or for re-exportation (reviewed in [10]). In foetal and neonatal liver LPL is synthesized in the liver. Throughout

development LPL gene expression decreases until it completely disappears in the adult [11]. Fenofibrate can induce the re-expression of the LPL gene in adult liver [12]. In the adult, the liver does not, however, synthesize LPL. Nevertheless, LPL activity can be detected in this organ. This LPL is delivered from the blood, and the liver constitutes the main site of LPL degradation [13]. The LPL activity present in very low amounts in the liver of adult animals (which increases slightly following Intralipid® administration or after 24 h starvation in late pregnancy) could hence be attributed to an influx of active LPL from other tissues. This LPL accumulates in capillaries of the hepatic circulation and remains active until its degradation [14].

It has been suggested that following partial hepatectomy the hepatocytes enter a phase of de-differentiation and that they acquire a phenotype similar to that of foetal liver cells [15]. This retro-differentiation is again reversed during liver regeneration and finally the normal adult enzyme pattern is restored once the regeneration is complete [16]. Here we attempt to determine whether LPL also appears in the liver of the adult rat during hepatic regeneration, and if so, whether this is due to the re-expression of the LPL gene in the regenerating liver, or whether the enzyme is derived from other tissues, as occurs in certain situations in the adult.

EXPERIMENTAL

Chemicals

BSA (essentially fatty acid-free), dithiothreitol, sucrose, Pipes and glycerol trioleate were obtained from Sigma Chemical Co. Hepes was from Boehringer-Mannheim, Barcelona, Spain. Glycerol tri[9,10-(n)-³H]oleate was obtained from Amersham International, Amersham, Bucks., U.K. All other reagents were of the highest purity available.

Abbreviations used: LPL, lipoprotein lipase; HL, hepatic lipase; LCAT, lecithin cholesterol acyltransferase; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein; WAT, white adipose tissue.

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Table 1 Food intake, body weight and organ weights

Food intake, body weight and organ weights in sham-operated (S) and hepatectomized (H) rats. Abbreviations: BAT, interscapular brown adipose tissue; WAT, the two epididymal fat pads. Data are means $\pm$ S.E.M. for 5–7 animals. The time after treatment is given in hours and also in days (in parentheses).

Time (h) (days)	Group	Food intake (g)	Body (g)	Adrenal (mg)	Heart (mg)	BAT (mg)	WAT (g)	Liver (g)
0		24.1 $\pm$ 0.8	229 $\pm$ 11	52 $\pm$ 3	844 $\pm$ 30	283 $\pm$ 70	34 $\pm$ 2	11.2 $\pm$ 0.4
3	S	0.6 $\pm$ 0.2	212 $\pm$ 16	41 $\pm$ 4	748 $\pm$ 70	291 $\pm$ 80	32 $\pm$ 2	9.1 $\pm$ 1.1
	H	0.4 $\pm$ 0.1	195 $\pm$ 3	49 $\pm$ 2	690 $\pm$ 10	203 $\pm$ 20	29 $\pm$ 1	3.1 $\pm$ 0.2
6	S	0.7 $\pm$ 0.3	189 $\pm$ 13	34 $\pm$ 7	660 $\pm$ 56	338 $\pm$ 30	28 $\pm$ 2	8.5 $\pm$ 0.5
	H	0.5 $\pm$ 0.1	166 $\pm$ 3	31 $\pm$ 6	599 $\pm$ 22	210 $\pm$ 20	25 $\pm$ 1	3.2 $\pm$ 0.4
12	S	0.4 $\pm$ 0.1	199 $\pm$ 17	40 $\pm$ 8	669 $\pm$ 38	174 $\pm$ 30	30 $\pm$ 3	7.5 $\pm$ 0.5
	H	0.3 $\pm$ 0.1	168 $\pm$ 4	39 $\pm$ 3	620 $\pm$ 20	150 $\pm$ 8	25 $\pm$ 1	2.9 $\pm$ 0.1
24 (1)	S	15.3 $\pm$ 0.7	215 $\pm$ 10	46 $\pm$ 10	740 $\pm$ 50	362 $\pm$ 90	32 $\pm$ 2	9.3 $\pm$ 0.4
	H	6.5 $\pm$ 1.2	190 $\pm$ 2	50 $\pm$ 3	686 $\pm$ 30	249 $\pm$ 20	29 $\pm$ 1	4.3 $\pm$ 0.2
48 (2)	S	23.1 $\pm$ 0.9	232 $\pm$ 4	52 $\pm$ 9	780 $\pm$ 20	269 $\pm$ 40	35 $\pm$ 1	10.6 $\pm$ 0.3
	H	11.3 $\pm$ 1.0	196 $\pm$ 3	50 $\pm$ 3	732 $\pm$ 20	264 $\pm$ 30	29 $\pm$ 1	6.0 $\pm$ 0.2
72 (3)	S	20.0 $\pm$ 3.0	236 $\pm$ 6	41 $\pm$ 4	720 $\pm$ 30	163 $\pm$ 20	35 $\pm$ 1	10.6 $\pm$ 0.6
	H	17.4 $\pm$ 2.1	196 $\pm$ 5	53 $\pm$ 3	707 $\pm$ 30	159 $\pm$ 22	29 $\pm$ 1	6.4 $\pm$ 0.2
120 (5)	S	21.8 $\pm$ 0.7	228 $\pm$ 5	38 $\pm$ 4	824 $\pm$ 20	244 $\pm$ 60	34 $\pm$ 1	10.7 $\pm$ 0.2
	H	23.1 $\pm$ 1.8	205 $\pm$ 9	41 $\pm$ 4	679 $\pm$ 30	259 $\pm$ 31	32 $\pm$ 2	7.8 $\pm$ 0.4
168 (7)	S	23.1 $\pm$ 1.2	247 $\pm$ 7	52 $\pm$ 2	771 $\pm$ 46	278 $\pm$ 50	37 $\pm$ 1	11.2 $\pm$ 0.2
	H	19.1 $\pm$ 1.0	213 $\pm$ 5	41 $\pm$ 4	688 $\pm$ 50	240 $\pm$ 40	32 $\pm$ 1	8.0 $\pm$ 0.3

Animals and surgery

Male Wistar rats (180–220 g) were used from our own colony. Animals were fed *ad libitum* with standard chow diet (65 % carbohydrate, 18 % protein, 3 % fat, 5 % fibre, 5 % minerals, and vitamins, all by wt.) and subjected to a 12 h-light/12 h-dark cycle (starting light at 08:00 h). Rats were anaesthetized with ether and subjected to midventral laparotomy (H) and subsequent removal of left lateral and median lobes (70 % of liver resection) by the method of Higgins and Anderson [1]. The liver was immediately frozen in liquid nitrogen. Sham-operated (S) rats subjected to the same manipulation but without liver excision, were used as controls. After surgery, the animals were allowed to recover for times ranging from 3 h to 7 days in the same conditions, and food intake was measured. Animals were killed by decapitation and plasma and tissues were immediately resected, weighed, frozen in liquid nitrogen and stored at -80°C until processed.

LPL activity assay

Hepatic endothelial lipase (HL) is an enzyme typically present in the liver but also present in plasma and steroidogenic tissues (adrenals and sexual organs) [17]. Since HL slightly cross-reacts in the lipolytic activity assay we use for LPL measurement, it is difficult to measure LPL activity accurately in tissues which co-express HL and LPL (e.g. plasma, adrenals and liver). Therefore the LPL assay was modified by using an anti-(rat HL) serum. Before incubation with the radioactive substrate, all samples were systematically mixed 1:1 with antiserum or preimmune serum and preincubated for 90 min at 4°C . The antiserum against rat HL has been described previously [18]; it was raised in rabbits by using active lipase purified from heparin-perfused rat livers.

LPL activity was determined by the method of Ramírez et al. [19] with minor modifications. The assay mixture contained 0.6 mM glycerol tri[9,10-(n)- ^3H]oleate (12 Ci/mol), 50 mM MgCl_2 , 0.05 % fatty acid-free BSA, 3 % rat serum (preheated 30 min at 56°C), 25 mM Pipes (pH 7.5) and 0.02 ml of sample in a final volume of 0.2 ml. The incubation was carried out for 30 min at 25°C . The reaction was stopped and [^3H]oleate

separated from substrate was quantified as described previously [20]. One unit of activity is the amount of enzyme that catalyses the release of 1 μmol of oleate per min.

RNA analyses and DNA-hybridization probes

Total RNA was extracted from frozen rat livers by the guanidine isothiocyanate method [21]. RNA dot-blots were prepared as recommended by Schleicher and Schuell, Inc., filtered through a Minifold apparatus, and immobilized on positively charged nylon membranes (Boehringer-Mannheim). The following cDNA fragments were used as probes: a 1.36 kb fragment from cDNA encoding rat LPL; a 0.75 kb fragment encoding chicken β -actin, and a 1.6 kb fragment from the cDNA (pRSA 57) clone for rat albumin. The levels of an oligo(dT) probe were used as a control for total mRNA. Digoxigenin-11-dUTP (Boehringer-Mannheim) was used for the random-primed labelling reactions of the cDNA according to the manufacturer's instructions. Prehybridization, hybridization and detection were performed as recommended in the DIG system user's guide from Boehringer-Mannheim.

Statistics

Results are given as means $\pm$ S.E.M. Statistical analysis of the data was performed by analysis of variance, followed by Bonferroni's *t* test (Graph PAD Instat, ISI software, San Diego, CA, U.S.A.).

RESULTS

Changes in weight of whole body and of different tissues

Following simulated operation (sham-operated animals, S) body weight decreased during the first few hours, but returned to initial values on the second day. In partially hepatectomized animals (H) the decrease in body weight was more important ($P \leq 0.01$ at 3 and 6 h versus $t = 0$ or normal intake approx. 10 g/100 g body wt.) and the recovery was less marked, so body weight remained below that of controls beyond day 1 after the operation (Table 1). These variations were related to changes in

Figure 1 LPL activity in liver and plasma and LPL mRNA in liver

LPL activity was determined in liver (m-units/g) and plasma (m-units/ml) of partially hepatectomized (H, ■) or sham-operated (S, ●) animals. Each point is the mean $\pm$ S.E.M. from 5–6 animals/group. Lower panels: liver mRNA was determined by dot-blot analysis. Details of RNA extraction, transfer and hybridization with LPL cDNA are given in the Experimental section. Each point is the mean $\pm$ S.E.M. from three animals/group (an example is shown in the lower panel).

the amount of food intake: rats, nocturnal animals, only eat solid food during the hours of darkness (Table 1). Sham-operated animals ingested less food during the first night after the operation ($P \leq 0.001$ versus $t = 0$), but by the second night they had recovered their normal intake. In contrast, hepatectomized animals continued to eat less than usual 7 nights after the operation ($P \leq 0.001$ versus $t = 0$).

The adrenal glands and the white adipose tissue (WAT) showed a slight reduction in weight (with a minimum at 6 h) which parallels the reduction in body weight, but, except in the first hours, the adrenal glands and WAT weights in hepatectomized are significantly different from those in sham-operated rats ($P \leq 0.01$). The weights of heart and brown adipose tissue were lower in hepatectomized rats than in the sham-operated group at all times studied. The remains of the liver did not begin to regain weight until 12 h after partial hepatectomy (Table 1). Thereafter, recovery was progressive and rapid and, after 7 days, the weight was 260 % of the initial value (8.0 g versus 3.1 g; $P \leq 0.001$). Liver weight was, however, still 71 % of the liver weight

Figure 2 LPL activity in adrenals, skeletal muscle and heart

LPL activity (m-units/g) was determined in adrenals, skeletal muscle and heart of partially hepatectomized (H, ■) or sham-operated (S, ●) animals. Each point is the mean $\pm$ S.E.M. from 5–6 animals/group.

of controls (8.0 g versus 11.2 g; $P \leq 0.01$). No differences were observed in WAT weight at any of the times studied (Table 1).

LPL activity in the liver (Figure 1)

In sham-operated animals (S) the LPL activity in the liver increased during the first 12 h, to double the normal value ($P \leq 0.001$ versus $t = 0$ h). In partially hepatectomized animals (H) LPL activity increased to nearly five times the normal level in the adult rat ($P \leq 0.001$ versus $t = 0$ h), being significantly higher than in S animals ($P \leq 0.05$ at 6 h). In both cases LPL activity returned to normal after 24 h. In order to establish whether the increase in LPL activity observed in the remnant liver following partial hepatectomy was attributable to the transport of LPL from extrahepatic tissue, we measured the activity of the enzyme in plasma and several tissues.

LPL activity in plasma and various tissues

The various tissues studied showed different levels of LPL activity. LPL activity was high in white and brown adipose tissues, heart and adrenal glands, whereas low levels were observed in skeletal muscle. The plasma LPL levels were very low. In plasma (Figure 1), adrenal glands (Figure 2) and brown

Figure 3 LPL activity in white and brown adipose tissues

LPL activity (m-units/g) was determined in white and brown adipose tissue of partially hepatectomized (H, ■) or sham-operated (S, ●) animals. Each point is the mean $\pm$ S.E.M. from 5–6 animals/group.

adipose tissue (Figure 3) a similar pattern of variation in LPL activity was observed. LPL activity increased to a maximum between 3 and 6 h after partial hepatectomy ($P \leq 0.01$ for plasma and $P \leq 0.05$ for adrenal glands at 6 h; $P \leq 0.01$ for brown adipose tissue at 3 h), and thereafter rapidly returned to basal levels. The largest differences between S and H animals were found in plasma ($P \leq 0.01$) and brown adipose tissue ($P \leq 0.05$). In skeletal muscle and heart (Figure 2) the pattern of variation of LPL activity is similar, nevertheless a maximum of LPL activity is also present at 3 h. In WAT, after the first few hours there is an increase in LPL activity with a maximum at 7 days after partial hepatectomy ($P \leq 0.01$ versus 0 h).

LPL mRNA in the liver

The increase in LPL activity in the liver following partial hepatectomy could be attributed to an increase of the LPL transported into the liver, or also to an increase in the local synthesis of the enzyme in the liver itself. To examine this second possibility, we determined the levels of LPL mRNA in the liver by dot-blot analysis. In intact adult animals no LPL mRNA could be detected in the liver [11]. At time zero in adult rats, we detected a non-specific RNA. Both in H and in S rats, hepatic LPL mRNA levels rose over the non-specific values to a maximum between 3 and 6 h after surgery. This increase was higher in H than in S groups ($P \leq 0.05$ between 3 and 24 h).

DISCUSSION

Alterations in weight and food intake

Surgical stress leads to changes in the amount of food intake, which consequently will translate into alterations in body weight. In the first 12 h the experimental animals ingested more food than the intact controls (1.7 g for S and 1.2 g for H animals

versus 0.2 g for controls) which is consistent with the observations of others [8]. In the hepatectomized animals we observed a more important decrease in body weight, since by day 7 post-hepatectomy the rats studied here had not yet fully recovered their initial body weight.

The progressive recovery of liver weight agrees with that reported by others [22], although Gove and Hems [8] describe the recovery of initial liver weight on day 4 post-hepatectomy. No references are available on weight changes in the different tissues following partial hepatectomy. The loss of weight that occurs during the first few hours appears to be due to surgical stress, since it is also found in sham-operated animals. However, recovery of weight, in the tissues studied, was slower in the H group than in the S group. This difference can perhaps be attributed to more important surgical stress and the lower food intake during the recovery period in the H group.

LPL activity in the various tissues

Only one study [23] addresses the changes in LPL activity in various tissues after hepatectomy. In this study an increase in LPL activity 20 min after hepatectomy was observed in the heart, adrenal gland and plasma. In agreement with this result, we observed a peak in LPL activity 3 h after partial hepatectomy in heart and brown adipose tissue, and after 6 h in the other tissues studied as well as in plasma. Many factors are involved in the regeneration process, in particular catecholamines, glucose, insulin and epidermal growth factor. Several of these factors can modulate LPL activity.

In the skeletal muscle a peak of LPL activity appears in both H and S rats. In rats, LPL increases progressively in the muscle during daylight hours, irrespective of whether the animal is fed or fasted, and reaches a maximal activity at the beginning of the dark period [24]. Therefore, the alterations produced following surgery may be due to the effect of catecholamines: after the operation both adrenaline and noradrenaline increase very rapidly and remain high for the next 2 days, although the levels in plasma are higher after partial hepatectomy than after a sham operation [25] and catecholamines have been reported to induce an increase in the residual LPL activity in three different fibres of skeletal muscle [26].

In the heart, which expresses LPL to a 10-fold higher level than in skeletal muscle, a rapid increase in LPL activity was observed after 3 h, which was attributable to the surgery since it occurred in both H and S groups. This agrees with the rise described by others 30 min after partial hepatectomy [23]. Similar to the situation in skeletal muscle, this rise does not coincide with the progressive increase in LPL activity found in the heart of control rats throughout the light period, which reaches a maximum at the beginning of the dark period, coinciding with the beginning of ingestion [24]. Glucagon and the catecholamines could be responsible for the rise in LPL activity observed here because it is known that these hormones increase LPL activity in the heart [4,24].

In the adrenal glands the increase in LPL activity was only observed in hepatectomized rats, which coincides with previous findings [23]. Treatment of guinea-pigs with a corticotropin (ACTH) analogue for 11 days leads to an increase in the activity and the mRNA of LPL in adrenal gland [27]. Although, according to other authors, glucocorticoids appear to have no direct effect on hepatic regeneration, they do affect the proliferation of hepatocytes, both *in vivo* and *in vitro* [5]. In a previous study we noted that dexamethasone increases LPL activity in neonatal hepatocytes [28]. Thus glucocorticoids could be involved, directly

or indirectly, in the increased activity of LPL observed in adrenal glands following partial hepatectomy.

In WAT, adrenaline [29] and glucagon [30] have been reported to reduce the LPL activity released by heparin and the total LPL activity of the tissue, irrespective of protein synthesis [31]. Meanwhile other authors report that adrenaline inhibits the synthesis of LPL and stimulates its degradation [32]. Moreover, adrenergic stimulation of the pancreas is known to reduce the secretion of insulin, a hormone that raises LPL activity in WAT [33]. However, we only observed a slight reduction in LPL activity following surgery, which could correspond to the diurnal reductions typical of intact animals [34]. The increase in LPL activity between day 1 and day 7 after surgery has not been described to date, and remains to be studied.

In brown adipose tissue the LPL activity (and the quantity of mRNA) typically increase in response to the cold via nor-adrenaline [35,36]. The peak of LPL activity that we observed in this tissue was at 3 h and greater in H than in S groups. This phenomena could be related to differential alterations in the body temperature produced during recovery from the operation.

LPL activity in the liver

Present results show that in the first few hours following partial hepatectomy there is an increase in the LPL activity in the remaining liver which is linked in time to a rise in the amount of active LPL in the circulation following an increased release of the enzyme from peripheral tissues. Following partial hepatectomy, the mass of the liver is reduced by about 70 %, and it is possible that the remaining liver may be unable to maintain the same rate of uptake/inactivation of LPL as occurs in the intact liver (i.e. a threefold increase in the rate per unit weight of tissue). If this is the case, the increase in circulating LPL activity detected following partial hepatectomy would not be the cause of the increase in LPL activity in the liver, but rather a consequence of the inability of the liver to clear circulating active LPL, due to saturation. However, in earlier studies of perfusion of the isolated liver we were unable to saturate the hepatic uptake of LPL, although we perfused livers with LPL activities 100 times higher than those detected in plasma after partial hepatectomy (results not published). Furthermore, 6 h after partial hepatectomy there was a fall in both hepatic and circulating levels of LPL, although there had not yet been any appreciable increase in the total mass of the liver, which suggests that the rate of LPL uptake–inactivation–degradation in the regenerating liver might be greatly increased to adapt to the new situation and become sufficient to take care not only of the circulating LPL but also of the LPL accumulated in the plasma and liver in this 6 h period.

An alternative hypothesis, which is not incompatible with either of the above, would be that the liver recovers the expression of the LPL gene, thus initiating the local synthesis of the enzyme. The results obtained in this study show a marked increase in the levels of LPL mRNA in the regenerating liver, coincident with high levels of LPL activity present in the liver. These results give support to this third hypothesis of endogenous re-expression. This is not the only case in which a gene that remains silent in the adult is re-expressed in the liver during regeneration. There are numerous references available on data of this kind. Haber et al. [3] describe up to 70 genes that are induced or repressed during hepatic regeneration. Following the terminology of these authors, the LPL gene in the liver corresponds to the 'immediate-early' type, since its maximum induction is between 1 and 6 h after partial hepatectomy, and transitory (it rapidly becomes silent again, recovering baseline values in 48 h). The expression pattern of the LPL gene (expression in neonatal liver, extinction during

development until its complete disappearance in the adult [11], and re-expression during hepatic regeneration) is similar to that of other genes, such as that of α -fetoprotein [37], stathmin [38] or laminin [39]. This is consistent with the hypothesis that during hepatic regeneration there is a de-differentiation of hepatocytes in the adult animal to foetal or neonatal hepatocyte stages, associated with the reappearance of foetal markers.

The factor and/or mediators that may be responsible for the induction of the expression of the LPL gene during hepatic regeneration are at present unknown, although there are other situations known in which the LPL gene can be re-expressed in the adult, such as with tumour necrosis factor [40] or fenofibrate [12] administration. Furthermore, fibric acid derivatives are known to influence hepatocyte proliferation and longevity [41], consistently with the hypothesis that fibrates might trigger a subtle form of hepatic de-differentiation.

Among the factors that could be involved in the new disappearance of LPL expression in the liver during hepatic regeneration, one should also consider glucocorticoid hormones. In fact, glucocorticoids are responsible for the disappearance of LPL gene expression in the liver during development [11], and also for the reduction in the expression of the α -fetoprotein gene in the liver [37].

After partial hepatectomy the liver rapidly traverses the cell cycle and enters a very rapid growth process, associated with marked alterations in the expression pattern of many genes. In this study we show that the LPL gene is also re-expressed and that the liver contains high LPL activity in the first few hours following partial hepatectomy. The presence of high quantities of active LPL in the regenerating liver that is actively growing could enable it to take up fatty acids from the circulating triacylglycerols in the VLDL and in the chylomicrons. These fatty acids are necessary for the generation of membranes. This utilization would agree with the increase in the amount of fatty acids described in the hepatic remnant and with the reduction of plasmatic VLDL [9].

The analysis of hepatic growth and its control has important clinical implications. The study of genes like that encoding LPL, which appears in the liver during the first few hours following partial hepatectomy, may contribute not only to a better understanding of the post-operative clinical complications but also may enhance our knowledge of the process of hepatic restoration.

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