Lipoprotein lipase in the kidney: activity varies widely among animal species

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Much evidence points to a relationship among kidney disease, lipoprotein metabolism, and the enzyme lipoprotein lipase (LPL), but there is little information on LPL in the kidney. The range of LPL activity in the kidney in five species differed by >500-fold. The highest activity was in mink, followed by mice, Chinese hamsters, and rats, whereas the activity was low in guinea pigs. In contrast, the ranges for LPL activities in heart and adipose tissue were less than six- and fourfold, respectively. The activity in the kidney (in mice) decreased by >50% on food deprivation for 6 h without corresponding changes in mRNA or mass. This decrease in LPL activity did not occur when transcription was blocked with actinomycin D. Immunostaining for kidney LPL in mice and mink indicated that the enzyme is produced in tubular epithelial cells. To explore the previously suggested possibility that the negatively charged glomerular filter picks up LPL from the blood, bovine LPL was injected into rats and mice. This resulted in decoration of the glomerular capillary network with LPL. This study shows that in some species LPL is produced in the kidney and is subject to nutritional regulation by a posttranscriptional mechanism. In addition, LPL can be picked up from blood in the glomerulus.

rat; mink; Chinese hamster; mouse; guinea pig; immunolocalization; nutritional regulation; transcription

The presence of (increased amounts of) LPL in this location might contribute to disease initiation and/or progression. There are many reports that LPL activity is suppressed in chronic renal disease in humans (20). The mechanism for this is not fully understood. These patients often have increased VLDL triglycerides and decreased levels of HDL cholesterol, and it has been suggested that the decreased LPL activity contributes to the dyslipidemia. Experimental chronic renal failure in animals is associated with decreased LPL expression in several tissues (27), but it is not known whether decreased production of LPL in the kidney itself is an important factor for the overall decrease in body LPL.

In view of the strong connection between LPL and kidney disease, it is surprising that there are no direct studies on LPL in kidney disease. This may be, at least in part, because it has been reported that LPL activity is low in the kidneys of rats (15, 30) and guinea pigs (7). An immunohistochemical study of LPL in guinea pig kidneys showed LPL in the glomerular capillaries (7). No LPL mRNA could be detected in any nearby cells by in situ hybridization, and the authors suggested that the lipase might have been picked up from the blood. On the other hand, there are reports of substantial amounts of LPL mRNA in mouse kidney (15), and some of us recently noted substantial levels of LPL mRNA, mass, and activity in kidneys from mink (18). This suggested that there may be large differences in the expression of LPL in kidneys between animal species. We have therefore studied LPL activity in several animal species, taking into account both the possibility that the enzyme is synthesized within the tissue and the possibility that the enzyme is picked up from the blood.

METHODS

Materials. Heparin was purchased from Leo Pharma (Malmö, Sweden), and the low-molecular-mass heparin preparation Fragmin was from Pharmacia (Stockholm, Sweden). Hypnorn was from Jansen (Bersee, Belgium), and Dormicum was from Roche (Basel, Switzerland). Bovine serum albumin, SDS, and Triton X-100 were from Sigma (St. Louis, MO). Protease inhibitor cocktail tablets (Complete mini) were from Roche.

Buffer A, used for homogenization of tissues, contained 0.025 M NaH2PO4, 5 mM Na2EDTA, 1 mg/ml bovine serum albumin, 10 mg/ml Triton X-100, 1 mg/ml SDS, and 5 IU heparin. One protease inhibitor tablet was added to 50 ml of this buffer, and the pH was adjusted to 8.2. Phosphate-buffered saline (PBS) comprised 0.01 M phosphate, 0.154 M NaCl, pH 7.4.
LPL was purified from bovine milk as previously described (1). The concentration of the stock preparation was \( \sim 1 \) mg/ml in 10 mM Bis-Tris, 1 M NaCl, pH 6.5. Antibodies to bovine LPL, raised in hens (22), were used for experiments in mice, rats, and mink. IgG were isolated from egg yolks and were then affinity-purified on an LPL-agarose column (35). Antisera to bovine LPL were also raised in rabbits and used for immunolocalization of injected bovine LPL in rats and mice. IgG were isolated from the rabbit antiserum on a protein A-agarose column, and specific antibodies were purified through affinity chromatography on LPL-agarose. The chicken and rabbit antibodies were eluted from the affinity column with 0.2 M glycine, pH 2.7, and 50 mM diethylamine, pH 12, respectively. The fractions were pooled and immediately dialyzed against 10 mM Tris-HCl, pH 7.4. For immunolocalization, the anti-LPL antibodies were detected with goat anti-chicken IgG or goat anti-rabbit IgG labeled with Alexa Fluor 488 (Molecular Probes, Leiden, The Netherlands). Goat serum, used for blocking, was obtained from Sigma. Preimmune chicken IgG (egg IgG) or preimmune rabbit IgG were used for control sections. Vectashield mounting medium was from Vector Laboratories (Burlingame, CA). Monoclonal antibody 5D2 to LPL was a kind gift from Dr. J. Brunzell, University of Washington (Seattle, WA).

Animal procedures. Male Sprague-Dawley rats weighing 180–220 g and male and female C57-black mice weighing \( \sim 20 \) g were obtained from Moellegaard Breeding Centre (Ejby, Denmark). Guinea pigs (all males) were from the same source and weighed 400–700 g. The animals were kept on a 12:12-h light-dark cycle whereby the light was turned on at 6 AM. The animals had free access to standard chow and water and were allowed 1 wk for acclimatization before the experiments. Mice designated to be in the fed state were killed between 6 and 8 AM. When they were to be fasted, the food was removed at 6 AM. Refeeding was ad libitum. Chinese hamsters were from a local breeding colony used for studies on spontaneous diabetes. Male nondiabetic animals weighing 25.5–31.5 g were used. The mink from a local breeding colony used for studies on spontaneous diabetes. Male nondiabetic animals weighing 25.5–31.5 g were used. The mink were killed by an overdose of Dormitor (11). Chinese hamsters and mice were killed through cervical dislocation, rats by decapitation, and guinea pigs by a blow on the neck. Tissues were rinsed free of blood, weighed, and stored for analysis of LPL activity.

In experiments were carried out at the Norwegian College of Veterinary Medicine (Oslo, Norway). Details on handling, caging, meals, and identification of LPL-deficient mink are given elsewhere (28). Mink were killed by an overdose of Dormitor (11). Chinese hamsters and mice were killed through cervical dislocation, rats by decapitation, and guinea pigs by a blow on the neck. Tissues were rinsed free of blood, weighed, and stored for analysis of LPL activity and mass (frozen at \(-70^\circ\)C in buffer A) or LPL mRNA and immunofluorescence (frozen in liquid nitrogen). The skeletal muscle sampled in mice was soleus. For pre- and postheparin blood samples, and for injection of bovine LPL to mice, the animals were anesthetized with either Hypnorm and Dormicur as previously detailed (26) or Ketalar (7.5 mg/kg body wt ip, Pfizer, Stockholm, Sweden) and Dormitor vet (50 \( \mu \)g/kg body wt ip, Orion Pharma, Espoo, Finland). The left and right jugular veins were exposed and used for injections and blood sampling. The local Animal Care Committee at Umeå University approved all animal procedures.

For the experiments in which LPL was injected into rats, the purified enzyme was diluted into heat-inactivated (56\(^\circ\)C, 1 h) rat serum to give a final concentration of 100 \( \mu \)g/ml. Each rat was given 1 ml of this solution per kilogram body weight, i.e., \( \sim 20 \) \( \mu \)g. To transform LPL to the inactive (presumably monomeric) form with low affinity for heparin (38), the solution of bovine LPL in rat serum was incubated at 45\(^\circ\)C for 90 min. Pilot experiments showed that this resulted in the loss of \( \sim 90\% \) of catalytic activity. With chromatography on heparin-agarose, this material eluted almost quantitatively in the earlier peak in the salt gradient, at \( \sim 0.5 \) M NaCl, similar to the position for the inactive form of LPL in rat blood (21). The resulting solutions were given by intravenous injections in the tail vein, without anesthesia in rats, and in an exposed jugular vein of mice. For injection of LPL to mice, the animals were anesthetized and given the same dose as the rats, 100 \( \mu \)g/kg body wt in 10 mM Bis-Tris, 1 M NaCl, pH 6.5 (the buffer used for purification on heparin-agarose) (1).

Assays. For determination of LPL activity and mass, frozen tissues in buffer A (9 ml buffer/g tissue) were thawed and homogenized with a Polytron homogenizer (PT-MR 3000; Kinematica, Littau, Switzerland). The homogenates were centrifuged for 15 min at 3,000 rpm, and the supernatants were used for assay. LPL activity was measured as described (4). Two microliters of the supernatant were assayed in a total volume of 200 \( \mu \)l. The substrate was an emulsion of 100 mg soybean triglycerides and 10 mg egg yolk phospholipids/ml containing a trace amount of triolein labeled with \( [\text{H}] \)oleic acid, kindly prepared by Fresenius-Kabi (Uppsala, Sweden). Incubation was for 30 min at 25\(^\circ\)C. Before assay of LPL in samples of mouse pre- and postheparin plasma, hepatic lipase activity was inhibited by preincubation of the sample with a rabbit antiserum to rat hepatic lipase (23).

LPL mass in tissues was measured using an ELISA as described for assay of rat LPL (4). For mink or rat LPL, we used affinity-purified, cross-reacting chicken antibodies raised against bovine LPL for the capture step and the monoclonal 5D2 antibody for the detection step. For mouse LPL, we used affinity-purified, cross-reacting chicken antibodies raised against bovine LPL for the capture step and the monoclonal 5D2 antibody for the detection step. The antibodies do not react sufficiently with LPL from guinea pigs or hamsters to make a useful ELISA. Calibration of the assay was with purified bovine LPL, and values for mouse, mink, and rat LPL were calculated as equivalents of bovine LPL. Hence the values are not absolute but rest on the unproven assumption that the antibodies have equal affinity for LPL from the different species.

For determination of LPL mRNA, total RNA was extracted from different tissues using TRIzol reagent (Life Technologies). cDNA was prepared from 5–10 ng total RNA using Moloney murine leukemia virus reverse transcriptase, RNase HMinus (M-MLV RT [H--]; Promega) and pd(N)_{6}, Random Hexamer (Amersham Biosciences). LPL mRNA and the endogenous control (18S ribosomal RNA) were quantified by multiplex PCR using TaqMan Universal PCR Master Mix and the ABI Prism 7700 Sequence Detection System (Applied Biosystems, Foster City, CA). LPL primers and probe were designed from the published sequences for mouse, rat, and mink LPL (corresponding GenBank Accession No. NM_008509, NM_012598, and AD223493, respectively). The sequence for probe and primers used for mink LPL is as follows: 5'-Fam-CTTGGAACGCGCGATCTGTTG-CAMRA (probe); primers for mouse and rat LPL: 5'-AAGCTGGTGGGGAATGATGGTG (sense), 5'-CCGTTCCTGCTCATCCTAAAGTGG (antisense); and primers for mink LPL: 5'-AGCTGGTGGGGAATGATGGTG (sense), 5'-GCCAGTATCTATGCTACATTGTTG (antisense). The probe was designed to span the entire exon region. The eukaryotic 18S rRNA endogenous control reagent set was supplied by Applied Biosystems. The expression of LPL was calculated as related to the LPL mRNA level in kidneys after normalization to 18S rRNA and determination of the difference between the values using the 2-Cr formula (User Bulletin 2, Applied Biosystems). All samples were analyzed in triplicate, and mean values were calculated.

Immunolocalization. Small pieces of kidney were mounted in Tissue-Tec OCT (Sakura Finetek Europe) and snap-frozen in propane chilled with liquid nitrogen. The tissue pieces were stored at \(-70^\circ\)C until sectioning. Cryosections were fixed for 10 min in 4% freshly made paraformaldehyde in PBS. After being rinsed, the sections were blocked in 5% goat serum for 10 min and then incubated overnight with the primary antibody. All of these procedures were performed at room temperature. Incubation with secondary antibody was done for 30 min at 37\(^\circ\)C. The sections were rinsed in PBS and mounted in Vectashield medium. The immunostained samples were viewed by confocal laser scanning microscopy (Leica SP2 or Nikon-D-Eclipse C1). Sections from one normal and one LPL-defective mink (see Table 1) and from several mice were studied.

Statistics. Unless otherwise specified, the data are means \( \pm \) SE for groups of five animals or more. Student’s t-test was used to evaluate statistical significance.
LPL in kidney

RESULTS

LPL in kidney in relation to heart and adipose tissue. The first step in this study was to compare the LPL activity in kidneys of some animal species with that in heart and adipose tissue. The results showed a great variability between the species studied, >500-fold (Table 1). In contrast, in heart and adipose tissue the ranges for LPL activities were less than six- and fourfold, respectively. Mink, Chinese hamsters, and mice kidneys had high LPL activity, whereas the activity was lower in rats and very low in guinea pigs. In an earlier study in mink, kidneys had high LPL activity, whereas the activity was lower in skeletal muscle (soleus) or in adipose tissue. Rats had much lower kidney LPL activity, ~120 mU/g, compared with ~900 mU/g in mice. In guinea pigs, LPL activity in the kidney was <10 compared with >3,000 in heart and >1,000 mU/g in adipose tissue.

We measured LPL mass in mink, mice, and rats. Our ELISA does not function for Chinese hamsters and guinea pigs. In all three species, the specific activity (mU/ng) of the enzyme was the same order of magnitude in kidney as in other tissues (Table 1). LPL mRNA was measured in mink and mice (Table 1). The amount of message was about the same in the defective and normal mink.

Physiological changes in LPL activity and mass in mouse kidney. We then questioned whether LPL activity and/or mass in mouse kidney is modulated in response to the physiological state. We chose mice for this study because, among the species found to have high LPL activity in the kidney, only the mouse is commonly used in studies of lipoprotein metabolism.

Previous studies have shown pronounced circadian rhythms for LPL in adipose tissue of rats (2) and mice (26). LPL activity in mouse kidney also showed a significant change with time of day (Fig. 1). The activity was highest at 10 AM, decreased to a minimum at 6 PM (P < 0.01), and then increased again. This is similar to the changes in adipose LPL in mice, but the amplitude of the changes was less in the kidney. LPL mass did not change significantly with the time of day (Fig. 1).

When food was withdrawn from mice, LPL activity in the kidney decreased by >50% in 6 h, from ~1,100 to ~500 mU/g (Fig. 2, P < 0.001). As fasting was continued to 24 and 48 h,
LPL activity decreased further to $\sim 260$ mU/g. Refeeding for 2 and 4 h after 24 h of fasting caused a rapid increase in LPL activity in the kidney to $445 \pm 29$ and $724 \pm 41$ mU/g, respectively (Fig. 2, $P < 0.05$). Other experiments showed that after 6 h, the activity had returned to fed levels (data not shown). LPL mRNA and mass did not change much during fasting for 30 h and refeeding for 24 h (relative LPL mRNA shown). LPL mRNA and mass did not change much during short-term fasting appears to require that a gene, separate from the lipase gene, be switched on (5). The experiment shown in Fig. 3 indicates that the same mechanism operates in mouse kidney. In this experiment, the LPL activity in the mouse kidney. In this experiment, the LPL activity in kidney decreased by 30–40% when food was withdrawn from mice for 6 or 9 h. When the mice were given actinomycin D before fasting was started, the decrease in LPL activity did not occur. When mice were given actinomycin after 6 h of fasting, LPL activity increased in 3 h to a value that was $\sim 10\%$ higher than the value before fasting.

Earlier experiments have shown that in rats, mice, and guinea pigs, there is a relatively large drop in adipose tissue LPL activity on fasting. The present study shows a similar drop in kidney LPL in mice. In contrast, there was no drop in LPL activity in either adipose tissue or kidneys of Chinese hamsters (Table 1). An earlier study in mink showed no difference of LPL activity in kidney with regard to nutritional state (28).

We also explored the effects of gender and age but did not find any large differences. The LPL activity in kidneys of 2-mo-old female mice was $539 \pm 45$ mU/g in the fed state, about one-half of that in male mice of comparable age. When the female mice were fasted for 24 h, LPL activity decreased to $235 \pm 42$ mU/g ($P < 0.002$). Thus the effect of fasting was similar to that in male mice, a decrease of $>50\%$. The LPL activity in kidneys of 4- and 8-mo-old fed female mice was significantly lower per gram tissue ($P < 0.02$) than in the 2-mo-old female mice, $359 \pm 36$ and $373 \pm 32$ mU/g, respectively.

To explore which fraction of kidney LPL is in contact with the circulating blood, we measured LPL activity before and 30 min after injection of a low-molecular-mass heparin preparation (Fig. 4). This type of heparin was used to ensure rapid absorption after intraperitoneal injection. Low-molecular-mass heparin preparations have been shown to cause efficient release of LPL both in whole body and in tissue perfusion experiments (9, 10). The injection resulted in a reduction of LPL activity by 49% in the kidneys ($P < 0.001$), 18% in the heart ($P = 0.055$), and 29% in white adipose tissue ($P < 0.01$). These results indicate that a comparatively large fraction of the LPL in kidneys is in contact with blood.

**Immunolocalization.** Most of the specific immunostaining with anti-LPL antibodies was associated with tubular epithelial...
was little or no periglomerular staining, but there was scattered staining inside the glomeruli.

The pattern of immunostaining in kidneys from mink and mice differed strikingly from that earlier observed in guinea pigs by Camps et al. (7). They found staining of the glomerular capillary network but little or no immunostaining in or along the tubuli. There was some immunostaining within the glomeruli in both mice and mink (Fig. 5), but it was clear that in these animals most of the immunostaining was associated with the tubuli. Camps et al. (7) suggested that the LPL found in the glomeruli might have been picked up from the blood. A way to test that hypothesis was to inject exogenous LPL. For these experiments, we used rats, which have low endogenous LPL activity in the kidney (Table 1), and mice.

Unpublished experiments by our laboratory have shown that a relatively small proportion of injected, labeled LPL (~2%) locates in the kidney of rats (Chevreuil O and Hultin M., unpublished observations). For the immunolocalization, we used rabbit anti-bovine LPL. These antibodies do not cross-react with rat or mouse LPL and gave no signal in kidneys from rats or mice not injected with LPL (not shown). Two minutes after injection of active bovine LPL, there was intense staining in the capillary network of the glomeruli (Fig. 6, A, B, and E) but very little along the capillaries surrounding the tubules or in tubular epithelial cells. When heparin was injected immediately before LPL, binding of the enzyme in the capillaries of the glomeruli was virtually abolished (Fig. 6, C and F). The staining was essentially unchanged at 15 min after the injection (not shown; studied only in rats). After 60 min, the staining was markedly reduced but was still confined to the capillary network of the glomeruli (not shown; studied only in rats). When we injected catalytically inactive LPL, which binds less strongly to heparin/heparan sulfate (38), there was only faint staining of the glomeruli (Fig. 6D; studied only in rats).

DISCUSSION

Our study demonstrates that there is LPL in the kidney and indicates that the enzyme is present in two different modes. In some of the species we studied, mice and mink, there were relatively high levels of LPL mRNA, protein, and activity in the kidney. Although there was a marked 35-fold difference in LPL catalytic activity between normal mink kidney and rat kidney, the specific activity was similar, ~0.5 mU/ng. Therefore, the difference in catalytic activity was not due to abnormal processing, as is the case with the enzyme in the LPL-deficient mink. The pattern of immunostaining indicated that in mink and mice the enzyme is associated with tubuli and capillaries around the tubuli, where it probably helps provide the tissue with energy substrates. A large fraction of the LPL in mouse kidney was washed out after injection of heparin. These results indicate that in mice, mink, Chinese hamsters, and, presumably, in several other species, the kidney is an important player in the metabolism of lipoproteins. There were some differences with gender and age in the mouse, but these were not large. This indicates that, at least in mice, the expression of LPL in kidney is a rather constant trait. The other main finding was that the capillary network in the glomeruli can pick up LPL from the blood. This was previously implied from a study in guinea pigs (7) and is here shown directly through the injection of exogenous LPL into rats and mice.
Immunolocalization in mice and mink, two of the species that express high LPL in kidney, showed that most of the enzyme was associated with tubuli. Immunostaining over tubular epithelial cells suggested that these are the main cells that produce the enzyme. This would be logical because the tubular epithelial cells consume much energy and derive it mainly from fatty acids. Experiences with other tissues indicate that the lipase is usually produced by the cells that will take up and metabolize fatty acids (25). In mink with the Phe214Leu mutation, there was immunostaining over the tubular cells, similar to that seen in normal mink, but there was no staining outside the cells. Earlier studies have shown that these mink have substantial amounts of the inactive lipase in the blood (11). Taken together, these findings suggest that after secretion the inactive lipase fails to bind to the cell surface of the lipase-producing cells or to the vascular epithelium. All of these results are in line with the hypothesis that in those animals that produce LPL in their kidneys, the functions of the enzyme are analogous to its functions in adipose tissue and muscles.
Studies with genetically modified mice have shown that expression of LPL only in the heart is enough to support normal triglyceride clearance (17, 25). Our results show that the activity in mouse kidney was as high as that in the heart per gram tissue and two to three times higher as calculated for the total tissue. The most obvious role for the lipase would be to present the underlying tubular cells with fatty acids for energy production. This is questioned, however, by findings in mink injected with radioactively labeled chylomicrons. Only a small fraction, <1%, of the radioactive fatty acids was found in the kidneys (28). Another possibility is that the kidney is a site where lipoprotein triglycerides are transformed to free fatty acids that mix into the plasma pool of free fatty acids and can be used throughout the body (13, 34). Like the heart, the kidney is a very well-perfused tissue.

In guinea pigs and rats, LPL activity in adipose tissue and muscles responds rapidly to changes in the nutritional state (3, 29). This is presumably an important aspect of energy homeostasis (25). The same regulation is seen also in mice, but the amplitude of the changes of LPL activity in adipose tissue and heart is less in mice (26). The present study shows that in mice, LPL activity in the kidney responds to the nutritional state. There was a marked reduction, ~50%, on fasting, and the activity returned to fed levels within a few hours after the refeeding of 24-h-fasted mice. This response was in the same direction and of similar magnitude as that in adipose tissue (26). The time course was also similar. In contrast, in kidneys of mink (28) and Chinese hamsters (Table 1) LPL activity did not change with the nutritional state. In these species, there was also no significant change in LPL activity with nutritional state in adipose tissue, heart, or any other tissue studied (28). The overall conclusion seems to be that the disposition of the LPL system varies considerably among species.

The mechanism for downregulation of adipose tissue LPL activity during fasting is posttranslational and appears to require that a gene, separate from the lipase gene, is activated (5). The product of this putative gene presumably acts to channel extracellular LPL toward an inactive form (37). The mechanism for downregulation of LPL activity in mouse kidney appears to be the same as in adipose tissue.
protein in their blood, in contrast to humans and many animals. This is a unique finding for a factor involved in lipoprotein metabolism.

The tissue activity was 7.6 mU/g tissue. If a 1% to the total LPL in the kidney was picked up from the circulating blood. This fraction, sometimes denoted “functional LPL,” can be probed by perfusion of the tissue with heparin (6, 16). In our experiments, 49% of the LPL was washed out from the kidneys within 30 min after administration of heparin. This indicates that a large fraction of kidney LPL is in contact with the circulating blood and can participate in lipoprotein metabolism. In fact, the fraction released from the kidney was higher than that for either heart or adipose tissue, two major sites of “functional LPL.”

Camps et al. (7) found that in guinea pigs there was immunostaining for LPL associated with the glomerular capillaries, but not in other parts of the kidney. They found no LPL mRNA (by in situ hybridization) in any cells within the glomeruli and suggested that the lipase had probably been picked up from the blood. All three layers of the glomerular filter, the capillary endothelium, the glomerular basement membrane, and the podocytes, exhibit strong negative charge and may thus provide “heparin-like” binding sites for LPL. To test this hypothesis, we injected exogenous lipase into rats and mice. This gave a very striking picture, with intense staining of the capillary network of the glomeruli but virtually no staining anywhere else in the kidney. The pattern was similar to that seen for endogenous LPL in guinea pig kidney (7). These data support the hypothesis that LPL can be picked up from the blood by the capillaries in the glomeruli. Binding was virtually abolished by preinjection of heparin, indicating that binding was, as suggested (7), to heparin-like sites. In further support of this, there was no binding of inactive, presumably monomeric LPL that is known to have much reduced affinity for heparin (19).

If there is equilibrium between LPL in the circulating blood and LPL bound in the glomeruli, the bound amount should reflect the concentration in the blood. We have not directly investigated this, but note that both pre- and post-heparin LPL is higher in fed compared with fasted mice (26). In guinea pigs, it appears that no LPL is produced in the kidney (7). If so, we can estimate the amount of LPL activity picked up from the blood. The tissue activity was 7.6 ± 2.6 mU/g tissue. If a similar amount of LPL is picked up from the blood by glomeruli in mice, this would contribute ~1% to the total LPL in the kidney. The function of LPL in the glomeruli, if any, is not obvious. The enzyme could provide fatty acids from lipoproteins as an energy substrate and/or precursor for other lipids in glomerular cells. The enzyme could also provide peroxisome proliferator-activated receptor ligands for regulatory processes (8, 39). Another possibility is that the enzyme, through its bridging action, enhances binding and endocytosis of lipoprotein particles (31). This effect of LPL is quite dramatic with the use of cultured mesangial cells (32).

A main conclusion from our study is that the expression of LPL in kidney varies widely among species. This is not a unique finding for a factor involved in lipoprotein metabolism. For instance, mice and rats have no cholesterol ester transfer protein in their blood, in contrast to humans and many animals (33). Rats have high hepatic lipase, whereas this enzyme is almost not present in guinea pigs (36). In mice the hepatic lipase circulates in the blood, whereas in most species it is bound in liver (24). More examples could be cited. With respect to LPL in the kidney, there is no information on whether humans are high or low expressers. This will be important to investigate in view of the close relationship between kidney disease and lipoprotein metabolism. Such studies may open new perspectives on the association among kidney disease, reduced LPL function, and deranged lipoprotein metabolism.

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