Depletion of Pre-\(\beta\)-high Density Lipoprotein by Human Chymase Impairs ATP-binding Cassette Transporter A1- but Not Scavenger Receptor Class B Type I-mediated Lipid Efflux to High Density Lipoprotein*

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The ATP-binding cassette transporter A1 (ABCA1) mediates the efflux of cellular unesterified cholesterol and phospholipid to lipid-poor apolipoprotein A-I (apoA-I). Chymase, a protease secreted by mast cells, selectively cleaves pre-\(\beta\)-migrating particles from high density lipoprotein (HDL\(_3\)) and reduces the efflux of cholesterol from macroparticles. To evaluate whether this effect is the result of reduction of ABCA1-dependent or -independent pathways of cholesterol efflux, in this study we examined the efflux of cholesterol to preparations of chymase-treated HDL\(_3\) in two types of cell: 1) in J774 murine macrophages endogenously expressing low levels of scavenger receptor class B, type I (SR-BI), and high levels of ABCA1 upon treatment with cAMP; and 2) in Fu5AH rat hepatoma cells endogenously expressing high levels of the SR-BI and low levels of ABCA1. Treatment of HDL\(_3\) with the human chymase resulted in rapid depletion of pre-\(\beta\)-HDL and a concomitant decrease in the efflux of cholesterol and phospholipid (2-fold and 3-fold, respectively) from the ABCA1-expressing J774 cells. In contrast, efflux of free cholesterol from Fu5AH chymase-treated and to untreated HDL\(_3\) was similar. Incubation of HDL\(_3\) with phospholipid transfer protein led to an increase in pre-\(\beta\)-HDL contents as well as in ABCA1-mediated cholesterol efflux. A decreased cholesterol efflux to untreated HDL\(_3\) was not, however, observed in ABCA1-expressing J774 with proculcin, an inhibitor of cholesterol efflux to lipid-poor apoA-I. Similar results were obtained using brefeldrin and gliburide, two inhibitors of ABCA1-mediated efflux. These results indicate that chymase treatment of HDL\(_3\) specifically impairs the ABCA1-dependent pathway without influencing either aqueous or SR-BI-facilitated diffusion and that this effect is caused by depletion of lipid-poor pre-\(\beta\)-migrating particles in HDL\(_3\). Our results are compatible with the view that HDL\(_3\) promotes ABCA1-mediated lipid efflux entirely through its lipid-poor fraction with pre-\(\beta\)-mobility.

Atherosclerosis is a disease characterized by accumulation of cholesterol in the arterial intima, the innermost layer of the arterial wall (1). Initially, cholesterol accumulates intracellularly, mostly in the intimal macrophages that scavenge oxidized low density lipoproteins. As the macrophages become cholesterol-loaded, they are transformed into foam cells, a key event in the early atherogenic process. Because macrophages are unable to down-regulate scavenger receptors or the inflow of cholesterol by this pathway, removal (efflux) of excess cellular cholesterol from these cells is of particular importance to prevent foam cell formation (2).

Efflux of cellular cholesterol is a complex and heterogeneous process promoted by many factors and requiring the presence of extracellular cholesterol acceptors (3–5). Desorption of free cholesterol by aqueous diffusion to phospholipid-containing lipoproteins is a nonspecific and relatively inefficient pathway that operates in all cells (6). A more efficient pathway of cholesterol efflux is mediated by the exchangeable apolipoproteins A, C, and E, the major apolipoproteins associated with HDL\(_1\) (7). Lipid-free or lipid-poor apolipoproteins promote the efflux of free cholesterol by interacting with the ATP-binding cassette transporter A1 (ABCA1) in the cell membrane (8). In contrast, mature HDL and other phospholipid-containing spherical particles are believed to acquire free cholesterol by simple aqueous diffusion or by facilitated diffusion mediated by the scavenger receptor class B, type I (SR-BI). Indeed, the rate of cholesterol efflux from SR-BI-expressing cells to phospholipid-containing acceptors is a linear function of the quantity and type of phospholipids present in the extracellular acceptors (9). However, it has also been reported that the presence of intact apolipoproteins may influence the ability of phospholipid-containing particles to promote cholesterol efflux (10, 11).

Experimental studies indicate that the ABCA1 is involved in the efflux of free cholesterol and phospholipid from different cell types, mediating the lipidation of apoA-I, a process thought to be responsible for the formation of pre-\(\beta\)-migrating HDL particles. These particles, in turn, interact with lecithin-cholesterol acyltransferase in plasma, which catalyzes the esteri-
fication of free cholesterol and the subsequent maturation of the pre-β particles to α-migrating HDL with a core of cholesterol esters (12, 13). Cholesterol efflux to purified, lipid-poor apoA-I has been well established as an ABCA1-mediated pathway for the removal of cellular sterols (14–16). However, although in some studies it has been observed that the ultracentrifugally isolated HDL3 fraction is able to induce ABCA1-mediated efflux of cholesterol (14, 17–19), the relative contributions of α- and pre-β-migrating particles in HDL3 to cellular cholesterol efflux via ABCA1 or other pathways of efflux have not been well characterized.

We have demonstrated previously that several proteases found in the arterial intima can degrade HDL3, in vitro and reduce its efficiency as an acceptor of cholesterol from macrophages. The mast cell proteases chymase (20) and tryptase (21) and some metalloproteinases (22) as well as plasmin and kallikrein (23) specifically deplete the small subpopulation of pre-β-migrating HDL particles and so impair the efflux of cholesterol from human macrophage foam cells promoted by HDL3. Because cholesterol efflux to HDL3 can be mediated by ABCA1-dependent and -independent mechanisms, we were interested to find out which of these two types of efflux is affected by proteolytic enzymes capable of depleting pre-β-migrating HDL particles. We selected human chymase as an example of a neutral protease present in the arterial intima because chymase, when bound to heparin, i.e. in its physiological form, is partially resistant to its natural inhibitors (24) and, thus, capable of proteolyzing HDL in the plasma (20) and in the aortic intimal fluid (24, 25).

To be able to define which type of efflux is impaired by treatment of HDL3 with chymase, we chose J774 murine macrophages incubated in the presence of CAMP to examine the ABCA1-dependent pathway of efflux (14, 26) and Fu5AH rat hepatoma cells to examine the SR-B1 pathway (27). In addition, to study in further detail the chymase-inhibition of lipid efflux, we used probucol for inhibition of efflux to lipid-free or lipid-poor apolipoproteins (26–30). The results using the two cell lines strongly suggested that chymase-induced proteolysis of HDL3 specifically impairs the component of efflux which is dependent on the function of ABCA1. The ABCA1 dependence of the efflux was confirmed by using brefeldin and gliburide, two inhibitors of ABCA1 (31, 32). Our results also demonstrate that HDL3 effectively promotes ABCA1-mediated efflux of lipids caused by the presence of pre-β-migrating lipid-poor particles.

EXPERIMENTAL PROCEDURES

Materials—Fetal calf serum (FCS), bovine serum albumin (BSA), 8-4-chlorophenylthio)-cAMP (CPT-cAMP), brefeldin, and gliburide were purchased from Sigma. Organic solvents were purchased from Merck. [1,2-3H]Cholesterol and [methyl-3H]Choline chloride were from Amersham Biosciences. Tissue culture flasks and plates were from Corning and Falcon. Dulbecco's modified Eagle's medium, RPMI 1640, and phosphate-buffered saline (PBS) were purchased from BioWhittaker (Walkersville, MD). The acetyl-CoA: cholesterol acyltransferase inhibitor, Sandoz 58-035, was a gift from Novartis (Basel, Switzerland). Fetal calf serum (FCS), bovine serum albumin (BSA), 8-(4-chlorophenylthio)-cAMP (CPT-cAMP), brefeldin, and gliburide were purchased from BioWhittaker (Walkersville, MD). The acetyl-CoA: cholesterol acyltransferase inhibitor, Sandoz 58-035, was a gift from Novartis (Basel, Switzerland). Materials—Fetal calf serum (FCS), bovine serum albumin (BSA), 8-4-chlorophenylthio)-cAMP (CPT-cAMP), brefeldin, and gliburide were purchased from Sigma. Organic solvents were purchased from Merck. [1,2-3H]Cholesterol and [methyl-3H]Choline chloride were from Amersham Biosciences. Tissue culture flasks and plates were from Corning and Falcon. Dulbecco's modified Eagle's medium, RPMI 1640, and phosphate-buffered saline (PBS) were purchased from BioWhittaker (Walkersville, MD). The acetyl-CoA: cholesterol acyltransferase inhibitor, Sandoz 58-035, was a gift from Novartis (Basel, Switzerland). Fetal calf serum (FCS), bovine serum albumin (BSA), 8-(4-chlorophenylthio)-cAMP (CPT-cAMP), brefeldin, and gliburide were purchased from BioWhittaker (Walkersville, MD). The acetyl-CoA: cholesterol acyltransferase inhibitor, Sandoz 58-035, was a gift from Novartis (Basel, Switzerland).


3Hcholine chloride. After the stimulation period in the presence of CPT-cAMP and the efflux time to the different acceptors (6 h), the medium was collected and centrifuged. Control cell monolayers were treated identically, except that CPT-cAMP was omitted from the incubation medium. After centrifugation, the supernatants were separated and the lipids extracted. The aqueous phase was aspirated, and, to remove any remaining free [3H]choline, the chloroform phase was washed three times with 10.5% (v/v) methanol/water. The chloroform phase was then dried under a stream of nitrogen (N2), and redissolved in 1 ml of toluene. A 700-μl aliquot of each sample was transferred to a liquid scintillation vial and quantified by scintillation counting. To analyze the cellular lipids, the monolayers of cells were washed three times with PBS, and the lipids were extracted by the addition of 1 ml of 2-propanol. The 2-propanol extracts were dried under a stream of N2, the free [3H]choline was extracted, and the chloroform phase was treated, as described above.

Statistical Analysis—Results are reported as the means ± S.D. Statistical significance was determined by two-tailed Student’s t test.

RESULTS

Ability of the Chymase-treated HDL3 to Promote Efflux of Cellular Cholesterol from J774 and Fu5AH Cells—We treated the HDL3 fractions isolated from human plasma with human chymase for various periods of time. The concentration of chymase used (0.5 μg/ml) was chosen to match the assumed concentration of chymase in the intimal fluid (24). After fully inhibiting the chymase activity, the untreated and chymase-treated HDL3 preparations were added to three cellular systems to test their ability to promote cellular cholesterol efflux. Aliquots of HDL3 were added to the cell cultures in the low range of acceptor protein concentration, in which the high affinity efflux of cholesterol dominates (25), and the release of cholesterol into the medium was measured after incubation for 4 h. The cell models used in these experiments were J774 macrophages and Fu5AH cells. Under basal conditions, J774 express low levels of ABCA1 and SR-BI and release membrane cholesterol to extracellular acceptors by passive diffusion, whereas stimulation with cAMP up-regulates ABCA1-mediated lipid efflux to apolipoproteins. In contrast, under basal conditions, Fu5AH cells express high levels of SR-BI in the plasma membrane, and thus the efflux of lipids depends on facilitated diffusion by this receptor. As shown in Fig. 1A, when unstimulated J774 cells (−cAMP) were used as cholesterol donor cells, pretreatment of HDL3 with chymase for up to 24 h did not have any influence on the rate of cholesterol efflux. However, upon cAMP stimulation of the cells (+cAMP), an increased efflux (2-fold) to the untreated preparation of HDL3 (0 h) was observed, and a short preincubation of HDL3 with chymase (2 h) was sufficient to prevent the cAMP-dependent increase in the efflux of cholesterol. In a control experiment, we used lipid-free apoA-I as cholesterol acceptor (Fig. 1B). As expected, after cAMP stimulation, the apoA-I-dependent efflux was increased (by 3-fold), confirming that the ABCA1-mediated pathway was stimulated. When 1 mg/ml apoA-I was incubated with 0.5 μg/ml chymase, small-sized polypeptides were formed, and the cholesterol efflux from the cAMP-stimulated cells was fully inhibited (not shown).

Analysis of HDL3 by agarose gel electrophoresis showed that the untreated HDL3 preparation contained both α- and pre-β-migrating species (estimated pre-β content 6%), and treatment with chymase totally depleted the pre-β-HDL subpopulation within 2 h of incubation (see Fig. 1A, inset). Throughout the whole incubation period, no change in the mobility of the α-migrating fraction of HDL3 was observed. The ability of chymase to deplete pre-β-HDL was also confirmed by two-dimensional polyacrylamide gradient gel electrophoresis analysis (see Fig. 5). Analysis of the untreated HDL3 by SDS-PAGE showed two major bands corresponding to apoA-I and apoA-II (not shown). As reported previously (25), treatment of HDL3 with chymase results in degradation of apoA-I with high efficiency and in degradation of apoA-II with low efficiency. ApoA-I immunoblotting of the gel revealed the appearance of an additional band with apparent molecular mass of 26 kDa which reflected degradation of apoA-I (32 ± 1%, data not shown). In this experiment, prolongation of chymase treatment beyond 2 h did not lead to further significant degradation of apoA-I.

In contrast to the results obtained with cAMP-stimulated J774 cells, chymase degradation of HDL3 for up to 24 h did not have any influence on the efflux of cholesterol from the Fu5AH cells (Fig. 2). Fu5AH cells express high levels of SR-BI; hence, these results indicate a lack of effect of chymase proteolysis on the cholesterol acceptor function of HDL3 in conditions where the SR-BI-facilitated cholesterol efflux mechanism dominates.

Because an effect of chymase treatment on HDL3 was observed only when using the J774 cells, we studied in further detail the efflux of cellular cholesterol from these cells. First, we determined the rate of efflux from control or cAMP-stimulated cell cultures in the presence of various concentrations of HDL3 (up to 50 μg/ml) (Fig. 3). The efflux of cholesterol from nonstimulated cells to untreated and chymase-treated HDL3 was similar and of low affinity (apparent Km about 50 μg/ml). In sharp contrast, the efflux of cholesterol from stimulated cells to untreated HDL3 was far more efficient (Km of 18 μg/ml; Vmax 20%/4 h) (Prism, GraphPad Inc., San Diego). Treatment of HDL3 with chymase for 2 h dramatically decreased the efficiency of this efflux process down to the level observed in the nonstimulated cells. Because ABCA1 expression is also up-regulated in cholesterol-loaded macrophages, we then studied the effect of chymase treatment of HDL3 on the efflux of cholesterol from cholesterol-loaded unstimulated J774. The results showed that chymase treatment for 2 h reduced cholesterol efflux from these cells by 40% (Student’s t test; p = 0.052) (data not shown).

![Fig. 1. Efflux of [3H]cholesterol from J774 to HDL3 treated with chymase for various lengths of time.](image-url)
that observed when nonstimulated cells were used (Fig. 4).

Symbols denote monolayers treated with CPT-cAMP; open symbols denote untreated control monolayers. Data are from a representative experiment with triplicate wells (n = 3). (CPT-cAMP for 12 h as described previously (see Fig. 1 and Experimental Procedures), then incubated with increasing concentrations of untreated HDL3 (solid and open squares) as cholesterol acceptors for 4 h. HDL3 was treated with chymase for 2 h under the conditions described in Fig. 1. Solid symbols denote monolayers treated with CPT-cAMP; open symbols denote control monolayers. Data are from a representative experiment with triplicate wells (n = 3). Values are expressed as the means ± S.D.

ABC1-mediated Phospholipid Efflux from J774 Macrophages to Chymase-treated HDL3—To measure the phospholipid efflux, the phospholipids in J774 cells were radiolabeled. Stimulation of the radiolabeled J774 cells with CPT-cAMP caused a 10-fold and a 3-fold increase in phospholipid efflux to apoA-I and to untreated HDL3 (at 0 h), respectively. Chymase treatment of HDL3 for 2 h prevented the cAMP-induced increase in the efflux of phospholipids, i.e. it remained at a level similar to that observed when nonstimulated cells were used (Fig. 4).

Effect of Chymase Treatment of HDL3 on Their Ability to Promote Cellular Cholesterol Efflux from cAMP-stimulated J774 Cells Under Conditions When Efflux to Lipid-poor Apolipoproteins or Efflux Facilitated by ABC1 Is Inhibited—To demonstrate further that the lipid-poor, pre-β-migrating component present in the HDL3 preparation was responsible for the ABC1-dependent efflux, we studied the effect of chymase treatment of HDL3 on efflux from cAMP-stimulated J774 cells in the absence or presence of 1) probucol, an inhibitor of the lipid efflux promoted by lipid-poor particles (28–30), and 2) brefeldin and gliburide, two inhibitors of ABC1 (31, 32). The results shown in Fig. 7 indicate that probucol is able to reduce
Fig. 5. Effect of chymase treatment on the particle composition of untreated HDL₃ (A) and PLTP-pretreated HDL₃ (B). Native HDL₃ and PLTP-pretreated HDL₃ were incubated with chymase for 2 h under the conditions described in Fig. 1. At the end of the incubation, the distribution of HDL subclasses was analyzed by two-dimensional electrophoresis, where agarose gel electrophoresis was followed by nondenaturing polyacrylamide gradient gel electrophoresis. Fractionated HDL₃ was then electroblotted onto a nitrocellulose membrane on which apoA-I-containing lipoproteins were detected with the use of a sheep anti-apoA-I antibody.

Fig. 6. Effect of the content of pre-β-HDL in HDL₃ on efflux of cellular [³H]cholesterol from CPT-cAMP-stimulated and unstimulated J774 cells. Monolayers of J774 cells were labeled with 3 μCi/ml [³H]cholesterol for 24 h, as described previously (see Fig. 1 and “Experimental Procedures”). The cells were then incubated for 12 h with 0.2% BSA in the presence (A) or absence (B) of 0.3 mM CPT-cAMP followed by incubation for 4 h with various HDL₃ preparations (all at 12.5 μg/ml) containing different amounts of pre-β-HDL. HDL₃ was preincubated in the absence (−PLTP) or presence (+PLTP) of PLTP for 24 h followed by incubation in the absence (−chymase) or presence (+chymase) of chymase for 2 h, as described under “Experimental Procedures.” Pre-β contents: 0% = −PLTP/+chymase; 4% = native HDL₃ (from the donor with the lowest pre-β content in this study); 6% = +PLTP/+chymase; 9% = −PLTP/+chymase; 18% = +PLTP−/chymase.

Fig. 7. Effect of probucol, brefeldin, and gliburide on [³H]cholesterol efflux from CPT-cAMP-stimulated J774 to untreated or chymase-treated HDL₃. Cell monolayers were labeled with 3 μCi/ml [³H]cholesterol for 24 h in RPMI medium with 1% FCS in the presence of 2 μg/ml acyl-CoA:cholesterol acyltransferase inhibitor. The cells were then stimulated for 12 h with 0.3 mM CPT-cAMP in 0.2% BSA. After this treatment, the monolayers were incubated for 2 h in the presence or absence of 10 μM probucol. In a parallel experiment 10 μM brefeldin was added during the stimulation time with CPT-cAMP. In an additional experimental gliburide was added to give a final concentration of 100 μM during the efflux period. Fractional efflux/4 h was determined for 12.5 μg/ml untreated HDL₃ (open bars) and 12.5 μg/ml chymase-treated HDL₃ (solid bars) (treatment with chymase for 2 h under conditions described in Fig. 1). Data are from a representative experiment with triplicate wells (n = 3). Values are expressed as the means ± S.D.

DISCUSSION

In the present study, we attempted to identify the cellular cholesterol efflux pathway associated with the high affinity component of the efflux to HDL₃, which is lost upon treatment of the acceptors with chymase (25). For this purpose, we studied the cholesterol efflux promoted by the chymase-treated HDL₃ from 1) J774 cells that express ABCA1 upon stimulation with cAMP, and 2) Fu5AH cells that physiologically express the SR-BI. Limited proteolysis of HDL₃ by chymase produced full depletion of the pre-β-migrating particles and completely abolished the ABCA1-mediated component of cholesterol efflux to the acceptor particles. Moreover, chymase treatment of HDL₃ inhibited phospholipid efflux, a process specifically mediated by ABCA1 (15, 16, 40).

Our results are compatible with the view that pre-β particles do not contribute to the ability of HDL₃ to promote cholesterol efflux by either simple or facilitated diffusion. This conclusion is also consistent with the observation that pre-β HDL does not participate in the cholesterol efflux to HDL₃ from cell systems poorly expressing ABCA1 (41). The fact that chymase treatment did not reduce the two diffusional efflux processes stimulated by phospholipid-rich acceptors indicates that chymase cleaved a pool of lipid-poor particles. This hypothesis was confirmed by our present observation that only efflux to untreated HDL₃, but not to chymase-treated HDL₃ (from which lipid-poor...
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particles had been depleted), was inhibited by probucol, an antagonist of cholesterol efflux to lipid-poor particles (28–30). The report that trypsin-labile apolipoproteins in preparations of HDL₃ are responsible for an apolipoprotein-dependent component of cholesterol efflux (19) is also consistent with the present findings. We and others (42, 43) observed recently that the C-terminal domain of apoA-I is necessary to promote chymase treatment on high affinity efflux of cholesterol to HDL₃; 3) enrichment of HDL₃ with pre-

REFERENCES

1. Ross, R. (1999) N. Engl. J. Med. 340, 115–126
2. Brown, M. S., and Goldstein, J. L. (1983) Annu. Rev. Biochem. 52, 223–261
3. Fielding, C. J. (1991) Curr. Opin. Lipidol. 2, 376–378
4. Johnson, W. J., Malberg, F. H., Rothblat, G. H., and Phillips, M. C. (1991) Biochim. Biophys. Acta 1063, 273–298
5. Fielding, C. J., and Fielding, P. E. (1991) Biochim. Biophys. Acta 1533, 175–189
6. Vayner, P. G., Bertnick, A. E., Kellner-Weigel, G., de la Llera-Moya, M., Phillips, M. C., and Rothblat, G. H. (2003) Arterioscler. Thromb. Vasc. Biol. 23, 712–719
7. Lee, M., Calabresi, L., Chiesa, G., Franceschini, G., and Kovanen, P. T. (2002) Arterioscler. Thromb. Vasc. Biol. 22, 1475–1481
8. Rothblat, G. H., de la Llera-Moya, M., Favari, E., Yancey, P. G., and Kellner-Weigel, G. (2002) Arterioscler. Thromb. 163, 1–8
9. Vayner, P. G., de la Llera-Moya, M., Swarnakar, S., Monzo, P., Klein, S. M., Connelly, M. A., Johnson, W. J., Williams, D. L., and Rothblat, G. H. (2000) J. Biol. Chem. 275, 36596–36604
10. Bernini, F., Calabresi, L., Pahlo, G., and Franceschi, G. (1996) Biochim. Biophys. Acta 1299, 103–109
11. Lee, M., Kovanen, P. T., Tedeschi, G., Oungré, E., Franceschini, G., and Calabresi, L. (2003) J. Lipid Res. 44, 539–546
12. Fielding, C. J., and Fielding, P. E. (1995) J. Lipid Res. 36, 211–228
13. Jonas, A. (1991) Biochim. Biophys. Acta 1084, 205–220
14. Bertnick, A. E., Rothblat, G., Happe, K. L., Royer, L. J., McNish, J., and Franceschi, G. (2000) J. Biol. Chem. 275, 26834–26840
15. Attie, A. D., Kastelian, J. P., and Hayden, M. R. (2001) J. Lipid Res. 42, 1717–1726
16. Remaley, A. T., Stonik, J. A., Demosky, S. J., Neufeld, E. B., Bocharov, A. V., Vishnyakova, T. G., Eggerman, T. L., Patterson, A. P., Duverger, N. J., Santamaria-Fojo, S., and Brewer, H. B., Jr. (2001) Biochim. Biophys. Res. Commun. 280, 818–823
17. Wang, N., Silver, D. L., Costet, P., and Tall, A. R. (2000) J. Biol. Chem. 275, 33053–33058
18. Forstch-Orozumere, M., Langmann, T., Heimerl, S., Boruszkowa, H., Kaminski, W. E., Drobnick, W., Honen, C., Schumacher, C., and Schmitz, G. (2001) J. Biol. Chem. 276, 12427–12432
19. Mendoza, A. J., and Orun, J. F. (1997) Biochim. Biophys. Acta 1346, 285–299
20. Lee, M., von Eckardstein A., Lindstedt L., Assmann G., and Kovanen, P. T. (1999) Arterioscler. Thromb. Vasc. Biol. 19, 1066–1074
21. Lee, M., Sommerhoff, C. P., von Eckardstein, A., Zelti, F., Fritz, H., and Kovanen, P. T. (2002) Arterioscler. Thromb. Vasc. Biol. 22, 2096–2091
22. Lindstedt, L., Saarinen, J., Kulkkinen, N., Welgus, H., and Kovanen, P. T. (1999) J. Biol. Chem. 274, 22627–22634
23. Lindstedt, L., and Kovanen, P. T. (2000) Biochim. Biophys. Res. Commun. 277, 552–557
24. Lindstedt, L., Lee, M., and Kovanen, P. T. (2001) Arterioscler. Thromb. Vasc. Biol. 21, 87–97
25. Lindstedt, L., Lee, M., Castro, G. H., Fruchtaj, J.-C., and Kovanen, P. T. (1996) J. Clin. Invest. 97, 2174–2182
26. Oram, J. F., Law, R. M., Garvin, M. R., and Wade, D. P. (2000) J. Biol. Chem. 275, 34508–34510
27. Jian, B., de la Llera-Moya, M., Ji, Y., Wang, N., Phillips, M. C., Swaney, J. B., and Tall, A. R., and Rothblat, G. H. (1998) J. Biol. Chem. 273, 5599–5606
28. Tsutita, M., and Yokoyama, S. (1986) Biochemistry 25, 13011–13029
29. Yokoyama, S. (1996) Biochim. Biophys. Acta 1302, 1–15
30. Sakr, S. W., Williams, D. L., Stoudt, G. W., Phillips, M. C., and Rothblat, G. H. (1999) Biochim. Biophys. Acta 1438, 85–98
31. Remaley, A. T., Schumacher, U. K., Stonik, J. A., Farsi, B. D., Nazih, H., and Brewer, H. B., Jr. (1997) Arterioscler. Thromb. Vasc. Biol. 17, 1813–1821
32. Wang, N., Silver, D. L., Thiele, C., and Tall, A. (2001) J. Biol. Chem. 276, 25742–25747
33. Kokkoni, K., Ovastiainen, M., and Kovanen, P. T. (1998) J. Biol. Chem. 261, 16067–16072
34. Franceschini, G., Vecchio, G., Gianfranceschi, G., Magani, D., and Sirtori, C. R. (1985) J. Biol. Chem. 260, 13621–13625
35. Schagger, H., and Von Jagow, G. (1987) Anal. Biochem. 166, 368–379
36. Huang, Y., von Eckardstein, A., and Kovanen, G. H. (1995) Arterioscler. Thromb. 15, 445–458
37. Vayner, P. G., Bielicki, J. K., Johnson, W. J., Lund Katz, S., Palgumachari, M. N., Anantharamaiah, G. M., Segrest, J. P., Phillips, M. C., and Rothblat, G. H. (1995) Biochemistry 34, 7965–7968
38. Jauhiainen, M., Metso, J., Pahlman, R., Blomqvist, S., van Tol, A., and Ehnholm, C. (1993) J. Biol. Chem. 268, 4032–4036
39. Lee, M., Metso, J., Jauhiainen, M., and Kovanen, P. T. (2003) J. Biol. Chem. 278, 13509–13545
40. Fielding, P. E., Nagao, K., Hakamata, H., Chimini, G., and Fielding, C. J. (2003) Biochemistry 39, 14113–14120
41. Sviridov, D., Miyazaki, O., Theodore, K., Haung, A., Fukumachi, I., and Nestel, P. (2002) Arterioscler. Thromb. Vasc. Biol. 22, 1482–1488
42. Faveri, E., Bernini, F., Tarugi, P., Franceschini, G., and Calabresi, L. (2002) Biochem. Biophys. Res. Commun. 296, 801–805
43. Panagiotopulos, S. E., Witting, S. R., Horace, E. M., Hui, D. Y., Maiorano, N. J., and Davidson, W. S. (2002) J. Biol. Chem. 277, 39477–39484
44. Lee, M., Uboldi, P., Giudice, D., Catapano, A. L., and Kovanen, P. T. (2000) J. Lipid Res. 41, 975–984
45. Kovanen, P. T. (1996) Curr. Opin. Lipidol. 7, 281–286
46. Sloop, C. H., Dory, L., and Roheim, P. S. (1987) J. Lipid Res. 28, 225–237
47. Asztalos, B. F., Sloop, C. H., Wang, L., and Roheim, P. S. (1993) Biochim. Biophys. Acta 1169, 301–304
48. Ghalim, N., Adlouni, A., Saile, R., Parra, H. J., Benslimane, A., Bard, J. M., and Fruchart, J.-C. (1996) Int. J Clin. Lab. Res. 26, 224–228
49. Fournier, N., Atger, V., Paul, J.-L., Sturm, M., Duverger, N., Rothblat, G. H., and Mauviel, N. (2000) Arterioscler. Thromb. Vasc. Biol. 20, 1283–1292
50. Kaartinen, M., Penttilä, A., and Kovanen, P. T. (1994) Arterioscler. Thromb. 14, 966–972
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