Active and low-active forms of serum phospholipid transfer protein in a normal Finnish population sample

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Abstract Human serum phospholipid transfer protein (PLTP) exists as a catalytically active (HA-PLTP) and a low-active (LA-PLTP) form. In this study, the association of PLTP activity and the concentrations of both forms with lipid and carbohydrate parameters were investigated. In a random Finnish population sample, serum PLTP concentration (n = 250) was 6.56 ± 1.45 mg/l, the mean lipoprotein-independent (PLTPexo) phospholipid transfer activity was 6.59 ± 1.66 μmol/ml/h, and the mean lipoprotein-dependent (PLTPendo) activity was 1.37 ± 0.29 μmol/ml/h. Of the serum PLTP concentration, ~46% was in a catalytically active form. HA-PLTP concentration correlated positively with serum PLTPexo activity (r = 0.380, P < 0.001), HDL cholesterol (r = 0.291, P < 0.001), and apolipoprotein A-I (r = 0.187, P < 0.01). Of the potential regulatory factors for PLTP, apolipoprotein E showed a weak positive correlation with serum PLTPexo (r = 0.154, P < 0.05) and PLTPendo (r = 0.192, P < 0.01) activity but not with PLTP concentration. Weak associations were also observed between PLTP parameters and determinants of glucose homeostasis (glucose, insulin, and homeostasis model assessment for insulin resistance). The present data on PLTP activity and concentration reveal novel connections of the two PLTP forms with lipid and carbohydrate metabolism.

Supplementary key words • apolipoproteins • lipid transfer proteins • enzyme-linked immunosorbent assay

Increased HDL concentration protects against coronary heart disease (1, 2), primarily by removing cholesterol from peripheral tissues (3). One important regulator of HDL metabolism is phospholipid transfer protein (PLTP) (4). It transfers phospholipids between different lipoproteins (5) and mediates HDL conversion (6, 7). Recent observations of the presence of PLTP in macrophage foam cells of atherosclerotic lesions suggest that PLTP could function either as an antiatherogenic molecule by facilitating cholesterol efflux or as a proatherogenic molecule by mediating lipid retention (8, 9). The involvement of PLTP in the reverse cholesterol transport process was recently suggested by Oram and colleagues (10), who demonstrated that PLTP interacts with ABCA1 on macrophages and facilitates cholesterol and phospholipid efflux. In addition to lipid metabolism, PLTP may also have a role in carbohydrate metabolism (11–13). In HepG2 cells, high glucose concentration increases both PLTP mRNA and activity levels (14).

Human plasma contains two forms of PLTP, a high-active form (HA-PLTP) and a low-active form (LA-PLTP). These two forms are associated with macromolecular complexes of different size (15, 16). At present, the processes that regulate the distribution of the HA- and LA-PLTP forms are unknown.

Although gene-targeted animal models (17–22) have been studied extensively, the physiological role of PLTP in human lipid metabolism is far from resolved. The present study was specifically carried out to clarify the relationships of PLTP concentration and activity with lipoprotein and carbohydrate metabolism in normolipidemic Finnish individuals participating in the Health 2000 Health Examination Survey. By measuring the concentration of both HA- and LA-PLTP forms (23) and studying the relationship...
ships between PLTP concentration and activity and selected serum parameters, we will increase our understanding of the regulation of PLTP activity and the distribution of the two PLTP forms. The aims of this study were to investigate the distribution of the two PLTP forms in a population sample, to test how the two PLTP forms relate to lipid and carbohydrate metabolism, and to find possible regulatory factors for PLTP.

MATERIALS AND METHODS

Subjects

For this study, 250 subjects (125 men and 125 women), age range 30-94 years, were randomly chosen as a subsample of the Health 2000 Health Examination Survey study (24) carried out in Finland. Serum samples were stored at -70°C before analysis.

Determination of PLTP concentration

Measurement of human serum PLTP concentration was performed essentially as described earlier (23). Briefly, the serum samples were incubated with 0.5% SDS for 30 min at 22°C in the sample buffer [10 mM NaPO4, 150 mM NaCl (PBS), pH 7.4, containing 0.1% Tween 20]. After the SDS pretreatment, the mixtures were diluted in the sample buffer and added in duplicate to microtiter plate wells coated with anti-human PLTP monoclonal antibody JH66. All subsequent steps were performed according to the PLTP ELISA method as described (25). The intra-assay and interassay coefficients of variation (CVs) were 8.5% (n = 8) and 9.7% (n = 12), respectively.

Separation of the two PLTP forms from each other was carried out by dextran sulfate-CaCl2 precipitation using the method of Kato et al. (26), with minor modifications. Briefly, 200 µl of serum was mixed with 300 µl of water and 200 µl of 1% dextran sulfate (Dextran Sulfate Sodium Salt; dextran molecular weight ~500,000; Amersham Pharmacia Biotech; dialyzed against water before use). The mixture was incubated on ice for 20 min with intermittent mixing. After this, CaCl2 was added to a final concentration of 0.1 M. The mixture was centrifuged (16,000 g) for 5 min at room temperature, and the clear supernatant was collected and assayed for PLTP activity and concentration. NaCl was added to the supernatant to a final concentration of 1 M before the PLTP activity assay. PLTP activity in the supernatant after precipitation was ~90% of that in the original serum sample. The LA-PLTP concentration was obtained by subtracting the HA-PLTP concentration measured in the dextran sulfate-CaCl2 supernatant from total serum PLTP concentration.

Assay of PLTP activity

PLTP-facilitated phospholipid transfer activity was measured in serum using two different radiometric methods.

1) In the exogenous, lipoprotein-independent assay (PLTPexo), [3H]phosphatidylcholine (PC)-liposomes (150 nmol of dipalmitoylphosphatidylcholine in 10 mM Tris-Cl, 150 mM NaCl, and 1 mM EDTA, pH 7.4) were incubated with isolated HDL containing 1.5 mM iodoacetate (28). After incubation, 320 µl of 10 mM Tris-Cl, 150 mM NaCl, and 1 mM EDTA, pH 7.4, were added, and then excess liposomes and apoB-containing lipoproteins were precipitated with 300 µl of 215 mM MnCl2·4H2O and 500 mM NaCl containing 445 U/ml heparin. The intra-assay and interassay CVs were 3.2% (n = 20) and 6.3% (n = 14), respectively.

2) In the endogenous, lipoprotein-dependent assay (PLTPend), [3H]PC-liposomes were mixed with 30 µl of undiluted serum and incubated for 30 min at 37°C in a final volume of 80 µl, containing 1.5 mM iodoacetate (28). After incubation, 320 µl of 10 mM Tris-Cl, 150 mM NaCl, and 1 mM EDTA, pH 7.4, were added, and then excess liposomes and apoB-containing lipoproteins were precipitated with 300 µl of 215 mM MnCl2·4H2O and 500 mM NaCl containing 445 U/ml heparin. The intra-assay and interassay CVs were 3.2% (n = 20) and 6.3% (n = 14), respectively.

In both assays, radioactivity was measured from the supernatants with a liquid scintillation counter (Wallac, Turku, Finland).

Apoe genotyping

Apoe-3937 and apoe-4075 variations were genotyped using the MassARRAY System (Sequenom, San Diego, CA), with the following protocol modifications: 30 ng of genomic DNA was amplified in a 5 µl reaction, using 0.25× BD Taq DNA Polymerase (BD Biosciences Canada, Mississauga, Ontario). The PCR program involved eight cycles at 95°C for 30 s and 72°C (~0.5°C/cycle) for 1 min, 37 cycles at 95°C for 30 s and 68°C for 1 min, followed by a 3 min extension at 68°C. PCR products were diluted 1:3 before the variation-specific extension reaction. Duplex extension reactions were done using the protocol specified by the manufacturer, with 100 µl. Genotypes were automatically called with SpectroCALLER software (Sequenom) and checked manually. The PCR primers used were 5′-ACGTTGATGACACTGCAGAAG-3′ and 5′-ACGTTGATGACCGGGCCCTGTGACTGTC-3′. The extension primer used for apoe-3937 was 5′-GGGACATGGGCAAGGTTG-3′, and that used for apoe-4075 was 5′-TGCCGATGACCTGCAAGG-3′. The terminator mix used was ACG (Sequenom).

General procedures

Protein concentration was determined by the method of Lowry et al. (29). ApoAIV, apoAI-II, and apoB concentrations were measured by immunoturbidimetric methods using commercial kits (Orion Diagnostica, Espoo, Finland; Boehringer-Mannheim, Mannheim, Germany) and a clinical chemistry analyzer (Olympus Diagnostic GmbH). ApoE concentration was measured using an ELISA (30).

Serum total cholesterol (TC) and triglyceride (TG) were analyzed using fully enzymatic methods (Olympus Diagnostica). HDL- and LDL-cholesterol (HDL-C and LDL-C) were measured using direct enzymatic methods (Roche Diagnostics GmbH).

Plasma glucose concentration was analyzed by a hexokinase method (Olympus Diagnostica), and insulin was analyzed by a microparticle enzyme immunoassay (Abbott Diagnostics Division, Axis-Shield, Oslo, Norway). Concentration of C-reactive protein (CRP) was determined by an immunoturbidimetric method (Orion Diagnostica). The homeostasis model assessment for insulin resistance (HOMA IR) was calculated from the fasting plasma glucose and serum insulin concentrations as follows: fasting insulin (µU/ml) × fasting glucose (mmol/l)/22.5 (31).

Statistical analysis

Comparisons of continuous variables between genders and apoe genotypes were tested for statistical significance with one-way ANOVA. Correlations of PLTP mass and activity with age, body mass index (BMI), and serum lipids were tested with the Pearson correlation test. All statistical analyses were performed using SPSS version 11.5.

RESULTS

Characteristics of the study population

The mean age of the study population, consisting of 125 male and 125 female subjects, was 55 years; the BMI
was 26.1 ± 4.0 (mean ± SD). The age, BMI, and CRP values did not differ significantly between genders (Table 1). The same was true for serum TG, LDL-C, apoB, apoA-II, apoE, and insulin, but there was a significant gender difference in TC, HDL-C, apoA-I, and glucose. The waist-to-hip ratio (WHR) was significantly higher among men.

**Serum PLTP activities**

PLTP activity assays were performed by two methods: the exogenous assay (PLTPexo) measures phospholipid transfer to exogenously added HDL (27), and the endogenous assay (PLTPendo) measures phospholipid transfer to endogenous serum HDL (28). Serum PLTP activity values, as measured by the two assays, are shown in Table 2.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>Men</td>
<td>55.29 ± 15.29</td>
</tr>
<tr>
<td>Women</td>
<td>54.94 ± 15.14</td>
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<tr>
<td>BMI (kg/m²)</td>
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<tr>
<td>Men</td>
<td>25.62 ± 3.12</td>
</tr>
<tr>
<td>Women</td>
<td>26.58 ± 4.73</td>
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<tr>
<td>WHR</td>
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<tr>
<td>Men</td>
<td>0.96 ± 0.05</td>
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<tr>
<td>Women</td>
<td>0.86 ± 0.06</td>
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<tr>
<td>CRP (mg/l)</td>
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<tr>
<td>Men</td>
<td>5.45 ± 1.08</td>
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<tr>
<td>Women</td>
<td>5.81 ± 0.94</td>
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<tr>
<td>TG (mmol/l)</td>
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<tr>
<td>Men</td>
<td>1.54 ± 1.32</td>
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<tr>
<td>Women</td>
<td>1.40 ± 0.66</td>
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<tr>
<td>LDL-C (mmol/l)</td>
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<tr>
<td>Men</td>
<td>3.53 ± 0.91</td>
</tr>
<tr>
<td>Women</td>
<td>3.70 ± 0.82</td>
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<tr>
<td>apoB (g/l)</td>
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<tr>
<td>Men</td>
<td>1.13 ± 0.26</td>
</tr>
<tr>
<td>Women</td>
<td>1.15 ± 0.26</td>
</tr>
<tr>
<td>HDL-C (mmol/l)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.26 ± 0.35</td>
</tr>
<tr>
<td>Women</td>
<td>1.48 ± 0.38</td>
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<tr>
<td>apoA-I (g/l)</td>
<td></td>
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<tr>
<td>Men</td>
<td>1.47 ± 0.27</td>
</tr>
<tr>
<td>Women</td>
<td>1.68 ± 0.29</td>
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<tr>
<td>apoA-II (g/l)</td>
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<tr>
<td>Men</td>
<td>0.35 ± 0.08</td>
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<tr>
<td>Women</td>
<td>0.56 ± 0.09</td>
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<tr>
<td>apoE (mg/l)</td>
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<tr>
<td>Men</td>
<td>25.76 ± 16.57</td>
</tr>
<tr>
<td>Women</td>
<td>27.02 ± 14.92</td>
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<tr>
<td>Glucose (mmol/l)</td>
<td></td>
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<tr>
<td>Men</td>
<td>5.62 ± 0.82</td>
</tr>
<tr>
<td>Women</td>
<td>5.33 ± 0.62</td>
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<tr>
<td>Insulin (mU/l)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>7.82 ± 8.37</td>
</tr>
<tr>
<td>Women</td>
<td>7.26 ± 6.94</td>
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<tr>
<td>HOMA IR</td>
<td></td>
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<tr>
<td>Men</td>
<td>2.01 ± 2.30</td>
</tr>
<tr>
<td>Women</td>
<td>1.78 ± 1.55</td>
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</table>

There were no significant gender differences in these activities. The serum PLTPexo activity was 6.59 ± 1.66 μmol/ml/h (mean ± SD), and the serum PLTPendo activity 1.37 ± 0.29 μmol/ml/h.

**Quantitation of serum HA- and LA-PLTP concentrations**

Using a method that enables us to quantitate separately the concentrations of the high- and low-active forms of serum PLTP (23), we evaluated the distribution of the two PLTP forms in sera from 250 randomly selected Finnish subjects. The mean PLTP concentration in serum was 6.56 ± 1.45 mg/l (range, 2.78–10.89 mg/l), and the mean LA-PLTP and HA-PLTP concentrations were 3.56 ± 1.14 mg/l (range, 1.20–8.43 mg/l) and 3.00 ± 1.21 mg/l (range, 0.92–7.63 mg/l), respectively (Table 2). The correlations between serum PLTP activity and concentration values are presented in Fig. 1. Serum PLTPexo activity showed a significant positive correlation with serum PLTP concentration (r = 0.45, P < 0.001; Fig. 1A) and HA-PLTP concentration (r = 0.38, P < 0.001; Fig. 1B), whereas the correlation with LA-PLTP concentration was weaker (r = 0.17, P < 0.01; Fig. 1C). PLTPendo activity demonstrated a weak positive correlation with HA-PLTP concentration, whereas no correlation to serum total PLTP or LA-PLTP concentration was evident (Table 3). A significant negative correlation was detected between serum LA- and HA-PLTP concentrations (Fig. 2).

**Correlation of PLTP with clinical and biochemical parameters**

None of the PLTP parameters correlated with gender or the inflammation marker, CRP (Table 4). Serum PLTP concentration correlated positively with age, and PLTPexo activity correlated with BMI and WHR, in accordance with earlier findings (12, 25).

PLTPendo activity showed a positive correlation with serum TC, TG, and LDL-C, whereas PLTPexo activity associated only weakly with TC and TG and not at all with LDL-C. ApoE concentration showed a positive but weak correlation with both PLTPexo and PLTPendo activity (Table 4). As
previous studies (32) have demonstrated that serum apoE concentration is dependent on the apoE polymorphism, we analyzed apoE allele distribution in the study population. ApoE allele frequencies were similar to those reported previously for Finns (33). Correlations between apoE genotypes and PLTP parameters were performed by subgrouping apoE isoforms as follows: group 1, E3/E3 (n = 137); group 2, E3/E4, E4/E4 (n = 78); group 3, E2/E2, E2/E3, E2/E4 (n = 17). Serum apoE concentration was highest in group 3, carriers of the ε2 allele, followed by groups 1 and 2 [group 1, 28.1 ± 14.5 mg/l; group 2, 20.7 ± 15.8 mg/l; group 3, 39.9 ± 18.6 mg/l (mean ± SD, P < 0.001)]. PLTP_{exo} activity and PLTP concentrations did not differ between the groups. The ε2 allele carriers (group 3), however, had increased serum TG levels [group 1, 1.45 ± 0.84 mmol/l; group 2, 1.42 ± 0.87 mmol/l; group 3, 2.12 ± 2.55 mmol/l (P < 0.05)] and increased PLTP_{endo} activity [group 1, 1.35 ± 0.18 μmol/ml/h; group 2, 1.35 ± 0.19 μmol/ml/h; group 3, 1.64 ± 0.88 μmol/ml/h (P < 0.001)].

A statistically significant positive correlation was observed between HDL-C and serum PLTP concentration, HA-PLTP concentration, and PLTP_{endo} activity. PLTP_{exo} activity, however, did not correlate with HDL-C. The main apolipoprotein component of HDL, apoA-I, correlated positively with HA-PLTP concentration and PLTP_{endo} activity. No correlation between LA-PLTP concentration and any measured lipid parameter was evident (Table 4).

PLTP activity has in previous studies been associated with carbohydrate metabolism (11, 34, 35). Therefore, we studied the correlations between PLTP parameters, glucose, and insulin. PLTP_{exo} activity correlated positively with serum glucose, and serum total PLTP concentration and HA-PLTP concentration showed a similar trend. However, the LA-PLTP concentration tended to associate with serum insulin. Interestingly, the insulin resistance calculated as the HOMA index displayed a trend of positive correlation with PLTP_{exo} activity in this normolipidemic, nondiabetic population sample.

**DISCUSSION**

PLTP is found in human serum in two distinct forms, one active in phospholipid transfer (HA-PLTP) and the
other low-active (LA-PLTP). Both forms associate with macromolecular complexes of different size, which, in turn, affects the reactivity of PLTP antibodies (23, 36). To quantitate HA- and LA-PLTP accurately, a pretreatment of samples with SDS, to denature the protein and reveal epitope, was used for the efficient detection of both forms of PLTP. The new ELISA (23) is an essential tool for addressing the mechanisms by which the two forms of PLTP. The mean serum PLTP concentration of 250 normolipidemic subjects was 6.6 ± 1.5 mg/l, which is similar to the values reported by Desrumaux et al. (34). Of this, ~50% represents the LA-PLTP form. A large individual variation, however, exists between the relative amounts of HA- and LA-PLTP. The prevalence of HA- and LA-PLTP in subjects with different forms of dyslipidemia cannot be concluded from this study, as the sample was composed of normolipidemic individuals.

We used two different radiometric assays to determine PLTP activity. The two activity assays resulted in quite different values for serum PLTP activity: 6.6 μmol/ml/h (PLTPexo) and 1.4 μmol/ml/h (PLTPendo). The two methods also resulted in different correlations to lipoprotein parameters and serum glucose. The PLTPendo assay is dependent on endogenous HDL levels (28) and will therefore, by definition, correlate with the HDL parameters apoA-I and HDL-C. The correlations with TC, TG, and LDL-C suggest that other lipoproteins also significantly affect the outcome of the assay. The PLTPendo activity does not correlate with serum PLTP concentration or LA-PLTP concentration, and only a marginal correlation was seen with HA-PLTP concentration. These data suggest that the PLTPendo assay reflects more the activity of PLTP as modulated by the composition of endogenous lipoproteins (28), whereas the PLTPexo assay reflects more directly the amount of active PLTP in serum.

Among normolipidemic Finnish subjects, relatively weak correlations were detected between PLTPexo activity and serum TC, TG, apoB, apoE, and glucose. Murdoch and colleagues (37) reported a similar correlation between PLTP activity and apoB. They also observed a positive correlation between PLTP activity and buoyant LDL (38). In the present study, no correlation between PLTPexo activity and LDL-C or HDL-C was evident. The correlations with TC, apoB, and TG suggest that PLTP activity correlates with VLDL, which is in agreement with the hypothesis of Murdoch et al. (38) that as VLDL apoB increases, PLTP activity also increases to facilitate the transfer of postlipolytic surface remnants to HDL. Subjects with hypertriglyceridemia display an increase in PLTP activity (12). This increase has been suggested to be attributable to insulin resistance. The correlation of PLTPexo activity to the surrogate marker for insulin resistance (HOMA IR) suggested by the present study is in agreement with these findings.

Because HA- and LA-PLTP in the circulation exist as different macromolecular complexes, their interaction with other proteins and lipids seems to modulate their function and distribution. The observations that apoE concen-

Fig. 2. Correlation between LA-PLTP and HA-PLTP concentrations.
that the increased PLTPendo activity is attributable to a dif-
ferration of PLTP-mediated pathway. However, the detailed mechanisms
by which glucose and insulin could modulate the PLTP
activity, total PLTP concentration, and HA-PLTP concentration
but not with LA-PLTP concentration. These data sug-
gest that PLTP activity and the distribution of the two
PLTP forms in serum are influenced not only by lipid but
also by glucose metabolism. Tu and Albers (14) have shown
that expression of the PLTP gene is subject to regulation
by glucose via a peroxisome proliferator-activated recep-
tor-mediated pathway. However, the detailed mechanisms
by which glucose and insulin could modulate the PLTP
subcellar distribution remain an interesting target for fu-
ture studies.

In conclusion, we still await large, preferably prospec-
tive studies on PLTP to assess whether PLTP concentra-
tion, activity, or both combined can be used as inde-
pendent markers for cardiovascular risk evaluation and
whether it is possible to reduce the risk by targeted drug
treatment.

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REFERENCES

1. Castelli, W. P., R. J. Garrison, P. W. Wilson, R. D. Abbott, S. Kalous-
dian, and W. B. Kannel. 1986. Incidence of coronary heart disease
and lipoprotein cholesterol levels. The Framingham Study. J. Am.

2. Kannel, W. B. 1983. High-density lipoproteins: epidemiologic pro-

verse cholesterol transport. J. Lipid Res. 36: 211–228.

2001. The impact of phospholipid transfer protein (PLTP) on HDL

5. Tollefson, J., S. Ravnik, and J. Albers. 1988. Isolation and charac-
terisation of a phospholipid transfer protein (LTP-II) from human

6. Jauhiainen, M., J. Metso, R. Pahlman, S. Blomqvist, A. van Tol,
causes high density lipoprotein conversion. J. Biol. Chem. 268: 4032–4036.

tein conversion mediated by human plasma phospholipid transfer

8. Desrumaux, C. M., P. A. Mak, W. A. Boisvert, D. Masson, D. Stu-
pholipid transfer protein is present in human atherosclerotic les-
sions and is expressed by macrophages and foam cells. J. Lipid Res.
44: 1453–1461.

pitz, D. Mangelsdorf, and P. Tontonoz. 2003. The phospholipid
transfer protein gene is a liver X receptor target expressed by mac-

2003. Phospholipid transfer protein interacts with and stabilizes
ATP-binding cassette transporter A1 and enhances cholesterol ef-

Plasma phospholipid transfer protein activity is related to insulin
resistance: impaired acute lowering by insulin in obese type II dia-
betic patients. Diabetologia. 41: 929–934.

F. H. de Man, A. van der Laarse, and A. van Tol. 2003. Decreased
PLTP mass but elevated PLTP activity linked to insulin resistance

O’Connor, and A. Van Tol. 2002. Relationship of phospholipid
transfer protein activity to HDL and apolipoprotein B-containing
51: 3389–3395.

of human genes relevant to HDL metabolism: responsive elements
for peroxisome proliferator-activated receptor are involved in the

15. Oka, T., T. Kujiroka, M. Ito, T. Egashira, S. Takahashi, M. N. Nan-
jee, N. E. Miller, J. Metso, V. M. Olkkonen, C. Ehnholm, M. Jauhi-
ainen, and H. Hattori. 2000. Distribution of phospholipid transfer
protein in human plasma: presence of two forms of phospholipid
transfer protein, one catalytically active and the other inactive. J.
Lipid Res. 41: 1651–1657.

Jauhiainen, and C. Ehnholm. 2002. Isolation and partial charac-
terization of the inactive and active forms of human plasma phos-

17. Jiang, X. C., C. Bruce, J. Mar, M. Lin, Y. Ji, O. L. Francone, and


