Human Apolipoprotein A-II Enrichment Displaces Paraoxonase From HDL and Impairs Its Antioxidant Properties

A New Mechanism Linking HDL Protein Composition and Antiatherogenic Potential

Vincent Ribas, José Luis Sánchez-Quesada, Rosa Antón, Mercedes Camacho, Josep Julve, Joan Carles Escolà-Gil, Luís Vila, Jordi Ordoñez-Llanos, Francisco Blanco-Vaca

Abstract—Apolipoprotein A-II (apoA-II), the second major high-density lipoprotein (HDL) apolipoprotein, has been linked to familial combined hyperlipidemia. Human apoA-II transgenic mice constitute an animal model for this proatherogenic disease. We studied the ability of human apoA-II transgenic mice HDL to protect against oxidative modification of apoB-containing lipoproteins. When challenged with an atherogenic diet, antigens related to low-density lipoprotein (LDL) oxidation were markedly increased in the aorta of 11.1 transgenic mice (high human apoA-II expressor). HDL from control mice and 11.1 transgenic mice were coincubated with autologous very LDL (VLDL) or LDL, or with human LDL under oxidative conditions. The degree of oxidative modification of apoB lipoproteins was then evaluated by measuring relative electrophoretic mobility, dichlorofluorescein fluorescence, 9- and 13-hydroxyoctadecadienoic acid content, and conjugated diene kinetics. In all these different approaches, and in contrast to control mice, HDL from 11.1 transgenic mice failed to protect LDL from oxidative modification. A decreased content of apoA-I, paraoxonase (PON1), and platelet-activated factor acetyl-hydrolase activities was found in HDL of 11.1 transgenic mice. Liver gene expression of these HDL-associated proteins did not differ from that of control mice. In contrast, incubation of isolated human apoA-II with control mouse plasma at 37°C decreased PON1 activity and displaced the enzyme from HDL. Thus, overexpression of human apoA-II in mice impairs the ability of HDL to protect apoB-containing lipoproteins from oxidation. Further, the displacement of PON1 by apoA-II could explain in part why PON1 is mostly found in HDL particles with apoA-I and without apoA-II, as well as the poor antiatherogenic properties of apoA-II–rich HDL.

(Circ Res. 2004;95:789-797.)

Key Words: atherosclerosis • homocysteine thiolactone • paraoxonase • high-density lipoprotein • oxidized LDL

The mechanisms by which high-density lipoprotein (HDL) modulates atherosclerosis susceptibility remain incompletely understood. HDLs are classified according to their content of major apolipoproteins: apolipoprotein A-I (apoA-I) and apoA-II. ApoA-I plays a protective role against atherosclerosis, as demonstrated by the analysis of apoA-I transgenic mice.\(^1\) In contrast, the role of apoA-II is less understood,\(^2,3\) and overexpression of mouse\(^4\) and human apoA-II has generally been found to be proatherogenic.\(^5-8\) One mechanism by which the apoA-II expression may promote atherogenesis is altered reverse cholesterol transport.\(^9,10\) A second proatherogenic mechanism may involve impaired inhibition of the oxidative modification of apoB-containing lipoproteins, as described in murine apoA-II transgenic mice.\(^11\) Although antioxidant properties have been ascribed to apoA-I and apoA-II,\(^12\) it is currently believed that an important part of HDL antioxidant properties is related to their associated enzymes. These are paraoxonase (PON1),\(^13-15\) platelet-activated factor acetyl-hydrolase (PAF-AH),\(^16\) lecithin:cholesterol acyltransferase (LCAT),\(^17\) and plasma glutathione selenoperoxidase (GPX3).\(^18\) PON1 is a calcium-dependent ester hydrolase\(^19\) that catalyzes the hydrolysis of organophosphates and oxidized phospholipids,\(^13,20\) including PAF,\(^21\) and also homocysteine thiolactone.\(^22\) PAF-AH hydrolyzes the acetyl moiety of the sn-2 position of PAF and also oxidized phospholipid with short-chain acyl moieties in the sn-2 position.\(^16\) The main known function of LCAT is cholesterol esterification; however, a role in hydrolyzing...
oxidized polar phospholipids generated during lipoprotein oxidation has also been described.\textsuperscript{17} This function is probably attributable to an apoA-I–independent LCAT phospholipase activity. GPX3 has been found associated with HDL in human plasma, and its hydroperoxide-reducing activity might be important in protecting the endothelium from the toxic effects of oxidized lipids.\textsuperscript{23}

In this study, we assessed whether the protection conferred by HDL against oxidative modification of apoB-containing lipoproteins is impaired in human apoA-II transgenic mice, an animal model of familial combined hyperlipidemia.\textsuperscript{8}

Materials and Methods

Animals

Male and female mice were used in equal proportions, unless otherwise stated. All animal procedures were in accordance with published recommendations.\textsuperscript{24} Human apoA-II transgenic mice (lines 25.3 and 11.1, which, in this study, presented plasma concentrations of human apoA-II of 18±5 mg/dL and 123±17 mg/dL, respectively) were developed as described previously.\textsuperscript{10} Mice were maintained on a cholate-containing atherogenic diet (high-fat high-cholesterol; ICN Pharmaceuticals) for up to five months. To obtain blood from fasted mice, food deprivation began at 5 PM, and samples were obtained between 8 AM and 10 AM.

Lipid and Apolipoproteins

Total cholesterol, HDL cholesterol (by photometric-photometric-MgCl\textsubscript{2} precipitation), triglyceride (Roche Diagnostics), phospholipid, free cholesterol (Wako), and human apoA-II (Kamiya) were measured using commercial methods adapted to a 911 Hitachi autoanalyzer, whereas total protein content in lipoproteins was measured by the Bradford method.\textsuperscript{25} Pure apoA-II was obtained from Sigma.

Quantification of Aortic Atherosclerosis and Immunohistochemistry

Hearts and proximal aortas were removed and rinsed in saline, fixed in 4% solution of paraformaldehyde with 1 mmol/L EDTA and 20 μmol/L butylated hydroxytoluene (BHT) to avoid oxidation for 1 hour, and fixed in sucrose-containing PBS (5% sucrose, 1 mmol/L EDTA, and 20 μmol/L BHT) overnight. Hearts were then mounted in OCT compound (Tissue-Tek) and frozen at ~80°C. Aortic 10-μm-thick sections were prepared through the sinus area and incubated with biotin-conjugated MDA-2 (monoclonal antibody against 4-hydroynonenal-modified lipoprotein [LDL]) and NA59 (monoclonal antibody against malondialdehyde [MDA]-modified low-density lipoprotein). Aortic sections were embedded in black fluorimeter microplates (Nunc) with 3 μmol/L CuSO\textsubscript{4} in a cuvette containing LDL (0.1 mmol/L phospholipids) or HDL (1 mmol/L cholesterol). Oxidation was started with 5.5 μmol/L CuSO\textsubscript{4} at 37°C in the dark for 150 minutes. Reaction was stopped with 50 μmol/L EDTA and 20 μmol/L BHT (final concentrations). An aliquot was loaded on agarose gel (Midigel). After electrophoresis, the gel was dried, stained with Sudan Black, and the relative mobility of LDL evaluated with Gel doc 2000 densitometer and Quantity One software (Bio-Rad).

9- and 13-Hydroxyoctadecadienoic Acid Content

Linoleic acid hydroxides (9-hydroxy-10,12-octadecadienoic acid [9-HODE] and 13-hydroxy-9,11-octadecadienoic acid [13-HODE]) were determined by gas chromatography/mass spectrometry as described previously. The HODE content of LDL in the LDL+HDL incubations was calculated by subtracting the HODE of HDL incubated without LDL.

Conjugated Diene Kinetics

Oxidation was started by adding 2.5 μmol/L CuSO\textsubscript{4} in a cuvette containing LDL (0.1 mmol/L phospholipids) or HDL (0.13 mmol/L phospholipids). Continuous monitoring of 234 nm absorbance was performed in a Biochrom 4060 spectrophotometer equipped with a seven-position cell changer (Pharmacia) at 30°C for four hours. The lag phase was calculated as described. Kinetics of the LDL in the LDL+HDL incubations were calculated by subtracting the kinetics of HDL incubated without LDL.

DCF Assay

2′,7′-Dichlorofluorescein diacetate (DCF) assay\textsuperscript{32} (Sigma) was performed in black fluorimeter microplates (Nunc) with 3 μg of human LDL apolipoprotein B, 2 nmol of HDL phospholipid, and 2 μg of DCF. Fluorescence was measured after three hours at 37°C.

Enzymatic Activities

Total plasma arylesterase activity was measured using phenylacetate as substrate.\textsuperscript{33} EDTA-sensitive plasma arylesterase (PON1) activity was calculated by subtracting the EDTA-resistant arylesterase. The latter was determined using 1 mmol/L EDTA in the reaction buffer instead of Cl\textsubscript{2} Ca, which was used to determine total arylesterase activity.\textsuperscript{34} PAF-AH activity was determined using a commercial kit (Cayman Chemical). GPX3 activity was measured using a coupled spectrophotometric assay.\textsuperscript{23} LCAT activity was measured against an exogenous substrate.\textsuperscript{30}
Liver Gene Expression

Liver total RNA was extracted using Trizol (Gibco/BRL) and repurified with RNAeasy columns (RNAeasy mini kit; Qiagen). Reverse transcription was performed with 2 μg of each RNA using Moloney murine leukemia virus reverse transcriptase H (Promega), and quantitative analysis was performed using real-time PCR (ABI Prism 7000; Applied Biosystems). The mRNA expression of the selected genes was studied using predesigned validated assays (Assays-on-Demand; Applied Biosystems).

Immunoblot

PON1 was determined after native gel electrophoresis (GGE; precast 4% to 20% acrylamide gels; Bio-Rad) and Western blot analysis using a specific goat anti-mouse antiserum (gift from Dr Trudy Forte, University of California in Berkeley). Murine apoA-I was determined after SDS polyacrylamide electrophoresis and Western blot with a specific antibody. Bands were evaluated with Gel doc 2000 densitometer and Quantity One software (Bio-Rad).

Statistical Analyses

Results are expressed as mean±SEM. Comparisons between groups were made by Newman–Keuls multiple comparison test after a one-way ANOVA test for normal data distribution. For small samples or when data did not show a Gaussian distribution, comparisons were performed using Kruskal–Wallis nonparametric ANOVA test followed by Dunn multiple comparison test. Comparisons were performed using GraphPad Prism 3.0 for Windows (GraphPad Software) and Microsoft Excel.

Results

Plasma Lipids

As in previous reports,19,30,36 11.1 transgenic mice presented with decreased cholesterol in HDL (0.73±0.13 versus 1.53±0.34 mmol/L in control mice) and increased apoB-containing lipoproteins that were both enriched in triglycerides (1.99±0.44 versus 0.50±0.03 mmol/L in control mice) and cholesterol (8.49±1.71 versus 5.41±1.48 mmol/L in control mice), whereas 25.3 transgenic mice presented a lipid and lipoprotein profile similar to that of control mice.

Morphometric and Immunohistochemical Analysis of Aortic Root Lesions

Atherosclerosis quantification and immunohistochemical analysis are shown in Table 1. After five months of atherogenic diet, control and 25.3 mice showed small, mainly fatty streak lesions. In contrast, 11.1 transgenic mouse aortas showed a 12-fold greater lesion area than control mice, and these lesions were complex, with fatty and fibroproliferative regions. The detection area of oxidized epitopes of LDL in the aortic root, as recognized by MDA-2 and NA-59 antibodies, was dramatically increased (17-fold greater in both cases) in 11.1 transgenic mice compared with control and 25.3 transgenic mice.

Markers of Plasma Oxidative Stress

Plasma 8-isoprostane showed no difference among the three mouse lines studied (control 166±34 pg/mL versus 170±34 and 176±20 pg/mL in 25.3 transgenic mice and 11.1 transgenic mice, respectively; n=10 in each group). No difference was found in TBARS content in plasma (control mice 2.3±0.2 nmol of MDA equivalents/mL versus 2.1±0.5 and 2.0±0.4 nmol in 25.3 and 11.1 transgenic mice, respectively; n=8 in each group). No carotene or lycopene was detected in plasma of these mice. Plasma retinol and HDL tocopherol

| TABLE 1. Morphometric and Immunohistochemical Analysis of Aortic Atherosclerotic Lesions |
|-----------------------------------------|-----------------|-----------------|
| Lesion area (m²/section)                | Control (n=12)  | Transgenic 25.3 (n=11) | Transgenic 11.1 (n=10) |
|                                           | 6.8±2.9         | 10.2±3.1         | 83.1±13.3*           |
| MDA-2 stained area (μm²/section)        | 2.5±0.8         | 3.7±1.3          | 43.6±7.2*           |
| NA-59 stained area (μm²/section)        | 2.1±0.7         | 3.4±1.0          | 34.9±4.8*           |
| Values are positive stained area×10⁵ μm²/section, expressed as mean±SEM. *P<0.001 vs control. |
were detectable, but no significant differences were observed among mouse lines (data not shown).

**HDL Protection Against LDL Oxidative Modification**

The ability of HDL to inhibit oxidation of apoB-containing lipoproteins was tested using different approaches. One was the study of the migration through agarose gel electrophoresis (relative electrophoretic mobility [REM]) of mouse VLDL and LDL coincubated with HDL under oxidizing conditions (Figure 1). When apoB-containing lipoproteins became oxidized, they increased their electrophoretic mobility. Control and 25.3 transgenic mouse HDL effectively inhibited this increase in REM, whereas 11.1 transgenic mouse HDL did not.

Because adequate volumes of apoB-containing lipoproteins from mice are difficult to obtain and human LDL oxidation has been extensively studied, human LDLs were used next. In this case, we implemented a standardization parameter to use the same amount of HDL from all mouse lines, as readily measured by phospholipid, cholesterol, or protein content (Figure 2). Again, control and 25.3 transgenic mouse HDLs were able to prevent LDL from increased electrophoretic mobility under these conditions, whereas LDLs coincubated with HDL from 11.1 transgenic mice were not.

A number of similar experiments were performed matching the HDL phospholipid of the different mouse lines and measuring REM, linoleic acid hydroxyde derivatives (9-HODE and 13-HODE), DCF fluorescence, and lag phase of the oxidation kinetics (Figure 3). The results clearly showed that in contrast to control mouse and 25.3 transgenic mouse HDL, coincubation of human LDL with HDL from 11.1 transgenic mice was not able to avoid the increase in REM (Figure 3A), HODEs (Figure 3B), or DCF fluorescence (Figure 3C). Also, in the conjugated diene kinetics, HDL...
from control and 25.3 mouse lines markedly delayed LDL oxidation, whereas LDL incubated with HDL from 11.1 transgenic mice showed a shorter lag phase (Figure 3D).

**Plasma Activity of Enzymes Related to Antioxidative Protection**

Plasmatic activities of HDL enzymes with antioxidant properties were analyzed. Results are shown in Table 2. Total plasma arylesterase activity of 11.1 transgenic mice was 75% that of control mice. Because PON1 is calcium-dependent, adding EDTA to the reaction buffer results in inhibition of this activity.19 Consistent with previous reports,37 we found EDTA-resistant arylesterase in plasma of all mice, and this was phenylmethylsulfonyl fluoride–sensitive (data not shown), in contrast to the EDTA-sensitive activity (referred to as PON1 activity hereafter). Plasma PON1 activity of 11.1 transgenic mice was 45% that of control mice. Also, plasma PAF-AH activity presented a 25% decrease in 11.1 plasma compared with that of control or 25.3 mice (Table 2). As reported previously,10 LCAT exogenous activity showed a nonsignificant tendency to be decreased in 11.1 transgenic mice compared with control or 25.3 mice (Table 2). Plasma GPX3 activities (control 14.2 ± 0.9 μmol/mL; 25.3 transgenic mice 13.0 ± 0.5 μmol/mL; 11.1 transgenic mice 14.9 ± 0.6 μmol/mL min; n = 10 in each group) did not differ among the three mouse lines.

**Liver Gene Expression of HDL-Associated Enzymes**

mRNA liver expression of apoA-I, apoA-II, human apoA-II, PON1, LCAT, and PAF-AH was measured by real-time RT-PCR. Excluding human apoA-II transcript, no significant difference was observed in the expression of any of these genes once corrected by GAPDH mRNA (supplemental Table I in the online data supplement available at http://circres.ahajournals.org).

**Incubation of Plasma and HDL With Human apoA-II**

When increasing quantities of isolated human apoA-II were incubated at 37°C with control plasma, PON1 activity decreased (Figure 5A). At an apoA-II concentration similar to that found in 11.1 mice, a 50% decrease in PON1 activity was observed, with no changes in PAF-AH or EDTA-resistant arylesterase activity. This decrease was also found in HDL fractions isolated by FPLC profile (Figure 5B). No decrease in PON1 activity was found when the incubation was performed at 4°C. Incubation of HDL isolated by ultracentrifugation with increasing human apoA-II at 4°C caused a tendency toward an increase in size of immunoreactive bands recognized by the PON1 antibody (Figure 5C) but no change in the measured activity of the enzyme (data not shown). However, PON1 immunoreactive bands were absent after the same incubations performed at 37°C (Figure 5C), and this was concomitant with absence of PON1 activity. PON1 inhibition was not observed when the isolated human apoA-II was subjected to lipid extraction and the extract added to the HDL of control mice (data not shown).

**Discussion**

We hypothesized that impaired protection of HDL against apoB-containing lipoprotein oxidation in the 11.1 transgenic mouse model could play a role in its enhanced atherosclerosis susceptibility. This line of human apoA-II in transgenic mice presented a relative increase in the area stained with antibodies that recognize LDL oxidation epitopes compared with

**TABLE 2. Plasma Activities of HDL-Associated Enzymes**

<table>
<thead>
<tr>
<th>Enzyme Activity</th>
<th>25.3 Transgenic Mice</th>
<th>11.1 Transgenic Mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma arylesterase (total), nmol/mL min⁻¹ (n=16)</td>
<td>32.6 ± 1.5</td>
<td>31.4 ± 1.6</td>
</tr>
<tr>
<td>Plasma arylesterase (EDTA-sensitive), nmol/mL min⁻¹ (n=16)</td>
<td>16.4 ± 1.0</td>
<td>15.6 ± 1.2</td>
</tr>
<tr>
<td>Plasma PAF-AH, nmol/mL min⁻¹ (n=8)</td>
<td>103.9 ± 7.9</td>
<td>107.7 ± 6.7</td>
</tr>
<tr>
<td>Plasma LCAT, nmol cholesterol esterified/mL h⁻¹ (n=5)</td>
<td>7.2 ± 1.7</td>
<td>ND</td>
</tr>
</tbody>
</table>

Values are mean ± SEM and No. of samples in each group is indicated. ND indicates not determined.

† p < 0.01 and ‡ p < 0.001 vs control.
control or 25.3 mice. However, a concomitant increase in plasma markers of oxidative stress was not found, which suggests that the level of oxidation of plasma lipoproteins was similar in the three mouse lines studied. Thus, the main difference in oxidation susceptibility may occur in the subendothelial space. In this milieu, the antioxidant and anti-inflammatory properties of HDL may confer vital protection.38

Lipoproteins that undergo oxidation are known to increase their electrophoretic mobility. This property can be used to establish the degree of LDL oxidation and has been used previously to assess HDL protectivity.39 Using this approach, HDL of 11.1 transgenic mice proved to have impaired protection capability. This was also observed when other experimental approaches, such as HODE content, DCF fluorescence, and conjugate diene lag phase formation, were applied. It is well known that some lipophilic antioxidants are able to prevent or delay lipoprotein oxidation.40 We measured antioxidant vitamins in HDL of our mice; however, only significant amounts of \( \alpha \)-tocopherol were detected, and its concentration did not differ among the different mouse lines. Other factors involved in lipoprotein protection against oxidation include certain apolipoproteins and antioxidant enzymes. Antioxidant properties of apoA-I have been described,12,38 and there was a considerable apoA-I deficiency in our apoA-II transgenic mice.9,10 However, mice lacking apoA-I do not show susceptibility to atherosclerosis.41 Thus, in addition to a partial apoA-I deficiency, apoA-II overexpression may cause absence or malfunction of HDL-associated enzymes such as PON1, PAF-AH, GPX3, and LCAT. A decreased liver gene expression of these enzymes (except that of GPX3, which was not measured) was ruled out. Plasma LCAT and GPX3 activities were found to be similar in the three lines of mice, although it is noteworthy that the measured activities could be poorly correlated with the activities related to LDL protection. In contrast, HDL from 11.1 transgenic mice had decreased PON1 activity in addition to the decreased plasma HDL mass.10 ApoA-I deficiency could affect stability or activity of PON1.42 Incubating isolated human apoA-II with control plasma at 37°C but not at 4°C decreased PON1 activity in plasma and HDL; PAF-AH activity, in contrast, was unchanged at both temperatures. This seems to be attributable to an apoA-II–induced displacement of PON1 from HDL. The temperature-dependent nature of this phenomenon, which is not the case of the known displacement of apoA-I by apoA-II,38 suggests the involvement of enzymatic activities. This could lead to a lipid-free enzyme with higher turnover in plasma, leading to decreased PON1 mass in HDL of transgenic mice. If this mechanism were to be relevant in vivo, the minimal apoA-II concentration

Figure 4. Representative apolipoprotein, lipid, and enzymatic HDL fractions isolated by FPLC. A, Apolipoprotein content in milligrams per deciliter for human apoA-II and arbitrary densitometric units for apoA-I determined by Western blot. B, Total cholesterol content. C, EDTA-sensitive arylesterase (PON1) activities. Inset, Western blot of PON1 of ultracentrifugally isolated HDL (10 μg of HDL protein loaded per lane). D, PAF-AH activities.
needed to induce PON1 displacement would be between 18 mg/dL (the average concentration of 25.3 transgenic mice, which shows normal PON1 activity) and 30 mg/dL where, indeed, a complete PON1 displacement was observed. Displacement of PON1 from HDL has also recently been shown to be induced by incubation with serum amyloid A and could be important for impaired HDL antioxidant properties during acute phase reaction.

PAF-AH is associated with HDL in mice and protects against lipoprotein oxidation and atherosclerosis development. In our mice, PAF-AH activity of 11.1 mice was moderately decreased in plasma and in HDL. Thus, our data suggest that decreased PON1, apoA-I, and PAF-AH in 11.1 transgenic mouse HDL may play a role in the decreased inhibition of LDL oxidation. The results presented here are partially consistent with those published previously in murine apoA-II transgenic mice. In this case, the decrease in PON1 activity was only observed when adjusted for HDL protein, and the HDL proved to be proinflammatory in a cell-based assay. Our findings, although this kind of assay was not used, do not suggest that human apoA-II transgenic mice HDL were pro-oxidant because human LDL incubated alone experienced more intense or rapid oxidation than that co-incubated with 11.1 HDL. This difference may be another species-specific difference in apoA-II that is likely attributable to the higher affinity of dimeric human apoA-II for HDL surfaces compared with monomeric murine apoA-II. It has also been shown that substituting the central domain of apoA-I by a segment of human apoA-II in transgenic mice impairs the protection of HDL against LDL oxidative modification. Another group also reported decreased plasma PON1 and PAF-AH in independently generated human apoA-II transgenic mice. This was concomitant with a relatively increased protection against VLDL oxidative modification in the transgenic mice, the origin of which was not clarified. The reason for this discrepancy in results between our studies is unclear; however, at least two factors may be of importance: first, their mice were fed a chow diet, and

Figure 5. Effect of purified human apoA-II on PON1 activity. A, EDTA-sensitive arylesterase (PON1) activities of plasma incubated with increasing concentrations of human apoA-II at 37°C for three hours. B, PON1 activities of HDL and lipoprotein-depleted fractions of plasma isolated by FPLC after the experiment shown in A. C, Western blot using antibodies to PON1 against HDL (1 mmol/L HDL phospholipid) from control mice incubated with purified human apoA-II and separated by native GGE.
second, their plasma human apoA-II concentration was lower than in ours. It is well known that long-term feeding with an atherogenic diet decreases PON1, whereas higher human plasma apoA-II concentrations may further impair the rest of the HDL antioxidant system form by apoA-I, PAF-AH, and LCAT.

In summary, we found evidence of impairment in HDL protection against oxidative modification of apoB-containing lipoproteins in mice overexpressing human apoA-II. Decreased apoA-I, concomitant with decreased PON1 and PAF-AH activities, is probably related to this impairment as well as to the increased atherosclerosis susceptibility of these mice. Further, the in vitro displacement of PON1 by physiologic concentrations of human apoA-II could explain, at least in part, why PON1 is mostly found in HDL particles without apoA-II and, thus, the lack of antiatherogenic properties of apoA-II–enriched HDL.

Acknowledgments
This work was funded by SAF 99-0104 from Ministerio de Ciencia y Tecnología, and FIS G03-181, C03-08, and C03-01. During part of this study V.R. was a predoctoral fellow and J.C.E.-G. a Ramón y Cajal researcher, both funded by the Ministerio de Ciencia y Tecnología. We are grateful to Christine O’Hara for editorial assistance.

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Circ Res. 2004;95:789-797; originally published online September 23, 2004;
doi: 10.1161/01.RES.0000146031.94850.5f

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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### Online Table 1. Liver mRNA expression of apoA-I, murine apoA-II, human apoA-II, PON1, PAF-AH and LCAT

<table>
<thead>
<tr>
<th></th>
<th>Control mice</th>
<th>11.1 transgenic mice</th>
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<tr>
<td></td>
<td>n = 5</td>
<td>n = 5</td>
</tr>
<tr>
<td>Apolipoprotein A-I</td>
<td>8.0 ± 1.5</td>
<td>7.1 ± 0.7</td>
</tr>
<tr>
<td>Apolipoprotein A-II (murine)</td>
<td>11.6 ± 2.0</td>
<td>14.2 ± 1.5</td>
</tr>
<tr>
<td>Apolipoprotein A-II (human)</td>
<td>__</td>
<td>1,083 ± 98</td>
</tr>
<tr>
<td>Paraoxonase-1</td>
<td>0.10 ± 0.03</td>
<td>0.11 ± 0.02</td>
</tr>
<tr>
<td>PAF-AH</td>
<td>0.015 ± 0.004</td>
<td>0.022 ± 0.004</td>
</tr>
<tr>
<td>LCAT</td>
<td>0.23 ± 0.02</td>
<td>0.33 ± 0.04</td>
</tr>
</tbody>
</table>

Values are transcript/GAPDH ratios and are mean ± SEM from liver RNA of control or 11.1 mouse line at three months of diet. Excluding human apoA-II transcript, no statistical difference was found.