Familial Combined Hyperlipidemia in Mexicans
Association With Upstream Transcription Factor 1 and Linkage on Chromosome 16q24.1

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Objective—To investigate the largely unknown genetic component of the common lipid disorder, familial combined hyperlipidemia (FCHL) in Mexicans, we analyzed the upstream transcription factor 1 (USF1) gene that was recently associated with FCHL and high triglycerides (TG) in Finns. We also analyzed the Mexican FCHL families for 26 microsatellite markers residing in the seven chromosomal regions on 2p25.1, 9p23, 10q11.23, 11q13, 16q24.1, 19q13, and 21q21, previously linked to FCHL in Whites.

Methods and Results—We genotyped 314 individuals in 24 Mexican families for 13 SNPs spanning an 88-kb region, including USF1. The FCHL and TG traits showed significant evidence for association with 3 SNPs, hCV1459766, rs3737787, and rs2073658, and haplotype analyses further supported these findings (probability values of 0.05 to 0.0009 for SNPs and their haplotypes). Of these SNPs, hCV1459766 is located in the F11 receptor (F11R) gene, located next to USF1, making it difficult to exclude. Importantly, the association was restricted to a considerably smaller region than in the Finns (14 kb versus 46 kb), possibly because of a different underlying linkage disequilibrium structure. In addition, 1 of the 7 regions, 16q24.1, showed suggestive evidence for linkage (a lod score of 2.6) for total cholesterol in Mexicans.

Conclusions—This study, the first to extensively investigate the genetic component of the common FCHL disorder in Mexicans, provides independent evidence for the role of USF1 in FCHL in an outbred population and links the 16q24.1 region to an FCHL-component trait in Mexicans. (Arterioscler Thromb Vasc Biol. 2005;25:1985-1991.)

Key Words: familial combined hyperlipidemia ■ USF1 gene ■ complex traits ■ Mexican population ■ coronary heart disease

Familial combined hyperlipidemia (FCHL) is a common heterogeneous disorder, characterized by the presence of multiple lipoprotein phenotypes that increase the risk of premature coronary heart disease (CHD).1 Families with this condition typically exhibit a mixed pattern of lipid abnormalities, with one or more family members affected by high levels of serum total cholesterol (TC) and/or triglycerides (TG). FCHL profiles are often associated with elevated apolipoprotein B (apoB) levels and with an unfavorable decrease in serum high-density lipoprotein cholesterol (HDL-C) levels.2,3 Although it has been evident for 30 years that FCHL has a strong genetic component,2 DNA sequence variants contributing to FCHL and its component traits are largely unknown, especially regarding the prevalence of variants with major effects.

Several genetic studies have been conducted in various ethnic groups to identify susceptibility genes for FCHL and its component traits.4–11 Evidence for a major FCHL locus was first found on chromosome 1q21-q23 in Finns,5 and subsequent replications were observed in US, German, Chinese, and Dutch populations.9–11 Linkage to the 1q21–23 region has also been replicated in 7 extended Mexican families.12 These 7 families comprise a portion of the samples investigated in this present study. Recently, Pajukanta et al (2004)13 reported that FCHL is linked and associated with the gene encoding the upstream transcription factor 1 (USF1) on chromosome 1q21. USF1 is the first major gene implicated in FCHL.

The ubiquitously expressed USF proteins are members of the basic helix-loop-helix leucine zipper (bHLH-zip)
family of transcription factors, and USF1 is known to control expression of several genes involved in glucose and lipid metabolism.\textsuperscript{14,15} Variation in USF1 has been shown to influence features of glucose and lipid homeostasis in the EARS II offspring study.\textsuperscript{16} Recently USF1 was also shown to stimulate apolipoprotein A-V (APOA5) promoter activity in an insulin-dependent manner, demonstrated by the reduced binding of USF1 to the APOA5 promoter in the presence of insulin.\textsuperscript{17} This connection between APOA5 and USF1 is especially noteworthy because variants of APOA5 have been linked to high TGs in the outbred population of Mexico. Previous studies have clearly demonstrated that the Mexican population has an increased predisposition to mixed dyslipidemias, including FCHL.\textsuperscript{22–24} However, this population has been under-investigated for the genetic factors conferring this susceptibility.

It is likely that alleles of multiple genes contribute to the complex FCHL phenotype. In fact, genome-wide scans have identified several chromosomal loci for FCHL and its component traits in Caucasian families with FCHL.\textsuperscript{6–8,25,26} Loci on chromosomes 1q21, 2q31, 10p11, 10q11, 16q, and 21q21 were identified in the Finnish FCHL families;\textsuperscript{5–6,26} loci on chromosomes 2p, 11p, 16q, and 19q in the Dutch FCHL families;\textsuperscript{7} and loci on 6q, 8p, and 11p in the British FCHL families,\textsuperscript{25} respectively. Therefore, we also analyzed the Mexican FCHL families for peak markers of 7 regions identified in the previous genome scans of Caucasian FCHL families.

### Methods

#### Subjects and Clinical Features

A total of 24 extended Mexican FCHL families with a history of premature CHD were included in this study, comprising 314 family members (Table 1a and 1b). These families were recruited in the Lipid Clinic of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ) in Mexico City. The ethnicity and race of these subjects reflect the general population of Mexico. Thus, the race of all of these subjects is mestizo who are a mixture of American Indian and white. Inclusion criteria for the probands were as follows: Elevated levels of serum TGs (≥90th age/sex-specific Mexican population percentile) and/or elevated levels of serum TC (≥90th percentile) and elevated levels of serum apoB (≥90th percentile). The positive family history of premature CHD before the age of 60 years was defined as the manifestation of myocardial infarction either in the proband or a first-degree relative of the proband. The age/sex-specific population percentiles for lipids were based on a previous survey of the Mexican population.\textsuperscript{23} In addition, at least 1 first-degree relative had a phenotype of high TC (≥90th percentile) or high TGs (≥90th percentile) different from that of the proband. Exclusion criteria for the probands were tendon xanthomas, renal disease, and thyroid disorders. All subjects completed a questionnaire about their medical history, medica-

### Table 1A. Phenotypic Characteristics of Family Members Included in the Study

<table>
<thead>
<tr>
<th></th>
<th>FCHL Affected</th>
<th>Unaffected Family Members</th>
<th>Spouses</th>
<th>FCHL Probands</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>144 (54/90)</td>
<td>123 (59/64)</td>
<td>32 (17/15)</td>
<td>24 (12/12)</td>
</tr>
<tr>
<td>Age, years</td>
<td>42.0±12.7/51.2±15.4</td>
<td>39.4±17.2/37.1±17.6</td>
<td>49.5±11.0/47.4±9.5</td>
<td>53.4±12.2/58.7±14.1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.6±38.2/27.4±3.2</td>
<td>23.9±4.6/24.1±3.6</td>
<td>26.0±18.7/26.5±3.4</td>
<td>26.8±3.3/27.1±5.9</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>6.7±0.6/7.0±0.8</td>
<td>5.4±0.8/5.4±0.9</td>
<td>4.8±1.0/5.1±0.9</td>
<td>6.5±0.6/7.3±1.4</td>
</tr>
<tr>
<td>TG, mmol/L</td>
<td>4.4±1.0/4.1±1.0</td>
<td>1.5±0.3/1.7±0.9</td>
<td>2.4±1.0/1.3±0.9</td>
<td>4.1±0.7/4.1±0.6</td>
</tr>
<tr>
<td>HDL-C, mmol/L</td>
<td>0.9±0.2/1.0±0.2</td>
<td>1.2±0.5/1.5±0.7</td>
<td>0.9±0.2/1.3±0.6</td>
<td>0.9±0.1/0.9±0.2</td>
</tr>
<tr>
<td>APOB, mg/dL</td>
<td>122.8±27.5/129.5±26.0</td>
<td>90.2±30.3/87.7±27.6</td>
<td>99.0±27.3/88.2±24.3</td>
<td>127.6±16.0/135.9±23.5</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>4.8±1.4/4.9±1.3</td>
<td>4.7±0.9/4.9±0.8</td>
<td>4.7±0.7/4.9±1.2</td>
<td>4.9±1.3/5.0±0.7</td>
</tr>
</tbody>
</table>

Values are mean±SD. Lipid measurements were available for 314 individuals. M/F indicates male/female; BMI, body mass index; TC, total cholesterol; TG, triglycerides; HDL-C, HDL-cholesterol; apoB, apolipoprotein B.

*FCHL status: TG and/or TC ≥90th age/sex-specific Mexican population percentile.

#### Table 1B. Structure of the 24 Mexican Families With FCHL

<table>
<thead>
<tr>
<th></th>
<th>Individuals With DNA available (M/F)</th>
<th>314 (147/167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probands (M/F)</td>
<td>24 (12/12)</td>
<td></td>
</tr>
<tr>
<td>Family structure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of families with 2 generations*</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>No. of families with 3 generations</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>No. of families with 4 generations</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>No. of families with less than 5 affecteds</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>No. of families with 5 affecteds</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>No. of families with more than 5 affecteds†</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>No. of affected subjects (M/F)</td>
<td>56 (24/32)/39</td>
<td></td>
</tr>
<tr>
<td>No. of independent affected sib-pairs</td>
<td>88 (30/58)/65</td>
<td></td>
</tr>
<tr>
<td>TG≥90th percentile (M/F)</td>
<td>34 (10/24)/18</td>
<td></td>
</tr>
<tr>
<td>TC≥90th percentile (M/F)</td>
<td>20 (12/8)/4</td>
<td></td>
</tr>
<tr>
<td>HDL-C≥10th percentile (M/F)</td>
<td>144 (54/90)/96</td>
<td></td>
</tr>
</tbody>
</table>

M/F indicates male/female; TG, triglycerides; TC, total cholesterol; HDL-C, HDL-cholesterol.

*The No. of genotyped generations with affected and unaffected individuals.
†The maximum No. of affected subjects was 14; 2 combined 28 phenotype: TC and TG≥90th age/sex-specific Mexican population percentile; §FCHL: TG and/or TC≥90th age/sex-specific Mexican population percentile. In addition, there are 198 nonindependent avuncular affected pairs and 127 nonindependent cousin affected pairs for FCHL in these families.
tion, as well as smoking and drinking habits. Body mass index (BMI) was determined for all subjects. Each subject provided a written informed consent. The protocol for this study was approved by the Institutional Committee of Biomedical Research in Humans of the INCNMSZ.

**Laboratory Analytical Methods**

All lipid levels for affected individuals were measured before treatment. The measurements were performed with commercially available standardized methods. Glucose was measured using the glucose oxidase method; serum TC and TGs were measured using an enzymatic method (SERA-PAK®); HDL-C levels were assessed using phosphotungstic acid and Mg2+; LDL-C concentrations were estimated by the Friedewald formula; and plasma apoB measurements were obtained using a commercially available assay (Beckman).

**Genotyping**

We genotyped 314 individuals from the 24 families for 13 SNPs, spanning USF1 and the 2 genes flanking USF1, F11 receptor (F11R), and a hypothetical gene LOC257106. Eight of these SNPs were reported previously. Five additional SNPs (rs1023115, rs1240334, rs2481084, rs2774279, and rs3813610) were selected from the dbSNP database. We genotyped 26 peak microsatellite markers for the previously linked regions on 2p25.1, 9p23, 10q11.23, 11q13, 16q24.1, 19q13, and 21q21, using the ABI Prism 3700 DNA Analyzer and the Genotyper 3.7 software.

**Statistical Analysis**

Because of the acknowledged difficulties to replicate results obtained in genetic analyses of complex traits, we used the same diagnostic criteria, the same methods, and the same markers as described previously with the USF1 gene and Dutch and Finnish genome scans. Accordingly, we tested the SNPs for association using the pyrosequencing technique on the automated PSQ HS96A platform. We genotyped 26 peak microsatellite markers for the previously linked regions on 2p25.1, 9p23, 10q11.23, 11q13, 16q24.1, 19q13, and 21q21, using the ABI Prism 3700 DNA Analyzer and the Genotyper 3.7 software.

Localization (in bp) of the SNPs and the pairwise LD between SNPs. a, LD between markers tested in spouses. b, LD between markers tested in probands. D’ is shown in the top left-hand triangle of the display. The scale for D’ is presented at the top. r2 is shown in the bottom right-hand triangle. The scale for r2 is presented on the right-hand side.

Two traits, high TG and FCHL, associated in the previous study were tested. The affection status for these traits was defined using the 90th Mexican age/sex-specific population percentiles of TC and TGs (the FCHL trait) and the 90th age/sex-specific percentiles of TGs (the high TG trait). The extent of pairwise linkage disequilibrium (LD) between the marker genotypes was tested using the JLIN: JAVA LD PLOTTER program available online (http://www.genepi.com.au/project/jlin).

For linkage analysis of microsatellite markers, we carried out the same parametric and nonparametric 2-point analyses as were used previously with the MLINK program of the LINKAGE package and the SIBPAIR program, as implemented in the ANALYZE package. We assumed a disease allele frequency of 0.006 under the dominant mode of inheritance and 0.1095 under the recessive mode of inheritance. Linkage analyses of the microsatellite markers were performed for the dichotomized FCHL, TG, TC, and low HDL-C traits, as described previously. Allele frequencies were estimated from all individuals using the DOWNFREQ program. The PedCheck program was used to assess the genotype data for pedigree inconsistencies. The multipoint analyses for 16q24.1 and 10q11.23 were performed using the GENEHUNTER program.
TABLE 2A. Association Analyses of Individual SNPs in the F11R-USF1 Region for the TG and FCHL Traits

<table>
<thead>
<tr>
<th>Gene</th>
<th>rs Number for the SNP</th>
<th>SNP Type</th>
<th>Distance Between SNPs (bp)</th>
<th>Het/Freq</th>
<th>Triglycerides</th>
<th>FCHL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FBAT P*</td>
<td>FBAT P*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P&lt;o</td>
<td>P&lt;e</td>
</tr>
<tr>
<td>F11R rs836</td>
<td>3'UTR</td>
<td>20190</td>
<td>21.390</td>
<td>0.37/0.25</td>
<td>0.02</td>
<td>0.002</td>
</tr>
<tr>
<td>F11R rs4339888</td>
<td>3'UTR</td>
<td>2197</td>
<td>0.35/0.22</td>
<td></td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>USF1 rs2073658</td>
<td>5'UTR</td>
<td>1239</td>
<td>0.35/0.22</td>
<td></td>
<td>0.05</td>
<td>0.005</td>
</tr>
<tr>
<td>USF1 rs2073656</td>
<td>5'UTR</td>
<td>1235</td>
<td>0.38/0.26</td>
<td></td>
<td>0.05</td>
<td>0.005</td>
</tr>
<tr>
<td>USF1 rs2073655</td>
<td>5'UTR</td>
<td>1780</td>
<td>0.34/0.22</td>
<td></td>
<td>0.05</td>
<td>0.005</td>
</tr>
<tr>
<td>USF1 rs2516838</td>
<td>5'UTR</td>
<td>3186</td>
<td>0.22/0.12</td>
<td></td>
<td>0.05</td>
<td>0.005</td>
</tr>
<tr>
<td>LOC257106 rs2774279</td>
<td>C-S</td>
<td>5083</td>
<td>0.21/0.12</td>
<td></td>
<td>0.05</td>
<td>0.005</td>
</tr>
<tr>
<td>LOC257106 rs3813610</td>
<td>I</td>
<td>4693</td>
<td>0.46/0.36</td>
<td></td>
<td>0.05</td>
<td>0.005</td>
</tr>
</tbody>
</table>

All results represent P values; *P values for association with HBAT, †P values for linkage and association with the gamete competition test; and ‡P values for linkage test using the options – o and – e, respectively. Analyses for cells left blank resulted in P values >0.05. Het/Freq indicates heterogeneity/allele frequency; E, exonic; C-S, coding-synonymous; I, intronic; IG, intergenic; F11R, F11R receptor gene; USF1, upstream transcription factor 1 gene; LOC257106, hypothetical protein LOC257106.

TABLE 2B. Haplotype Analysis for the TG and FCHL Traits

<table>
<thead>
<tr>
<th>Haplotype of SNPs</th>
<th>Haplotype of SNPs</th>
<th>TG</th>
<th>FCHL</th>
<th>TG</th>
<th>FCHL</th>
</tr>
</thead>
<tbody>
<tr>
<td>hCV1459766-rs3737787</td>
<td>rs3737787-rs2073658</td>
<td>0.0009</td>
<td>0.02</td>
<td>0.004</td>
<td>0.03</td>
</tr>
<tr>
<td>Haplotype 11</td>
<td>Haplotype 22</td>
<td>0.001</td>
<td>0.02</td>
<td>0.002</td>
<td>0.02</td>
</tr>
</tbody>
</table>

All results represent P values for association with the HBAT – e option. Only P values 0.05 or less are reported. The segregating susceptibility haplotype was 1-2 (1 indicates the major allele) in all of the analyses above. The haplotype 2-2 (2 indicates the minor allele) was less transmitted, protective haplotype in all of the analysis above.

Statistical Significance

We performed 2 classes of analyses. In the study of USF1, two traits were tested for association with 13 SNPs. The Bonferroni correction for the probability values obtained in these analyses can be considered overly conservative, because we investigate highly correlated SNPs and traits. We are conducting the same analyses seen in Pajukanta et al13 and are examining the results in aggregate to see if SNPs and traits. We are conducting the same analyses seen in

Results

To investigate the underlying genetic component for FCHL within the USF1 region in the Mexican population, we genotyped a total of 13 SNPs spanning an 88-kb region, including three genes, USF1, F11 receptor (F11R), and hypothetical gene LOC257106 (Table 2a). The F11R and haplotypic gene LOC257106 were investigated besides USF1 in Mexicans, because in Finns the associated region extended to an 146-kb region that also covered the F11R gene, specifically in TG-affected Finnish males.13

One F11R SNP, hCV1459766, and 2 USF1 SNPs, rs3737787 and rs2073658, within a 14-kb region, showed evidence for association with the FCHL and TG traits (Table 2a and 2b). Specifically, the TG trait produced the most significant signal for association, resulting in probability values of 0.001, 0.005, and 0.001 for SNPs hCV1459766, rs3737787, and rs2073658, respectively, when testing for linkage and association in nuclear families using the FBAT option – e (Table 2a). When testing for association and accounting for linkage using the FBAT option – e, the SNPs hCV1459766 and rs3737787 resulted in probability values of 0.04 and 0.02 (Table 2a). These results are in accordance with the results obtained when testing for linkage and association in the extended families using the gamete competition test (Table 2a). Moreover, haplotype analysis for SNPs hCV1459766-rs3737787 provided evidence of association with both traits, TGs (P=0.0009) and FCHL (P=0.02) using the HBAT option – e (Table 2b). Although these 3 SNPs are in strong LD with one another, their pairwise r2 measurements of
TABLE 3. Two-Point Linkage and ASP Analyses for
Chromosome 16q24.1 with the TC Trait

<table>
<thead>
<tr>
<th>Marker</th>
<th>Position* (cM)</th>
<th>LOD Score†</th>
<th>ASP LOD Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>D16S507</td>
<td>105.17</td>
<td>0.1 (0.3)</td>
<td>1.1</td>
</tr>
<tr>
<td>D16S505</td>
<td>108.96</td>
<td>0.6 (0.1)</td>
<td>2.6</td>
</tr>
<tr>
<td>D16S3091</td>
<td>111.12</td>
<td>0.2 (0.3)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

ASP indicates affected sib-pair test.
*The position is based on the Marshfield Center for Medical Genetics Database. †Maximum LOD scores using a dominant mode of inheritance. The recombination fractions are given in parentheses.

Discussion

Our results taken in aggregate provide evidence that variants in USF1 are associated with FCHL and TGs in Mexican FCHL families. The SNPs hCV1459766, rs3737787, and rs2073658 showed significant evidence for association with both traits. As in the original study, the most significant association was observed with the high TG trait. Furthermore, haplotype analysis for SNPs hCV1459766-rs3737787 showed significant evidence for association with both traits, TGs (P = 0.0009) and FCHL (P = 0.02). As in the Finns, the major alleles and haplotypes formed by the major alleles were associated with FCHL and TGs. Similarly, the transmission of the haplotype of minor alleles to the affected individuals was reduced. However, there were differences in these results when compared with the Finns, possibly because of a different underlying LD structure. First, the most significant evidence for association was observed with the haplotypes of the SNPs hCV1459766-rs3737787 (versus the SNPs rs3737787-rs2073658 in Finns). Second, the association was restricted to a 14-kb region in the Mexican families with FCHL when compared with the 46-kb in the TG-affected Finnish males.

In spite of the compelling evidence for the replication of the original association in the Mexican population, it is important to emphasize the need to sequence the USF1 genes in the Mexicans in future studies. We could fail to detect additional, possibly even coding variants that are associated in the Mexican population, as well as important differences in LD structure and allelic heterogeneity. Therefore, a gene-based approach that considers all common variations within a gene jointly is needed to resolve the possible inconsistencies arising from population differences.

Here we also report a region on chromosome 16q24.1 to show suggestive evidence for linkage with TC in the Mexican families. Previous data from a combined analysis of the Dutch and Finnish genome-wide scans for FCHL provided evidence that the 16q24.1 region is linked to low HDL-C, producing a parametric multipoint LOD score of 3.6 for the low HDL-C trait. Importantly, this region on 16q24.1 has also been linked to HDL-C in an independent
study of Mexican Americans.\textsuperscript{38} In the combined analysis of the Dutch and Finnish FCHL families,\textsuperscript{7} the maximum 2-point LOD score of 2.0 was obtained with marker D16S505 for low HDL-C; whereas for TC, the adjacent marker D16S3091 (2.1 cM apart) produced the highest 2-point LOD score of 1.6. Interestingly, the TC trait produced the highest evidence for linkage in the Mexican FCHL families, resulting in a 2-point ASP LOD score of 2.6 with marker D16S505 and a multipoint NPL score of 2.2. Although the maximum LOD scores for this region on 16q24.1 were observed for different traits in the Mexicans than in the Finns and Dutch, we assume that the complexity of the genetic and environmental processes that regulate the expression of the complex FCHL phenotypes in each population contributes to this difference.

Several studies have demonstrated that the Mexican population has a high genetic predisposition to the type 2 diabetes mellitus, metabolic syndrome, and some primary forms of dyslipidemias.\textsuperscript{22–24} In Mexicans, at age 50, 27.6\% of men and 21\% of women exhibit mixed dyslipidemia.\textsuperscript{23} These data suggest that the most common causes of mixed dyslipidemias, such as type 2 diabetes mellitus and FCHL, are common abnormalities in the Mexican population. Therefore, it is critical to identify genetic variants that confer susceptibility to high serum lipid levels in this population. The present study is the first report to extensively investigate the genetic component of the common FCHL disorder in the Mexican population.

Acknowledgments
This research was supported by the UC-MEXUS CONACYT grant, National Institutes of Health grants HL-28481 and HL-70150, as well as American Heart Association grant 0430180N. A.H.V. received support through CONACyT fellowship. We thank the family members for participating in this study. We thank S. Ramirez and M. Rodriguez for technical support.

References
22. Stern MP, Knapp JA, Hazuda HP, Haffner SM, Patterson JK, Mitchell BD. Genetic and environmental determinants of type II diabetes in...


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Arterioscler Thromb Vasc Biol. 2005;25:1985-1991; originally published online June 23, 2005; doi: 10.1161/01.ATV.0000175297.37214.a0

Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1079-5642. Online ISSN: 1524-4636

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