Preliminary evidence of genetic determinants of adiponectin response to fenofibrate in the Genetics of Lipid Lowering Drugs and Diet Network.

Submitted by arnett on Mon, 08/19/2013 - 12:58pm

Preliminary evidence of genetic determinants of adiponectin response to fenofibrate in the Genetics of Lipid Lowering Drugs and Diet Network.

Title
Preliminary evidence of genetic determinants of adiponectin response to fenofibrate in the Genetics of Lipid Lowering Drugs and Diet Network.

Publication Type
Journal Article

Year of Publication
2013

Authors
Aslibekyan, S, An, P, Frazier-Wood, AC, Kabagambe, EK, Irvin, MR, Straka, RJ, Tiwari, HK, Tsai, MY, Hopkins, PN, Borecki, IB, Ordovas, JM, Arnett, DK

Journal
Nutr Metab Cardiovasc Dis

Volume
23

Issue
10

Pagination
987-94

Date Published
2013 Oct

ISSN
1590-3729

Keywords
Adiponectin, Adipose Tissue, White, Adult, Cadherins, Chromosomes, Human, Pair 12, Drug Resistance, Female, Fenofibrate, Gene Frequency, Genome-Wide Association Study, Humans, Hypolipidemic Agents, Linkage Disequilibrium, Male, Middle Aged, Minnesota, Oligonucleotide Array Sequence Analysis, Polymorphism, Single Nucleotide, Siblings, Utah

Abstract
BACKGROUND AND AIMS: Adiponectin is an adipose-secreted protein that has been linked to changes in insulin sensitivity, high-density lipoprotein cholesterol levels, and inflammatory patterns. Although fenofibrate therapy can raise adiponectin levels, treatment response is heterogeneous and heritable, suggesting a role for genetic mediators. This is the first genome-wide association study of fenofibrate effects on circulating adiponectin.

METHODS AND RESULTS: Plasma adiponectin was measured in participants of the Genetics of Lipid Lowering Drugs and Diet Network (n = 793) before and after a 3-week daily treatment with 160 mg of fenofibrate. Associations between variants on the Affymetrix Genome-Wide Human SNP Array 6.0 and adiponectin were assessed using mixed linear models, adjusted for age, sex, site, and family. We observed a statistically significant (P = 5 × 10⁻⁸) association between rs2384207 in 12q24, a region previously linked to several metabolic traits, and the fenofibrate-induced change in circulating adiponectin. Additionally, our genome-wide analysis of baseline adiponectin levels replicated the previously reported association with CDH13 and
suggested novel associations with markers near the PCK1, ZBP1, TMEM18, and SCUBE1 genes. The findings from the single marker tests were corroborated in gene-based analyses. Biological pathway analyses suggested a borderline significant association between the EGF receptor signaling pathway and baseline adiponectin levels.

**CONCLUSIONS:** We present preliminary evidence linking several biologically relevant genetic variants to adiponectin levels at baseline and in response to fenofibrate therapy. Our findings provide support for fine-mapping of the 12q24 region to investigate the shared biological mechanisms underlying levels of circulating adiponectin and susceptibility to metabolic disease.

DOI: 10.1016/j.numecd.2012.07.010
Alternate Journal: Nutr Metab Cardiovasc Dis
PubMed ID: 23149075
PubMed Central ID: PMC3578131
Grant List: U01 HL072524 / HL / NHLBI NIH HHS / United States
U01HL072524-04 / HL / NHLBI NIH HHS / United States