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Title: Genome-wide association study of the plasma triglyceride response to an n-3 polyunsaturated fatty acid supplementation

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Source: JOURNAL OF LIPID RESEARCH **Volume:** 55 **Issue:** 7 **Pages:** 1245-1253 **DOI:** 10.1194/jlr.M045898 **Published:** JUL 2014

Times Cited in Web of Science Core Collection: 9

Total Times Cited: 9

Usage Count (Last 180 days): 1

Usage Count (Since 2013): 5

Cited Reference Count: 33

Abstract: Studies have shown a large interindividual variability in plasma TG response to long-chain n-3 PUFA supplementation, which may likely be attributable to genetic variability within the populations studied. The objective is to compare the frequency of SNPs in a genome-wide association study between responders (reduction in plasma TG levels >= 0.01 mM) and nonresponders (increase in plasma TG of >= 0 mM) to supplementation. Genomic DNA from 141 subjects who completed a 2-week run-in period followed by 6-week supplementation with 5 g of fish oil daily (1.9-2.2 g EPA and 1.1 g DHA daily) were genotyped on Illumina HumanOmni-5-QuadBeadChip. Thirteen loci had frequency differences between responders and nonresponders (P < 1 x 10(-5)), including SNPs in or near IQCJ-SCHIP1, MYB, NELL1, NXPH1, PHF17, and SLIT2 genes. A genetic risk score (GRS) was constructed by summing the number of risk alleles. This GRS explained 21.53% of the variation in TG response to n-3 PUFA supplementation when adjusted for age, sex, and BMI (P = 0.0002). Using Fish Oil Intervention and Genotype as a replication cohort, the GRS was able to explain 2% of variation in TG response when adjusted. In conclusion, subjects who decrease their plasma TG levels following n-3 PUFA supplementation may have a different genetic profile than individuals who do not respond.

Accession Number: WOS:000338017400005

PubMed ID: 24847101

Language: English

Document Type: Article

Author Keywords: nutrigenetics; single nucleotide polymorphism; responders; fish oil; genetic risk score

KeyWords Plus: BODY-MASS INDEX; CARDIOVASCULAR BIOMARKER RESPONSE; DENSITY-LIPOPROTEIN; FISH-OIL; TRIACYLGLYCEROL RESPONSE; POLYMORPHISM; CHOLESTEROL; RISK; GENE; GENOTYPE

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Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC

Publisher Address: 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA

Web of Science Categories: Biochemistry & Molecular Biology

Research Areas: Biochemistry & Molecular Biology

IDS Number: AJ9GZ

ISSN: 0022-2275

eISSN: 1539-7262

29-char Source Abbrev.: J LIPID RES

ISO Source Abbrev.: J. Lipid Res.

Source Item Page Count: 9

Funding:

Funding Agency	Grant Number
Canadian Institutes of Health Research (CIHR)	MOP229488
Heart and Stroke Foundation of Canada	
CIHR	MSH95330
Fonds de recherche du Quebec - Sante (FRQS)	
Biotechnology and Biological Sciences Research Council	

This work was supported by an operating grant from Canadian Institutes of Health Research (CIHR) (MOP229488). F. Guenard received a research fellowship award from the Heart and Stroke Foundation of Canada. O. Barbier received a scholarship from the CIHR (New Investigator Award, MSH95330). P. Couture received a scholarship from the Fonds de recherche du Quebec - Sante (FRQS). M-C. Vohl holds a Tier 1 Canada Research Chair in Genomics Applied to Nutrition and Health. The Fish Oil Intervention and Genotype Study was supported by the Biotechnology and Biological Sciences Research Council. The authors do not declare any conflicts of interest.

Open Access: No

Output Date: 2017-08-02

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