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FADS polymorphisms and plasma levels of omega-3 fatty acids

Michael H. Davidson
Omthera Pharmaceuticals, Inc., USA

Until recently, plasma levels of long-chain marine omega-3 fatty acids were thought to be exclusively affected by dietary intake. Short-chain omega-3 fatty acids, primarily alpha-linolenic acid, is abundant in the diet, but only small amounts are converted to the longer-chain EPA and even less elongated to DHA by the desaturase enzymes (delta-5 and delta-6) However, it is now widely recognized that LC-PUFA that are formed by these desaturases are affected significantly by genetic polymorphisms that code for these enzymes (FADS1–3). These FADS polymorphisms are relatively common and potent and may explain up to 30% of the variability in LC-PUFA levels (both omega-6 and omega-3) For example, about 80% of African Americans have a FADS polymorphism (rs174537) that is associated with more effective conversion of SC-PUFA to LC-PUFA by desaturase-5, and therefore, they have both higher levels of arachidonic acid (AA) and EPA, even though their fish consumption is lower on average than that of whites . Therefore, it is intriguing to hypothesize that African Americans who have higher levels of disorders such as hypertension, asthma, and aspirin resistance can be linked to a higher inflammatory state driven by an overproduction of prostaglandins and leukotrienes that are synthesized from AA. On the other hand, Hispanic individuals more commonly have a different FADS polymorphism (rs17454) that results in less conversion of SC-PUFA to LC-PUFA, and they consequently have lower levels of AA and EPA (Figure 2) (12). This FADS polymorphism is associated with dyslipidemia (high triglycerides [TGs] and low high-density lipoprotein cholesterol [HDL-C]) that is in part modulated by PUFA intake. Therefore, this polymorphism may explain the high prevalence of hypertriglyceridemia in the Hispanic population, whereas the rs1745237 polymorphism found predominantly in African Americans and associated with higher EPA levels may lead to their lower incidence of elevated TGs and higher HDL-C levels. The same FADS polymorphisms associated with lower levels of EPA and DHA are also linked to other diseases such as inflammatory bowel disease) and attention deficit/hyperactivity disorder (ADHD) for which clinical trials in humans have supported a potential benefit with increased omega-3 fatty acid intake. Further studies are needed to define the function of FADS1 and FADS2 polymorphisms relative to the mechanisms involved in the development of atherosclerosis, dyslipidemia, and other diseases that may be linked to either AA overproduction or deficiencies in marine LC-PUFAs.

Biography

Michael H. Davidson, M.D., is Professor of Medicine and Director of the Lipid Clinic at the University of Chicago. He also serves as Chief Medical Officer and Executive Vice President for Omthera. Pharmaceuticals, a subsidiary of Astra Zeneca Pharmaceuticals. He is a leading expert in the field of Lipidology. He has conducted over 1000 clinical trials, published more than 300 medical journal articles and written three books on Lipidology. His research background encompasses both pharmaceutical and nutritional clinical trials including extensive research on statins, novel lipid-lowering drugs, and omega-3 fatty acids. He was a founding board member of the National Lipid Association and initiated the self-study modules that lead to formation of board certification in lipidology. He founded the Chicago Center for Clinical Research, which became the largest investigator site in the United States and was acquired by Pharmaceutical Product Development in 1996. He was also the co-founding Chief Medical Officer of Omthera Pharamceuticals in 2008 that was acquired by Astra Zenece Pharmaceutical in 2013 for $440M. He is board-certified in internal medicine, cardiology, and clinical lipidology. He is a Fellow of the American College of Cardiology and the American College of Chest Physicians. In addition, he was President (2010-2011) of the National Lipid Association. He was named in *The Best Doctors in America* for the past 10 years and was named Father of the Year by the American Diabetes Association, 2010.

mdavidsonmd@gmail.com