

SNPs affect folate metabolism in study of Puerto-Rican adults

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Researchers at Tufts University have gained further understanding of the genomic basis for altered folate metabolism and the content of uracil in blood DNA. In a study published in October's *American Journal of Clinical Nutrition*, senior author Jimmy Crott, PhD, and colleagues studied nine single nucleotide polymorphisms (SNPs) in five genes involved in folate uptake and retention: folate hydrolase (FOLH1), folate polyglutamate synthase (FPGS), γ -glutamyl hydrolase (GGH), proton-coupled folate transporter (PCFT), and reduced folate carrier (RFC1) in a cohort of 991 Puerto Rican adults residing in and around Boston. In addition, four SNPs in two genes involved in folate metabolism previously associated with altered blood folate and homocysteine concentrations were studied: methylenetetrahydrofolate reductase (MTHFR) and methionine synthase (MTR).

SNPs are variations in the sequence of nucleotides, or building blocks, that make up genes. Humans possess two copies of every gene. For each SNP, there are three possible genotypes depending on the presence of "normal" and "variant" copies of the gene; two normal copies, one normal and one variant or two variant copies.

Diseases, such as some cancers, have been associated with diminished blood folate concentrations and abnormal folate metabolism. Crott, a scientist in the Vitamins and Carcinogenesis Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts, and first author Lauren DeVos of Pennsylvania State University found that several SNPs affect folate metabolism, as evidenced by altered

concentrations of blood homocysteine, folate, and DNA uracil.

"Perhaps the most intriguing results of this study involve these SNPs that affected the concentration of uracil in DNA. Uracil accumulation has the potential to cause DNA breakage, a mutagenic event that may increase the risk for cancer," Crott said.

With respect to the MTHFR 677C>T SNP, those with two copies of the variant gene (TT genotype) displayed a 33.8% lower blood DNA uracil content than those with one or less copies of a variant gene (CC and CT genotypes). This observation fits with previous work showing that, under certain conditions, those with the TT genotype have a significantly lower risk for colorectal cancer than CC and CT genotypes. In addition, a significant association was detected between the -124T>G SNP in GGH gene and DNA uracil content. Individuals with one copy of the variant GGH gene (-124TG genotype) had DNA uracil levels 30% higher, while those with two copies of the variant gene (-124GG genotype) had a uracil level 73% higher than wildtypes (-124TT genotype). The authors speculate that this change might feasibly increase these individuals' risk for cancer.

Differences in blood folate concentrations were also associated with two of the SNPs studied. After correcting for other potentially confounding factors, those with the MTHFR 677TT genotype displayed folate concentrations 4.6% lower than CC genotypes and CT genotypes. Those with at least one copy of the variant T gene of the FOLH1 1561C>T SNP had blood folate concentrations 10.8% higher than those with the CC genotype. "Although the changes we see here are rather modest, low blood folate concentrations are associated with several diseases including colorectal cancer and neural tube defects," Crott said.

This study was a nested cohort within the ongoing Boston Puerto Rican Health Study (BPRHS). Puerto Rican adults between the ages of 45 and

75 were identified in blocks containing at least 10 Hispanic occupants in the 2000 census, and one per household (randomly selected) interviewed in his or her home. In addition to answering health-related and anthropometric questions, participants filled out a population-validated, food-frequency questionnaire.

"The current study is part of a body of research exploring whether a diet lacking essential nutrients like B vitamins and antioxidants plays a role in health disparities in older Puerto Rican adults," said co-author Katherine Tucker, a professor at the Friedman School of Nutrition Science and Policy, director of the Dietary Assessment and Epidemiology Research Program at the JM USDA HNRCA, and principal investigator of the BPRHS.

"The BPRHS is building on previous Tufts research which demonstrates that older Puerto Rican adults living in Boston are more likely to develop chronic health conditions such as depression and diabetes compared to older non-Hispanic whites living in the same neighborhoods," Tucker continued. "We hypothesize these health disparities are triggered by stress associated with poverty, perceived discrimination and poor nutrition among other challenges."

Source: Tufts University, Health Sciences

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