Association of functional polymorphism rs2231142 (Q141K) in the ABCG2 gene with serum uric and gout in 4 US populations

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Abstrak

A loss-of-function mutation (Q141K, rs2231142) in the ATP-binding cassette, subfamily G, member 2 gene (ABCG2) has been shown to be associated with serum uric acid levels and gout in Asians, Europeans, and European and African Americans; however, less is known about these associations in other populations. Rs2231142 was genotyped in 22,734 European Americans, 9,720 African Americans, 3,849 Mexican Americans, and 3,550 American Indians in the Population Architecture using Genomics and Epidemiology (PAGE) Study (2008-2012). Rs2231142 was significantly associated with serum uric acid levels (P = 2.37 × 10(-67), P = 3.98 × 10(-5), P = 6.97 × 10(-9), and P = 5.33 × 10(-4) in European Americans, African Americans, Mexican Americans, and American Indians, respectively) and gout (P = 2.83 × 10(-10), P = 0.01, and P = 0.01 in European Americans, African Americans, and Mexican Americans, respectively). Overall, the T allele was associated with a 0.24-mg/dL increase in serum uric acid level (P = 1.37 × 10(-80)) and a 1.75-fold increase in the odds of gout (P = 1.09 × 10(-12)). The association between rs2231142 and serum uric acid was significantly stronger in men, postmenopausal women, and hormone therapy users compared with their counterparts. The association with gout was also significantly stronger in men than in women. These results highlight a possible role of sex hormones in the regulation of ABCG2 urate transporter and its potential implications for the prevention, diagnosis, and treatment of hyperuricemia and gout.