Genome-wide association analyses identify 18 new loci associated with serum urate concentrations

Elevated serum urate concentrations can cause gout, a prevalent and painful inflammatory arthritis. By combining data from > 140,000 individuals of European ancestry within the Global Urate Genetics Consortium (GUGC), we identified and replicated 28 genome-wide
significant loci in association with serum urate concentrations (18 new regions in or near TRIM46, INHBB, SFMBT1, TMEM171, VEGFA, BAZ1B, PRKAG2, STC1, HNF4G, A1CF, ATXN2, UBE2Q2, IGF1R, NFAT5, MAF, HLF, ACVR1B-ACVRL1 and B3GNT4). Associations for many of the loci were of similar magnitude in individuals of non-European ancestry. We further characterized these loci for associations with gout, transcript expression and the fractional excretion of urate. Network analyses implicate the inhibins-activins signaling pathways and glucose metabolism in systemic urate control. New candidate genes for serum urate concentration highlight the importance of metabolic control of urate production and excretion, which may have implications for the treatment and prevention of gout.