Meta-analysis of 28,141 individuals identifies common variants within five new loci that influence uric acid concentrations.

Abstract:
Elevated serum uric acid levels cause gout and are a risk factor for cardiovascular disease and diabetes. To investigate the polygenetic basis of serum uric acid levels, we conducted a meta-analysis of genome-wide association scans from 14 studies totalling 28,141 participants of European descent, resulting in identification of 954 SNPs distributed across nine loci that exceeded the threshold of genome-wide significance, five of which are novel. Overall, the common variants associated with serum uric acid levels fall in the following nine regions: SLC2A9 (p = 5.2x10(-201)), ABCG2 (p = 3.1x10(-26)), SLC17A1 (p =
3.0 \times 10^{-14}), SLC22A11 (p = 6.7 \times 10^{-14}), SLC22A12 (p = 2.0 \times 10^{-9}), SLC16A9 (p = 1.1 \times 10^{-8}),
GCKR (p = 1.4 \times 10^{-9}), LRRC16A (p = 8.5 \times 10^{-9}), and near PDZK1 (p = 2.7 \times 10^{-9}). Identified
variants were analyzed for gender differences. We found that the minor allele for rs734553 in SLC2A9
has greater influence in lowering uric acid levels in women and the minor allele of rs2231142 in
ABCG2 elevates uric acid levels more strongly in men compared to women. To further characterize
the identified variants, we analyzed their association with a panel of metabolites. rs12356193 within
SLC16A9 was associated with DL-carnitine (p = 4.0 \times 10^{-26}) and propionyl-L-carnitine (p =
5.0 \times 10^{-8}) concentrations, which in turn were associated with serum UA levels (p = 1.4 \times 10^{-57}) and
p = 8.1 \times 10^{-54}, respectively), forming a triangle between SNP, metabolites, and UA levels. Taken
together, these associations highlight additional pathways that are important in the regulation of
serum uric acid levels and point toward novel potential targets for pharmacological intervention to
prevent or treat hyperuricemia. In addition, these findings strongly support the hypothesis that
transport proteins are key in regulating serum uric acid levels.