Common variants in P2RY11 are associated with narcolepsy.

Abstract:

Growing evidence supports the hypothesis that narcolepsy with cataplexy is an autoimmune disease. We here report genome-wide association analyses for narcolepsy with replication and fine mapping across three ethnic groups (3,406 individuals of European ancestry, 2,414 Asians and 302 African Americans). We identify a SNP in the 3' untranslated region of P2RY11, the purinergic receptor subtype P2Y?? gene, which is associated with narcolepsy (rs2305795, combined P = 6.1 x 10^-18, odds ratio = 1.28, 95% CI 1.19-1.39, n = 5689). The disease-associated allele is correlated with reduced expression of P2RY11 in CD8(+) T lymphocytes (339% reduced, P = 0.003) and natural killer (NK) cells (P = 0.031), but not in other peripheral blood mononuclear cell types. The low expression variant is
also associated with reduced P2RY11-mediated resistance to ATP-induced cell death in T lymphocytes (P = 0.0007) and natural killer cells (P = 0.001). These results identify P2RY11 as an important regulator of immune-cell survival, with possible implications in narcolepsy and other autoimmune diseases.