A common variant mapping to CACNA1A is associated with susceptibility to exfoliation syndrome

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Exfoliation syndrome (XFS) is the most common recognizable cause of open-angle glaucoma worldwide. To better understand the etiology of XFS, we conducted a genome-wide association study (GWAS) of 1,484 cases and 1,188 controls from Japan and followed up the most significant findings in a further 6,901 cases and 20,727 controls from 17 countries across 6 continents. We discovered a genome-wide significant association between a new locus (CACNA1A rs4926244) and increased susceptibility to XFS (odds ratio (OR) = 1.16, P = 3.36 × 10(-11)) . Although we also confirmed overwhelming association at the LOXL1 locus, the key SNP marker (LOXL1 rs4886776) demonstrated allelic reversal depending on the ancestry group (Japanese: ORA allele = 9.87, P = 2.13 × 10(-217) ; non-Japanese: ORA allele = 0.49, P = 2.35 × 10(-31)) . Our findings represent the first genetic locus outside of LOXL1 surpassing genome-wide significance for XFS and provide insight into the biology and pathogenesis of the disease.

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