Association of the del443ins54 at the ARMS2 locus in Indian and Australian cohorts with age-related macular degeneration.

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Abstract

PURPOSE:

The ARMS2/HTRA1 genes at the 10q26 locus have been associated with risk of age-related macular degeneration (AMD), with the most significantly associated variants being A69S (rs10490924), del443ins54 (EU427539) and rs11200638. We wished to explore the association of the del443ins54 in two ethnically different populations from India and Australia.

METHODS:

The del443ins54 was screened in a large cohort of ~1500 subjects from these two populations by a combination of PCR-based agarose gel electrophoresis and validated by resequencing. Statistical analysis comprised the calculations of allele, genotype and haplotype frequencies along with their p values and corresponding odds ratios (OR), and 95% confidence intervals (95% CI) and measures of linkage disequilibrium (LD).

RESULTS:

The del443ins54 was significantly associated with AMD in both the Indian ($p=1.74 \times 10(-13)$; OR = 2.80, 95%CI, 2.12-3.70) and Australian cohorts ($p = 2.78 \times 10(-30)$; OR = 3.15, 95%CI, 2.58-3.86). These associations were similar to those previously identified for the A69S and the rs11200638 variant in these populations that also exhibited high degrees of LD (D' of 0.87-0.99). A major risk haplotype of "T-indel-A" ($p = 5.7 \times 10(-16)$; OR = 3.16, 95%CI, 2.34-4.19 and $p=6.33 \times 10(-30)$; OR = 3.15, 95%CI, 2.57-3.85) and a protective haplotype of "G-wild type-G" ($p=2.35 \times 10(-11)$; OR = 0.39, 95%CI, 0.29-0.52 and $p=1.02 \times 10(-30)$; OR = 0.31, 95%CI, 0.25-0.38) were identified in the Indian and Australian cohorts, respectively.

CONCLUSIONS:

These data provide an independent replication of the association of del443ins54 variant in two different ethnicities, despite differences in allele and haplotype frequencies between them. High levels of LD in both populations limit further genetic dissection of this region in AMD.