Volume 73, Issue 4, October 2003, Pages 780-790

A Genomewide Scan for Age-Related Macular Degeneration Provides Evidence for Linkage to Several Chromosomal Regions

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https://doi.org/10.1086/378505

We report the results of a genomewide scan for age-related macular degeneration (AMD) in 158 multiplex families. AMD classification was based on fundus photography and was assigned a grade ranging from 1 (no disease) to 5 (exudative disease). Genotyping was performed by the National Heart, Lung, and Blood Institute Mammalian Genotyping Service at Marshfield (404 short tandem repeat markers). The sample included 158 families with two or more siblings with AMD, 490 affected individuals, 101 unaffected individuals, and 38 whose affection status was unknown. Relative pairs included 511 affected sibling, 28 avuncular, 53 cousin, 7 grandparent-grandchild, and 9 grand-avuncular pairs. Two-point parametric and multipoint parametric and nonparametric analyses were performed. Maximum two-point LOD scores of 1.0â€“2.0 were found for markers on chromosomes 1, 2, 8, 10, 14, 15, and 22. Multipoint analyses were consistent with the two-point results for chromosomes 1, 2

Multipoint analyses were consistent with the two-point results for chromosomes 1, 2, 8, 10, and 22 and provided evidence for additional linkage regions on chromosomes 3, 6, 8, 12, 16, and X. Our signals on chromosomes 1q, 6p, and 10q are consistent with some other previously published results. Significant linkage to AMD was found for one marker on chromosome 2, two adjacent markers on chromosome 3, two adjacent markers on chromosome 6, and seven contiguous markers on chromosome 8, with empirical P values of .00001. The consistency of many of the other signals across both two-point and multipoint, as well as parametric and nonparametric, analyses indicate several other regions worthy of follow-up.

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* The first two authors contributed equally to this manuscript.

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