

Identification of a Novel Locus for Autosomal Dominant Primary Open Angle Glaucoma on 4q35.1-q35.2.

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PURPOSE: Primary open angle glaucoma is the most prevalent type of glaucoma and the leading cause of irreversible blindness worldwide. The genetic basis is poorly understood. Of 14 loci associated with this disease, only two genes have been identified, accounting for approximately 4% of cases. The authors investigated the genetic cause of primary open angle glaucoma in a large four-generation family with an apparent autosomal dominant mode of inheritance.

METHODS: Twenty-three family members underwent comprehensive phenotyping by a single ophthalmologist, and the MYOC gene was sequenced in all affected family members for whom DNA was available. Parametric genomewide linkage analysis was performed on 10 affected family members and one unaffected family member. Within the critical region, mutation analysis of candidate genes LRP2BP, CYP4V2, and UFSP2 was carried out by direct sequencing.

RESULT: No mutations were identified in MYOC. Genomewide linkage analysis generated one significant LOD score of 3.1 (maximum affected-only LOD score of 2.8) centered on chromosome 4 at 4q35.1-q35.2, a critical region that does not contain any of the previously reported primary open angle glaucoma loci. A 1.866-Mb (7.2 cM) region was identified containing 17 known or hypothetical genes. No mutations were identified in the candidate genes LRP2BP, CYP4V2, and UFSP2.

CONCLUSION: This study identifies a new primary open angle glaucoma locus, GLC1Q, in a region on chromosome 4 not previously associated with glaucoma.

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