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Address for correspondence and reprints: Dr. Joël Zlotogora, Hadassah University Hospital, P.O. Box 12000, Jerusalem 91120, Israel.

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The Distinction Between Juvenile and Adult-Onset Primary Open-Angle Glaucoma

To the Editor:

Because of the significant differences between the juvenile and adult forms of open-angle glaucoma, especially with regard to inheritance, prevalence, severity, and age of onset, we read with interest the recent publication by Morissette et al. (1995), describing a pedigree with a phenotype that overlaps the distinctive features of juvenile-onset open-angle glaucoma (JOAG) and adult-onset primary open-angle glaucoma (usually abbreviated as POAG or COAG). These authors conclude that a gene mapped to human chromosome 1q21-q31 (GLC1A) can be responsible for both juvenile and adult forms of open-angle glaucoma. The implications of such a result could be extremely important, in light of the high prevalence of the adult form of the disease. However, while the data presented in this report suggest that variable expressivity of the GLC1A gene may lead to a broader range of onset for this form of juvenile glaucoma, these data do not identify the GLC1A gene as an important cause of POAG. To prevent misleading interpretations of this and similar studies, we wish to clarify the distinction between the juvenile and adult forms of open-angle glaucoma.

Glaucoma is a term used to describe a disease process that results in a loss of retinal ganglion cells, causing a characteristic degeneration of the optic nerve. Typically the deterioration of the optic nerve is associated with an elevation of intraocular pressure that is probably related to the pathogenesis of the disorder. The ocular structures comprising the fluid pathways that contribute to the variation in intraocular pressure are located in the "angle" created by the junction of the cornea with the iris. Clinical descriptions of the various types of glaucoma often refer to the appearance of the angle; in particular, glaucoma is frequently divided into the open-angle and closed-angle subtypes. Closed-angle glaucoma is very rare and is usually caused by anatomical abnormalities. Open-angle glaucoma is much more common and is likely to result from a number of different, and as yet undefined, physiological and biochemical abnormalities. Although glaucoma eventually causes a complete loss of sight, the destructive process is usually very slowly progressive, and most patients are unaware of a loss of vision, or any other symptom, until quite late in the course of the disease. Of the many different types of glaucoma, the most common is POAG, which affects individuals in the later decades of life, with an onset usually after the age of 50 years (Armaly 1962, 1969). A rare form of glaucoma that has been recently well studied is the primary open-angle glaucoma of juvenile-onset (JOAG). Unlike the adult-onset disease, the juvenile type almost always develops before the age of 40 years and is an unusually severe form of the disease, frequently causing substantial visual impairment in affected individuals (Wiggs et al. 1995). While the adult form of the disease is likely to be inherited as a complex trait, without an obvious segregation pattern, the juvenile form is inherited as an autosomal dominant Mendelian trait with high penetrance. One locus for JOAG has been mapped to human chromosome 1q21-q31 (Sheffield et al. 1993; Richards et al. 1994; Wiggs et al. 1994). The clinical phenotype of the pedigrees shown to be linked to the 1q21-q31 region is remarkably uniform (Johnson et al. 1994; Wiggs et al. 1995).

In the recent publication by Morissette et al. (1995), a common haplotype derived from microsatellite markers located in the 1q21-q31 region segregates with the disease phenotype in 40 individuals included in this study. Of these 40, 36 were documented to develop the disease before the age of 40 years and consequently were designated as JOAG. The remaining four were first diagnosed at ages 44, 47, 53, and 62 years. Because the disease

was diagnosed after the age of 40 years, these individuals were felt to have clinical features more in line with the adult form of the disease (POAG or COAG). Hence, the authors conclude that the gene located in the 1q21-q31 region can be responsible for both the juvenile and adult forms of the disease. We contend that onset before age 40 years is an arbitrarily defined distinction between the two forms of the disease. The severity of the glaucoma afflicting the majority of the affected members of this pedigree and the demonstration of simple Mendelian inheritance suggest that the phenotype described in this report is an example of variable expression of the JOAG phenotype rather than true POAG. Moreover, because of the insidious character of the glaucoma disease process, clinically pinpointing the actual onset of the disease is quite difficult. The possibility exists that these four individuals had developed the disease prior to age 40 years. The data presented in this report suggest that the age at onset of the form of juvenile glaucoma caused by GLC1A may occasionally extend beyond the age of 40 years. However, one should not conclude from these data that the GLC1A gene is commonly responsible for the very prevalent adult-onset form of the disease.

JANEY L. WIGGS,[1,2] KARIM F. DAMJI,[4] JONATHAN L. HAINES,[3] MARGARET A. PERICAK-VANCE,[5] AND R. RAND ALLINGHAM[4]

[1]*Department of Ophthalmology, Tufts University School of Medicine,* [2]*Genetics Division, Tufts University, Sackler School of Graduate Biomedical Sciences, and* [3]*Molecular Neurogenetics Unit, Massachusetts General Hospital, Boston; and* [4]*Department of Ophthalmology and* [5]*Division of Neurology, Department of Medicine, Duke University Medical Center, Durham*

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Address for correspondence and reprints: Dr. Janey L. Wiggs, Molecular Genetics Unit, Department of Ophthalmology, New England Medical Center, 750 Washington Street, Box 450, Boston, MA 02114. E-mail: jwiggs_gla@opal.tufts.edu

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