Documenting the Corneal Phenotype Associated with the *MIR184* c.57C>T Mutation

Ten years ago, we published the clinical features of a novel hereditary anterior-segment dysgenesis, which we termed EDICT syndrome for endothelial dystrophy, iris hypoplasia, congenital cataracts, and stromal thinning.[1] We followed this with a report on the linkage of this dysgenesis to chromosome 15q.[2] Hughes et al. later published a report of a family with hereditary keratoconus and cataracts, which linked to a region within the EDICT interval.[3,4] Recently, Hughes et al. identified a mutation in *MIR184*, encoding microRNA 184 (MIM 613146), and this mutation is responsible for the disease of keratoconus and cataracts noted in their family.[5] We have reported that the same mutation (c.57C>T) in *MIR184* causes EDICT syndrome.[6] Since the publication of our report linking *MIR184* (c.57C>T) to EDICT syndrome, we have additionally used next-generation sequencing to rule out any potential coding variant that might modify the phenotype caused by the mutation. Although both our study and the study by Hughes et al. report congenital cataracts, there are considerable differences in the description of the corneal phenotype. We described nonectatic thinning and uniform, steep corneal topography in all affected family members. Additionally, we described the histopathology of the proband's cornea taken at the time of a penetrating keratoplasty. We noted stromal thinning, degeneration of keratocytes, and polymorphic vacuoles containing osmiophilic structures within and between collagen lamellae. Prominent posterior nodules characteristic of Fuchs corneal dystrophy (MIM 136800) were present in the Descemet membrane, and the endothelium stained positively for cytokeratin, a feature also found in posterior polymorphous corneal dystrophy (MIM 122000). Hughes et al. describe "progressive astigmatism" and "cones" in affected family members and state that surgery was performed on some affected family members for the treatment of their corneal disease. Therefore, there is presumably tissue that Hughes et al. can study to confirm the diagnosis of keratoconus in their family. Also, photographic slit-lamp biomicroscopy and corneal topography of affected members would be useful for the documentation of a keratoconus phenotype. Furthermore, it would be helpful if Hughes et al. could provide a description of the iris of affected family members and note any abnormalities if present. Iris hypoplasia was a prominent phenotypic feature of EDICT syndrome. It is essential that phenotypes of novel genetic diseases be comprehensively described so that variability across different familial cases can be accurately assessed.

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Web Resources

The URL for data presented herein is as follows:

Online Mendelian Inheritance in Man (OMIM), http://www.omim.org

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Response to Iliff et al.

We thank Iliff et al. for their interest in our work, and we are pleased to reply. We reported that a mutation in *MIR184* (MIM 613146) causes autosomal-dominant keratoconus with early-onset anterior polar cataracts (KTCNCT [MIM 614303]) in a large Irish family.[1] The corresponding authors described a US family with a similar ocular phenotype of endothelial dystrophy, iris hypoplasia, congenital