Involvement of L/M Opsin Polymorphisms in Cone Dystrophy

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Summary
There are numerous examples in the literature of cone dystrophy patients presenting with a color vision defect.10 Here we present a case of a patient presenting with progressive cone dystrophy, who was subsequently found to harbor a mutation in his L/M opsin gene. The specific genotype explains both his inherited color vision defect and his progressive loss of cone function. These results suggest that the involvement of the L/M gene locus in cone dystrophy may be more common than previously thought.

Clinical Presentation
A 32-year-old man was diagnosed with color blindness and progressive vision loss beginning in grade school that has stabilized over the past few years. The patient has a family history of typical red-green color blindness not associated with vision loss. Previous testing showed normal photopic ERG oscillatory potentials and normal dark-adapted visual function. The patient has a family history of typical red-green color blindness not associated with vision loss. Previous testing showed subnormal photopic ERG oscillatory potentials and normal dark-adapted visual function. These results suggest that the involvement of the L/M gene locus in cone dystrophy may be more common than previously thought.

L/M-Opsin Gene Analysis
DNA was extracted from a blood sample, and the L/M gene array was examined. This patient's congenital red-green color vision deficiency is Explained by the presence of C203R, a novel mutation in the L/M-opsin gene. The missense mutation changes a conserved threonine residue to an unconserved leucine. This change is predicted to affect the sequence of L/M-opsin and may affect protein function. This patient has normal rod function and a family history of typical red-green color blindness not associated with vision loss. Previous testing showed subnormal photopic ERG oscillatory potentials and normal dark-adapted visual function. These results suggest that the involvement of the L/M gene locus in cone dystrophy may be more common than previously thought.

Disruption of the Foveal Cone Mosaic
We used the Bioptigen SD-OCT (Bioptigen, Inc., Research Triangle Park, NC) to obtain high-resolution images of the foveal mosaic. A and vertical, B. We used the Cirrus HD-OCT (Zeiss, Dublin, CA) to obtain a map of macular thickness (C), which showed significant thinning compared to the normal values predicted by the macular (version 5.1.1). From the horizontal Bioretinal OCT scan, we were able to assess foveal thickness. This was compared to data for our normal controls (plotted line represents the normal mean, shaded gray region is ±2 standard deviations, dashed orange line is the patient presented here). As shown in panels D-F, the central thickness is reduced from normal and this can be attributed to a reduction in OPL thickness. Arrows in A & B represent the extent of the foveal photoreceptor mosaic shown in Figure 4.

Conclusions
-Cone dystrophies likely represent many different diseases, though they often present similarly in the clinic with poor central vision and reduced color vision. As such, they are usually grouped together without further pursuit of etiology.
-Examination of the L/M-opsin gene locus (as well as other previously identified cone dystrophy loci) may be a useful way to refine the clinical classification of these patients.
-Retinal disorders with reduced cone function, though present in the presence of an otherwise normal rod mosaic (OD). These imaging results are similar to our patient (Figures 3 and 5).

References

Apparance of the Peripheral Photoreceptor Mosaic
Show images are of the peripheral photoreceptor mosaic in a normal control (a) and the patient reported above (b). Normal images were acquired at approximately 5 deg (a) and 10 deg (b) from fixation. Patient images are from -5 deg (a), -5 deg (b), -7 deg (d), and -9 deg (f) from fixation. In the normal mosaic, the cones appear as bright spots surrounded by a dark ring, which presumably represents the inner segment. Numerous inner segments are visible in the patient, albeit at reduced frequency than normal. Cone and rod density was calculated at various locations and compared to that reported for normal cones in Dubin et al.10. On the right, rod density was consistent with normal values, though cone density was reduced by about 25% from normal. Rod density in the patient is consistent with normal densities. This result is consistent with the expected for the S-cone mosaic. Thus, the residual cone structure likely includes S-cones as well as some L-cones.

Similar Imaging Results from Typical BCM
We have imaged a number of patients with cone dystrophy and yellowish SCI. Show images are from two patients, whose defect is caused by a C205R mutation in their single L/M photopigment. The foveal mosaic shown in A is of a normal control. The normal mosaic, the cones appear as bright spots surrounded by a dark ring, which presumably represents the inner segment. Numerous inner segments are visible in the patient, albeit at reduced frequency than normal. Cone and rod density was calculated at various locations and compared to that reported for normal cones in Dubin et al.10. On the right, rod density was consistent with normal values, though cone density was reduced by about 25% from normal. Rod density in the patient is consistent with normal densities. This result is consistent with the expected for the S-cone mosaic. Thus, the residual cone structure likely includes S-cones as well as some L-cones.