Notes from Dr. Irene Maumenee's presentation at the CRB1 research symposium March 23, 2013

Dr. Maumenee picked up with the mission statement: to outline the present level of knowledge and develop paths to treatment and prevention. She spoke about the confusing classification of retinal dystrophies. Clinicians describe diseases based on symptoms and natural history, whereas geneticists consider mutations. Mutations in the same gene can cause different retinal dystrophies, and, conversely, the same clinical entity can result from mutation in more than one gene (called genetic heterogeneity).

Historically, LCA has been considered an early-onset, severe form of retinitis pigmentosa, but the separation is arbitrary, Dr. Maumenee said. LCA affects 1-2 out of 100,000, accounting for 5% of inherited retinal dystrophies. It causes nystagmus, sluggish pupillary responses, and a markedly reduced ERG. Clinical diagnosis isn't reliable until 15 months of age. Dr. Maumenee said many children report the ocular-digital sign as comforting, but it can cause atrophy of fat behind the eyes, which can progress to growth of a cone-like structure on the cornea (keratoconus).

Sixteen LCA genes have been identified, but there may be as many as 30. The genes are involved in protein transport; photoreceptor development and maintenance, and polarity; protein folding; vitamin A cycling; Muller cell-photoreceptor interaction; neuroprotection; and cellular energetics. The percentage of cases due to different mutations varies in populations. In India and Saudi Arabia, only 30% of patients have mutations in known genes.

A strong founder effect (same mutations through inheritance through shared ancestors) is seen among LCA families in Puerto Rico. *CRB1* mutations (a 7 base pair deletion and a missense mutation) affect the inner segments of photoreceptors.

Dr. Maumenee suggested that some mutations may manifest in only a certain genetic background (the rest of the genome). Dr. Selzer added that populations probably include people with *CRB1* mutations who have normal vision, but they do not come to a practitioner's attention. This was a recurring theme in the meeting.