Genetic etiology and clinical consequences of complete and incomplete achromatopsia

Alberta AHJ Thiadens1,3, Susanne Roosing3, Niki WR Slingerland1, Mary J van Schooneveld5, Janneke JC van Lith-Verhoeven4, Norka van Moll-Ramirez6, L Ingeborgh van den Born7, Carel B Hoyng4, Frans PM Cremers3 & Caroline CW Klaver1,2

Introduction
Achromatopsia (ACHM) is a rare autosomal recessive cone dysfunction disorder, which can be divided into complete and incomplete ACHM subtypes. Patients with the complete subtype have no recordable cone function on electroretinogram (ERG), while those with incomplete ACHM retain some residual cone function on ERG, and presumably have a better clinical outcome.

Study Questions
1. What is the genetic cause of complete and incomplete ACHM?
2. Are disease-causing mutations associated with ACHM subtype and visual prognosis?

Subjects and Methods
All ophthalmologic clinical data of probands with complete ACHM (N=35) and incomplete ACHM (N=26) available during lifetime, were registered from medical charts and updated by ophthalmologic examination. Mutations in the CNGB3, CNGA3, and GNAT2 gene were analyzed by direct sequencing.

Conclusions
1. **CNGB3** is by far the most important causal gene, and p.T383IfsX13 the most frequent mutation
2. Genetic mutations did not predispose to either ACHM subtype
3. Deducing from our findings, the clinical distinction between complete and incomplete ACHM subtypes has no clinical value, and the assumption of a stationary nature is misleading