Genetic etiology and clinical consequences of complete and incomplete achromatopsia

Alberta AHJ Thiadens[1,3], Susanne Roosing[3], Niki WR Slingerland[1], Mary J van Schooneveld[5], Janneke JC van Lith-Verhoeven[4], Norka van Moll-Ramirez[6] L Ingeborgh van den Born[7], Carel B Hoyng[4], Frans PM Cremers[3] & Caroline CW Klaver[1,2]

Erasmus Medical Center, Rotterdam: 1. Dept of Ophthalmology, 2. Dept of Epidemiology & Biostatistics. Radboud University Nijmegen Medical Center: 3. Dept of Human Genetics, 4. Dept of Ophthalmology. 5. University Medical Center Utrecht, Dept of Ophthalmology. 6. Sensis, Center for care, education and services for visually impaired people, Grave. 7. The Rotterdam Eye Hospital, the Netherlands

Correspondence address: a.thiadens@erasmusmc.nl

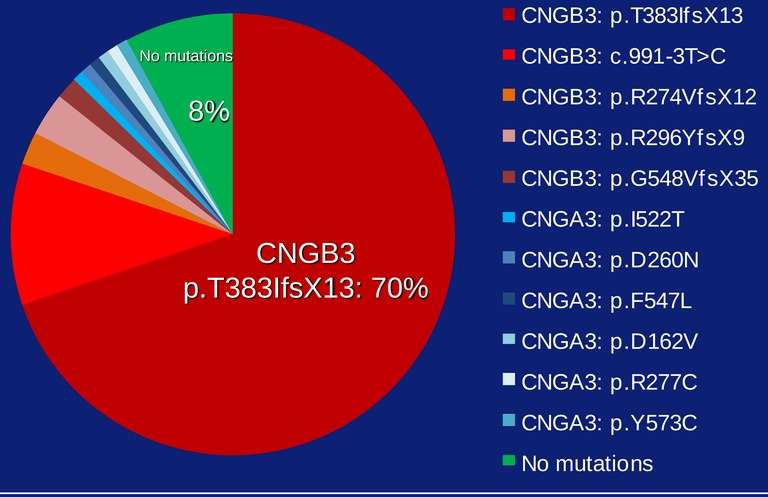
Introduction

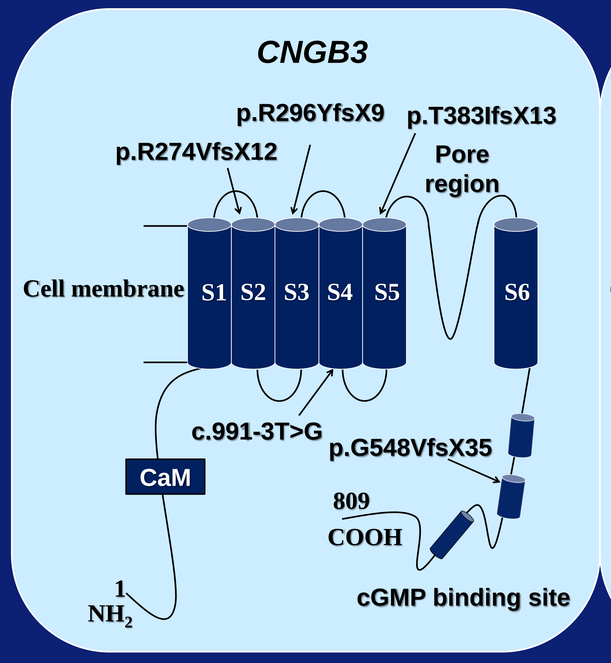
Achromatopsia (ACHM) is a rare autosomal recessive cone dysfunction disorder, which can be divided into complete and incomplete ACHM subtypes. Patients with the complete subtype have no recordable cone function on electroretinogram (ERG), while those with incomplete ACHM retain some residual cone function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

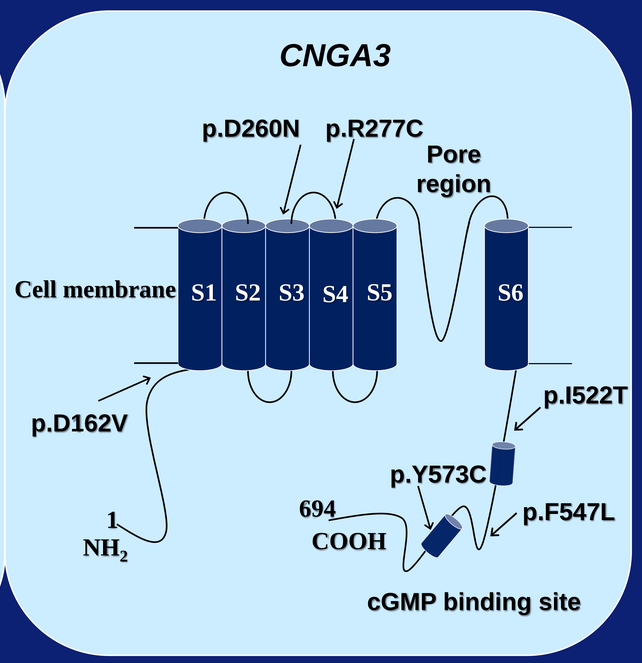
Study Questions

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

	Allele frequency		Color vision defects		Visual acuity childhood				Visual acuity adulthood			
Diagnosis	p.T383IfsX13	P value	Mild/ Medium	Severe	0.16-0.20	0.10	<0.10	P value	0.16-0.20	0.10	<0.10	P value
Complete ACHM (N=35)	74%	0.8	0	100%	29%	60%	11%	0.6	20%	57%	23%	0.5
Incomplete ACHM (N=26)	76%		4%	96%	31%	54%	15%		23%	46%	31%	







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**

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.