Novel CNGA3 and CNGB3 mutations in two Pakistani families with achromatopsia.

Abstract:
To identify the genetic defect in two Pakistani families with autosomal recessive achromatopsia. Two families (RP26 and RP44) were originally diagnosed with retinal dystrophy based upon their medical history. To localize the causative genes in these families, homozygosity mapping was performed using Affymetrix 10K single nucleotide polymorphism (SNP) arrays. Sequence analysis was used to find the mutations in candidate genes cyclic nucleotide-gated channel alpha-3 (CNGA3; family RP26) and cyclic nucleotide-gated channel beta-3 (CNGB3; family RP44). Control individuals were analyzed by allele-specific PCR for the CNGA3 mutation and BstXI restriction analysis for the CNGB3 mutation. After genetic analysis, clinical diagnosis was re-evaluated by electroretinography and color vision testing. During the course of this study, selected affected members of family RP26 were given pink glasses as supportive therapy. Sequence analysis of the positional candidate genes identified a novel missense mutation in CNGA3 (c.822G>T; p.R274S) in family RP26, and a novel CNGB3 frameshift mutation (c.1825delG; p.V609WfsX9) in family RP44. Clinical re-evaluation after genetic analysis revealed that both families have segregating autosomal recessive achromatopsia. Genetic analysis of two Pakistani families with retinal disease.
enabled the establishment of the correct diagnosis of achromatopsia. Two novel mutations were identified in CNGA3 and CNGB3 that are both specifically expressed in cone photoreceptors. Re-evaluation of the clinical status revealed that both families had achromatopsia. The use of pink glasses in patients was helpful in reducing photophobia and enabled rod-mediated vision.