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Titel des Beitrags: X-linked retinitis pigmentosa: RPGR mutations in most families with definite X linkage and clustering of mutations in a short sequence stretch of Exon ORF15

Abstract: PURPOSE. A comprehensive screening was conducted for RP2 and retinitis pigmentosa GTPase regulator (RPGR) gene mutations including RPGR exon ORF15 in 58 index patients. The frequency of RPGR mutations was assessed in families with definite X-linked recessive disease (xIRP), and a strategy for analyzing the highly repetitive mutational hot spot in exon ORF15 is provided. METHODS. Fifty-eight apparently unrelated index-patients were screened for mutations in all coding exons of the RP2 and the RPGR genes, including splice-sites, by single-strand conformation polymorphism (SSCP) analysis, except for RPGR exon ORF15. A strategy for directly sequencing the large repetitive stretch of exon ORF15 from a 1.6-kb PCR-product was developed. According to pedigree size and evidence for X linkage, families were subdivided into three categories. RESULTS. Screening of 58 xIRP families revealed RP2 mutations in 8% and RPGR mutations in 71% of families with definite X-linked recessive inheritance. Mutations clustered within a similarato500-bp stretch in exon ORF15. In-frame sequence alterations in exon ORF15 ranged from the deletion of 36 bp to the insertion of 75 bp. CONCLUSIONS. Mutations in the PPGR gene are estimated to cause 15% to 20% of all cases of RP, higher
than any other single RP locus. This report provides a detailed strategy to analyze the mutational hot spot in RPGR exon ORF15, which cannot be screened by standard procedures. The discrepancy of the proportion of families linked to the RP3 locus and those having RPGR mutations is resolved in a subset of families with definite X linkage.