Syndromic and non-syndromic forms of retinitis pigmentosa: a comprehensive Italian clinical and molecular study reveals new mutations

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ABSTRACT. Mutations in more than 60 different genes have been associated with non-syndromic and syndromic retinitis pigmentosa (RP), a heterogeneous group of inherited retinal dystrophies. To increase the understanding of the molecular epidemiology of the disease in Italy, we analyzed 56 patients with syndromic and non-syndromic forms of RP attending the Retinitis Pigmentosa Center of San Paolo Hospital (Milan, Italy). Patients underwent detailed clinical examination. Genomic DNA isolated from peripheral blood samples was screened for mutations in different genes according to RP form by direct sequencing analysis. The impact of novel missense mutations on protein functions was predicted by in silico analysis and protein sequence alignment. Cosegregation analysis was performed between available family members. Forty-one of the 56 probands analyzed had non-syndromic and 15 had syndromic RP forms. Putative disease-causing mutations were identified in 19 of 56 unrelated RP
probands. Mutation screening identified a total of 22 different heterozygous variants. Notably, 12 of these putative pathogenic mutations have not been previously reported. New variants were found to be located on the USH2A, RPGR, EYS, and RHO genes. All 3 new variants detected in X-linked RP probands were confirmed in other affected family members. We found a positivity rate of 24.4% and 60% for probands with non-syndromic and syndromic RP, respectively. This is the first report of RPGR X-linked RP proband-ORF15 mutations in Italian patients with X-linked (XL)-RP. In addition, this is the first report of data regarding the association between EYS mutations and non-syndromic RP forms in the Italian population.

Key words: Bardet-Biedl syndrome; Molecular screening; Retinitis pigmentosa; Usher syndrome