Retinitis pigmentosa (RP) is a heterogeneous group of inherited retinal disorders characterized by progressive night blindness, and loss of visual fields, ultimately leading to complete blindness. To date, few studies have offered explanations for the wide range in clinical variability that may be observed even within the same family carrying the same mutation. The purpose of this study is to assemble and analyze data relating to the degree of affectation in patients with RP to determine whether protein variation in trans to the disease locus is associated with clinical severity. The specific disorder is a form of autosomal dominant RP (adRP) caused by an Arg677stop mutation in the RP1 gene, found in an adRP family with over 100 living, affected family members. All of the data, including ophthalmologic records, fundus photographs, patient self-report questionnaires, and genetic data for the study were previously collected as part of an ongoing study. We developed three forms of severities (age-, fundus-dependent, and a combination of the two) and assigned scores. A total of 35 individuals were ascertained.

No statistically significant effect was observed on the course of adRP disease severity by gender alone or parent of origin. Age at diagnosis was significantly associated with fundus-dependent severity, with combined severities alone and with respect to gender; suggestive for age-dependent severity by itself; and significant for age-dependent severity when evaluated by gender. Age at loss of peripheral vision (LOPV) demonstrated significance for fundus-severity and combined severity, and was suggestive for age-dependent severity. Furthermore, age at night blindness (NB) was suggestive for age-dependent severity only.

In terms of genetic modifying factors, males with allele 3 were diagnosed with RP at a younger age compared to females with the same allele, as well as individuals with different alleles. In terms of biologic validity, several amino acid sequences are highly conserved throughout mammalian species and haplotype sequences 1 and 3 are significantly different from...
each other y computational analysis. Based on these findings, appropriate counseling for males with allele 3 is suggested to address both clinical management and psychosocial issues relating to earlier disease onset.