

Trinucleotide Repeat Expansions in the *junctophilin-3* Gene Are Not Found in Caucasian Patients with a Huntington's Disease-like Phenotype

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Huntington's disease (HD) is characterized by movement abnormalities and psychiatric symptoms and is caused by a CAG repeat expansion in the *IT15* gene encoding huntingtin.¹ Recently, a family of African American ethnicity was reported with HD-like (HDL) features mapping to chromosome 16q23, designated HDL-2.² Subsequently, a CAG/CTG repeat expansion in the *junctophilin-3* gene was identified in this family and shown to cosegregate with the disease in 10 affected individuals.³ Additional patients of African origin were identified as carrying a repeat expansion in the *junctophilin-3* gene.

To investigate whether a CAG/CTG repeat expansion in the *junctophilin-3* gene may underlie the HDL features in Caucasian patients, we analyzed the CAG/CTG repeat in a group of 1,600 patients who were referred to DNA laboratories in Germany and Austria.⁴ All patients have been referred by neurologists. None of the patients carried a CAG repeat expansion of more than 37 units in the *IT15* gene, thus excluding HD as the genetic cause of the symptoms. A total of 147 patients are known to have a family history of choreatic symptoms. For approximately 50% of the remaining patients, there was no history of movement disorders within the family. Repeat sizes of 10 to 27 units were found in our patients (Fig). The allele frequencies showed a bimodal distribution with peak values at 14 and 16 repeats. None of the patients had an expanded allele in the *junctophilin-3* gene. As nearly all German centers for quality assessment of HD analysis have participated in this study, it is unlikely that a CAG/CTG repeat expansion in the *junctophilin-3* gene plays a major role among Caucasians. In this respect, it is interesting to note that HDL-2-positive patients reported so far are of African origin.³ It

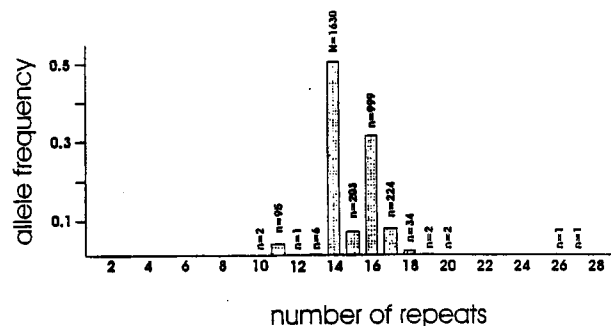


Fig. Allele frequency of the CAG/CTG repeat in the *junctophilin-3* gene in 1,600 patients of Caucasian origin with Huntington's disease-like symptoms.

will therefore be important to estimate the frequency of CAG/CTG repeat expansions in HDL-2 in Africans and to consider HDL-2 in choreatic patients of African origin for which CAG repeat expansions in the *IT15* gene have been excluded.

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