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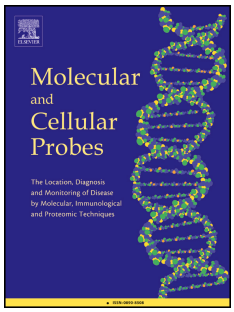

The search for modifier genes in Huntington disease - multifactorial aspects of a monogenic disorder

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The search for modifier genes in Huntington disease - multifactorial aspects of a monogenic disorder

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Abstract

It is becoming increasingly evident that the underlying mutation of a single locus is often insufficient for the prediction of the comprehensive phenotype in human Mendelian disorders, implicating that there is no clear distinction between monogenic and complex traits. By definition, monogenic traits show a classic pattern of inheritance and are strongly influenced by variation within a single gene. However, many Mendelian traits that result in genetic disorders can have phenotypes that differ in subtle or profound ways such as severity, onset age and other associated phenotypic characteristics. Among the factors that may explain these differences in disease expression are modifier genes. This review focuses on the role of modifier genes using the example of Huntington Disease (HD), an autosomal dominantly transmitted, progressive neurodegenerative disorder. The advantages and limitations of candidate gene approaches versus genome-wide association studies (GWAS) as well as its implications for diagnostic, prognostic, and therapeutic interventions are discussed.

Keywords

Huntington disease; modifier genes; candidate genes; genome-wide association studies; phenotype