Identification of Three Mutations in the Cu, Zn-Superoxide Dismutase(Cu,Zn-SOD) Gene with Familial Amyotrophic Lateral Sclerosis

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摘要.

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder affecting motor neurons. Although most cases of ALS are sporadic, approximately 10% are inherited as an autosomal dominant trait. Mutations in the Cu/Zn superoxide dismutase gene (SOD 1) are responsible for a fraction of familial ALS (FALS). Screening our FALS kindreds by SSCP, we have identified mutations in 15 families, of which 9 have not been previously reported. Two of the new mutations alter amino acids that have never been implicated in FALS. One of them affects a highly conserved amino acid involved in dimer contact, and the other one affects the active-site loop of the enzyme. These two mutations reduce significantly SOD 1 enzyme activity in lymphoblasts. Our results suggest that SOD 1 mutations are responsible for > or = 13% of FALS cases

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