

Publication

A novel SOD1 splice site mutation associated with familial ALS revealed by SOD activity analysis

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**ID** 1196238**Author(s)** Birve, Anna; Neuwirth, Christoph; Weber, Markus; Marklund, Stefan L; Nilsson, Ann-Charloth; Jonsson, Per Andreas; Andersen, Peter M**Author(s) at UniBasel** [Weber, Markus](#) ;**Year** 2010**Title** A novel SOD1 splice site mutation associated with familial ALS revealed by SOD activity analysis**Journal** Human molecular genetics**Volume** 19**Number** 21**Pages / Article-Number** 4201-6

More than 145 mutations have been found in the gene CuZn-Superoxide dismutase (SOD1) in patients with amyotrophic lateral sclerosis (ALS). The vast majority are easily detected nucleotide mutations in the coding region. In a patient from a Swiss ALS family with half-normal erythrocyte SOD1 activity, exon flanking sequence analysis revealed a novel thymine to guanine mutation 7 bp upstream of exon 4 (c.240-7T). The results of splicing algorithm analyses were ambiguous, but five out of seven analysis tools suggested a potential novel splice site that would add six new base pairs to the mRNA. If translated, this mRNA would insert Ser and Ile between Glu78 and Arg79 in the SOD1 protein. In fibroblasts from the patient, the predicted mutant transcript and the mutant protein were both highly expressed, and despite the location of the insertion into the metal ion-binding loop IV, the SOD1 activity appeared high. In erythrocytes, which lack protein synthesis and are old compared with cultured fibroblasts, both SOD1 protein and enzymic activity was 50% of controls. Thus, the usage of the novel splice site is near 100%, and the mutant SOD1 shows the reduced stability typical of ALS-associated mutant SOD1s. The findings suggests that this novel intronic mutation is causing the disease and highlights the importance of wide exon-flanking sequencing and transcript analysis combined with erythrocyte SOD1 activity analysis in comprehensive search for SOD1 mutations in ALS. We find that there are potentially more SOD1 mutations than previously reported.

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