



Session P10 - Neuromuscular disorders

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P10.01A / A - Whole exome sequencing of patients with amyotrophic lateral sclerosis

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Poster Area

Authors

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Disclosures

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Abstract

Introduction: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease. Genetic factors play a key role in ALS and uncovering its genetic background may bring us closer to fully understand its pathomechanism, therefore the aim was to identify rare damaging variants in major and minor genes involved in pathways annotated to ALS.

Patients and methods: The investigated sporadic patients fulfilled the revised El Escorial criteria for ALS. Whole exome sequencing of 21 Hungarian patients affected by ALS was carried out. The patients were prescreened for *C9ORF72* repeat expansion, *SOD1*, *ANG*, *FUS*, *SETX*, *TARDBP* and *UBQLN2* genes. Exome sequencing was performed using Illumina NextSeq sequencer and data analysis was performed according to the best practices to identify single nucleotide variants and small insertions/deletions. The detected variants were confirmed by Sanger sequencing.

Results: Exome sequencing revealed a novel non-synonymous variant (T338I) in *NEFH* gene that encodes neurofilament heavy polypeptide; a previously described nonsense mutation (G1177X) in the alsin (*ALS2*) gene that leads to premature stop codon and may affect endosomal and vesicle transport; and finally a recurrent variant (R261H) in the *NEK1* gene, encoding NIMA related kinase-1, that has recently been associated with ALS in the Caucasian population.

Conclusion: Disease causing variants have been detected in approximately 28% (3/21) of this sporadic cohort. Our study contributed to the better understanding of the genetic background of the disorder and indicated that complex approaches are needed to understand the genetic heterogeneity of this disease.

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