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PRESS RELEASE

The new gene responsible for more than one third of familial ALS cases identified

A new gene, responsible for the familial and sporadic forms of Amyotrophic Lateral Sclerosis (ALS), has been identified. Over the last 10 years, researchers from all over the world have tried to identify the gene that they knew was located on chromosome 9. The study was accepted and published today, just after two weeks from this finding, on 'Neuron', the most important and authoritative international scientific journal in the field of neurology. The following institutions participated in the research study: Laboratory of Neurogenetics, National Institutes of Health (Bethesda, USA, headed by Dr. Bryan J. Traynor); ALS Centre, Department of Neuroscience of the Molinette Hospital of Turin (headed by Professor Adriano Chiò); Molecular Genetics Unit, OIRM Sant'Anna Hospital of Turin (headed by Dr. Gabriella Restagno); ALS Centre, Università Cattolica del Sacro Cuore university (headed by Professor Mario Sabatelli); and ALS Centre, University of Cagliari (headed by Dr. Giuseppe Borghero).

In the collaborative study 268 US, German and Italian familial ALS cases were analysed along with 402 Finnish familial and sporadic ALS cases. The study showed that 38% of familial cases and 20% of sporadic cases carried an alteration of the gene called *c9orf72*. The identified alteration consists in a hexanucleotide (GGGGCC) expansion in the first intron of the gene. The frequency of ALS patients carrying such mutation is double compared to that of the SOD1 gene, the first ALS gene identified in 1993.

The mechanism through which the *c9orf72* causes ALS is yet to be clarified. The c9orf72 protein is usually located within the nucleus, whereas, in the mutation, it is mainly localised in cytoplasm. This means that an alteration in the protein localization may be at the basis of its malfunctioning. In addition, the hexanucleotide expansion alters the DNA transcription by taking away normal proteins and RNAs involved in the regulation of the same transcription.

This finding represents a step forward in identifying the causes of ALS and its treatment, in particular since it gives an explanation of the causes of ALS in a high percentage of familial and sporadic cases.

The contribution of the Italian Amyotrophic Lateral Sclerosis Genetic (ITALSGEN) Consortium was pivotal for the success of the study. The Consortium brings together 14 university and hospital departments to fight against ALS. The study was funded by the Italian Football Federation (FIGC), the Vialli and Mauro Foundation for Research and Sport and the Ministry of Health (targeted research).

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