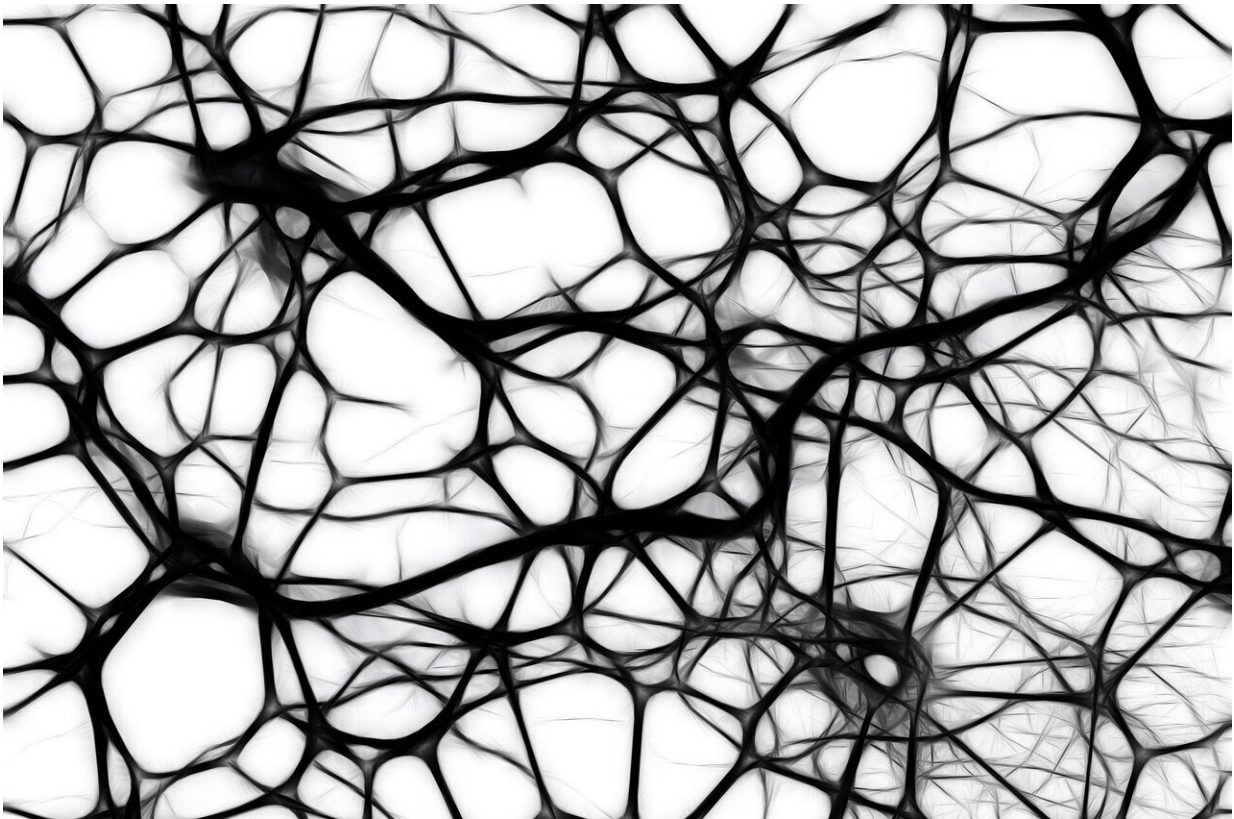


New molecular structures associated with ALS

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Researchers from the University of Seville and the University of Pavia have identified a link between Amyotrophic Lateral Sclerosis (ALS) and the accumulation of DNA-RNA hybrids in the genome. The

accumulation of these hybrids causes increased genomic damage and boosts genetic instability. This finding will make it possible to better understand the molecular basis of the disease, as well as to propose new solutions to curb it.

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease of the central nervous system, characterized by progressive degeneration of motor neurons leading to muscle paralysis. Classified as a [rare disease](#), there is no cure despite efforts to understand the disease's molecular basis and research devoted to identifying therapies that can at least slow its evolution.

At the CABIMER center, the group from the University of Seville led by Professor Andrés Aguilera, in collaboration with the group led by Dr. Cristina Cereda from the Mondino Foundation at the University of Pavia, have identified a link between this disease and the accumulation of DNA-RNA hybrids in the genome. The researchers have observed that patient-derived mutations in TDP-43, a protein of the RNA metabolism whose deficiency is associated with ALS, result in the accumulation of these hybrids in both neuronal and non-[neuronal cells](#), thereby causing increased genomic damage and genetic instability.

This discovery has led to a new perception of the disease's molecular basis related to the role of the TDP-43 protein in the cellular cytoplasm. The mutations analyzed cause a TDP-43 deficiency in the [cell nucleus](#), thus leading to the accumulation of these aberrant structures in the DNA. This research opens up new avenues of exploration to understand the disease's [molecular basis](#), as well as new approaches to try to slow its evolution.

More information: Marta Giannini et al. TDP-43 mutations link Amyotrophic Lateral Sclerosis with R-loop homeostasis and R loop-mediated DNA damage, *PLOS Genetics* (2020). [DOI:](#)

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