

# Research uncovers new insights on ALS and points to a potentially promising treatment strategy

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New research provides a better understanding of the mechanisms behind the development of amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, and points to a potential treatment strategy. The work was led by investigators at the Healey Center for ALS at Massachusetts General Hospital (MGH) and is published in *Molecular Neurobiology*.

ALS, a degenerative condition without a cure, attacks brain and spinal cord nerve cells to progressively affect individuals' ability to move, speak, eat, and even breathe. Previous studies have implicated dysfunction within mitochondria, which generate energy within cells, as playing an important role in the development of ALS. Also, studies in Alzheimer's disease have linked changes in mitochondrial function to interactions between an abnormal form of tau, which accumulates in the brains of patients with Alzheimer's disease, and a mitochondrial protein called dynamin-related protein 1 (DRP1). Piecing these bits of information together, Ghazaleh Sadri-Vakili, Ph.D., director of the NeuroEpigenetics Laboratory at the MassGeneral Institute for Neurodegenerative Disease and the Healey Center for ALS at MGH, and her colleagues examined whether interactions between this abnormal tau with DRP1 might also promote mitochondrial dysfunction in ALS, and whether reducing tau could be a novel and promising therapeutic approach to fight the disease.

The team found that in brain tissue from deceased patients who had ALS, the abnormal form of tau is present, is located where tau is not normally found, and interacts with DRP1. When cells were grown in contact with deceased ALS patients' [brain tissue](#) that contained abnormal tau, the cells' mitochondria fragmented and oxidative stress increased. Importantly, reducing tau with a specific degrader reversed these effects, reducing mitochondrial fragmentation and lowering oxidative stress.

"We demonstrated for the first time that targeting tau with a new class of small molecules that selectively degrade it can reverse the ALS-induced

changes in mitochondria's shape and function, highlighting tau as a potential therapeutic target," says Sadri-Vakili.

**More information:** Tiziana Petrozziello et al, Targeting Tau Mitigates Mitochondrial Fragmentation and Oxidative Stress in Amyotrophic Lateral Sclerosis, *Molecular Neurobiology* (2021). [DOI: 10.1007/s12035-021-02557-w](https://doi.org/10.1007/s12035-021-02557-w)

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