NATIONAL PRESS ALERT – PARIS – 02 FEBRUARY 2026

UNDER EMBARGO **UNTIL 05 FEBRUARY 2026, 8 PM, PARIS TIME**

Discovery of a key mechanism to halt the most common genetic form of ALS

A specific molecular mechanism has been identified as the cause of the most frequent genetic forms of amyotrophic lateral sclerosis (ALS, also known as Charcot's disease) and frontotemporal dementia (FTD). By neutralising the genetic abnormality shared by these two neurodegenerative disorders, a research team from the CNRS[1], in collaboration with scientists from Harvard University, has succeeded in preventing the premature degeneration of neurons, and motoneurons in several cellular and animal experimental models. The results will be published in *Science* on 05 February 2026.

In nearly half of familial cases of ALS and FTD, the same abnormality affects the C9ORF72 gene. This gene contains repetitive sequences located within an intron, a segment normally removed before protein synthesis. In patients with ALS or FTD, this elimination process is defective: the intron persists and is inappropriately translated, leading to the production of abnormal and toxic proteins that accumulate in neurons and motoneurons and drive their rapid degeneration.

The scientists precisely identified the starting point of this aberrant translation: a codon[2] recognised by the ribosome[3] as an atypical start signal. Targeted modification of this unique signal through the introduction of a single mutation is sufficient to completely abolishes the synthesis of the toxic proteins responsible for neuronal degeneration. This approach, validated in mouse models and in human ALS patient-derived motoneurons following CRISPR-Cas9–mediated genome editing, prevents disease development in mice and rescues the cellular lifespan to levels comparable with healthy cells. These findings pave the way for the development of new therapeutic strategies directly targeting the underlying cause of these disorders.

Notes

1. Working at the CNRS laboratory Architecture et réactivité de l'ARN.
2. Short sequence of three "letters" of the genetic code that instructs the cell when to start, continue, or stop protein synthesis.
3. Small cellular "machine" that reads genetic instructions and use them to assemble proteins, which are essential for cell survival.

Bibliography

Blocking RAN translation without altering repeat RNAs rescues *C9ORF72*-related ALS/FTD phenotypes. Xin JIANG and al., Franck MARTIN and Clotilde LAGIER-TOURENNE, *Science*, 05 February 2026

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