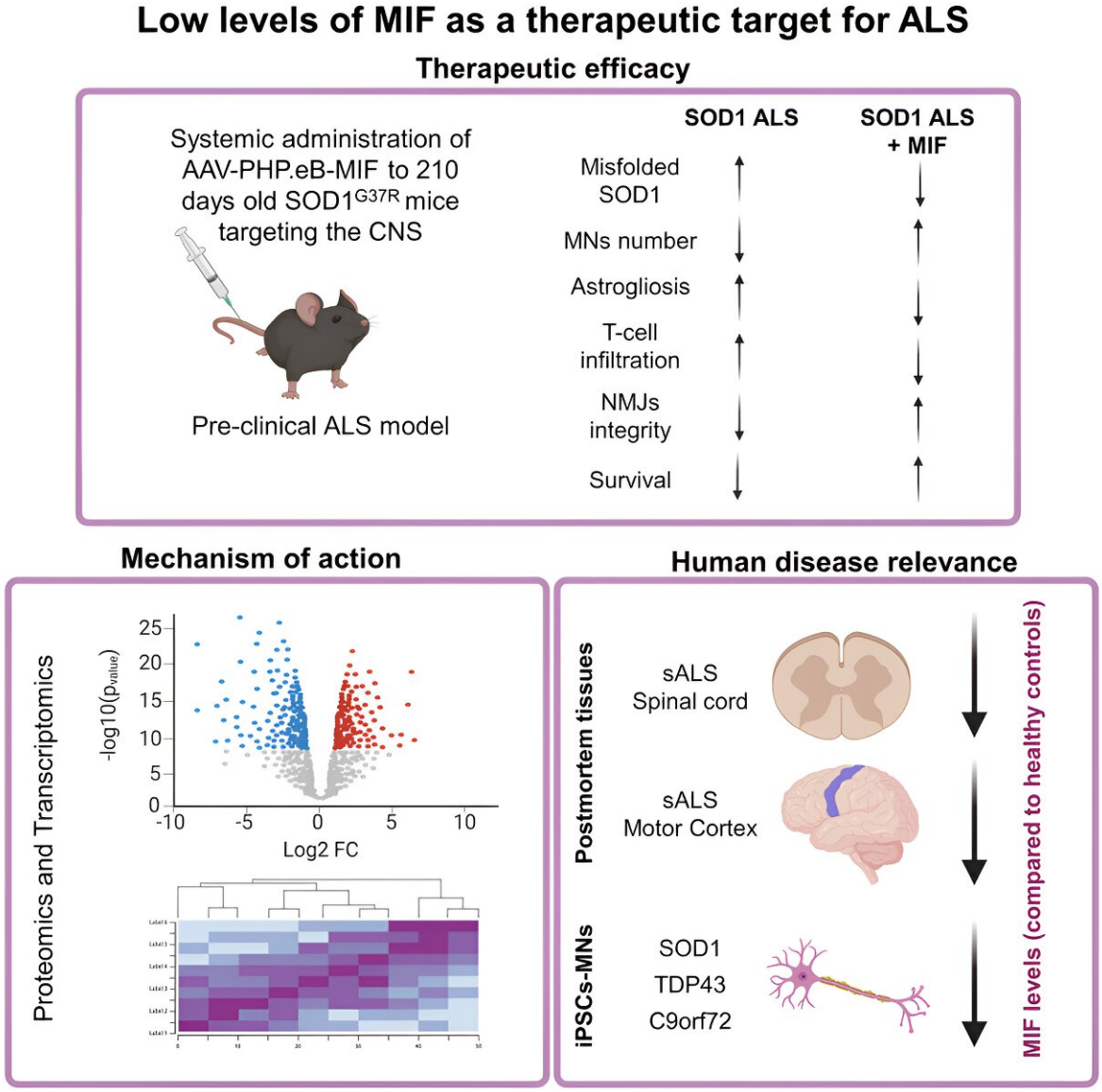
# Researchers discover therapeutic potential of increasing MIF protein levels to treat amyotrophic lateral sclerosis

May 29 2024




Graphical abstract. Credit: *Cell Reports Medicine* (2024). DOI: 10.1016/j.xcrm.2024.101546

A recent collaborative research endeavor, published in *Cell Reports Medicine*, highlights a promising therapeutic avenue for amyotrophic lateral sclerosis (ALS). Led by researchers from Ben-Gurion University

of the Negev in conjunction with counterparts from Germany, the U.S., and Canada, the study delves into the potential of augmenting macrophage migration inhibitory factor (MIF) protein levels as a novel approach to tackling ALS.

ALS, often referred to as Lou Gehrig's disease, is a devastating neurodegenerative condition characterized by the progressive loss of motor neurons, leading to muscle weakness, paralysis, and ultimately respiratory failure. While the etiology remains elusive in the majority of cases, a subset of about 10% is attributed to genetic factors. Typically striking individuals aged 40 to 60, ALS carries a grim prognosis with a median survival of two to five years post-diagnosis.

Approximately 20% of genetic ALS cases stem from mutations in the superoxide dismutase (SOD1) gene. Extensive research has elucidated that these mutations, numbering over 180 variants, induce motor neuron degeneration through some form of toxicity. Yet, the precise mechanisms driving this selective toxicity remain unresolved.

A few years ago, Israelson and colleagues identified the multifunctional protein MIF to directly inhibit mutant SOD1 misfolding and binding to intracellular organelles. Elevated expression of MIF was shown to suppress accumulation of misfolded SOD1 and extend survival of mutant SOD1-expressing motor neurons.

Recently, a study led by Dr. Leenor Alfahel at Professor Adrian Israelson's laboratory at BGU, in collaboration with Professor Susanne Petri's team at Hannover Medical School, Germany, and other international collaborators, demonstrated the efficacy of exogenous MIF administration via viral vectors in a SOD1 mouse model of ALS. This intervention effectively delays motor function decline, modulates critical

pathways, and extends lifespan.

Moreover, the study identifies diminished MIF levels in motor neurons derived from familial ALS patients with various genetic backgrounds, as well as in the motor cortex and spinal cord of sporadic ALS cases, suggesting broader implications beyond SOD1-linked pathology.

These collaborative efforts underscore MIF's potential as a therapeutic candidate for ALS, opening up new possibilities for treatment. However, comprehensive investigations are warranted to fully elucidate the underlying mechanisms of MIF's efficacy and its translational implications.

**More information:** Leenor Alfahel et al, Targeting low levels of MIF expression as a potential therapeutic strategy for ALS, *Cell Reports Medicine* (2024). DOI: 10.1016/j.xcrm.2024.101546

Provided by Ben-Gurion University of the Negev