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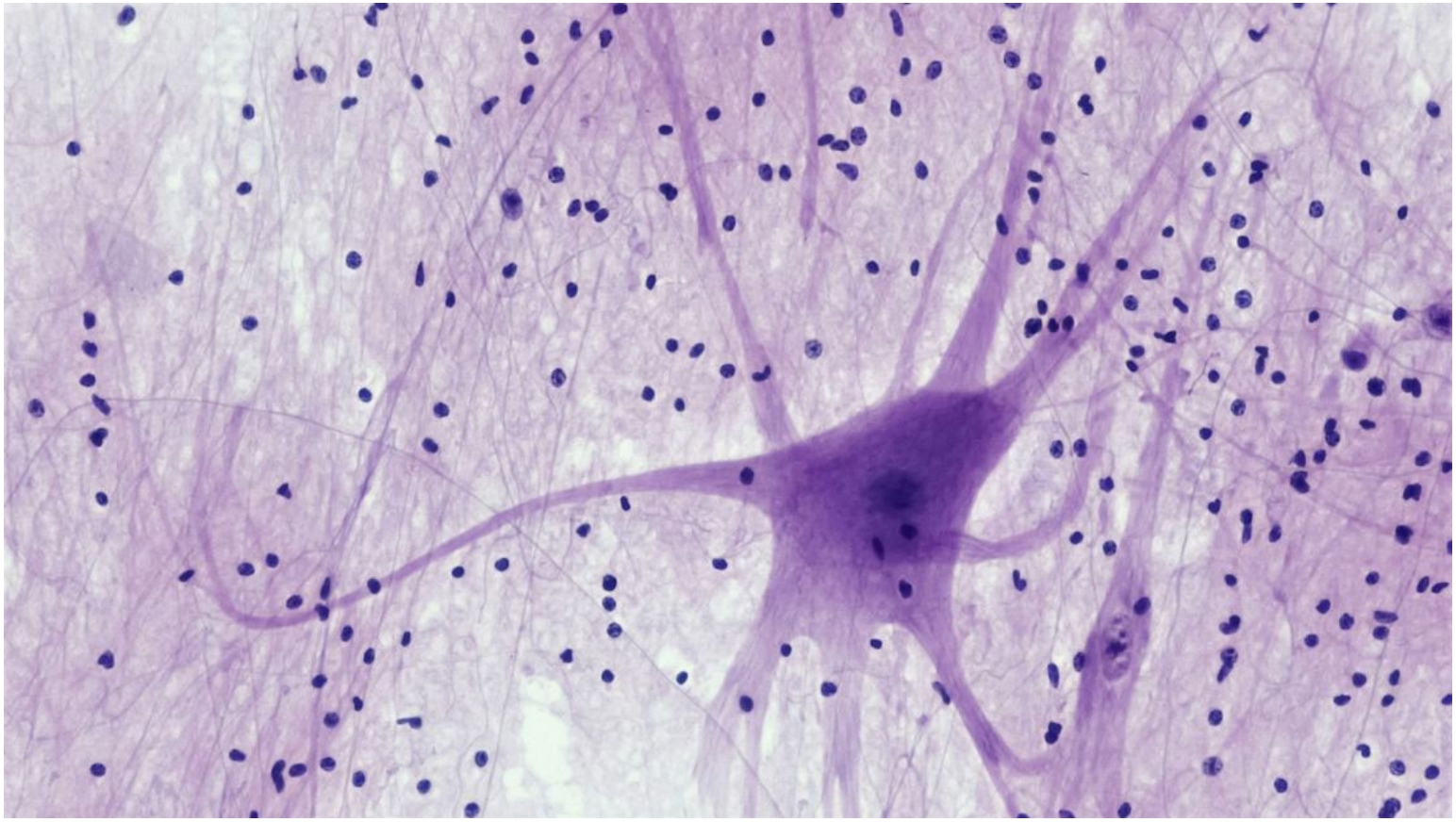
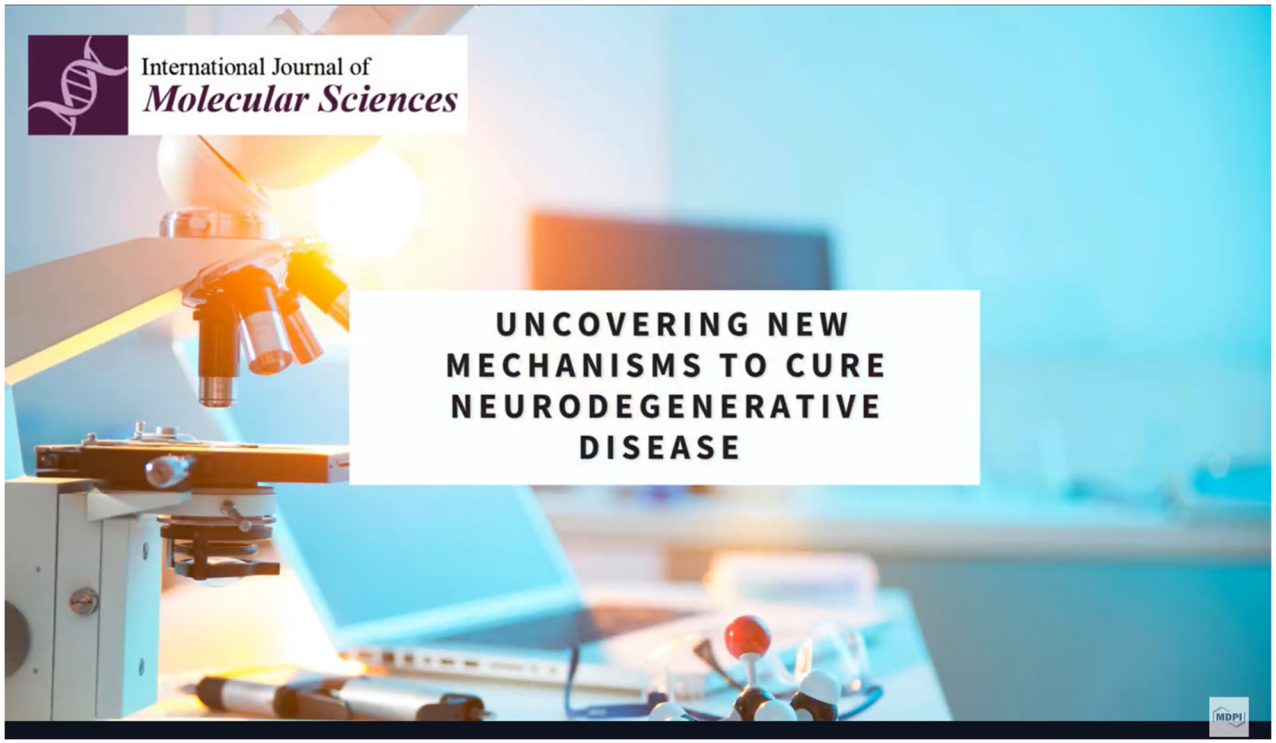


Uncovering New Mechanisms to Cure Neurodegenerative Disease

An Open Access study published in the *International Journal of Molecular Sciences*, presents new mechanisms contributing to neurodegeneration, a key component of Alzheimer's, Parkinson's and other neurodegenerative diseases.

The study finds a possible cause for the reduction of 4E-BP2, a critical protein in the brain which, when absent, causes memory impairment and contributes to the development of neurodegenerative disease.

This important research is vital to seeking a cure for debilitating neurodegenerative diseases affecting millions worldwide.



The impact of neurodegenerative disease

Neurodegenerative disease (ND) is an umbrella term that includes conditions such as Alzheimer's Disease (AD), Parkinson's Disease, and multiple sclerosis. They are caused by damage to the nervous system, and are usually ageing diseases; however, they may also occur earlier on in life in rare cases.

The impact of ND is debilitating. For example, AD is a dementia-type disease, causing a range of symptoms such as significant memory impairment, changes in mood and behaviour, and can be immensely challenging for both the afflicted and their loved ones. Parkinson's Disease is a neurodegenerative disease that affects the brain's ability to regulate and control muscle movements. This results in symptoms such as constant tremor, balance issues and slowing down of movements. Parkinson's disease also causes non-motor symptoms such as memory issues, mental health issues, and pain. Research to understand how ND manifests is important for the development of efficient treatment, and eventually a cure.

The aforementioned study looks at the critical 4E-BP2 protein, which plays an important role in memory retention.

The role of the 4E-BP2 protein in neurodegenerative disease

As mentioned, ND is categorised by the destruction of the nervous system. This occurs through numerous ways, primarily the imbalance of proteins in nerve cells that leads to damage to the cells.

4E-BP2 is a protein found in cells, including nerve cells. Normally, 4E-BP2 binds to another regulatory protein called eIF4E, forming a complex that prevents further protein synthesis.

Previous research found that 4E-BP2 undergoes deamidation exclusively in neurons – the process by which the amino acid of the protein is changed from asparagine to aspartic acid, hence, the protein's shape changes. Once deamidation occurs, 4E-BP2 binds to another protein instead of eIF4E, significantly shifting the course of protein translation and communication between neurons.

It was found that this mechanism of deamidation was related to protein recycling due to damage from oxidative stress in the cells. Since the discovery of these findings, the deamidation of 4E-BP2 has been established as playing a critical role in protein synthesis in the brain. Importantly, its dysregulation is linked to the development of neurodegenerative disease.

The research conducted by Davis Joseph set out to confirm how 4E-BP2 deamidation exclusively takes place in neural cells, and why this may be the case.

The axonal environment accelerates 4E-BP2 deamidation

The author of the study, Dr. Davis Joseph, found that excessive 4E-BP2 takes place in axons (the long part of the nerve cell away from the cell body), due to their 'proteasome-poor environment'.

Proteasomes are cellular structures dedicated to degrading damaged or unwanted proteins. The author carried out western blots from retinal ganglia, optic nerve, dorsal root ganglia, the sciatic nerve and the whole brain from mice. The results confirmed that deamidation of 4E-BP2 occurs in the axons and at a significantly higher rate in myelinated axons of the whole brain.

"This experimentally validated discovery of the link between 4E-BP2 deamidation and axons is of seminal importance because it explains what causes a post-translational modification in the brain of all mammalian species, which has been conserved for over 90 million years. It paves the way to developing effective treatments against neurodegenerative diseases, such as Alzheimer's, Parkinson's, and many others." – The Fundamental Neurobiological Mechanism of Oxidative Stress-Related 4E-BP2 Protein Deamidation,

These novel findings are important to address another possible cause of neurodegeneration, and to work towards establishing better treatment and a cure for all neurodegenerative diseases.

Read more about this research by accessing the journal *IJMS*, or access a full list of Open Access journals here.