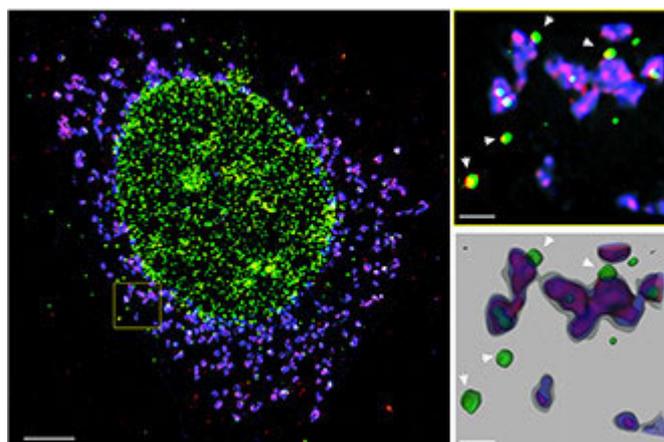


Blocking inflammation in motor neurone disease

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Melbourne researchers have uncovered how inflammation in motor neurone disease (MND) is triggered — a breakthrough that serves as a potential first step towards a new treatment for the disease.

By blocking an immune sensor called STING, the team could dramatically prevent inflammation in MND patient cells, paving the way for a new class of drugs to be developed for people with neurodegenerative disorders. Their discovery has been published in the journal [Cell](#).

MND is an incurable condition in which the nerve cells controlling the muscles that enable us to move, speak, swallow and breathe fail to work. One in 10,000 Australians will be diagnosed with MND in their lifetime and the average life expectancy from diagnosis is just two years.

Most people suffering from MND have an accumulation of a protein called TDP-43 within cells of the central nervous system. This build-up is associated with an inflammatory response that precedes the major symptoms of MND.

Researchers from the [Walter and Eliza Hall Institute of Medical Research](#) (WEHI), working with colleagues from [The University of Melbourne](#) and the [Hudson Institute of Medical Research](#), set out to investigate how the disease-causing inflammation is triggered in MND. According to WEHI's Associate Professor Seth Masters, "This unexpectedly identified that an immune sensor called STING is activated downstream of TDP-43. Fortuitously, our team had already studied the role of STING in other inflammatory diseases and are now working out how to block it."

The team then used new inhibitors — drug-like compounds — to block different components of this inflammatory pathway. Assoc Prof Masters explained, "Using cells from patients with MND that we can turn into motor neurons in a

dish, we showed that blocking STING dramatically prevented inflammation and kept the cells alive longer. This is an exciting first step before taking these inhibitors into the clinic for treatment for MND.”

Assoc Prof Masters said the research had also established activation of STING in people who had passed away due to MND, stating, “We are now aiming to validate a biomarker of the pathway earlier in the disease progression. Once this neuroinflammatory biomarker is validated, we will better understand which patients will benefit the most from treatments targeting the pathway.

“With this knowledge, there is the potential to develop a treatment for patients with MND.

“Interestingly, our preclinical models suggest that although the anti-inflammatory drugs that inhibit STING did not prevent disease onset, they did slow the degenerative progression of disease.”

The discovery thus offers hope for people diagnosed with what is otherwise a debilitating condition. Assoc Prof Masters said, “We are hopeful this research could lead to a treatment for people with established MND, who currently have very few treatment options and a life expectancy post diagnosis of just two to five years.

“While it isn’t a cure, we hope it might extend life expectancy and dramatically improve the quality of life for people diagnosed with MND.”

A future treatment might also be effective in slowing the progression of other neurodegenerative disorders. Assoc Prof Masters concluded, “We are hoping to develop a new class of drugs that would act as STING inhibitors to stop the progression of neurodegenerative disorders, such as MND, frontotemporal dementia and Parkinson’s disease.”

Image caption: Almost all patients with MND have evidence of TDP-43 (red) being in the wrong place inside motor neuron cells. Mitochondria (blue) provide power to motor neurons, but if invaded by TDP-43, they leak out their DNA (green), which triggers a virus sensor called STING. Drugs targeting STING prevent inflammation and keep MND patient motor neurons alive longer in laboratory tests.

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