New anti-inflammatory molecule could halt MS progression

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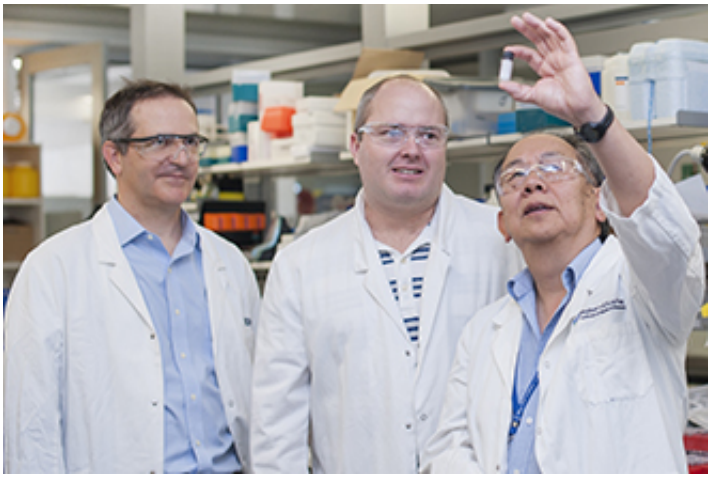

Associate Professor Guillaume Lessene, Dr Ueli Nachbur, Professor Andrew Lew (L-R) and colleagues developed a new drug-like molecule that prevents inflammation and could lead to a new treatment for MS. Credit: Walter and Eliza Hall Institute

Walter and Eliza Hall Institute scientists have developed a new drug-like molecule that can halt inflammation and has shown promise in preventing the progression of multiple sclerosis (MS).

Dr Ueli Nachbur, Associate Professor John Silke, Associate Professor Guillaume Lessene, Professor Andrew Lew and colleagues developed the molecule inhibit a key signal that triggers inflammation.

Multiple sclerosis is an inflammatory disease that damages the central nervous system including the brain, spinal cord and optic nerves. There is no cure and there is a desperate need for new and better treatments.

Inflammatory diseases such as MS were triggered by an over-active immune system, Dr Nachbur said. "Inflammation results when our immune cells release hormones called cytokines, which is a normal response to disease," he said. "However when too many cytokines are produced, inflammation can get out-of-control and damage our own body, all of which are hallmarks of immune or inflammatory diseases."

To apply the brakes on this runaway immune response, institute researchers developed a small drug-like molecule called WEHI-345 that binds to and inhibits a key immune signalling protein called RIPK2. This prevents the release of inflammatory cytokines.

Professor Lew said they examined WEHI-345's potential to treat immune diseases in experimental models of MS.

"We treated preclinical models with WEHI-345 after symptoms of MS first appeared, and found it could prevent further progression of the disease in 50 per cent of cases," he said. "These results are extremely important, as there are currently no good preventive treatments for MS."

Associate Professor Lessene, who developed the molecule with colleagues in the institute's ACRF Chemical Biology division, said WEHI-345 had potential as an anti-inflammatory agent."This molecule will be a great starting point for a drug-discovery program that may one day lead to new treatments for MS and other inflammatory diseases," Associate Professor Lessene said.

Dr Nachbur said institute scientists would use WEHI-345 to further investigate the signalling pathway that produced inflammatory cytokines

and to develop a better, stronger inhibitor of RIPK2 for treating inflammatory disease. "This signalling pathway must be finely balanced, because WEHI-345 only delayed signalling rather than blocked it. Nevertheless, this delay is enough to completely shut off cytokine production," he said.

"Not only is this a potential new treatment, it is a great tool we can use to unravel this signalling pathway and identify other important proteins that control inflammation that could be a drug target."

The research was published today in the journal *Nature Communications*.

Provided by Walter and Eliza Hall Institute