Cooling 'brains on fire' to treat Parkinson's

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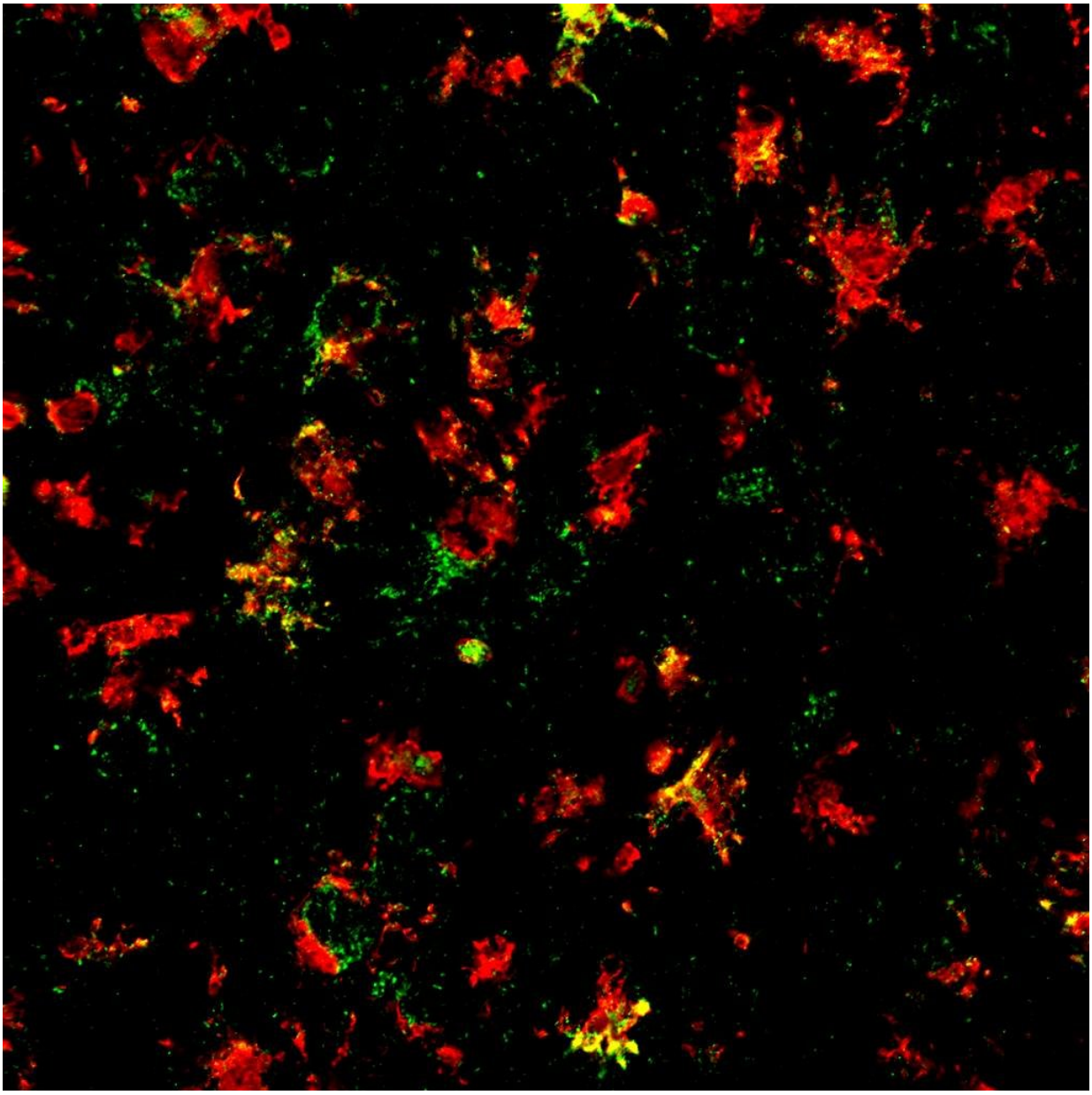

The NLRP3 inflammasome (green) is expressed by immune cells (red) in the

brains of people with Parkinson's disease. Credit: University of Queensland

A promising new therapy to stop Parkinson's disease in its tracks has been developed at The University of Queensland.

UQ Faculty of Medicine researcher Associate Professor Trent Woodruff said the team found that a small molecule, MCC950, stopped the development of Parkinson's in several animal models.

"We have used this discovery to develop improved drug candidates and hope to carry out human clinical trials in 2020," Dr. Woodruff said.

"Parkinson's disease is the second-most common neurodegenerative disease worldwide, with 10 million sufferers, whose control of body movements is affected.

"The disease is characterised by the loss of brain cells that produce dopamine, which is a chemical that co-ordinates motor control, and is accompanied by chronic inflammation in the brain.

"We found a key immune system target, called the NLRP3 inflammasome, lights up in Parkinson's patients, with signals found in the brain and even in the blood.

"MCC950, given orally once a day, blocked NLRP3 activation in the brain and prevented the loss of brain cells, resulting in markedly improved motor function."

There are no medications on the market that prevent brain cell loss in Parkinson's patients, with current therapies focusing on managing symptoms rather than halting the disease.

UQ Institute for Molecular Bioscience researcher Professor Matt Cooper said drug companies had traditionally tried to treat neurodegenerative disorders by blocking neurotoxic proteins that build up in the brain and cause disease.

"We have taken an alternative approach by focusing on immune cells in the brain called microglia that can clear these toxic proteins," he said.

"With diseases of ageing such as Parkinson's, our immune system can become over-activated, with microglia causing inflammation and damage to the brain.

"MCC950 effectively 'cooled the brains on fire', turning down microglial inflammatory activity, and allowing neurons to function normally."

The study is published in *Science Translational Medicine*, and was made possible by generous support from The Michael J. Fox Foundation for Parkinson's Research and Shake it Up Australia Foundation, which fund innovative research into therapies for Parkinson's disease.

"We are extremely grateful to our funders who have supported multiple research projects on this target at UQ, and to their donors who support medical research for those living with Parkinson's," Dr. Woodruff said.

The study was undertaken at the School of Biomedical Sciences and involved UQCCR Group Leader in Clinical Neuroscience Dr. Richard Gordon, an Advance Queensland Research Fellow, and Ph.D. student Eduardo Albornoz.

"The findings provide exciting new insight into how the spread of toxic proteins occurs in Parkinson's disease and highlights the important role of the immune system in this process," Dr. Gordon said.

"With continued funding support, we are exploring new treatment strategies including repurposing drugs to target mechanisms by which the immune system and the inflammasome contribute to disease progression."

More information: R. Gordon el al., "Inflammasome inhibition prevents α-synuclein pathology and dopaminergic neurodegeneration in mice," *Science Translational Medicine* (2018). stm.sciencemag.org/lookup/doi/ … scitranslmed.aah4066

Provided by University of Queensland