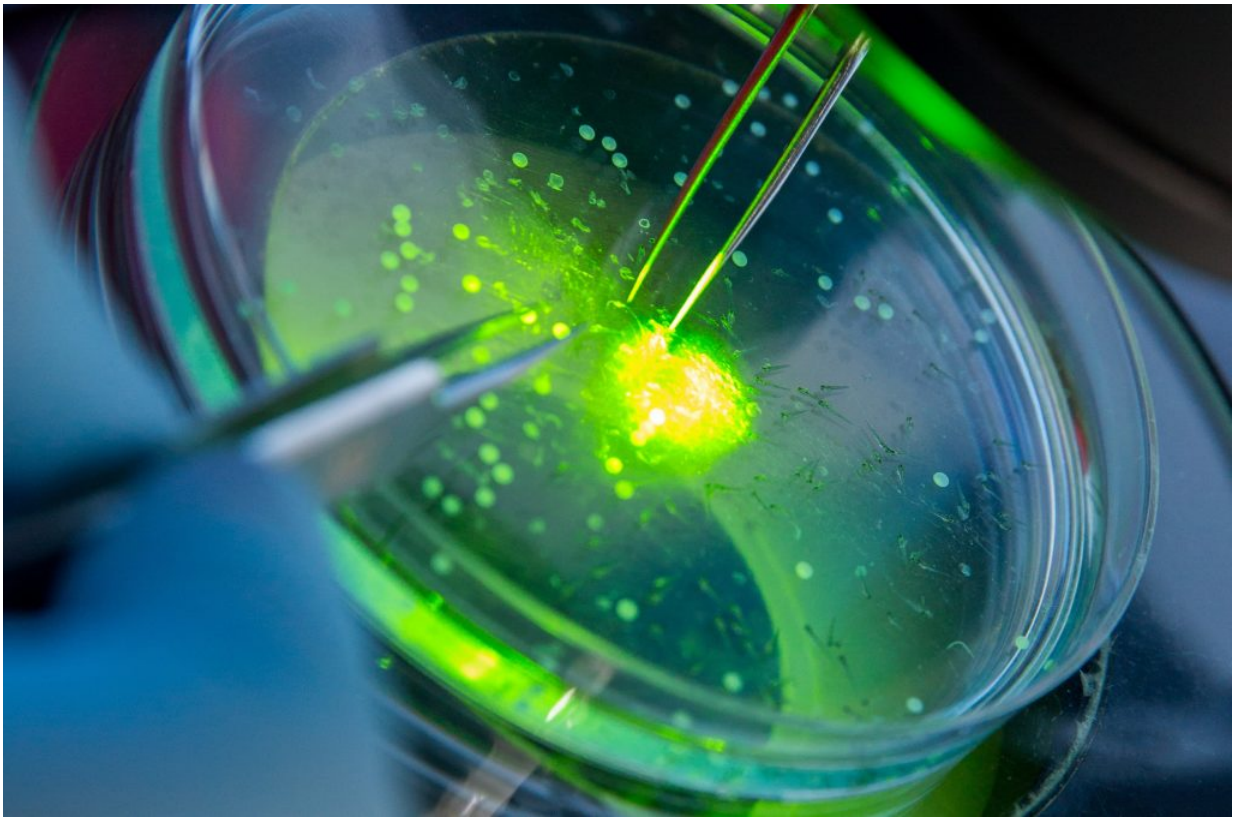
Zebrafish discovery could hold the key to better understanding motor neuron disease

February 13 2017



Credit: Chris Stacey

Researchers from Macquarie University's MQ Health are the first in the world to use a refined UV laser ablation technique to study the cellular behavior of MND in living zebrafish. New findings, published in the

Journal of Visualized Experiments on 3 February 2017, aim to better-understand how the disease spreads from neuron to neuron, through the body, in order to ultimately stop the debilitating disease in its tracks.

Postdoctoral fellow in Biomedical Sciences at Macquarie University's MQ Health, in Sydney, Marco Morsch, and his research team, have discovered a new, targeted combination technique that is capable of stressing, or killing, an individual unhealthy cell, without affecting any neighbouring healthy cells. This method is a first of its kind for potentially unlocking the secrets of MND.

"We know that some neurons contain a collection of proteins that play an important role in the cause and progression of MND," said Morsch.

"However, what the scientific community still doesn't know is how exactly the disease spreads to other parts of the body. By visualising how these disease-related proteins get cleared, or manage to move to another cell, we may be able to identify ways to interfere with this mechanism of propagation in order to slow, or ideally, stop progression."

Understanding this is critical, especially in relation to the neurodegenerative condition MND – also known as ALS, and which was at the centre of the worldwide 'Ice Bucket Challenge' phenomenon – which affects motor neurons in the brainstem, motor cortex and spinal cord, severely limiting a patient's quality of life.

MND targets and kills motor neurons, gradually weakening the muscles and leading to the inability to walk, speak, swallow, and eventually, breathe. MND has a three-to-five year life expectancy after diagnosis.

"Being able to actually visualise the death of a motor neuron and its short-term consequences in a living, transparent zebrafish provides the opportunity to better-understand the disease progression, and hopefully,

over time, stop it from further developing in patients," said Morsch.

"Our approach is unique – and especially exciting for MND – as we are able, for the first time, to target only a single cell that we know is expressing the MND protein (fluorescently labelled) and then follow it up with single-cell resolution microscopy. Together, this could allow us to decipher, in great detail, the 'route' of these proteins after their host has died."

Zebrafish have emerged as an attractive model system to study neurogenerative diseases because of its short maturity time, visual access to the nervous system and ease of transgenesis – the act of introducing a gene that will then be passed on to its offspring. Much of a human's protein-coding genes are related to genes found in the zebrafish, making it a perfect specimen for studying.

"The main cellular processes are very similar and applicable between different species."

"Understanding the fundamental disease mechanisms will ultimately help to improve the quality of life for these patients and families, and will be essential to find a much-needed cure for this devastating disease," Morsch concluded.

Provided by Macquarie University