Enlisting the brain's immune cells to fight MS

Specialist cleaning cells in the brain play a key role in neurodegenerative diseases, and they may also hold the secret to new treatments for the likes of MS and Alzheimer's.

Professor Colin Pouton and his team at the Monash Institute of Pharmaceutical Sciences found a way to isolate microglia, the immune cells of the brain, from stem cells. They also made the cells fluorescent so their activity can be tracked, opening up new avenues of research.

Professor Trevor Kilpatrick and his colleagues at the Florey Institute of Neuroscience and Mental Health think Colin's engineered cells could be the key to creating a revolutionary treatment for multiple sclerosis.

Trevor, a clinical neurologist who leads work on MS at the Florey and the Royal Melbourne Hospital, has been studying a molecule produced by microglia called MERTK. This molecule latches on to dead cells and debris in the brain and triggers microglial cells to clean them up.

This clean-up is a necessary first step to let the body's own repair mechanisms get to work.

"Even though the microglia doesn't directly coordinate the repair—other cells regrow the myelin sheaths on nerve cells that are destroyed in MS—the repair won't work properly unless the debris has been cleaned up," Trevor says.

Trevor's studies have shown that MERTK function may be corrupted in a significant proportion of people with MS. Injecting molecules that stimulate MERTK seems like a possible treatment, but the molecules are too large to cross the blood-brain barrier.

"Microglia seem to be involved in most of the degenerative diseases, but it's only recently we've been able to study them."

Instead, Trevor's team are hoping to create MERTK-producing microglia and inject them into MS patients. The theory is that the injected cells will migrate to the brain and help the body fight off MS.

At present the research is studying the effects of microglial transplants in animals, but the next step will need human cells—and that's where Colin's cells come in.

"Colin's group are already characterising the activity of their stem-cell derived microglia, detailing how well they take up debris. Once we're confident that the cells are behaving the way we think they will, we can try to establish a proof of principle for tests in humans."

And it's not only in MS where microglia are significant—Colin is studying their role in other neurodegenerative diseases such as Alzheimer's and Parkinson's.

"The first thing that disappears in degenerative diseases is functional synapses, the connections between neurons. When cells make fewer contacts with other neurons, they go into programmed cell death and once that starts there's no going back. We're interested in that initial process of loss of synapses, and microglia are right in amongst it," Colin says.