MS, the immune system and a sneaky intruder

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Professor Michael Pender

Australian immunological researchers have a strong tradition of being on the cutting edge - 20 years ago, Australian Professor Peter Doherty AC was awarded the Nobel Prize in Medicine for discovering how T cells, a critical part of the immune system, recognise foreign invaders. These T cells are the assassins of the immune system patrolling our bodies guarding against infection by viruses and bacteria.

In keeping with this strong Australian immunological research tradition, Professor Michael Pender, who is based at the University of Queensland, the Royal Brisbane and Women's Hospital, and the QIMR Berghofer Medical Research Institute, is investigating the role of T cells and EBV (Epstein Barr Virus) in the development of MS.

There is considerable evidence to suggest that EBV infection plays a role in MS, but exactly what is its role is unclear. EBV usually causes non-specific viral illness in childhood, but is also the cause of the illness glandular fever (also known as infectious mononucleosis). While around 90-95% of the general population will have been infected with EBV during their life, for people with MS, almost 100% have been infected by the virus.

Professor Pender has been extensively funded by MS Research Australia for over 9 years has just recently published a study, in the journal *Clinical & Translational Immunology*.
Professor Pender and his team have been investigating differences in the immune system of people with MS, and how they interact with EBV. Typically, once a person is infected with the virus, there is an active stage (technically called the lytic phase), and then the immune system kicks in and suppresses the virus - the immune system can't fully eliminate the virus but manages to keep it suppressed. The virus then goes into hiding, otherwise known as a latent phase. The virus specifically hides in the immune cells called B-cells. These are the cells in the immune system that generate antibodies that helps us fight infection. However, the virus hides in and hijacks some of the cells that make antibodies and potentially disrupts their normal functions.

In people without MS the immune system can use T cells to kill the EBV hijacked B cells to help suppress the latent infection, but Professor Pender has shown in his latest study that in people with MS their T cells fail to fully contain the EBV-hijacked B cells. As the duration of MS in individuals lengthens, the T cells become further exhausted and weakened. This appears to be specific for the EBV virus as the scientists demonstrate that the immune system can still shut down a similar virus called CMV.

The scientists postulate that this lack of control specifically of EBV leads to an increase in the number of hijacked B cells and that these cells might end up targeting the central nervous system of people with MS. Evidence has been building in recent years that B-cells play a key role in MS, and this has been supported by the efficacy of some of the newer MS medications that target B-cells.

Professor Pender's results suggest that during a relapse and at the early onset of the disease there is an increase in the number of EBV-infected B cells. These results will help tease out the role of EBV in MS, and potentially suggest targeting EBV may be another strategy to combat MS.

To this end, Professor Pender and his collaborators at the Queensland Institute of Medical Research have already commenced a very early stage, phase I, clinical trial of a treatment that aims to boost the ability of an individual's own T-cells to recognise and destroy EBV infected cells. MS Queensland is kindly partnering with MS Research Australia to fund this very important clinical trial.