BEGINNINGS OF A UNIQUE NEW APPROACH FOR TREATING MS

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Our blood brain barrier is an amazing part of the body that keeps the brain and spinal cord highly protected, allowing through only those cells and nutrients that are needed to keep the brain healthy.

This barrier prevents the majority of immune cells in the blood from entering the brain, reducing the risk of misguided inflammatory attacks on cells in the CNS. However, in MS, this barrier is breached and immune cells pass through causing the damaging attacks of MS.
One of the MS drugs, natalizumab, works by blocking the activity of a 'docking' molecule, the integrin-alpha 4 receptor (ITGA4). Immune cells use this molecule to dock onto and pass through the blood brain barrier. Blocking this molecule makes the drug highly effective in reducing the risk of relapses. However, as with many medications, there are a number of potential risks associated with natalizumab. In particular, this almost total block on immune cell entry and surveillance can also leave the brain vulnerable to the risk of viral infections.

With an MS Research Australia Incubator Grant, generously supported by the MS Society of WA, Dr Rakesh Veedu from Murdoch University, WA, and his colleagues have begun developing a cutting-edge gene technology treatment that aims to 'turn down' this docking station so that relapses can be prevented, but still allows the protective immune surveillance to continue.
They have published their important preliminary work in the highly prestigious *Nature Scientific Reports*. In this paper they describe how they have optimised the production of a gene-technology tool called a DNAzyme to target the receptor 'docking station'. DNAzymes are molecules that can be adapted to target and digest specific parts of the cell machinery that read the genetic code and convert it into the cell's components, in this case the docking molecule.
They have successfully developed a relatively stable DNAzyme, an important requirement for something that will be used as a medicine in the body, that was still able to reduce the amount of the receptor in question present in the cells.

This exciting gene technology approach to targeting the immune system is at the frontier of the next generation of medicines. It will allow the researchers to carefully turn down the production of the 'docking' protein to fine-tune the number of immune cells entering the brain to eliminate the risk of MS relapses, but still allow enough immune cells to enter to carry out their important surveillance role and against viruses.

This is the beginning of unique work that could lead to innovative, targeted MS therapeutics that can control only the 'bad' effects of the immune system, but leave the 'helpful' parts untouched, potentially greatly reducing the risks associated with some medications.