How does vitamin D change immune cell genes?

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Living further from the equator increases your risk of developing an immune disease such as MS.

This 'latitude effect' has been attributed in part to a lack of vitamin D, which may result from reduced sunlight exposure, as our bodies produce vitamin D in response to being exposed to ultraviolet rays.

Just how vitamin D might help prevent an autoimmune disease from occurring is not known. In this latest study published in *Genes and Immunity*, Professor David Booth and this team from Westmead Institute for Medical Research and The University of Sydney, investigated how gene activity changed in immune cells following vitamin D treatment.

At the cellular level, vitamin D interacts with a protein on the surface of cells called the vitamin D receptor (VDR). This protein then travels and sticks to the DNA in the cells, changing which genes are switched on or off. Professor Booth's team investigated how specific immune cells, called monocytes and dendritic cells might respond to vitamin D and to see what genes the cells would use in response to vitamin D.

They found that the VDR protein travels to the DNA and can bind to (or sticks to) the DNA at thousands of different spots around the genome. These spots are not random, but corresponds to areas of the genome which encode genes that the VDR protein manipulates. The team was particularly interested to see if these areas of DNA were the same in a subset of immune cells called monocytes and dendritic cells (both important in the development of MS).

They found that these common areas of the genome encoded for genes that determine the fate of a cell, or genes that tell a cell what to do. One of the important genes was called BAFT. Once VDR binds to the DNA next to BAFT it induces the cells to use the BAFT gene, which then goes on to makes even more genetic changes, which controlled the overall behaviour of these immune cells, for example making them more "inflammatory"- promoting inflammation, or made the cells less likely to attack the cells around them, and therefore less likely to induce an autoimmune disease.

For people with MS, this might influence whether the immune cells attack the cells of the brain and/or spinal cord, or whether they leave them alone. In other studies, a laboratory model that lacked this BAFT gene did not develop a MS-like disease. More research is needed but Professor Booth's results suggest that it might be possible to modify which genes a cell uses to modify the development and progression of a person's MS.

A clinical trial testing whether vitamin D supplements can help to prevent MS is currently being funded by MS Research Australia, the MS Prevention Trial, PrevANZ and we await the outcome of this trial with great interest. PrevANZ uses an oral dose of vitamin D. Other chemicals that mimic vitamin D have also been developed, but can have side-effects. Professor Booth's new research reveals more potential targets for future medications to treat MS by targeting certain immune cells to make them more tolerant, thus preventing further damage to the brain and/or spinal cord.