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Scientists 're-train' immune system to prevent attack of healthy cells

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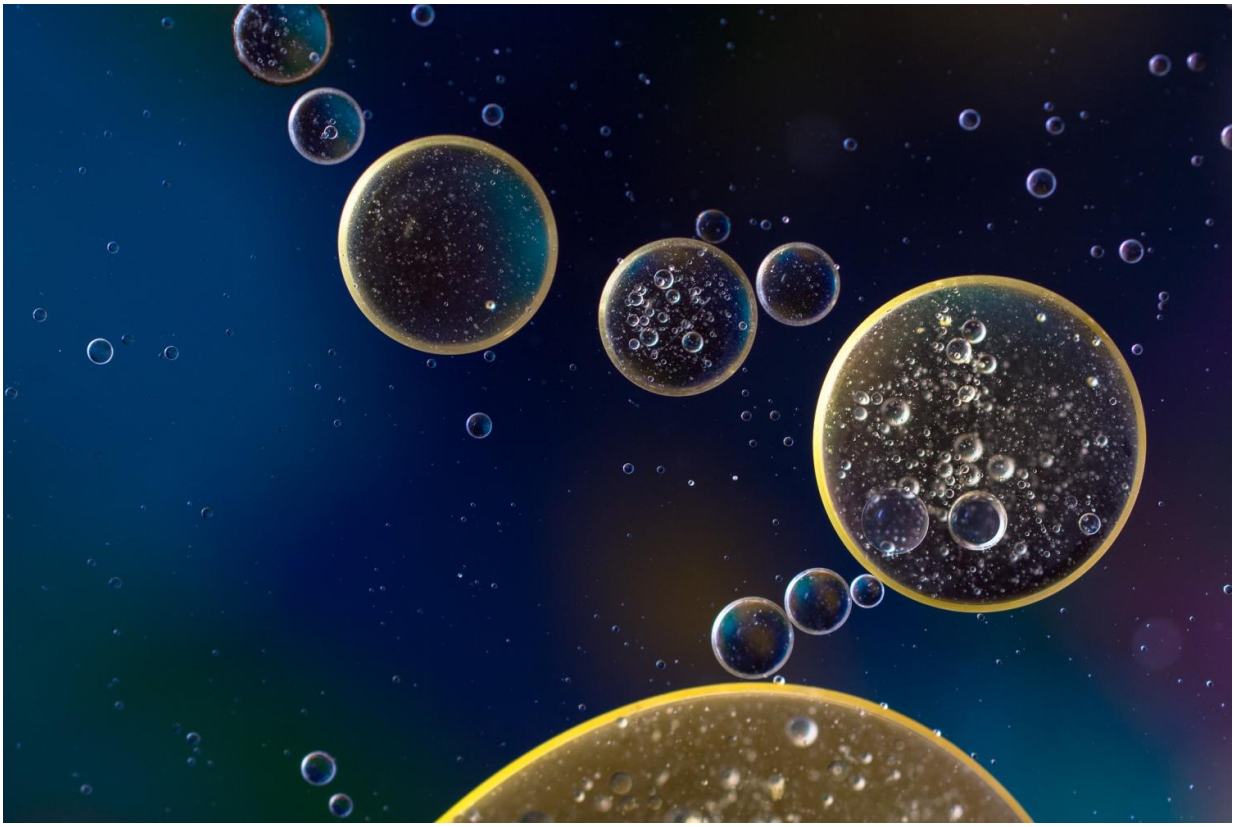

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The body's immune system can be re-wired to prevent it from recognizing its own proteins which, when attacked by the body, can cause autoimmune diseases like multiple sclerosis, a significant new

study by UK scientists has found.

Autoimmune diseases are caused when the immune system loses its normal focus on fighting infections or disease within and instead begins to attack otherwise healthy cells within the body. In the case of multiple sclerosis (MS), the body attacks proteins in myelin—the fatty insulation-like tissue wrapped around nerves—which causes the nerves to lose control over muscles.

Led by a multi-disciplinary team from the University of Birmingham, scientists examined the intricate mechanisms of the T-cells (or white blood cells) that control the body's immune system and found that the cells could be 're-trained' to stop them attacking the body's own cells. In the case of multiple sclerosis, this would prevent the body from attacking the Myelin Basic Protein (MBP) by reprogramming the immune system to recognize the protein as part of itself.

Supported by the Medical Research Council, the two-part study, published today in *Cell Reports*, was a collaboration between two research groups led by Professor David Wraith from the Institute of Immunology and Immunotherapy and Professor Peter Cockerill from the Institute of Cancer and Genomic Sciences.

The first stage, led by Professor Wraith showed that the immune system can be tricked into recognizing MBP by presenting it with repeated doses of a highly soluble fragment of the protein that the white blood cells respond to. By repeatedly injecting the same fragment of MBP, the process whereby the immune system learns to distinguish between the body's own proteins and those that are foreign can be mimicked. The process, which is a similar type of immunotherapy to that previously used to desensitize people against allergies, showed that the white blood cells that recognize MBP switched from attacking the proteins to actually protecting the body.

The second stage, saw gene regulation specialists led by Professor Peter Cockerill probe deep within the white blood cells that react to MBP to show how genes are rewired in response to this form of immunotherapy to fundamentally re-program the immune system. The repeated exposure to the same protein fragment triggered a response that turns on genes that silence the immune system instead of activating it. These cells then had a memory of this exposure to MBP embedded in the genes to stop them setting off an immune response. When T cells are made tolerant, other genes which function to activate the immune system remain silent.

Professor David Wraith said: "These findings have important implications for the many patients suffering from autoimmune conditions that are currently difficult to treat."

Professor Peter Cockerill, said: "This study has led us to finally understand the underlying basis of immunotherapies which desensitize the immune system"

Further longer term clinical trials will be needed to determine whether antigen-specific immunotherapies can indeed deliver lasting benefits. If this is successful, the study published today will be the first study defining the actual mechanisms of how T-cells can be made tolerant to the body's own proteins in a context that may lead to further advances in the battle to overcome autoimmunity.

More information: Sarah L. Bevington et al, Chromatin Priming Renders T Cell Tolerance-Associated Genes Sensitive to Activation below the Signaling Threshold for Immune Response Genes, *Cell Reports* (2020). DOI: 10.1016/j.celrep.2020.107748

Provided by University of Birmingham