Breakthrough opens door to safer lupus drugs

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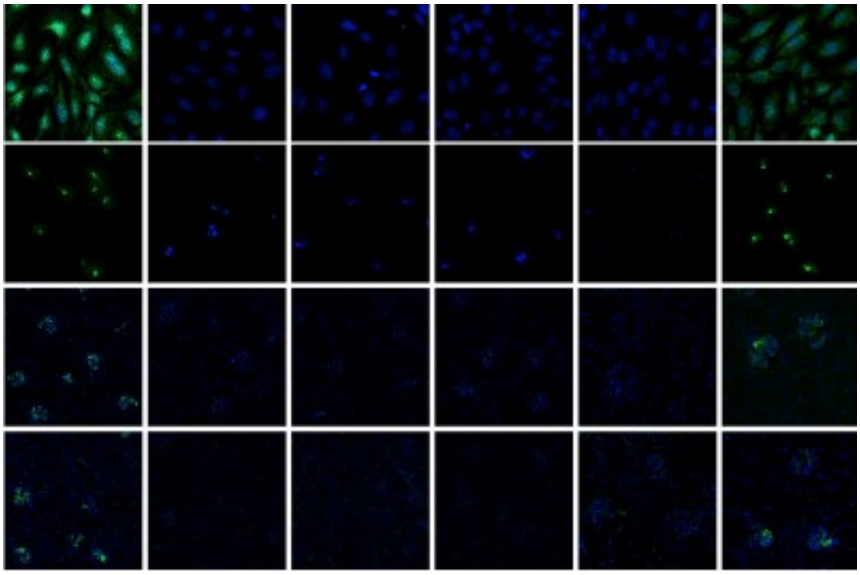

A ground-breaking discovery by Monash University researchers could revolutionise treatments given to lupus sufferers, saving thousands of people each year from serious illness or death caused by secondary infections.

Lupus is a vicious and widespread autoimmune disease that can attack any part of the body. It affects one in 1,000 Australians and 5 million people worldwide, and its victims are typically young women. Indigenous and Asian people suffer higher rates than other groups.

Current treatments for lupus essentially 'switch off' the patient's immune system to stop it attacking their body, according to lead researcher Dr Will Figgett, from Monash University's Department of Immunology.

This leaves patients vulnerable to any passing infection, and given that they are often in hospital due to the severity of lupus, the risk of exposure to another disease is high.

Dr Figgett and colleagues, working with world leader in immunology, Professor Fabienne Mackay, from the Department of Immunology – have found a way to stop lupus without stopping the immune system by focussing on a specific receptor found on B cells – the 'soldiers' of the immune system.

In healthy people, B cells attack diseases by producing antibodies that destroy invading pathogens. In lupus sufferers, B cells are misdirected to produce autoantibodies – cells that destroy the patient's own healthy tissue. Most commonly, lupus affects the skin and joints, but it can also strike the brain, kidneys and almost anywhere in the body.

In order to survive, B cells rely on a particular protein – called B cell Activating Factor of the TNF Family (BAFF), however too much BAFF causes lupus to develop. Each B cell carries three different kinds of receptor that detect BAFF in the blood stream. The receptors are known as BAFF-R, BCMA, and TACI. It is the TACI receptor that responds to excesses of BAFF, becoming overstimulated and triggering production of even stronger autoantibodies to attack healthy tissue.

Researchers found that if the TACI receptor is deleted, the B cells remain intact but lupus doesn't develop no matter how much BAFF is in the blood.

Dr Figgett said that while B cells are vital to a healthy immune system,

the TACI receptor itself is not crucial - the cell can fight most diseases without it.

"Among current lupus drugs, the most recent advancement is belimumab, which was thought to work by 'mopping up' the large amounts of extra BAFF in the patients and limiting the production of new B cells while under treatment," he said.

"This does help, but patients are left defenceless against a host of other illnesses. We have discovered that where the TACI receptor had been deleted from the genome, high BAFF levels don't get lupus even though they should.

The first step to make a new medicine is to find a suitable target. This is a better way to try and cure lupus because most of the natural immune system will remain intact to protect the patient," Dr Figgett said.

Provided by Monash University