Scientists discover 'how to stop your immune system from killing you'

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(Medical Xpress) -- Scientists at the University of Birmingham have discovered a 'molecular hoover' with the potential to prevent autoimmune conditions.

Research findings published today in the journal *Science* by Dr David Sansom and his team in the MRC Centre for Immune Regulation at Birmingham show how a protein, called CTLA-4, keeps the immune system damped down during day-to-day activities and prevents inappropriate aggressive behaviour from T cells, the 'command centre of our immune response'.

'Only when we are truly infected with invading microbes is the alarm system allowed to work properly, unleashing the full force of our immune system in the right place and at the correct time,' says Dr Sansom.

'We all take our immune system for granted,' he explains. 'Every day we are faced with a constant barrage of infectious agents just dying to make our bodies their home. To prevent this invasion, our immune system deploys a range of weapons designed to eat, poison and ultimately kill unwanted and potentially dangerous guests. On the whole, the immune system is remarkably good at its job.'

Why does this potent arsenal of weapons not kill us? 'The fact is that a number of diseases can be caused by such collateral immune damage, indeed rheumatoid arthritis, Type 1 diabetes and inflammatory bowel

syndrome are all thought to be examples of autoimmune conditions where the immune system attacks our bodies in some way,' says Dr Sansom.

One essential component of our immune system is CTLA-4, a protein found on T cells, he says. 'Without CTLA-4 T cells start to recognise our bodies, leading to the attack of many different organs in a manner which is fatal.'

While immunologists have known for a long time that CTLA-4 is required to prevent immune responses against ourselves, how it works has remained a mystery. The Sansom lab's work puts in place a critical piece of the puzzle by illustrating that CTLA-4 acts as a hoover removing the alarm signals that can drive unwanted and damaging immune responses against our bodies.

The work was funded by the Biotechnology and Biological Sciences Research Council (BBSRC) and the findings provide a new way of thinking about how to gain better control of our immune response and may help in the design of drugs to treat autoimmune diseases such as arthritis and diabetes.

Dr Sansom adds: 'Alternatively, by discovering new ways to prevent CTLA-4 working, it may be possible to encourage our immune cells to attack cells of our own bodies which could be desirable in cancers.'

In either case, he says, understanding how CTLA-4 works and learning how to manipulate its behaviour represents a significant step in understanding self-control in the immune system.

Provided by University of Birmingham