Medical Xpress

New pathway reveals how immune system is regulated, gives hope for chronic diseases

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Researchers from the University of Birmingham have identified an important new way in which our immune systems are regulated, and hope that understanding it will help tackle the debilitating effects of type 1 diabetes, rheumatoid arthritis and other serious diseases.

The team discovered a novel pathway that regulates the movement of pathogenic immune cells from the blood into tissue during an inflammatory response.

A healthy, efficient immune system ordinarily works to damp down inflammation and carefully regulate the magnitude of the response to infection and disease. In diseases such as diabetes and arthritis, as well as when we age, our immune system becomes less stringently regulated and this can lead to an exaggerated inflammatory response - allowing inappropriate access of immune cells to vulnerable tissues. The new study shows that beneficial effects of the new pathway are lost in these diseases, as well as during normal ageing.

The study, published in *Nature Medicine*, details how a key molecule regulates this aspect of our immune response. Importantly, the team were then able to show how the addition of this molecule to immune cells from patients with diabetes and arthritis could regain control of the movement of their immune cells, thereby reversing the pathogenic changes seen in these diseases.

Professor Ed Rainger, from the University of Birmingham, explained,

"Our immune system becomes progressively less effective over the years and this can become harmful leading to disease. Being able to understand the link between ageing and pathology will help us to reduce the risk of ill health associated with increasing age."

"Our discovery of this new pathway is very exciting. Not only does it reveal new ways in which our bodies control inflammation, it also indicates that we may be able design new drugs to reverse the disease and age specific loss of this pathway."

"The fact that the new pathway is relevant to both diabetes and rheumatoid arthritis, which are quite different diseases, implies a broad applicability to many chronic inflammatory and autoimmune diseases. This is an area of research we are keen to follow, and will be working with doctors from other specialities to determine whether this is the case and whether new therapies might be more broadly applicable"

The global healthcare landscape is undergoing a significant shift, with some populations experiencing a sharp increase in life expectancy. However, an ageing population comes with a rise in the prevalence of debilitating diseases, which in turn passes on a significant burden to the patients, their families and their health service providers.

Professor Rainger added, 'The link between the decline of this pathway and normal ageing is also very interesting, as this is a natural process. It means that patients with diseases such as rheumatoid arthritis may have accelerated decline of this pathway so that individuals as young as 20 have the immune function of 70 year olds. If we can identify patients at risk of developing this disease we may be able to artificially restore some vigour to their immune systems and reduce the burden of disease for the individual patient as well as their families and the NHS."

The next step is to use the findings in clinical studies that will investigate

the viability of treatments and therapies targeting this pathway.

Professor Peter Weissberg, Medical Director at the British Heart Foundation, said: "This is a superb piece of research that appears to have identified a new way to regulate chronic inflammation. It helps to explain why autoimmune diseases like rheumatoid arthritis become more common with age."

"It remains to be seen whether these findings will have any direct relevance to cardiovascular disease. However, coronary heart disease tends to be more common in people with chronic inflammatory conditions such as rheumatoid arthritis, so if this research leads to better treatments for these conditions, it might be expected that this will lead to fewer heart attacks in these patients."

More information: Homeostatic regulation of T cell trafficking by a B cell-derived peptide is impaired in autoimmune and chronic inflammatory disease, *Nature Medicine*, DOI: 10.1038/nm.3842

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