Medical Xpress

Antibodies in patients with rare disorder may have role preventing type 1 diabetes

July 14 2016

People with a rare autoimmune disorder produce autoimmune antibodies that appear to be linked to a reduced occurrence of Type 1 diabetes, new research has found. The study, published in *Cell*, suggests these antibodies could limit immune-related diseases and may have therapeutic potential.

In an international study led by King's College London, samples were taken from 81 people with a rare autoimmune disorder, called autoimmune polyendocrine syndrome type 1 (APECED), who have defects in the autoimmune regulator gene. Defects in this gene mean it can no longer fulfil its role as a regulator that helps purge the body of autoreactive immune cells termed T cells that can react against the body's own proteins, mistaking them for a foreign invader.

Professor Adrian Hayday, senior author of the study from Department of Immunobiology at King's College London and Group Leader at the Francis Crick Institute, said: 'APECED is a rare and poorly understood autoimmune disease. The defect in the autoimmune regulator gene should put APECED patients at severe risk of developing myriad autoimmune diseases, including type 1 diabetes, multiple sclerosis, lupus and rheumatoid arthritis in which an immune system that has not been purged of autoreactive cells attacks vital organs. Yet it's very unusual - possibly unprecedented - for APECED patients to develop multiple sclerosis or lupus, and most do not develop type 1 diabetes. So why don't they get these diseases? We wondered whether we could find out a lot more from these patients about basic human immunology and how their

immune systems might be keeping these diseases at bay.'

The researchers found that increased T cell auto-reactivity in patients with APECED was linked with increased B cell auto-reactivity. B cells are a type of immune cell that produce antibodies. The auto-reactive B cells produced autoantibodies that mistakenly targeted proteins within their own body, in particular targeting immune inflammatory molecules called interferons and interleukins. Each patient had about 100 different autoantibodies in their blood, but since each patient had different autoantibodies, the 81 patients collectively had antibodies to thousands of different human proteins.

Professor Hayday added: 'This is very significant because antibodies make up one of the largest sectors of the pharmaceutical market, and one of the great quests in the pharmaceutical industry is to be able to routinely generate antibodies against human proteins implicated in diseases. Rather than committing immense resources and expense to drug discovery, which is at best a very uncertain path, the findings suggest a route to drug recovery, in which naturally arising highly efficacious autoantibodies can be isolated from patients whose clinical information guides us as to the diseases most likely to benefit from those antibodies.'

To discover if APECED patients' autoantibodies could have therapeutic potential, the team tested them in a mouse model of psoriasis, an autoimmune condition that causes red, itchy and scaly skin. They found that injecting the mice with autoantibodies from the APECED patients could inhibit the development of psoriatic pathology.

Professor Hayday commented: 'After establishing the antibodies could protect mice from a form of psoriasis, there came the realization that perhaps the antibodies were actively limiting disease in the APECED patients themselves. Perhaps this was why the patients were arguably not

so ill as they might have been expected to be.'

The autoantibodies commonly produced by people with APECED include one that is a marker of type 1 diabetes, called glutamic acid decarboxylase autoantibody (GAD). Since GAD autoantibodies are closely associated with developing type 1 diabetes, the authors note that it is surprising that only 10 to 20 per cent of people with APECED develop diabetes.

To investigate why the APECED patients were not developing diabetes, they compared blood samples from eight APECED patients with type 1 diabetes with 13 APECED patients who had GAD autoantibodies but had not developed diabetes.

The patients without diabetes produced autoantibodies that completely impaired the activity of a subtype of interferon known as interferon-alpha, which is produced by the immune cells and may cause inflammation. By contrast, such potent antibodies were not produced by patients with diabetes. Therefore the authors suggest the naturally-arising autoantibodies could be inhibiting the effect of interferon-alpha which some have suggested may be linked to the development of type 1 diabetes.

Dr Hayday observes: 'Such striking correlations with type 1 diabetes were not evident for any other naturally arising anti-interleukin or anti-interferon antibodies, providing perhaps the strongest evidence yet in humans that interferon-alpha may contribute critically to the natural progression of type 1 diabetes.'

'This study provides correlational evidence for active anti-interferon antibodies providing protection from type 1 diabetes, but more research is needed to prove causation in humans. These findings give a firm foundation for exploring the potentials of autoantibodies from APECED

patients to ameliorate type 1 diabetes and other important autoimmune diseases that are rarely, if ever, present in APECED patients.'

For this study, Professor Hayday led an international collaboration of scientists and clinicians, who, together with the APECED/APS1 Patients' Association, established a start-up company, ImmunoQure AG that co-planned and supported work conducted in the investigators' academic institutions, including King's College London and the London Research Institute of Cancer Research UK, now part of the Francis Crick Institute. The international collaboration continues in the hope of addressing some of the key questions raised by this research.

Provided by King's College London

Citation: Antibodies in patients with rare disorder may have role preventing type 1 diabetes (2016, July 14) retrieved 4 May 2024 from https://medicalxpress.com/news/2016-07-antibodies-patients-rare-disorder-role.html