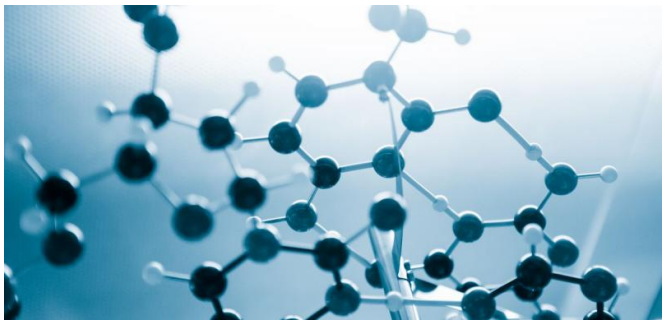
Study paves the way for new autoimmune disease treatments with fewer side effects

3 November 2016



Study paves the way for new autoimmune disease treatments with fewer side effects. Credit: University of Oxford

New research has raised the possibility of minimising the side effects of treatment for patients with autoimmune diseases, such as multiple sclerosis and inflammatory bowel disease.

A research team has been using genetics to explore ways of producing new treatments for autoimmune diseases, but with significantly fewer side effects.

Many of the current treatments for autoimmune diseases, which include multiple sclerosis, rheumatoid arthritis and inflammatory bowel disease, involve deliberately weakening the body's immune system. This leaves patients at greater risk of developing other opportunistic illnesses.

By studying 'experiments of nature' - naturally-occurring genetic variants that influence normal biological mechanisms - an Oxford-led team of scientists has been able to gauge the balance between efficacy and side effects.

The team has specifically investigated how genetic variation affects the function of a gene called TYK2. The TYK2 protein produced by this gene plays an important role in the processes that help the body fight off infection and cancer, but its activity can also promote autoimmune diseases.

The scientists found that a single genetic variant in TYK2 strongly protects against multiple different autoimmune diseases. This protective effect is mediated by a molecular change in the TYK2 protein that reduces its function and dampens down the activity of the immune cells, which could otherwise promote disease development.

The study, published in *Science Translational Medicine*, suggests that pharmaceutically mimicking the impact of the protective TYK2 variant could pave the way for new autoimmune disease treatments that balance the need for efficacy as well as safety.

Professor Lars Fugger of the Nuffield Department of Clinical Neurosciences, University of Oxford, who led the research, said: 'Developing new drugs is a costly and time-consuming process. On average it costs over £1 billion and takes over 10 years to bring a new drug to market, and more than 90% of drugs that enter into clinical trials are not ultimately approved. This is because the majority of drugs fail to demonstrate sufficient efficacy to treat disease or they are associated with severe unwanted side effects.

'While our research indicates that TYK2 could be a good drug target for treating autoimmune diseases, drugs that block the activity of immune cells have been known to leave patients vulnerable to infections and to increase the risk of cancer.

'However, by interrogating data available through the UK Biobank, the most comprehensive health study in the UK, we found that people carrying the protective TYK2 genetic variant were no more likely to have serious infections or to develop cancer than people without the variant.'

More information: C. A. Dendrou et al. Resolving TYK2 locus genotype-to-phenotype differences in autoimmunity, *Science Translational Medicine* (2016). DOI: 10.1126/scitranslmed.aag1974

Provided by University of Oxford