Probing the genetics of autoimmune disease

January 25 2023, by David Bradley

Credit: Pixabay/CC0 Public Domain

There are many forms of autoimmune disease, but by definition they all have one thing in common—they arise when the body's immunological defenses go awry and attack our cells or trigger biochemical changes that lead to inflammation and other responses that can be detrimental to our health. There are at least 150 different autoimmune diseases, some of them have the status of rare disease while others, such as type I diabetes and inflammatory bowel disease, are quite common.

Research in the *International Journal of Bioinformatics Research and Applications* has looked at several autoimmune diseases using bioinformatics to help improve our understanding of these important diseases.

Durbadal Chatterjee, Jyoti Parkash, and Arti Sharma of the Central University of Punjab in Bathinda, India, have focused on eight autoimmune diseases: Addison's disease, Graves' disease, Hashimoto's thyroiditis, myasthenia gravis, pernicious anemia, psoriatic arthritis, systematic lupus erythematosus, and vasculitis. They explain that science is yet to determine the genetic and biochemical pathways that give rise to these diseases.

The researchers point out that some autoimmune diseases don't tend to become apparent clinically at a single moment but symptoms gradually emerge in the patient ultimately leading to a diagnosis. Unfortunately, the problems are difficult to disentangle from the observations of autoimmune disease as some run in families, some are triggered by infection, and others arise because of environmental factors. It is possible that a combination of factors underpins the emergence of some diseases and that the specifics might be different from patient to patient. It is worth noting that genetics will inevitably have some role to play even if it is not the entire explanation.

The team has probed the U.S. National Center for Biotechnology Information (NCBI) database of genetic information surrounding these conditions and identified 668 genes associated with this group of diseases. The team found that most of these genes are involved in processes related to the activity of the immune system, intracellular signaling, and metabolism. However, while these genes are expressed and active in healthy people, they are silenced or have altered activity levels in people with these various autoimmune diseases.

The researchers found that one gene in particular, PTPN22, was present in seven of the eight diseases we studied. PTPN22, or protein tyrosine phosphatase non-receptor type 22 is a member of the so-called PEST family of protein tyrosine phosphatases. It acts to lower T cell receptor (TCR) signaling, which keeps activity and biochemistry steady, it maintains homeostasis, in T cells until they are needed by the immune system to fight disease.

The findings open up the possibility of finding pharmaceuticals that might be used to control errant behavior of the proteins associated with the given gene and so perhaps modulate the problematic autoimmune response in patients. The work might also provide useful clues as to how more targeted immunotherapy and stem cell treatments might be developed, that would again allow medicine to control the harmful immune response in these diseases.

"With the development of proteomics, genomics, and metabolomics, far more sensitive and specific methodologies will be developed in the future. Improved understanding of protein-protein interactions and specific targets anticipate further improvements in challenges of autoimmune diseases," the team concludes.

More information: Jyoti Parkash et al, Bioinformatics Approach in Solving the Puzzle of Autoimmune Diseases, *International Journal of Bioinformatics Research and Applications* (2022). DOI: 10.1504/IJBRA.2022.10052770

Provided by Inderscience