Excerpts from "Parkinson's and Autoimmunity" <https://journeywithparkinsons.com>
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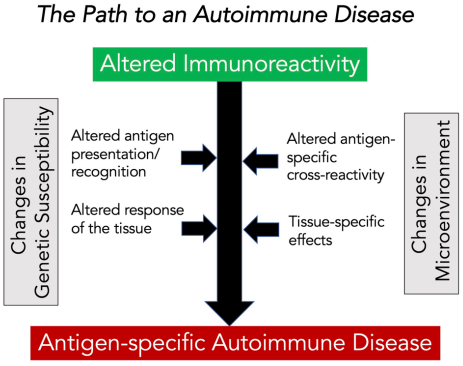
What is the Definition of an Autoimmune Disease? Davidson and Diamond (2001) defined an autoimmune disease as a clinical syndrome caused by the activation of T cells or B cells, or both, in the absence of an ongoing infection or other discernible cause." Thus, an autoimmune disease is the inappropriate activation of the host's immune system to attack self-antigens (that is, you).

Three Requirements for Autoimmunity to Occur-

- First, an individual must express MHC molecules that efficiently present a peptide derived from the target self-antigen. In other words, the MHC molecules you inherit play a role in determining your susceptibility to an autoimmune disease.
- Second, an individual must produce T and, in some cases, B cells with receptors that recognize a self-antigen. A mix-and-match strategy makes our immunologic diversity so that everyone is different from everyone else. Thus, by chance, a person will produce lymphocytes whose receptors recognize a self-antigen.
- Third, environmental factors must lead to the breakdown of the tolerance mechanisms, which have been designed to eliminate self-reactive lymphocytes. The current favorite hypothesis is that microbial attack (bacterial or viral) triggers the event as a 'last straw' that leads to autoimmune disease- we call it "molecular mimicry."



Abnormal Immune Response Promotes the Development of Parkinson's- The occurrence of intracellular inclusions named Lewy bodies is associated with the development of Parkinson's. A major component of Lewy bodies is aggregates of the protein alpha-synuclein (αSYN). A possible scenario leading to Parkinson's in older adults includes αSYN aggregation in dopaminergic neurons. The response to αSYN aggregation is cytokine-driven neuroinflammation, which enables an age-linked immunologic dysfunction. There is also evidence that αSYN, usually an intracellular protein, becomes an autoantigen by being released into the extracellular neuronal cell spaces and then aggregates, which further activates the immune response to engage the now deranged neuronal cells. Thus, over time, the afflicted neuron becomes dysfunctional and continues to be engaged by the inflammatory and immunological systems; dopaminergic neurons are destroyed, and Parkinson's begins.

Linking Autoimmunity to Parkinson's- Neuroinflammation is related to the etiology of Parkinson's. Now we link autoimmunity. It began with the epidemiological linkage of common genetic loci between Parkinson's and autoimmune diseases. They have found that patients with multiple sclerosis, Graves' disease, Hashimoto disease, and pernicious anemia have an increased risk of developing Parkinson's. Recently, Genome-wide association studies (GWAS) found seventeen shared loci between autoimmune diseases and Parkinson's; this includes type 1 diabetes, Crohn's disease, ulcerative colitis, coeliac disease, psoriasis, rheumatoid arthritis, and multiple sclerosis.

Summary-These results suggest a group of autoimmune disorders is linked to Parkinson's. The peripheral immune system is chronically turned-on and able to actively produce inflammatory mediators that fuel the neuroinflammatory flame that promotes the pathogenesis of Parkinson's. However, we need a more in-depth understanding of this immunological process and mechanism that links Parkinson's to autoimmune diseases. From this knowledge, novel immunomodulation therapies could evolve to slow or delay the progression of Parkinson's hopefully.