The changes in the brain that cause multiple sclerosis (MS) have baffled scientists since it was first described as a disease in 1868. There are genetic factors predisposing individuals to developing MS, as well as potential environmental, nutritional, and communicable disease exposure-related factors, but whether or not someone at risk will develop symptoms is still impossible to predict. What is known is that the effects of MS are largely the result of an autoimmune response—a malfunction that causes white blood cells to attack the self as it would a foreign invader.

The range of neurological symptoms that MS patients experience, (including partial paralysis, blindness, and cognitive impairment), are all linked to a loss of the fatty myelin coating that lines and protects nerve cell axons. The symptoms often appear suddenly as part of an acute episode and disappear within a week or more, probably because the body is able to regenerate myelin, a function that diminishes with age.
The Value of Basic Research

The symptoms of MS progress as each episode inflicts additional damage by stripping away more myelin and, in areas where myelin has already been completely destroyed, by producing plaque-like scars and lesions (reflected in the disease’s name) directly on axons. That damage blocks nerve impulses from flowing along neural pathways, which creates the symptoms of MS.

Given the complex origin of MS, the Harvard Stem Cell Institute (HSCI) has brought together experts across the medical sciences (immunologists, geneticists, cell biologists, etc.). Our investigators are focused on understanding the basic biology behind the development, replication, and regeneration of neurons and their associated components, like axons and myelin, both in healthy individuals and in those with neurological diseases. Some of this research is exploring facets of MS in great detail with an eye toward clinical application.

Clinical Applications

HSCI’s Director of Translational Medicine and Executive Committee member Lee Rubin, PhD, identified an antibody that blocks a type of white blood cell from traversing the blood brain barrier. His discovery led to the development of Tysabri®, one of the most effective drug treatments at slowing the progression of MS. The treatment reduces autoimmune damage by inhibiting the ability of T-cells to invade the nervous system and attack myelin.

Executive Committee member Amy Wagers, PhD, and Principal Faculty member Paola Arlotta, PhD, have recently shown that it is possible to reverse some of the effects of MS (especially those linked to aging) by restoring some of the myelin the disease has destroyed. In one case, Wagers linked the blood systems of two rodents, one young and healthy and the other older and with neural injuries similar to those found in MS patients. The older rodent partially restored some lost myelin due to the regenerative capacity of the younger mouse. When looking at the problem of regenerating myelin, Arlotta discovered that a compound identified fifty years ago (at the time thought not to have much biological impact) has promising capacity to coax adult stem cells to regenerate myelin much faster than the normal rate.

Promising Therapies

Additionally, HSCI investigators are working on basic immune system biology that should lead to new insights and promising therapies for MS. For example, HSCI Co-Founder Douglas Melton, PhD, is conducting a project in diabetes with “humanized mice” that are designed to let us see when the immune system attacks the beta cells in the pancreas. This same approach could be used to explore the conditions that cause an MS-related autoimmune attack.

On the therapeutic end, another example is found in the recent work of Affiliated Faculty member Jack Strominger, MD. Since several autoimmune diseases, including MS and diabetes, have been reported to have a deficiency in the number or function of regulatory T-cells, Strominger is focused on developing ways to increase the production of regulatory T-cells that would secrete high levels of a key signaling molecule cytokine, IL-10. If successful, this approach could provide a permanent protection from MS and other autoimmune diseases.

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