BENAROYA RESEARCH INSTITUTE
Virginia Mason

MULTIPLE SCLEROSIS RESEARCH FACT SHEET

Multiple sclerosis (MS) is an autoimmune disease in which the body's immune system destroys myelin, the protective sheath that covers nerve fibers. This affects the brain and spinal cord, leading to pain and disability. MS affects approximately 400,000 Americans (1 in 1,000), but is much more common in the Northwest where approximately 12,000 (2 in 1,000) people have MS. Some likely factors that contribute to this geographic effect are vitamin D deficiency from lack of natural sunlight, genetic predisposition in the North European/Scandinavian heritage and an environmental trigger, possibly a virus, found between 20 and 40 degrees latitude worldwide.

There are four types of MS. Relapsing-remitting multiple sclerosis (RRMS) is characterized by partial or total recovery after attacks. It is the most common form of MS. Eighty-five percent of people with MS experience a relapsing-remitting form of the disease. Other forms of the disease, in which symptoms generally do not subside and people experience steadily worsening disease, are less common and include primary-progressive, secondary-progressive and progressive-relapsing multiple sclerosis.

BRI and MS Research

BRI has a robust MS clinical research program with extensive experience in local and national clinical trials including studies with the most recent and dramatically efficacious immunotherapies.

- Clinical trials are led by Mariko Kita, MD, BRI Principal Investigator, Director of the Virginia Mason Multiple Sclerosis Center and head of the Department of Neurology at Virginia Mason.
- In 2007, the MS registry was added to the BRI Translational Research Program led by Jane Buckner, MD. This allows scientists and doctors to study patients' medical histories and data to understand disease treatment and progression.
- In 2008, BRI received a Washington State Life Sciences Discovery Fund grant that propelled MS research at BRI into a full-fledged program including basic, translational and clinical research, particularly focused on studies of genetic factors that influence the immune-mediated targeting of myelin in MS patients. BRI scientists are using the blood samples donated by research participants to advance understanding of how and why MS develops.
- In 2009, a prominent immunologist, Estelle Bettelli, PhD, joined BRI to start a new laboratory within the Immunology Program that focuses on multiple sclerosis as well as other diseases.
- In 2013, BRI received an NIH grant to find marks in the human genome which can explain why some white blood cells cause damage to the spinal cord and brain in MS. This is the first study to look for genomic changes responsible for the devastation caused by MS and will help determine how these cells can be regulated in models systems of MS and in humans.

Clinical Research

- BRI's clinical trials in MS often include evaluating new medications to determine whether they can decrease the number of MS relapses for RRMS, comparing the use of a combination of drugs versus a single drug and testing alternate dosages. New clinical trials are always becoming available.
- For information about BRI's current clinical trials in MS, please call (206) 342-6524 or email CRP@BenaroyaResearch.org.

Laboratory Research

- Estelle Bettelli, PhD, along with other scientists, discovered a subset of immune system cells, which when deregulated can lead to the development of MS and other autoimmune diseases. Dr. Bettelli is studying these cells to determine how to inhibit their harmful function. She has also developed model systems that recapitulate different forms of MS and allow investigation of how the immune system influences disease development and progression. The Bettelli lab's research focuses on a subset of CD4+ T cells that produces a cytokine known as IL-17. Her team aims to understand how these cells mediate their pathogenic functions and contribute to tissue destruction during the course of autoimmune diseases such as MS. The therapeutic goal of this research is to identify the pathways which modulate Th17 cells and develop strategies to block or enhance their functions.
- Karen Cerosaletti, PhD, BRI faculty member in the Translational Research Program, is also studying MS to better understand the nature of disease initiation and progression. Her work is focused on the molecular genetics of autoimmune disorders such as MS. She directs the Genotyping Core Laboratory at BRI, which investigates repository samples for specific genetic variants that have been associated with susceptibility to MS. Her group's research utilizes cellular and molecular assays of immune cells isolated from genotyped healthy controls and autoimmune research participants to identify the mechanism of action of genetic variants and the cellular consequences.
- Jane Buckner, MD, studies why the myelin specific T cells in MS patients are not "turned off" by the immune systems regulatory responses and why some RRMS patients are more resistant to treatment than others. This breakdown in the systems that control autoimmunity may be the key to why MS patients have flares of their disease and could be a target of therapy. Utilizing samples from BRI's MS registry, Buckner's group has found that T cells of RRMS patients with active disease are able to avoid suppression by regulatory T cells and that resistance to T cell suppression is correlated with sensitivity to IL-6. Furthermore, they found that when signals generated by IL-6 were blocked, the resistance to suppression was reversed. We now know that the IL-6 signaling pathway may be leveraged as a novel biomarker of MS disease activity and as a target for new therapies. Current studies now focus on understanding how to reverse the process of failed regulation during an MS flare.

Community Support

BRI needs community support to continue its crucial work of finding the causes and cures to eliminate autoimmune diseases. For more information about supporting BRI call (206) 583-6083 or visit BenaroyaResearch.org/donate-now.