

## Multiple Sclerosis Research Fact Sheet

# BENAROYA RESEARCH INSTITUTE



UNLOCKING THE IMMUNE SYSTEM

### BRI and Autoimmune Diseases

Autoimmune diseases strike one in 20 Americans, with conditions such as multiple sclerosis, Type 1 diabetes, rheumatoid arthritis, lupus, scleroderma, Crohn's disease and many others. Autoimmune diseases happen when the body's immune system, designed to protect the body, attacks it instead. There are more than 80 different autoimmune diseases. No tissue or organ is immune from autoimmune disease.

BRI is one of the few research institutes in the world devoted to discovering causes and cures to eliminate autoimmune diseases. The work of BRI scientists is generating new knowledge and opportunities for novel therapeutics, through a unique approach in which the patient's genetics and immune properties are carefully evaluated. BRI's research aims to block autoimmunity and to develop therapies to reverse disease by redirecting faulty immune systems so they won't attack healthy tissues.

### Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune disease in which the body's immune system destroys 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. Other factors are still unknown.

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, primary-progressive, secondary-progressive, and progressive-relapsing multiple sclerosis are less common, in which symptoms generally do not subside and people experience steadily worsening disease.

### BRI and MS Research

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

- Clinical trials are led by Mariko Kita, MD, BRI Principal Investigator and Director of the Virginia Mason Multiple Sclerosis Center.
- 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. The response of patients has been unprecedented with a group of 400 individuals participating in the study, with 163 individuals donating samples in 2010 alone. 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 2010, Damien Chaussabel, PhD, joined BRI to launch the Systems Immunology program that will develop a way to profile people's immune systems to pioneer new approaches to diagnosis, prognosis and therapy.

## Clinical Research

- Five clinical research trials in MS are currently being conducted at BRI. The newest study is an Immune Tolerance Network (ITN) study that is a phase II clinical trial evaluating the efficacy and safety of Abatacept in adult patients with RRMS. The ITN is an international consortium supported by the National Institute of Allergy and Infectious Diseases. Gerald Nepom, MD, PhD, Director of BRI is also Director of ITN. Abatacept is a biologic drug that selectively modulates the body's immune system. It has been approved by the FDA for the treatment of moderate-to-severe rheumatoid arthritis in adults. This study is open for enrollment.
- Other active trials include testing several oral medications to find out if they can decrease the number of MS relapses during a certain time period for RRMS, comparing the use of a combination of drugs versus using the drugs alone in RRMS and testing different doses of different drugs in RRMS. Listings of MS trials can be found on the BRI website, [www.benaroyaresearch.org](http://www.benaroyaresearch.org).

## Laboratory Research

- Dr. Bettelli, along with other scientists, discovered a subset of immune system cells which are believed to be potent inducers of MS and other autoimmune diseases. She is studying these cells to determine how to inhibit their harmful function. She also developed system models which can recapitulate different forms of MS to understand how the different arms of the immune system influence disease development and progression. Dr. Bettelli'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 are generated and how they can mediate their pathogenic functions that 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 focuses on developing novel biometric tools, called "tetramers," for monitoring disease prognosis and progression, and for evaluating the response to therapy in MS. These tetramers, developed and produced in BRI's tetramer production facility, are bioengineered molecules specific for MS autoantigens have the potential to directly detect antigen-specific CD4+ T cells in samples of peripheral blood from MS patients using flow cytometry.
- Dr. Jane Buckner's group focuses on discovering why some RRMS patients are more resistant to treatment than others. The goal of these studies is to determine why the myelin specific T cells in MS patients are not "turned off" by the immune systems regulatory responses. 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. Scientists at BRI have begun to solve that puzzle with the help of the MS registry. We now know that during a disease flare, T cells of MS patients seem impervious to regulation, while the T cells of patients in remission can be regulated in the same manner as in healthy individuals. Our current studies now focus on understanding how we can reverse the process of failed regulation during an MS flare.

## Community Support

BRI needs community support to continue its crucial work of unlocking the immune system and eliminating autoimmune diseases. For more information about supporting BRI please call (206) 583-6083 or visit [BenaroyaResearch.org/donate-now](http://BenaroyaResearch.org/donate-now).