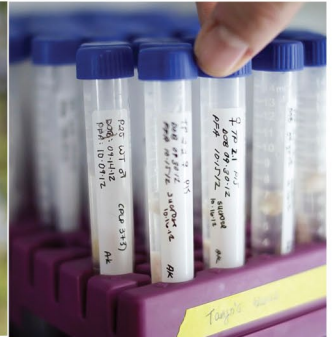


# PATHWAYS TO CURES

November 2023

JENNIFER  
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## Society Commits \$4.4 Million for New Studies to Drive Pathways to Cures

The National Multiple Sclerosis Society has committed \$4.4 million in multi-year funding to launch new MS research projects. This is part of the Society’s ongoing strategy to align the global MS research community around the most promising areas outlined in the Pathways to Cures roadmap to stop MS, restore function and end MS.

The new projects include five new research grants targeting recovery of functions for people with MS and nine pilot projects that focus on understanding the role of viruses such as Epstein-Barr in MS. These targeted research initiatives were designed to fill knowledge gaps and to take advantage of new opportunities to drive progress toward cures for everyone living with MS.

These new studies are part of the Society’s annual investment of over \$30 million for more than 200 new and ongoing MS research studies around the world.

Here are a few of the new research projects:

### STOPPING MS in its tracks:

A team at the University of Verona in Italy is working to identify molecules that may play a role in the connection that the Epstein-Barr virus has to MS-specific nervous system inflammation. (see p. 3)

### RESTORING what’s been lost:

Researchers at Massachusetts General Hospital are testing whether combining rehabilitation for walking with a pharmacological treatment can enhance their benefits. (see p. 8)

### ENDING MS forever:

Yale University scientists are using cutting-edge technology to explore tissues from people newly diagnosed with MS to understand how the Epstein-Barr virus may activate the immune system to launch MS. (see p. 14)

### NEW PROJECTS SUMMARIZED INSIDE

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## Pathways to Cures: STOPPING MS

Stopping MS is defined as achieving a state of no new disease activity, no worsening of daily living or quality of life, and no change in disease manifestations or clinical activity in people living with either relapsing or progressive forms of MS. Two key objectives have been targeted for the next three years to advance the STOP pathway: early detection before symptoms appear, and precision medicine for individualized treatment and lifestyle strategies to prevent further progression.

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### **Bonnie Dittel, PhD**

Versiti Blood Research Institute  
Milwaukee, Wisconsin

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$110,000

**Title:** Development of a mouse model to study the impact of Epstein Barr Virus on multiple sclerosis

**Summary:** Scientists at the Versiti Blood Research Institute are developing a mouse model to study the impact of the Epstein-Barr virus on MS.

**Background:** Infection with Epstein-Barr virus (EBV) has long been associated as a risk factor for developing MS. One recent study found that individuals infected with EBV in adulthood had a higher risk of developing MS than those who had been infected in childhood or adolescence.

Unfortunately, one obstacle to studying the link between EBV and MS has been the lack of good animal models, since EBV only infects humans. So, researchers use a similar virus in mice called gammaherpesvirus 68 (MHV68). There is evidence that mice infected with MHV68 suffer more severe EAE, a mouse model of MS.

**The Study:** Dr. Dittel and her team are developing a model of EBV/MS in mice using MHV68. They will try to discover how EBV works in humans by determining how long after MHV68 infection of mice EAE is more severe and whether immune cells linked to MS are altered. They are also determining whether infection in newborn and young mice leads to more severe EAE in their adulthood or whether it provides protection.

**What is the potential impact for people with MS?** This study hopes to develop a mouse model of EBV/MS that will allow future studies to investigate how EBV infection in early and late life contributes to the onset and underlying activity of MS. The model could lead to a strategy for reducing the incidence of multiple sclerosis in the future.

**Marc Horwitz, PhD**

University of British Columbia  
Vancouver, British Columbia, Canada

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$25,462, Plus co-funding by MS Canada

**Title:** Fighting the Hidden Enemy:

Therapeutic strategies targeting latent gammaherpesvirus infection in an autoimmune animal model of MS

**Summary:** A team at University of British Columbia is testing known EBV-targeting treatments in MS models to determine if they can reduce the severity or even prevent MS-like disease.

**Background:** The growing body of evidence implicating EBV as a causal factor in MS has sparked interest in the potential of using EBV-targeted therapies to treat or prevent disease. Existing EBV-targeted therapies, however, have been largely unsuccessful so far in trials, likely due to their inability to completely remove the virus, which usually stays dormant in the body. Therefore, there is a need to investigate novel EBV specific therapies to further understand the mechanisms linking EBV to MS and to determine if directly targeting the virus is a feasible and effective approach to alter disease development in individuals affected by MS.

**The Study:** Prof. Horwitz and colleagues are investigating three strategies to directly target the virus in the context of

MS, using a mouse model for EBV infection and MS previously developed in their lab. They will administer treatments prior to or after induction of MS-like disease in mice to mimic what could be done in people before and after they are infected with EBV and/or diagnosed with MS. The team has intentionally selected three treatment approaches that are currently in human clinical trials for other conditions and are therefore known to be tolerable and safe in people.

**What is the potential impact for people with MS?** These studies can determine if eliminating dormant EBV infection before or after MS-like disease onset can either stop disease in its tracks or prevent it altogether, bringing us much closer to trials of these strategies in people living with MS.

**Roberta Magliozzi, PhD**

University of Verona  
Verona, Italy

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$100,000

**Title:** Meningeal lymphoid-like structures as secret EBV hideout in multiple sclerosis.

**Summary:** Researchers at the University of Verona in Italy are working to identify molecules that may play a role in the Epstein-Barr virus's connection to MS-specific inflammation.

**Background:** Chronic inflammation is being looked at as one of the main mechanisms in MS progression. Growing

evidence suggests a key role for the Epstein-Barr virus (EBV), a herpes virus that persists for life after infection, as a possible driver of this chronic inflammation. Research has found that people with MS have more EBV-infected immune B cells in the brain than people who don't have MS. However, the exact way that EBV infection may contribute to chronic inflammation and nervous system damage in MS remains unknown.

**The Study:** Dr. Magliozzi and team will examine autopsied brain tissues of 20 people who had MS, looking for biomarkers for EBV and for specific structures associated with more rapid and severe disease progression. Tracking the real extent of EBV infection in MS brain tissue will contribute to a deeper understanding of how EBV may be involved in MS-specific inflammation and nervous system damage. The researchers are also attempting to identify the main molecules and pathways involved in the interaction between EBV and inflammation in the tissues (meninges) that surround the brain and spinal cord.

**What is the potential impact for people with MS?** Finding biomarkers of EBV infection could prove useful for both early diagnosis of MS and for monitoring EBV infection and its effects. Identifying molecules involved in MS-specific chronic inflammation and damage could lead to potential new anti-viral therapies that halt EBV activity in people with MS.

## Pathways to Cures: RESTORING FUNCTION

Multiple sclerosis can result in many different symptoms, including vision loss, pain, fatigue, sensory loss, impaired coordination, mobility, and cognitive changes. Translation of knowledge from basic mechanisms to functional impact is needed to optimize treatment, manage symptoms, and ultimately restore function for people living with both relapsing and progressive forms of MS. Two key objectives have been targeted for the next three years to advance the RESTORE pathway: remyelination and restoration of function.

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### Dawn Ehde, PhD

University of Washington  
Seattle, Washington

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2026

**Funding:** \$725,451

**Title:** Increasing Physical Activity via Provider Prescription and Engagement: Efficacy of Exercise Rx for Adults with MS

**Summary:** A team at the University of Washington is testing a novel electronic platform that bridges the communication gap between providers and people with MS to increase physical activity and restore function in people with MS.

**Background:** Regular physical activity improves mobility, balance, fatigue, and other symptoms in people with MS, and may even alter the disease course. However, only 20% of adults with MS get

the recommended amount of weekly physical activity. Research has shown that there are ways to facilitate being active, such as support and guidance from healthcare providers, tracking physical activity, setting appropriate goals, having an accountability partner, and using self-management skills to minimize potentially interfering symptoms such as fatigue. Prof. Ehde's team developed ExerciseRx, an innovative approach to promoting physical activity that helps individuals and healthcare providers communicate about ways to get more active through use of an app on a smartphone and the electronic health record.

**The Study:** Prof. Ehde's team will conduct a controlled trial in which adults with MS who are insufficiently active are randomly assigned to either ExerciseRx or usual care. They hope to answer the question of whether ExerciseRx increases physical activity and improves common symptoms like fatigue, pain, and depression. They will also look at functional outcomes, such as participation in social roles and activities. The team will also conduct qualitative interviews of a subset of participants and their providers to get their perspectives on the ExerciseRx platform, such as its ease of use.

**What is the potential impact for people with MS?** This study could accelerate the use of ExerciseRx in the routine care of people with MS and ultimately increase wellness on many levels.

### **Bo Fernhall, PhD**

University of Massachusetts Boston  
Boston, Massachusetts

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2026

**Funding:** \$719,399

**Title:** Targeting vascular mechanisms of functional outcomes via home-based exercise training among persons with multiple sclerosis who have hypertension  
**Summary:** UMass Boston researchers are testing a home-based exercise program to see if it can improve blood pressure, cognition and mobility in people with MS who have high blood pressure.

**Background:** Some common symptoms experienced by people with MS include walking difficulties and problems with cognition – in particular, processing information. Exercise has been shown to be beneficial for these problems, and has also been found to reduce high blood pressure in the general population. Often exercise programs are done in person, with professional oversight. Often people lose motivation to continue exercising outside of this kind of in-person study. Prof. Fernhall and collaborators want to tackle mobility and cognitive problems particularly in people with MS who have high blood pressure, a condition that is common in MS and can make these problems worse.

**The Study:** This team will test a home-based exercise program that involves online coaching and FitBit-style activity

monitors. The team already had success with this program in a previous study that did not involve people with high blood pressure. Now they will compare people randomly assigned to undergo 12 weeks of stationary bike training or 12 weeks of a stretching program. The bikes will be installed by professionals who will ensure their proper use. Both groups will be evaluated in person before and after for cardio fitness, blood pressure, cognition, walking speed and other measures of function.

**What is the potential impact for people with MS?** If this exercise program proves beneficial on multiple functions including cognition, mobility and blood pressure, it could have far-reaching consequences for people with MS especially since it is home-based.

**Anna Kratz, PhD**

University of Michigan  
Ann Arbor, Michigan

**Award:** Strategic Initiative

**Term:** 10/1/2023-9/30/2024

**Funding:** \$16,809

**Title:** A Nationwide Survey of Psychosocial Wellness in MS

**Summary:** Researchers are leading an effort to survey people with MS with the purpose of gathering data to enhance psychosocial wellness.

**Background:** As part of the National MS Society's and its global partner's efforts to drive research on the Pathways to Cures

roadmap, we seek to optimize the extent to which wellness behaviors, rehabilitation, self-care, and exercise can stop disease and restore function in people with MS. The Society convenes a Wellness Research Work Group to promote scientific evidence that supports lifestyle, behavioral, and psychosocial approaches for enhancing wellness in people living with MS.

**The Study:** On behalf of the Psychosocial Wellness Research Work Group, Dr. Anna Kratz is leading the team in developing and administering a survey to over 1,000 people with MS from across the US to gain new insights about psychosocial wellness in MS and to generate data that will guide future research to enhance psychosocial wellness in people with MS. The survey will help to establish what psychosocial wellness means to people with MS, what outcomes should be measured in research (for example, resilience, well-being), and what social determinants of health (such as income, neighborhood, access to care) play a role in psychosocial wellness.

**What is the potential impact for people with MS?** The survey results will help to establish a strategy for improving research on interventions to enhance psychosocial wellness in people with MS.

## Fast Forward Funds Study Targeting CNS Repair

### Yuta Fujimoto, MBA

J-Pharma Co., Ltd.

Yokohama, Kanagawa, Japan

**Award:** Commercial Research Funding

**Term:** 8/18/2023-8/17/2024

**Funding:** \$600,000

**Title:** IND enabling studies on a novel amino acid transport inhibitor to promote CNS repair in MS

**Summary:** This commercial funding opportunity supports studies that are necessary before a novel molecule that might promote nervous system repair can be tested in people with progressive MS.

**Background:** Current MS therapies do not completely stop the damage to the nervous system that leads to disease progression. Harmful, persistent pockets of inflammation may be the cause of this damage. A novel small molecule taken by mouth was able to decrease inflammation in the brain and spinal cord in mice with MS-like disease. It also increased the repair of nerve-insulating myelin and improved symptoms. The molecule, JPH034, targets this inflammation and may create a permissive environment for myelin repair.

**The Study:** A brief study to determine toxicity has been performed in lab models, with no serious adverse effects. However, before the molecule can be tested in people with MS, longer-term studies are needed to evaluate the safety of this molecule. The Society's Fast Forward funding will enable these studies, so that this strategy can be further developed for potential testing in people with progressive MS.

**What is the potential impact for people with MS?** This funding will help to launch an experimental therapy that has future potential to restore function to people with progressive MS.

**Prudence Plummer, PhD, PT**

MGH Institute of Health Professions  
Boston, Massachusetts

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2026

**Funding:** \$725,913

**Title:** Dalfampridine combined with physical therapy for mobility impairment in people with multiple sclerosis

**Summary:** Mass General researchers are testing whether walking can be improved by combining rehabilitation with a pharmacological treatment for walking.

**Background:** People with MS frequently experience difficulties with walking, due to slowed nerve signaling and damage. A “walking pill,” dalfampridine, is available to help to speed up nerve signals between the brain and muscles, but it doesn’t work for everyone. Once a person stops taking it, the improvement is lost. Physical therapy (PT) can also improve walking in people with MS by helping the brain to make new connections, but this requires a lot of practice. So, improvements from PT do not occur as quickly as with the “walking pill.” However, because PT may create changes in the brain, the improvements can last longer, even after a person stops PT. Prof. Plummer wants to know whether the two treatments can complement each other and improve recovery of walking ability and sustain the benefits of therapy longer.

**The Study:** The team will recruit people with MS with walking problems and who are suitable for taking dalfampridine. All participants will take the tablet for 6 weeks to assess how much it helps them. Then, after stopping the medication for 2 weeks, participants will be randomly assigned to resume the medication while getting PT for 6 weeks, or to remain off the medication and receive PT for 6 weeks. Before and after each treatment, the team will assess walking, balance, fatigue, and take a brain scan (MRI). The assessments will be repeated 12 weeks after the final treatment to evaluate if improvements have been sustained.

**What is the potential impact for people with MS?** This study will provide new information about whether combining these two treatments can improve difficulties in walking more than either treatment on its own, and whether brain rewiring from PT can be accelerated to improve how fast the nerves can send signals between the brain and the muscles.



**Carly Wender, PhD**

Kessler Foundation Research Center  
East Hanover, New Jersey

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2026

**Funding:** \$725,498

**Title:** A Novel Combinatory Approach to Maximize Functional Recovery of Learning and Memory in Multiple Sclerosis

**Summary:** Kessler Foundation researchers are testing a combined approach to improving cognitive function in people with MS, involving cognitive rehabilitation and exercise.

**Background:** Cognitive impairment, such as problems with learning and memory, is a common symptom in people with MS and can create challenges and barriers to independence, maintaining employment, and completing daily activities of living, such as housekeeping or grocery shopping. People with MS who also have mobility problems and have greater disease progression feel the consequences of impaired learning and memory much more strongly. An effective treatment to improve new learning and memory deficits is a cognitive rehabilitation technique called Kessler Foundation modified Story Memory Technique® (KF-mSMT). However, this technique was developed to improve learning lists of words, which is only one specific aspect of new learning and memory. To date, this treatment alone has not shown broad improvements in new learning and memory that have translated to benefits in everyday life.

**The Study:** Dr. Wender's team is trying a new approach that combines KF-mSMT with an innovative exercise training program to improve new learning and memory more globally. The team is conducting a trial in which participants will be randomly assigned to KF-mSMT alone or combined with exercise. Participants engage in 3 days a week for in-person sessions over 12 weeks. Before and after the program, participants will complete testing of new learning and memory and will complete a brain scan to measure the volume and function of an area of the brain (hippocampus) that plays a major role in learning and memory.

**What is the potential impact for people with MS?** Since all participants in this study receive the KF-mSMT treatment, all are likely to see benefits. However, the combined intervention may show greater improvements that will translate better to new learning and memory in everyday life. The results can also fuel the testing of other combinatory approaches involving cognitive rehabilitation, exercise, and virtual reality to improve other aspects of cognition that can be problems for people with MS.

**E. Yeh, MD**

The Hospital for Sick Children  
Toronto, Ontario, Canada

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2026

**Funding:** \$134,789, Plus co-funding by MS Canada

**Title:** An Exercise Training Intervention for Depressive Symptoms in Youth with MS: A Randomized Controlled Feasibility Trial

**Summary:** University of Toronto researchers are testing an exercise program that uses coaching to increase physical activity and possibly reduce depression and fatigue in children with MS.

**Background:** Prof. Yeh and colleagues have previously shown that moderate to vigorous exercise in children with MS may lead to decreased disease activity and lower depression and fatigue. However, they also have found that young people with MS are generally inactive and deconditioned, and may lack self-confidence in the ability to start and maintain an exercise program. Introducing exercise with an intervention program may be a non-pharmaceutical way to improve symptoms like depression and fatigue in kids with MS.

**The Study:** This team is conducting a multi-center trial to test the feasibility of a 20-week exercise program aimed at reducing depression in kids with MS, compared to a control group that only receives mobility and flexibility training.

The exercise program comprises three weekly home-based exercise sessions of 30 to 45 minutes. Kids will be assigned coaches to help motivate them, help them create weekly exercise goals, and provide support throughout the program. The control group will engage in a non-exercise program focused on improving mobility and flexibility three times a week. Children in both groups will receive testing prior to starting, including a physical examination, an MRI scan and cognitive testing. They will be asked to complete questionnaires focused on depression, fatigue and quality of life. Testing will be repeated at the end of the 20-week trial.

**What is the potential impact for people with MS?** If this approach is effective, it could inform programs to increase activity in kids with MS, which could lead to lower levels of depression and fatigue.

## Pathways to Cures: ENDING MS

Ending MS is defined as no new cases of MS. Two key objectives have been targeted for the next three years to advance the END pathway: primary prevention and secondary prevention. Primary prevention involves limiting exposures to MS risk factors in the general population. Secondary prevention focuses on individuals at high risk for MS and developing and deploying interventions in the period prior to preclinical/clinical stages of disease to reduce or eliminate the risk for developing MS.

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### Alexander Boyden, PhD

The University of Iowa  
Iowa City, Iowa

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$110,000

**Title:** Impact of gamma herpesvirus infection on required B cell:CD4 T cell interactions in a novel B cell-dependent, antibody-independent EAE model

**Summary:** Researchers at the University of Iowa are working to discover how a virus infection affects certain immune cell interactions in a mouse model of MS.

**Background:** That the Epstein-Barr virus (EBV) has a role in MS onset is increasingly recognized, but it's still not clear how this happens. EBV infects and resides inside immune cells, called B cells, which are known to be involved in driving the disease in some way. However, this relationship is difficult to model in mice, as

most mouse models do not require B cells for the disease to develop.

**The Study:** To better understand how MS develops, Dr. Boyden and his team of researchers are looking at interactions between B cells and CD4 T cells (cells that help coordinate the immune response), outcomes of their interactions, and how a viral infection may influence them. They have established a new mouse model that requires B cell-CD4 interactions for disease to develop in mice. This will make it possible to test how an EBV-related mouse virus influences these interactions. An advantage of this new mouse model is that it is affected by therapies that target B cells and mimics some aspects of human MS.

**What is the potential impact for people with MS ?** This work may establish a way to answer questions about EBV and MS, which in turn could explain more about how viral infections potentially cause MS by altering B cell function. The researchers hope their work will lead to an understanding of the origin of the disease—and eventually maybe stop it from happening in the first place.

**Judith Greer, PhD**

The University of Queensland  
Brisbane, Queensland, Australia

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$100,000

**Title:** Using a novel humanized mouse model to investigate how EBV infection at different ages potentiates development of CNS demyelinating disease

**Summary:** Researchers at the University of Queensland in Australia are trying to find the link between the age a person is infected with Epstein-Barr virus and the likelihood of developing MS.

**Background:** The Epstein-Barr virus (EBV) is thought to play a role in the development of multiple sclerosis.

Research also suggests that the risk of MS increases the older someone is at their first exposure to EBV. However, EBV exposure alone is not enough to trigger MS and a person's genetic background and environment are also factors. Previous research has identified over 200 common gene variants that can contribute to susceptibility to MS.

**The Study:** Dr. Greer's team is developing a mouse model with a human-like immune system, either mimicking that of people with MS or that of people without MS. This would enable exploration of the links between age at infection with EBV and subsequent development of MS. By studying immune cells in the 'humanized' mice with contain immune cells from

people with MS, Dr. Greer will attempt to answer such questions as: Do the 200+ gene variants that are linked to developing MS influence the life cycle of EBV and how the immune system responds to EBV? Are mice infected with EBV at a young age more resistant to developing MS-like disease than mice infected as adults?

**What is the potential impact for people with MS ?** This work will aid in building an animal model that facilitates research on the role of EBV in the development of MS. If this mouse model is successful, it could be used to test such possibilities as the effects of vaccinating against EBV as a possible way to prevent MS.

**Marc Horwitz, PhD**

University of British Columbia  
Vancouver, British Columbia, Canada

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$25,594, Plus co-funding by MS Canada

**Title:** Novel preclinical humanized mouse models of MS to investigate the ins and outs of EBV's role in disease initiation

**Summary:** University of British Columbia researchers are developing MS models for studying how EBV may trigger MS and how to prevent it.

**Background:** Epstein-Barr virus (EBV) is a member of the herpesvirus family that maintains a life-long infection in most people without causing major health problems. Based on population and clinical

studies from multiple research groups over the past few decades, EBV has been identified as a uniquely specific risk factor for MS. Because EBV infection often occurs early in life without causing symptoms, determining the mechanisms by which EBV could influence susceptibility to MS is difficult to investigate clinically.

Importantly, EBV is a human specific virus, and cannot infect regular mouse models that are typically used to study MS.

**The Study:** To overcome this problem, this team plans to generate mice with human immune systems, called humanized mice, which contain human immune cells that can be infected with EBV directly. These mice will be induced with one of two different protocols for generating relapsing or progressive-like disease. This will allow Prof. Horwitz and colleagues to determine consistent or unique mechanisms EBV uses to affect different types of MS.

**What is the potential impact for people with MS?** Creating new mouse models wherein EBV infection can be directly studied will allow researchers to determine the underlying reasons why EBV is such a strong risk factor for MS. Targeted preventative strategies and therapies can then be developed and tested.

**Theodore Jardetzky, PhD**

Stanford University  
Stanford, California

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$78,753

**Title:** Isolation of antibodies to prefusion EBV gB using humanized mice

**Summary:** Stanford University researchers are attempting to find antibodies that can block virus infection.

**Background:** Strong data link Epstein-Barr virus (EBV) infection with the development of MS. EBV is known to exist permanently in people in a latent form, with periodic reactivation leading to bursts of viral replication and an increase in viral load. It is possible this reactivation may trigger MS relapses and conversely, controlling EBV replication may reduce MS relapse severity. However, few antibodies targeting EBV have been isolated, and this possibility has yet to be tested clinically.

**The Study:** Using a protein known as EBV gB, Dr. Jardetzky and his team seek to identify novel antibodies that target EBV and that react better against the virus and could potentially be harnessed to alleviate MS symptoms. These antibodies will also be useful for both basic research and producing applied results, such as developing an EBV vaccine. The researchers will use complementary approaches that include mice whose immune systems have been “humanized.” This offers the ability to identify fully

human antibodies directly from these experiments, making them likely to be more usable for people.

**What is the potential impact for people with MS?** It is possible that therapies that suppress EBV activity in people with MS could help limit the immune responses to EBV proteins and disease activity. Anti-EBV antibodies developed by this work could also be useful for testing the theory that suppressing EBV will reduce disease symptoms and improve the quality of life for people with MS.

**Erin Longbrake, MD, PhD**

Yale University  
New Haven, Connecticut

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$110,000

**Title:** Epstein-Barr Virus in Patients with New Onset Multiple Sclerosis

**Summary:** Yale University scientists are exploring tissue obtained from people newly diagnosed with MS to determine what role EBV plays in activating the immune response in MS.

**Background:** Multiple sclerosis occurs when the immune cells attack the nervous system. There has been much speculation on the role of Epstein Barr virus (EBV) based on studies of populations at risk for developing MS. But the role of EBV is not clear; particularly, how it may trigger chronic disease in MS. Dr. Longbrake's team is looking specifically at throat tissue,

where EBV often presents itself, in people newly diagnosed with MS. They are determining whether this virus activates a process within immune cells in this tissue.

**The Study:** People who are newly diagnosed with MS will be recruited to provide paired blood and throat tissue samples. Samples from people without MS will be studied as well. Cells collected in this manner will be evaluated using cutting edge molecular and genetics technology.

**What is the potential impact for people with MS?** This study may open new avenues of understanding about the ways in which EBV may contribute to MS onset. This information may lead to a more complete understanding of how to stop MS in its tracks or even prevent it.

**Joseph Sabatino, MD, PhD**

University of California, San Francisco  
San Francisco, California

**Award:** Request for Applications

**Term:** 10/1/2023-9/30/2024

**Funding:** \$110,000

**Title:** Identification of viral-specific lymphocytes associated with novel autoantibody signature in multiple sclerosis

**Summary:** A team at UCSF is exploring a possible mechanism by which EBV may trigger the immune response that damages the nervous system in people with MS.

**Background:** Epstein Barr virus (EBV) has been strongly linked to the development of MS. However, the mechanisms by which EBV may contribute to MS remain poorly understood. Dr. Sabatino and colleagues suggest that infection with EBV leads to the activation of virus-specific immune cells, including B cells and T cells. These cells can then inappropriately injure components of the central nervous system.

**The Study:** The team has obtained immune cells from eight people with MS who share a unique pattern of antibodies against EBV-related proteins. B cells and T cells will be directly isolated from these individuals' blood samples, which have already been collected and stored. They will use a sophisticated technology that allows for the isolation of single immune

cells and identification of B cells and T cells specific for these viral proteins.

**What is the potential impact for people with MS?** Identifying immune cells that react to EBV could permit identification of individuals who are at risk for MS but are still without symptoms. For individuals with MS, these findings could permit the specific targeting of disease-relevant immune cells rather than broad immune suppression.