RESEARCH PRIORITY AREAS TO DRIVE BREAKTHROUGHS

The National MS Society invests in promising research to drive breakthroughs that will stop MS, restore function and end MS forever. To do this, we support collaborations and innovation, convene thought leaders, leverage new technologies and data, invest in training to ensure a robust future workforce, and learn from other diseases, funders and people living with MS. The following five focus areas are critical to advancing breakthroughs that will identify solutions for people living with MS today and ultimately lead to prevention and a cure.

**Define the contribution of genetics, risk factors and their modifiers to the risk for developing MS and disease course, and develop strategies to prevent, treat and cure all forms of MS “Why do some people get MS and others don’t?”**

Although tremendous progress has been made in identifying key biological pathways that contribute to MS risk, the cause is still unknown. Preventing MS for future generations requires a deep understanding of what triggers MS, how triggers lead to the development of the disease, and how to protect against it. High impact research areas include:

- Studying how pathogens, lifestyle factors and behaviors like diet and exercise, and environmental exposures impact the risk of developing MS and influence the disease course.
- Elucidating the role of the microbiome in MS risk and disease course
- Identifying additional risk variants and their epigenetic modifiers, and determining the genetic influence on clinical/imaging phenotype

**Understand MS pathology and pathophysiology “What is the cause of MS?”**

Much has been learned about immune system activity in the relapsing-remitting phase of MS and this knowledge has led to the development of effective disease-modifying therapies. Less understood is the relationship between initial immune activity and progressive neurodegeneration and how innate immunity participates in the progressive phase of MS. Identifying the causes of MS, and the underlying mechanisms and biological pathways involved in MS injury to the brain and spinal cord, will expose new targets for the development of treatments to stop the damage that causes disability. High impact research areas include:

- Clarifying the destructive and protective roles of the adaptive and innate immune system, including both infiltrating and compartmentalized cells
- Determining the causes of tissue injury at different stages of disease, and whether neurodegeneration and demyelination can be independent events in MS
- Determining how evolving MRI sequences relate to pathological changes in the central nervous system
- Leveraging big data and transformative technologies to identify and interrogate relevant biological pathways and clinical/demographic features that influence disability progression
Ensuring access to human central nervous system tissues/cells from MS patients and healthy controls for the purpose of gaining a thorough understanding of the neuropathology of MS

Understand and treat MS progression “How do we stop MS progression?”
MS progression often occurs early in the disease, even while the brain compensates for injury and even in people successfully treated for relapses. Progression is not easily measured and usually happens over long periods of time, making it hard to quickly detect whether a therapy is impacting the course of disease. This has made the development of therapies for progressive stages of MS a challenge. Diagnosing progressive disease based on biomarkers, in addition to clinical presentation would enable the testing of therapies earlier, promising better ways of protecting the nervous system from MS injury. High impact research areas include:

- Determining the specific pathologic underpinnings of MS progression
- Identifying objective indicators of disease activity that mark the transition to progression, measure treatment impact, and predict an individual’s course and response to therapy
- Determining mechanisms underlying the causes of progression in the absence of acute inflammation or relapses, the transition from relapsing to secondary progressive MS, and whether primary progressive and secondary progressive MS have similar biological underpinnings
- Developing better animal models that recapitulate human pathology to inform the study of the mechanisms underlying MS and progression
- Developing tools that allow better treatment decision making and personalized medicine, including therapy risks/benefits
- Testing approaches for the prevention and treatment of MS progression including repurposed/repositioned FDA-approved therapies, impact of early aggressive treatment vs. step therapy, and cell-based therapy

Identify strategies for neuroprotection and nervous system repair
“How do we repair the damage caused by MS?”
The hopes of people living with MS today rest on finding a way to stop disease worsening by preventing neurodegeneration and reversing the damage to restore lost function. The brain can repair myelin and also rewire itself around damaged areas, but in order to significantly impact disease, this natural ability needs to be enhanced. In addition to developing treatment strategies, there is a crucial need for non-invasive ways to determine quickly whether neuroprotective and repair strategies are working. High impact research areas include:

- Exploring remyelination and neuroprotective therapies (including stimulation of endogenous repair and cell-based approaches) and testing whether they have synergistic benefit with immune modulatory therapies
- Developing imaging biomarkers that detect demyelination/remyelination of white and gray matter and better outcome measures to track neuroprotection and repair
- Determining the extent that individuals’ behaviors (e.g. rehabilitation and exercise) can promote repair and plasticity
Elucidate the cause of MS symptoms, the impact of comorbidities, and identify rehabilitation, wellness behaviors and lifestyle approaches that impact disease course, symptoms and overall health. “How do we reverse symptoms and promote wellness?” Emerging evidence suggests that wellness behaviors and lifestyle factors can influence the risk for developing MS, disease course, severity of symptoms and quality of life. Finding ways to understand and address the variable and unpredictable symptoms caused by MS will have a profound impact on people’s quality of life. In addition, people with MS often live with other chronic medical conditions. Understanding how these other health conditions affect MS disease course and symptoms represents an important research opportunity. Focusing on opportunities to improve the design and conduct of clinical trials and providing strategies people can incorporate to enhance their wellbeing should be emphasized. High impact research areas include:

- Studying the impact of dietary interventions, supplements, and complementary approaches on the course of disease and quality of life
- Determining the optimal study designs, regimen, and safety of exercise/physical activity and rehabilitation approaches
- Determining the effectiveness of behavioral interventions such as mindfulness, resilience, positive psychology, problem solving, yoga, stress reduction and other strategies on disease activity and emotional health
- Understanding the cause and exploring potential treatment approaches to address symptoms including pain, spasticity, incontinence, sexual dysfunction, fatigue, cognitive impairment, and symptoms caused by lack of mobility
- Revealing the potential of adaptive technologies and advanced rehabilitation strategies
- Identifying causes of depression, anxiety and other emotional health issues in MS, and the best approaches to treatment and suicide prevention
- Assessing the effects of co-morbidities, aging and symptoms on disease course and related economic/life impacts
- Testing strategies to enhance health care access and quality to improve the lives of people living with MS