Plain Language Description
This summary will explain the details of your project to people without a scientific background who are affected by MS. It is used by our Community Review of MS Research Committee, nonscientists who review the plain language description and provide a score for relevance to MS.

Of Note:
- Please define terms that are not lay-friendly. For example, dendritic cells (immune cells that present fragments of foreign molecules to other immune cells).
- Please spell out abbreviations at first use. For example, “myelin oligodendrocyte protein” rather than “MOG.”
- Please avoid using judgmental phrases such as “suffers from” MS, or “MS victim.”
- Please have non-scientists read your plain language description to get feedback before submitting, to ensure that it is understandable.

Your response to each question should be no more than 1800 characters (with spaces - about 300 words).

What is the problem related to multiple sclerosis that you are addressing with this project? Please share your overall hypothesis(es) in plain language.

How do you propose to address the problem? Please summarize your aims using plain language.

Describe the steps that you are taking to achieve these aims. Please be specific about the experiments you are conducting, and whether studies involve humans (with cohort details such as age, race, gender, etc.), models of MS, or cell cultures (human or animal).

For studies that include people, please describe what is involved for participants in this study (number, frequency, and timing of visits; physical examinations; clinical measures; sample retrieval; imaging scans; symptom recording; etc.).

How might the results of this study potentially make life better for people affected by multiple sclerosis? Please include a time frame.

Following are three examples of plain-language summaries of basic science, rehabilitation, and epidemiology studies. For additional resources, you may:
- download a slide deck of tips about writing about research in plain language, or
- visit this website for tips on plain language writing and readability from the Multi-Regional Clinical Trials Center of Brigham and Women’s Hospital and Harvard
Example 1 – Basic Science

What is the problem related to multiple sclerosis that you are addressing with this project? Please share your overall hypothesis(es) in plain language.

Diagnosis and treatment of MS remain challenging, in part because there is no single laboratory test that can identify whether a person has MS, or predict a person’s expected disease activity in the future. Researchers have been working to identify “biomarkers,” or biological signals, that could serve as indicators or predictors of MS. Myeloperoxidase (MPO) is a protein found in large amounts in MS lesions and contributes to tissue damage. We hypothesize that MPO promotes active disease in MS by causing damage to the nervous system, including nerve-insulating myelin, and by sending signals that promote the initial stages of inflammation. We have shown that MPO activity can be tracked noninvasively using a technique that allows us to examine this phase of inflammation for the first time. Now we are working to confirm MPO’s role in MS-like disease activity, track its levels noninvasively during different disease stages, and to find ways to inhibit its effects. The results may yield a biomarker that can track and predict disease activity in MS, and present a target for novel therapeutic strategies.

How do you propose to address the problem? Please summarize your aims using plain language.

Our goals are to (1) to investigate whether using magnetic resonance imaging (MRI) to locate MPO in the brain can be used as a biomarker of disease activity in mice with progressive and relapse-remitting MS-like disease called EAE, 2) to understand the relationship between myeloperoxidase signaling and early immune system activity and damage to myelin (the substance that insulates nerve fibers and is a target of the immune response in MS), (3) to study whether experimental treatments can reduce myeloperoxidase signaling and thereby inhibit disease activity in progressive and relapse-remitting mouse models. These well-studied mouse models represent specific aspects of MS in people, and have proven valuable for assessing the potential of therapies before they are brought to human clinical trials.

Describe the steps that you are taking to achieve these aims. Please be specific about the experiments you are conducting, and whether studies involve humans (with cohort details such as age, race, gender, etc.), models of MS, or cell cultures (human or animal).

Mice will be examined in a series of experiments. The relapsing-remitting mice with be examined during relapses and remissions, and the progressive mice during onset of disease and chronic phases. Weights will be recorded daily. Clinical assessment for disease activity will be performed daily using a five-point scale of disease activity. MRI scanning will be performed 1 day after the onset of symptoms, then at remission, and again at 1 day after the next relapse (or for progressive disease, at chronic stage). We will track disease-related fluctuations of MPO levels. We will also inject MPO into mice at various timepoints and then observe its effects using imaging and also studying the tissues themselves postmortem. We will watch the effects on specific immune cells and also on damage to the brain and spinal cord. We will investigate the relationship between imaging data and data obtained by examining the tissues themselves. We also will examine how certain experimental treatments affect MPO activity by administering them to the mice and then tracking the results. To avoid experimental bias, blinding will be performed by assigning each mouse to a treatment group randomly. Those performing the outcome measurements will be blinded as to the group assignment of the mice.
For studies that include people, please describe what is involved for participants in this study (number, frequency, and timing of visits; physical examinations; clinical measures; sample retrieval; imaging scans; symptom recording; etc.).
N/A

How might the results of this study potentially make life better for people affected by multiple sclerosis? Please include a time frame.
These results may lead to the development of MPO as a biomarker that can enable the earlier detection of MS using a noninvasive test. Earlier diagnosis may improve outcomes by enabling earlier treatment to stop the advance of the disease. If the research is successful, these potential results could come to fruition within ten years. In addition, this work also may open up new treatment strategies that target MPO-mediated brain inflammation. This could ultimately lead to better treatments that may slow or stop the process of brain damage and better address progressive stages of MS.

Example 2 – Rehabilitation

What is the problem related to multiple sclerosis that you are addressing with this project? Please share your overall hypothesis(es) in plain language.
Many people with MS may eventually experience difficulty with walking. The term “gait” refers more specifically to the manner or pattern of walking (for example “unsteady gait“). Studies suggest that half the people with relapsing-remitting MS will need some assistance with walking within 15 years of their diagnosis. Gait problems in MS are caused by a variety of factors. MS frequently causes fatigue, which can limit walking endurance. MS damage to nerve pathways may hamper coordination and/or cause weakness, poor balance, numbness, or spasticity (abnormal tightness of muscles). Problems with vision or thinking and information processing can also interfere with walking. Concerns about falling and fears of appearing impaired in public cause problems too, sometimes leading to social isolation. Some approaches to assisting walking have been shown to improve strength, balance, coordination and/or gait in persons with MS who have significant mobility impairments. These approaches include body-weight supported treadmill and conventional over-ground walking training, but generally their benefits have been short-lived. For this reason, we have been investigating the potential of a robotic device that fits over torso to provide motorized assistance to move the hip and knee joints during walking. The result is a walking pattern guided by robotics with less exertion and physical demand in the upper body. As exoskeleton home units may be available to people with MS in the near future, such training could offer longer-term solutions for improving walking ability and exercise maintenance.

How do you propose to address the problem? Please summarize your aims using plain language.
The primary objective of this study is to test the feasibility of an exoskeleton-assisted walking for persons with advanced MS. We define a feasible intervention as one that is (a) accessible and safe, (b) tolerable, (c) acceptable, and (d) learnable. Secondarily, we will collect pilot data to assist with planning and implementing future and larger studies to determine the effectiveness of exoskeleton-assisted walk training.
Describe the steps that you are taking to achieve these aims. Please be specific about the experiments you are conducting, and whether studies involve humans (with cohort details such as age, race, gender, etc.), models of MS, or cell cultures (human or animal).

Since this is a preliminary study, we plan to recruit only 12 eligible participants who have been diagnosed with any form of multiple sclerosis who have an EDSS score 5.0 to 7.5 (this indicates disability ranging from severe enough to impair full daily activities, to unable to walk beyond approximately 16 feet with or without aid). Those with uncontrolled cardiovascular conditions (i.e., heart failure, angina, hypertension), osteoporosis, or other conditions with risk of bone fracture from weight bearing will be excluded for safety reasons.

Participants will be scheduled for 8 weeks of exoskeleton-assisted walking instruction at 3 sessions per week. We will track compliance and accessibility by participation (eligibility, enrollment, and attendance), and reasons for non-participation (late or missed sessions, and study drop out). We will also monitor for potential adverse events. Participants will be measured for exercise duration and intensity (heart rate, blood pressure, and perceived exertion) during each session, and evaluate trends in these parameters over time. Before and after the training, we will measure walking speed and ability using the timed “up and go” test, which measures the time it takes to stand up from a chair, walk briefly, and then sit down. We also will measure patient-reported outcomes, including changes in spasticity (extreme muscle tightness), pain, sleep disturbance, and fatigue, using validated questionnaires.

For studies that include people, please describe what is involved for participants in this study (number, frequency, and timing of visits; physical examinations; clinical measures; sample retrieval; imaging scans; symptom recording; etc.).

Participants will be required to travel to the center to receive 8 weeks of exoskeleton-assisted walking instruction sessions 3 times per week. Sessions will include instruction on how to put on and take off the device; sit-to-stand and stand-to-sit maneuvers; balance and fall protection training; walking on smooth (up to 30 min, 60 min, or 90 min as tolerated) and rough surfaces; turns; managing doors, elevators, and cupboards, and stopping on command. Most sessions will last from 1 to 2 hours, but participants can rest as needed or stop a session at any time. Walking tests and questionnaires will be administered before the first session and at the end of the last session.

How might the results of this study potentially make life better for people affected by multiple sclerosis? Please include a time frame.

We expect to have results from this study within two years. If the results of this study show exoskeleton-assisted walking to be safe, we will use the results to design a larger study that can determine its effectiveness at improving walking and other MS symptoms. This likely will take five years to complete. A demonstration of successful exoskeleton walking in MS may translate into a new rehabilitation treatment modality and a means of independent home or community exercise and/or independent ambulation for individuals with MS. This pilot study will examine the feasibility of exoskeleton-assisted walking for persons with MS, and will inform the design decisions for more robust studies to examine its effectiveness.
Example 3 – Epidemiology

What is the problem related to multiple sclerosis that you are addressing with this project? Please share your overall hypothesis(es) in plain language.

Multiple Sclerosis (MS) is a common immune-mediated disorder that involves immune attacks and inflammation in the brain and spinal cord (collectively they comprise the central nervous system). The cause of MS remains subject to intense investigation. Many common genes have been linked to susceptibility to MS, but carrying MS-linked genes alone does not mean a person will develop MS. Other factors, such as lifestyle and environmental factors, are also thought to play a triggering role.

Exposure to air pollution (an environmental factor) has been implicated in a wide variety of diseases, such as heart disease and stroke, and it is thought to cause inflammation and other negative effects in the body. However, the effects of air pollution on diseases of the central nervous system have not been thoroughly explored. Although some research has linked air pollution to higher rates of MS relapse, no study has answered the question of whether air pollution affects the risk of developing multiple sclerosis. Our team proposes to evaluate whether exposure to a specific type of air pollution, known as particulate matter, may increase susceptibility to developing MS. Particulate matter is a mixture of extremely small particles and liquid droplets, of different sizes and can be made up of many components, including acids, organic chemicals, metals, and soil or dust particles. Our hypothesis is that air pollution may be one of the triggering factors that contribute to making a person susceptible to developing MS.

How do you propose to address the problem? Please summarize your aims using plain language.
We will conduct a large study of particulate matter exposure and MS risk using two existing cohorts (study groups that are being followed over time). These cohorts include hundreds of thousands of women in the Nurses Health Study (followed from 1998 through 2004) and the Nurses Health Study II (followed from 1988 through 2007). The study participants periodically reported their residential addresses throughout the study, as well as their health status, including whether they developed MS. Air pollution measures for each woman in the study are derived from their residential address using a geographical information system. We will link individual places of residence at different ages with location-specific air pollution levels, and examine whether air pollution levels are related to risk of developing MS.

Describe the steps that you are taking to achieve these aims. Please be specific about the experiments you are conducting, and whether studies involve humans (with cohort details such as age, race, gender, etc.), models of MS, or cell cultures (human or animal).
This study involves the careful use of statistical methods to explore possible linkages between exposure to air pollutants, different timeframes, and the health outcomes of the Nurses Health Study participants. The identity of the participants is not revealed so their privacy is preserved. Using accepted statistical modeling techniques, we will evaluate the cumulative average exposure to different sizes of particulate matter pollutants up to the time of onset of MS, and compare highest exposures to lowest for contrast, and compare these factors in women who developed MS and those who did not. We will also do analyses restricted to women who did not move during the course of their time in the Nurses Health Study. We will conduct additional analyses to understand the possible influences of smoking status, region of residence the US, and age. Using accepted methods of analysis, we will adjust findings for participants’ age, ancestry, smoking status, body mass index at age 18,
region of residence, population density, latitude at age 15, and ultraviolet index of their residence. The purpose of this adjustment is to try to mitigate the possible influence of other possible risk or protective factors linked to MS, such as adolescent obesity (risk), tobacco smoking (risk), and exposure to UV light (protective).

For studies that include people, please describe what is involved for participants in this study (number, frequency, and timing of visits; physical examinations; clinical measures; sample retrieval; imaging scans; symptom recording; etc.).

This study uses previously collected data about the study participants, so there will not be any clinic visits or other activities required of them.

How might the results of this study potentially make life better for people affected by multiple sclerosis? Please include a time frame.

Since air pollution is already known to contribute to many other health issues, these results could bolster the argument for major public health initiatives and legislation to reduce sources of air pollution. This impact could occur within a few years of the conclusion of this study.

Longer term, understanding what causes MS is critical for finding better ways to treat it and even to prevent this disease in future generations. If air pollution is identified through this and other studies as a definite risk factor that contributes to the cause of MS, it would open the door to scientists who could try to trace the biological mechanisms and pathways that underlie this risk. This in turn could uncover new ways to prevent the biological events that lead to MS, and also possible ways to stop the events in people who already have the disease.