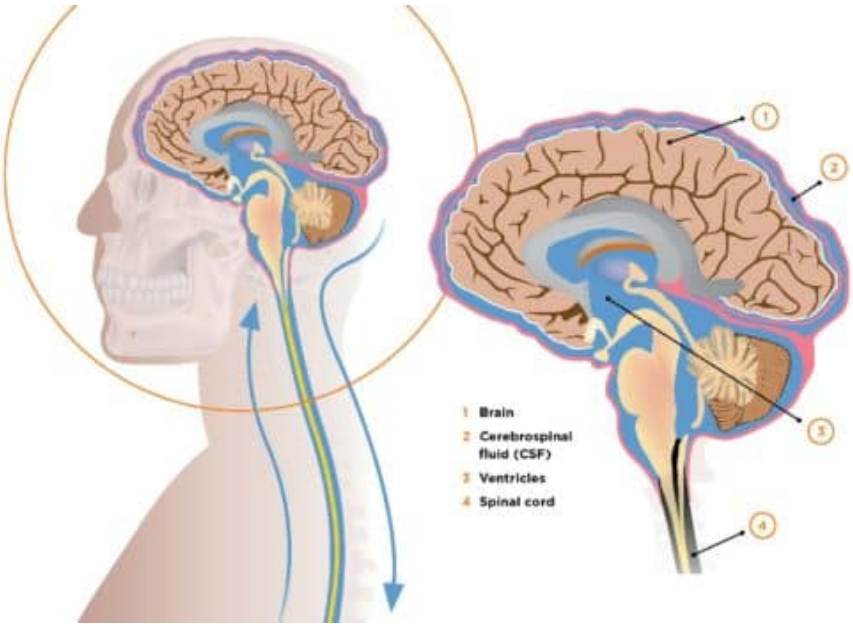
Varied response



Barancik Prize winner focuses on how different treatments affect people with MS.

by Mary E. King, PhD

Amit Bar-Or, MD, and his team have devised a novel platform for studying immune cells.

Amit Bar-Or, MD, has received the 2022 Barancik Prize for Innovation in MS Research for his work focusing on how people with multiple sclerosis will respond to various treatment

options.

Bar-Or is the Melissa and Paul Anderson President's Chair, professor of neurology, at the University of Pennsylvania's Perelman School of Medicine in Philadelphia, where he serves as chief of the Division of Multiple Sclerosis and Related Disorders. He also is founding director of the Center for Neuroinflammation and Neurotherapeutics.

Bar-Or and his team have devised a unique approach to tease out the important differences in immune responses among people with MS, including the use of what he calls a novel "precision neuroimmunology platform." This platform is a set of highly specialized measurements of immune cells and how they respond in various situations: for example, in the presence of an MS therapy.

Their goals are to learn more about MS, who will respond to different medications and if and when therapy could be safely stopped in an individual — that is, to stop MS. "We want to ultimately predict and monitor the best options for each individual person with MS," Bar-Or says. "What should we initiate, and when might we switch or stop treatments? And, importantly, can we achieve a safe, durable remission?"

Bar-Or brought an interest in both neurosciences and immunology to the treatment of MS during his medical residency. He realized that MS could affect relatively young people just starting their professional careers. This differentiated MS from some other neurological diseases, like Alzheimer's disease, that mostly affect older people.

At the time, MS also had only recently been reclassified from a completely untreatable condition to one that could be partially treated, he says. Bar-Or realized how much more research was needed, especially to stop disease progression. He began to focus his research on MS, while continuing to look at how discoveries in MS can help, as well as be informed by, studies of other neurologic and immune-mediated diseases.

The precision neuroimmunology platform

Bar-Or's precision neuroimmunology platform uses both blood and cerebrospinal fluid (CSF). CSF is a clear fluid that surrounds the brain and spinal cord and cushions them from injury. Studying the two compartments can provide complementary information. While studying CSF and its cells can be particularly informative, it requires lumbar puncture, which is not always practical to do repeatedly, in contrast to blood sampling, which can allow researchers to analyze many more samples over time, he says.

Bar-Or's approach to testing how an individual's immune system behaves is innovative in another way, as well. He points out that most of our immune cells are relatively quiet most of the time, but they activate in tissues when an immune response is triggered. So, looking at a simple blood test is not enough.

What is the Barancik Prize?

The Barancik Prize for Innovation in Research was created in 2014 by the Charles and Margery Barancik Foundation and is administered by the National Multiple Sclerosis Society. Chuck and Margie Barancik were also major personal supporters of MS research projects for more than 20 years. They developed the Barancik Prize to recognize exceptional scientists who have demonstrated outstanding innovation and originality in MS research. Barancik Prize winners receive $100,000 that can be used at their discretion.

Instead, Bar-Or's platform evaluates how the immune cells respond to something that triggers an immune response. They do this in one of two ways: They can take a blood or CSF sample from any individual and activate the immune cells in the laboratory, or the immune cells can be activated while still inside an individual in response, for example, to an MS therapy or vaccination. Importantly, by measuring the responses of not just one cell type, but multiple cell types at the same time, they can study which immune cells respond and how each type of immune cell behaves. For example, one cell type might respond by releasing molecules that affect another type of immune cell, perhaps causing the second cell type to be more active or slowing/stopping its activity in ways that are relevant to MS.

As they learn more about what happens in the blood or CSF sample, Bar-Or's team is using this information to add more tests and to refine the existing tests.

"The process of how we measure and what we measure is the product of many years of work not just by us, but also by many others trying to understand the different immune abnormalities that can contribute to MS," Bar-Or says.

Bar-Or and his colleagues can also follow individual patients before and during treatment with an existing therapy or during a clinical trial. In this way, they learn how an individual's immune system changes over time with the introduction of a treatment. Bar-Or's approach allows researchers to see how various parts of an individual's immune system respond to that treatment and compare this spectrum of results to what is seen in other individuals with MS. He explains that the best opportunity to do this is during clinical trials of a proposed therapy, when they can evaluate all the clinical trial data together, including imaging and other testing.

Impact on clinical trial design

By studying people with MS in this way during clinical trials, Bar-Or hopes to expand what is known about how and why various individuals respond differently to a new treatment in a more detailed and nuanced fashion than simply observing MS symptoms or changes seen on an MRI.

"It has been gratifying to see efforts like ours contribute to changing the culture of clinical trials," he says. "Sponsors are now realizing the importance of building in carefully designed

biological assessments in trials going forward. We can recognize and study immune responses to a new therapy across the study participants during the trial and provide additional valuable information about both the new therapy as well as MS.

“Using this type of platform to study immune responses in people who don’t have MS also contributes to our knowledge,” Bar-Or says. “And because the animal models of MS only approximate the human form of the disease, we think that studying the condition in humans with MS and non-MS controls gives us the best sense of the variability of responses across individuals in health and disease. We need to understand the wide range of healthy immune diversity in addition to the range of responses in those living with MS.”

Pandemic challenges

Bar-Or says the pandemic affected his laboratory in two ways.

“The pandemic had a major impact on any patient-facing research,” he says. “Our studies of patient samples came to a near-standstill, so we initially focused on laboratory work without human participants to keep patients and staff as safe as possible. Like many others, we dealt with back orders and problems getting certain supplies, too. But it brought out a great deal of creativity, including the ability to get things done with less.”

Bar-Or says the pandemic also taught everyone how to pivot research quickly to focus on what is important to people with MS, such as vaccines.

“I never thought we would be viewed as experts in vaccinology, but we learned a tremendous amount about vaccines in people with MS, including those on various therapies,” he says.

Research in general is still in a flux, with some aspects back to the way things were before the pandemic, but with other changes still in place indefinitely, such as wearing masks and staffing the lab in shifts to allow for distancing.

Support for the nomination

V. Wee Yong, PhD, professor at the University of Calgary, Canada research chair in Neuroimmunology, and director of the Alberta MS Network, supported Bar-Or’s nomination for the Barancik Prize, stating, “He is now internationally recognized as one of the top MS clinician-scientists worldwide and one of the premier authorities on the immunology of B cells.”

Yong points to the precision neuro-immunology platform in particular. “These investigations have enabled Bar-Or to be a world leader in the profiling of an individual’s functional immune response,” Yong says. He adds that Bar-Or has used this platform to provide novel insights into the biology of MS and the changes to the immune system that occur as the disease evolves in an individual.

“His scientific, clinical and translational neuroimmunology and leadership contributions place him as one of the most impactful researchers on MS currently and for the foreseeable

future.”

Future research

Bar-Or emphasizes his long-term goal of stopping MS.

“One of the holy grails of research in autoimmune disease is to get the immune system back to a state where it is no longer injuring the patient,” he says. “We want to achieve durable remission in each person, so they no longer need to be continuously treated, to stop MS while eliminating the burden and risks of chronic treatment.”

He hopes his team’s approach, including the precision neuroimmunology platform, will contribute to further understanding an individual’s needs for treatment and the selection of therapies that can help each individual attain a durable remission.

Mary E. King, PhD, is a freelance medical writer in Boulder, Colorado.