The next frontiers of MS research

Emerging treatments are increasingly looking to existing therapies and adapting them for use in MS.

by Mary E. King, PhD

Intriguing clues about possible new therapies for multiple sclerosis were presented at a recent American Academy of Neurology (AAN) meeting. MS researchers are still buzzing about studies that investigated repurposing certain therapies, currently used for other conditions, as MS treatments. Here's a look at some of the most promising research presented in that meeting. Stay tuned for results from this year's meeting, happening later this spring.

Eyeing vitamin A cousins

An experimental oral treatment—currently known as IRX4204—has a chemical structure similar to vitamin A. Researchers say that IRX4204 may slow or prevent inflammation and promote the repair of myelin that has already been damaged by immune attacks in MS.

"Naturally occurring vitamin A–like molecules, called retinoids, are known to be critically important for controlling the fate of immune system cells, [including] autoimmunity," explains Randolph Noelle, PhD, professor of microbiology and immunology at the Geisel School of Medicine at Dartmouth in Hanover, New Hampshire.

"In our study, we found that IRX4204 partially suppresses disease in a mouse model of MS called experimental autoimmune encephalomyelitis, or EAE."

Dr. Noelle, senior investigator on the study, adds, "We are beginning to understand what

retinoids do normally in humans, and now we have more active drug forms [like IRX4204] that may allow us to maneuver the immune system the way we want."

Dr. Martin Sanders
Photo courtesy of Dr. Martin Sanders

Dr. Martin Sanders, chairman and CEO of Io Therapeutics, which developed IRX4204, highlights two other key findings from the studies his company sponsored. First, "IRX4204 gets into the brains of healthy rats [in about the same concentration that] it shows up in the blood," a sign of excellent brain penetration, he says. Second, he says, "The treatment increased the production of myelin in a genetic model of rat cells."

If these IRX4204 results can be replicated in clinical trials in people with MS, "this one-two punch could be a powerful combination that would both stop immune responses that lead to nervous system damage and also repair what has been lost," notes Bruce Bebo, PhD, executive vice president of Research at the National MS Society.

Repurposing a cancer therapy
Researchers often look at current treatments to see if they may be helpful for other diseases. For example, a biological agent called ofatumumab targets and eliminates a type of white blood cell called a B cell, and is used to treat B cell cancers. Some studies suggest B cells also may play a role in MS disease activity. One recent trial tested ofatumumab in people with relapsing-remitting MS.

Dr. Amit Bar-Or

Photo courtesy
of Dr. Amit
Bar-Or

Dr. Amit Bar-Or, a neurologist and neuro-immunologist at the Montreal Neurological Institute and Hospital, is principal investigator of this new study, which compared multiple doses of ofatumumab versus placebo in 232 people with relapsing-remitting MS. Ofatumumab caused a 65 to 90 percent reduction in the number of new active brain lesions detected by MRI compared with those in the people who received placebos. Dr. Bar-Or explains that these results suggest that targeting B cells is a very promising approach for further investigation of MS treatments.

“A unique aspect of this study is the exciting demonstration that substantial benefit can be obtained with doses that only partially remove B cells,” Dr. Bar-Or says. “Confirming these results in larger studies will not only highlight the important role of particular subsets of B cells in MS but also guide a new research approach. It may be possible to selectively target B cell subsets, which would allow us to achieve maximal benefit with minimal impact on the immune system.” (B cells play an important role in the healthy immune system, so removing all of them with a medication can cause other problems.)

A cholesterol treatment for progressive MS
A therapy that is known to lower cholesterol levels may also have a role in reducing brain atrophy (shrinkage) in MS.

Studying statins

A clinical trial randomly assigned 140 people with secondary-progressive MS to receive either the cholesterol-lowering drug simvastatin or placebo. Those who received simvastatin had a significantly lower rate of brain shrinkage—43 percent lower, in fact—than those who received placebo.

Rates of brain atrophy per year:

0.288%

Simvastatin group

0.584%

Placebo group

Dr. Jeremy Chataway
Photo courtesy of Dr. Jeremy Chataway

At the AAN meeting, Dr. Jeremy Chataway, consultant neurologist at the National Hospital for Neurology and Neurosurgery, University College London Hospitals, along with his colleagues, provided results from a seven-year study in 140 people with secondary-progressive MS. (The research was also reported more fully in The Lancet in June.) Half the group received a statin (in this case, simvastatin, also known by its brand name, Zocor®) and half received a placebo in a double-blind trial—a type of study in which neither the participants nor the researchers know who received the investigated medication or the placebo until the study is over.

The rate of brain atrophy was slower in the people who took the statin daily, compared with those who took the placebo, a very encouraging result in a disease course that has very few disease-modifying treatments. “It reduced the rate of shrinkage by about 40 percent, which is really quite dramatic,” Dr. Chataway says. “Simvastatin may therefore have a neuroprotective role. Another possibility is that it has a protective effect on blood vessels; we’re not sure, and further work will be done.”

And even though the trial was designed to specifically evaluate brain atrophy, researchers noted slowing in some measures of disability progression, as well. Those who took the statin

received it at a very high dose—double the maximum level normally prescribed to lower cholesterol—but they tolerated it well.

Dr. Chataway is cautiously optimistic about the results of this study. “Even though brain atrophy has been linked to disability in MS, of course we need to make sure this can definitely translate into clinical benefit,” he says. “This will require a large, randomized phase 3 trial to thoroughly test the safety and efficacy in a much larger number of people with secondary-progressive MS.”
He stresses that, at this point, even though the study results are promising, there is not enough evidence to recommend treatment of MS with statins.

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For more on these and other emerging therapies, visit nationalmssociety.org/aan2014.