Immune System May Be a New Target for Slowing ALS

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Host: ALS Association Chief Scientist Lucie Bruijn, Ph.D.
Guest Speaker: Howard Weiner, M.D.

Our body’s immune system protects us from infection. But when it is overactive, or is focused on the wrong target, it can cause harm, as it does in the immune disease multiple sclerosis (MS). Does the immune system also cause problems in ALS? That’s the hypothesis of Howard Weiner, M.D., who spoke in a recent ALS Association webinar about his work. Dr. Weiner is Professor of Neurology at Harvard Medical School, with a long career as a researcher in MS. Recently, he has turned his attention to ALS, to try to understand how cells of the immune system may be damaging motor neurons.

“Dr. Weiner’s knowledge in the field of multiple sclerosis is very valuable to us in ALS,” said ALS Association Chief Scientist Lucie Bruijn, Ph.D., who hosted the webinar. “The Association has funded Dr. Weiner’s search for a marker in the bloodstream that may reveal the involvement of the immune system in the disease.”

In the central nervous system (CNS), motor neurons are protected by cells called microglia. Microglia are similar in many ways to immune system cells in the periphery (that is, outside the CNS), especially in their ability to send and receive chemical messages to other immune cells.

A major advance from Dr. Weiner’s lab was the development of a way to distinguish microglia from immune cells called monocytes, which enter the CNS from the bloodstream and are in many ways similar to microglia. The ability to tell these two types of cells apart led them to observe that microglia release an attractant chemical (“like a perfume,” Dr. Weiner said) that attracts monocytes to come into the CNS. Once there, they can be harmful to motor neurons.

“Our basic observation is that the monocytes coming out of the bloodstream go into the spinal cord and cause damage,” he said. “We want to stop them.” While his team originally observed this phenomenon in ALS mice, they have since seen similar behavior in the immune systems of ALS patients.

“We think this opens up a new therapeutic avenue for the treatment of ALS.” By stopping the infiltration of the monocytes, or by altering their behavior to be less harmful, it may be possible to slow the disease. “Monocytes aren’t the whole story in ALS, but they appear to be part of the story.”

Dr. Weiner has begun to focus on two important molecules made by the monocytes that influence their behavior. One, called Ly6C, appears on the surface and seems to appear in the monocytes that do the most damage. That raises the possibility that blocking the molecule with
a drug may be therapeutic. In Dr. Weiner’s lab, they have early results showing that such a strategy may be promising.

The second molecule, called miRNA-155, occurs within the cell and also seems to be involved in promoting damage. It was observed that reducing the monocyte’s ability to make miRNA-155 increased survival dramatically in ALS mice. “This gives us another target, after Ly6C,” Dr. Weiner said.

“These discoveries provide some very exciting leads for developing new therapies,” Dr. Bruijn agreed.

Finally, Dr. Weiner noted, since the monocytes occur in the periphery before they enter the CNS, they may be a useful and simple-to-measure biomarker for the progression of the disease. That could be valuable for tracking response to new therapies, even if monocytes themselves aren’t targeted.

The full webinar can be viewed by clicking on this link: https://alsa.webex.com/alsa/ldr.php?AT=pb&SP=MC&rID=65893192&rKey=88f6eb79aee923cc

Those interested in the details of Dr. Weiner’s research can obtain a copy of a recent scientific paper by emailing Dr. Bruijn at researchupdate@alsa-national.org