

Medical Update Memo

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Molecule Strikes Balance in Immune System and May Be Key to Autoimmune Attack in MS

SUMMARY

Researchers funded by the National MS Society and others report that a molecule called the aryl hydrocarbon receptor – which helps the immune system respond to environmental toxins – seems to regulate the balance between inflammatory and anti-inflammatory cells in MS-like disease in mice. The results may eventually help tease out the effects of environmental factors that may trigger the launch of autoimmune attacks against the nervous system in MS.

Details

Francisco J. Quintana, PhD, Howard Weiner, MD (winner of the 2007 Dystel Prize for MS Research) and colleagues at Harvard Medical School, Boston, report their findings in *Nature* (2008 May 1;453[7191]:65-71). This study was funded by the National MS Society and the National Institutes of Health among others. Marc Veldhoen, PhD (MRC National Institute for Medical Research) and colleagues report similar findings in a separate article, funded by the Medical Research Council UK (2008 May 1;453[7191]:106-9).

Multiple sclerosis occurs when the immune system attacks the brain and spinal cord. The disease is thought to occur when individuals whose genes make them susceptible encounter some unknown triggering factor in their environment. Numerous cells and proteins participate in the immune attack. Immune cells called T helper 17 (Th17) cells incite inflammation, whereas T reg cells are regulatory cells that can suppress the attack. In people with MS, however, T reg cells fail to do their jobs, and the attack goes unchecked. A molecule called aryl hydrocarbon receptor (AHR), best known for regulating the immune response to toxins such as dioxin, exists on the surface of both Th17 cells and T reg cells; previous research indicates

that it may play a role in their interaction.

Working separately, the two research teams studied AHR in mice with EAE, an MS-like disease. Dr. Veldhoen's group found that inducing EAE in mice lacking AHR reduced the number of Th17 cells, without increasing the number of T reg cells. Dr. Quintana's group showed that the results of activating AHR in EAE depended on the toxin used for activation. In mice given dioxin, T regs increased their regulatory activity, decreasing the capabilities of Th17 cells and suppressing EAE. In mice given FICZ (another toxin), Th17 cells increased their activity and EAE worsened.

Taken together, the results may eventually help tease out the effects of environmental factors that may trigger the launch of autoimmune attacks against the nervous system in MS. In an accompanying editorial, Drs. Emily Stevens and Christopher Bradfeld (University of Wisconsin, Madison) explain that the therapeutic ramifications of these findings, although intriguing, are still unclear. The key may lie in discovering why different chemicals affect AHR differently, which may mimic cues that a developing T cell receives from the environment. This understanding is crucial to applying these findings to therapeutic strategies for autoimmune diseases such as MS.

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