TSPO — a biomarker of brain injury and inflammation

By Tara Ann Cartwright

Tomas Guilarte, Ph.D., addressed NIEHS scientists Sept. 10 as part of the Inflammation Faculty Seminar Series. Guilarte’s talk, “TSPO: A Biomarker of Injury and Inflammation in the Brain and in Other Organ Systems,” addressed the potential of translocator protein (TSPO) to indicate inflammation in organs. The protein is a known biomarker of brain inflammation and can be detected through noninvasive testing.

The Inflammation Faculty was organized following the NIEHS 2012-2017 Strategic Plan, which designated inflammation as one of six high-priority areas of focus across the institute (see story). Guilarte’s seminar was co-hosted by Inflammation Faculty members Mamta Behl, Ph.D., toxicologist in the NIEHS Systems Toxicology Group, and Andrew Rooney, Ph.D., deputy director of the National Toxicology Program (NTP) Office of Health Assessment and Translation and co-coordinator of the group.

Both Behl and Rooney were intrigued by Guilarte’s research, because of the potential use of TSPO as a marker of inflammation caused by exposure to environmental chemicals. “TSPO is an exceptional biomarker of brain injury, which may have potential for assessing inflammatory damage in multiple organ systems,” Rooney said.

**TSPO detectable with PET scan**

Guilarte is a longtime NIEHS grantee, and professor and chair of the Department of Environmental Health Sciences at the Columbia University Mailman School of Public Health. He and his team have successfully developed and validated TSPO as a clinical biomarker for brain injury and neurodegeneration. The protein is involved in the translocation of cholesterol from the outer to the inner mitochondrial membrane, a prerequisite for steroid synthesis. Under normal physiological conditions, expression of the protein in the brain is relatively low. However, when cerebral inflammation is triggered by brain injury, TSPO expression increases markedly in activated glial cells, especially in the microglia and astrocytes.

TSPO levels can be detected in vivo by positron emission tomography (PET), thus providing researchers such as Guilarte with a real-time picture of where inflammation caused by injury occurs in humans. Guilarte has also demonstrated that following neurotoxicant exposure, TSPO expression is selectively upregulated in damaged rodent brain regions.

**Potential biomarker for inflammation in other organs**

These brain studies led Guilarte to ask if TSPO could be used to examine inflammation in other organ systems, such as the heart. In recent studies, he demonstrated that TSPO expression was increased in the hearts of male mice and in men with myocarditis compared with women, due to testosterone.

To date, little is known about the function of TSPO in glial or peripheral cells, nor is there an explanation of why TSPO expression is upregulated during inflammation. However, Guilarte has evidence to suggest that it may be related to oxidative stress.

As he concluded his talk, Guilarte described an agenda for using both cell sorting and flow cytometry to examine TSPO expression in normal peripheral blood cells and in other disease states that exhibit inflammation.

(Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group).
Chris McPherson, Ph.D., a biologist in the NTP Neurotoxicology Group, is interested in the effects of inflammation on neurogenic self-repair in the brain. (Photo courtesy of Steve McCaw)

Rooney, standing, explained that TSPO is produced in both monocytes and macrophages outside the brain, which may explain why it is associated with inflammation. (Photo courtesy of Steve McCaw)