

Study finds a new marker for assessing heart inflammation

By Sheila Yong

You might not think to look to the brain to measure inflammation in the heart. Yet, NIEHS grantee [Tomás Guilarte, Ph.D.](#) (<http://www.mailman.columbia.edu/our-faculty/profile?uni=trg2113>), discovered that a widely used biomarker for diagnosing brain injury can also help determine the severity of heart inflammation - a condition known as myocarditis.

Funded in part by NIEHS, Guilarte's [findings](#) (<http://www.ncbi.nlm.nih.gov/pubmed/24402571>) were published Jan. 9 online in the Journal of Cardiovascular Translational Research.

Revolutionizing the assessment of heart inflammation

Guilarte, professor and chair of environmental health sciences at the Columbia University Mailman School of Public Health, has been studying the translocator protein 18 kDa (TSPO) for almost two decades. His previous research established TSPO as a clinical biomarker for brain injury and neurodegeneration. The advantage of TSPO is that it can be imaged and quantitatively measured in the living human brain or in experimental animals, using noninvasive techniques, such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

The findings from Guilarte's brain studies led him to wonder if TSPO could also be used to examine inflammation in other organs, such as the heart. To address this possibility, Guilarte and his collaborators assessed TSPO levels in tissues obtained from myocarditis patients and mice. The mice had been previously exposed to coxsackievirus B3, which often causes myocarditis in humans. Using SPECT, the researchers found higher levels of TSPO in male mice compared to healthy controls.

SPECT can directly measure the extent of inflammation in the heart, without a biopsy or extensive surgical procedures. This is because when the heart is inflamed, it becomes filled with immune cells expressing the CD11b marker, the same cells that also express high levels of TSPO.

The clinical implications of TSPO levels in the heart

Interestingly, the researchers also observed a gender difference in TSPO expression - male patients and male mice with myocarditis expressed higher levels of TSPO than their female counterparts. Further experimentation with myocarditis mice revealed that the male hormone, testosterone, increases TSPO expression during myocarditis, specifically in the immune cells in the heart. Hence, the authors concluded that testosterone amplifies the inflammation, leading to permanent heart damage and failure. These findings also explain why men are at greater risk for myocarditis and other heart conditions related to inflammation.

Guilarte is excited about integrating his TSPO findings from the brain and heart studies to better understand the clinical implications of TSPO expression. "Our latest study is a major milestone, because it demonstrates that we can take what we learned about TSPO in the brain and draw lessons for the heart," Guilarte said in a Columbia University [press release](#). (<http://www.mailman.columbia.edu/news/brain-biomarker-shows-promise-heart>)

"At the same time, we should be able to take what we are learning about TSPO in the heart and apply it to our continuing TSPO research in the brain."

Guilarte believes there is a huge potential for how TSPO can impact not only myocarditis, but also cardiovascular diseases in general. "We have evidence that we can slow down neurodegeneration by controlling levels of TSPO in the brain," he explained. "This approach may eventually prove to have therapeutic value in the heart as well."

[Annette Kirshner, Ph.D.](#), NIEHS Division of Extramural Research and Training program administrator for Guilarte's funding, is impressed with his accomplishments in TSPO research. "TSPO is an exceptional molecular biomarker of brain injury and inflammation that can also be used to assess recovery from injury and the effectiveness of therapeutic strategies," she said. "Since TSPO is found in many regions of the body, expanding the use of this biomarker is very exciting."

The researchers plan to conduct a clinical trial at the Mayo Clinic, to see if TSPO can detect myocarditis-related inflammation in



Guilarte is also a member of the NIEHS National Advisory Environmental Health Sciences Council. (Photo courtesy of Steve McCaw)

patients with the condition. Their ultimate goal is to develop a reliable diagnostic method for myocarditis that can replace current procedures, which are often invasive and less accurate.

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