

# Brain biomarker shows promise in heart

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A biomarker widely used to diagnose brain injury has shown early promise for assessing the severity of heart inflammation, or myocarditis, find researchers at Columbia University's Mailman School of Public Health, Johns Hopkins, and the Mayo Clinic.

The study is published online in the January issue of the *Journal of Cardiovascular Translational Research*.

At present, there is no noninvasive method to confirm diagnosis of myocarditis, which can progress to [heart](#) failure and death. The current standard of biopsy is risky and often misses the disease. For this reason, there may be many people who aren't aware they have the condition.

To address this deficiency, the researchers looked at whether a

biomarker for inflammation in the brain can be used in the heart. When scientists want a clear picture of the extent of damage from a [brain injury](#), they use a PET scan to look for elevated levels of translocator protein 18 kDa, or TSPO. It turns out that TSPO is present in immune cells throughout the body.

In the study, the scientists assessed levels of TSPO in tissue biopsied from patients with myocarditis and in mice with myocarditis related to exposure to coxsackievirus B3—the same virus that often brings about the condition in humans. Using single-photon emission computed tomography (SPECT) imaging adapted to mice in collaboration with Martin Pomper, MD, PhD, in the department of Radiology at Johns Hopkins Medical School, they found higher levels of TSPO in male mice than in controls. Genetic tests revealed elevated levels of TSPO in men with myocarditis and male mice. Similar results were seen with levels of CD11b, a marker for the type of immune cells that host TSPO.

Differences between males and females can be chalked up to sex hormones, explains co-first author DeLisa Fairweather, PhD, associate professor of Environmental Health Sciences at Johns Hopkins Bloomberg School of Public Health. TSPO plays a key role in the metabolism of sex hormones. Heightening levels of the male hormone, testosterone, worsens inflammation.

"Testosterone amplifies inflammation in a bad way that leads to permanent damage in the heart and heart failure," Dr. Fairweather says. "This is why men are at greater risk for myocarditis and all heart conditions related to inflammation."

While levels of TSPO were much greater in males with myocarditis, the biomarker has potential for women too. "We should be able to detect the acute stage of inflammation in women and determine if they are at a risk to progress to heart failure," she says.

## TSPO: Beyond a Biomarker

TSPO appears to be much more than a simple biomarker. Previously scientists thought that TSPO expression was a simple snapshot of levels of inflammation. Now they believe that the protein is in fact driving disease. "TSPO is directly related to whether patients are going to develop severe myocarditis and [heart failure](#)," explains Dr. Fairweather. "That means it's important to look at for its prognostic value."

The next step is to conduct a small trial at Mayo Clinic to see if TSPO can detect inflammation in patients with myocarditis. "This could dramatically increase our understanding of what TSPO is doing in the human body and help us determine how it is related to atherosclerosis or an enlarged heart, which is the main reason people need a heart transplant, as well as other kinds of heart disease," she says.

From there, the researchers hope to extend the study to larger numbers, adding normal, non-inflamed patients, to see if they can determine a threshold level for TSPO that corresponds to a diagnosis of myocarditis. The outcome of these clinical trials could be that patients are finally able to get a definite diagnosis without submitting to an invasive biopsy. "Early diagnosis could open the door to new interventions to slow progression," Dr. Fairweather adds.

"There is huge potential for how TSPO can impact [myocarditis](#) but also cardiovascular disease in general," says senior author Tomás R. Guilarte, PhD, professor and chair of Environmental Health Sciences at Columbia's Mailman School. "In the brain, there is evidence that we can control levels of TSPO to slow neurodegeneration. This approach may eventually prove to have therapeutic value in the heart as well."

Dr. Guilarte, a pioneer in TSPO research has lead studies over the past 18 years that have validated the biomarker for clinical use in the brain.

While performing studies in the brain, he realized that TSPO could be useful for examining [inflammation](#) in other organ systems and started the heart studies with Dr. Fairweather.

"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. Indeed, TSPO will likely have implications for other organ systems," says Dr. Guilarte. "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."

**More information:** "Sex differences in Translocator Protein 18 kDa (TSPO) in the Heart: Implications for Imaging Myocardial Inflammation," *Journal of Cardiovascular Translational Research*: [link.springer.com/article/10.1007/s12265-013-9538-0](https://link.springer.com/article/10.1007/s12265-013-9538-0)

Provided by Columbia University's Mailman School of Public Health

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