

A urine test for Kawasaki disease

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A set of proteins detected in urine by researchers at Boston Children's Hospital may prove to be the first biomarkers for Kawasaki disease, an uncommon but increasingly prevalent disease which causes inflammation of blood vessels that can lead to enlarged coronary arteries and even heart attacks in some children. If validated in more patients with Kawasaki disease, the markers could make the disease easier to diagnose and give doctors an opportunity to start treatment earlier.

The discovery was reported online by a team led by members of the Proteomics Center and the departments of Pathology and [Rheumatology](#) at Boston [Children's](#) on Dec. 20 in the journal *EMBO Molecular Medicine*.

While only about two in 10,000 children in the United States develop [Kawasaki disease](#) annually, the disease is on the rise both here and worldwide; in Japan the prevalence approaches one in 100 among children under the age of 5. No one knows what triggers the disease, and though it can occur at any age, it most often appears in children under 5.

Kawasaki disease is highly treatable—approximately 80 percent of children diagnosed with it require only one round of treatment—but making a diagnosis is often a significant challenge. And if it is not detected early, Kawasaki disease can have serious consequences: About 25 percent of children with untreated Kawasaki disease develop [coronary artery](#) aneurysms.

"The symptoms of Kawasaki disease, including fever, rash and enlarged

lymph nodes, mimic those found in many common viral or bacterial infections in children," said Susan Kim, MD, MMSc, a rheumatologist with the Kawasaki Disease Program at Boston Children's. "The process of diagnosis includes considering a long list of possibilities. Especially in children with an incomplete presentation, a diagnosis of Kawasaki can be delayed or even missed.

"We'd like to have a test that we can use to proactively distinguish children with Kawasaki disease from those with other causes of fever," she continued. "This would allow us to start treatment much earlier and greatly reduce the risks of long-term complications."

In order to develop an effective diagnostic test, Kim worked with proteomics experts Alex Kentsis, MD, PhD, and Hanno Steen, PhD, to screen the protein content of urine from patients with Kawasaki disease using mass spectrometry and enzyme-linked immunosorbant assays. Kentsis and Steen had previously identified urine [biomarkers](#) for acute appendicitis, an effort aimed at reducing the numbers of children who either underwent unnecessary appendectomies or who had a ruptured appendix that did not show up on an imaging scan.

The team identified 190 proteins found only in the urine of children with Kawasaki disease. When validated in samples from 107 children seen at Boston Children's with suspected Kawasaki disease (53 of whom were ultimately diagnosed with it), two of the proteins—filamin C and meprin A, which are associated with injury to blood vessel and cardiac muscle cells as well as inflammation—proved to be 98 percent accurate at distinguishing children with Kawasaki disease from ones with conditions mimicking the disease. Levels of the markers also closely tracked treatment response and, in one patient, disease recurrence.

Other Kawasaki-associated markers detected in the study included proteins involved in immune activation, immune regulation and pathogen

recognition.

The researchers caution that for the moment the markers are still research tools and that they are working to refine and validate the findings in a larger group of patients. "We are working with the hospital's Technology Innovation and Development Office to find corporate partners with which to develop a clinical-grade test," said Steen, who directs the Proteomics Center.

"This is very exciting and our results are very promising," said Kim. "Of course we need to validate the results in a broader cohort of patients, ideally in collaboration with other centers. We are hopeful that these findings will help us to develop a test that can help specifically and proactively detect or rule out Kawasaki in suspected patients in the future."

Provided by Children's Hospital Boston

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