HEIDELBERG, 20 December 2012 – Researchers have discovered **proteins in human urine** that offer **new opportunities** for the **diagnosis**, study and maybe even the **treatment of Kawasaki disease**. Mass spectrometry-based proteomic analysis of the human urine proteome, the entire set of proteins found in human urine, uncovered molecular markers that offer significant improvements for the diagnosis of the disease. The results are reported in a new study published in *EMBO Molecular Medicine*.

“There is no diagnostic test for Kawasaki disease. Currently available diagnostic markers lack the specificity and sensitivity needed for reliable detection of the disease which has motivated our decision to use proteomics to identify new, improved biomarkers,” said Susan Kim, a rheumatologist at Boston Children’s Hospital and an instructor at Harvard Medical School. “Kawasaki disease is often difficult to diagnose and is the most prevalent cause of acquired childhood heart disease in the developed world. Failure to detect it can lead to coronary artery aneurysms and in some cases death, particularly in children who are not diagnosed early enough or when the diagnosis is not considered and acted upon due to the presence of only some of the classic symptoms.”

Kawasaki disease can occur at any age but is most commonly found in children under the age of five years. The disease appears to influence the immune system in such a way that it attacks its own tissues. This leads to inflammation that can damage blood vessels, most notably around the heart. If untreated, Kawasaki disease leads to coronary artery aneurysms in up to 25% of

cases.

The researchers used highly sensitive mass spectrometry techniques to profile the proteome of urine samples collected from children who had symptoms of Kawasaki disease. Several molecules were discovered that were exclusively present in the urine of patients with the disease. In particular, elevated levels of filamin C and meprin A were detected in both human blood and urine samples and show considerable potential for use as diagnostics.

Filamin C is a protein that helps maintain the structural integrity of heart and skeletal muscle. Meprin A is an enzyme that breaks down proteins and which is known to regulate the activities of other proteins linked to inflammation. Both of these markers could be used to identify patients with Kawasaki disease accurately using tests that are readily amenable for routine medical use.

“The urine proteome consists of thousands of protein molecules. Patients with Kawasaki disease have a unique urinary proteome that is distinct from the proteome observed for children with other causes of fever,” remarked Hanno Steen, director of the Proteomics Center at Boston Children’s Hospital and associate professor at Harvard Medical School. “In a group of 107 patients, we were able to distinguish children with Kawasaki disease from those with mimicking conditions much more reliably and accurately than currently available testing by measuring their levels of meprin A and filamin C in urine.” The researchers note that further validation of the diagnostic markers is needed and this work is in progress.

The researchers suggest that the development of clinical tests using these new markers may improve the accuracy of diagnosis of children with suspected Kawasaki disease and assist in the development of new treatments. For this purpose, the scientists have made the analyzed proteomes openly available at the Peptide Atlas (www.peptideatlas.org).

Urine proteomics for discovery of improved diagnostic markers of Kawasaki disease

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