Finding Better Ways to Diagnose Heart Attacks

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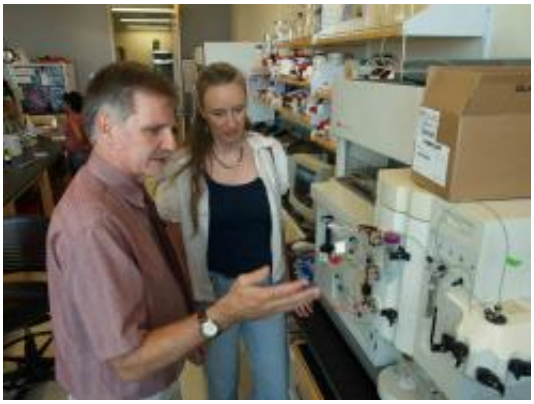

Jeff Walker explains how he and his colleagues purify samples of blood serum to analyze it by mass spectrometry to Lindsey Luke, who suffered a cardiac arrest and subsequent heart failure due to a genetic heart defect that was unknown at the time.

(PhysOrg.com) -- UA biochemistry researchers apply Nobel Prize technology to develop better diagnostics for heart attacks. Their work also could help predict individual risks of heart disease.

When a patient is whisked into the emergency room with symptoms of a heart attack, doctors run a test to determine Troponin-I levels in the bloodstream - the molecular aftermath of a traumatic event damaging the heart muscle.

"Unfortunately, the Troponin-I test doesn't tell the whole story," said

Jeff Walker, a professor in The University of Arizona department of physiology who is also a member of the UA's BIO5 Institute and the Sarver Heart Center. "The kits used to determine the levels of this protein don't tell doctors anything about the exact nature of the damage inflicted on the heart."

Troponin-I normally is found inside heart muscle cells, where it interacts with other protein molecules, causing the heart to squeeze and pump blood. During a heart attack, the cells in the affected area begin to die and disintegrate, spilling their contents, including Troponin, into the bloodstream.
A blood test that comes back positive for Troponin tells doctors that a patient has suffered damage to the heart muscle. Knowing the exact level of Troponin-I could give doctors important clues to the exact nature of a heart attack, the best mode of treatment and the patient's individual risk of a recurring event that might be fatal.

"With the existing tests, this is very difficult to do," Walker said. "They are fairly blunt weapons."

His research group, which works on sharpening those weapons through the use of a sophisticated analytical method called mass spectrometry, has garnered worldwide recognition for overcoming a seemingly insurmountable obstacle: the limitation of mass spectrometry to very small molecules.

On the scale of atoms and molecules, Troponin-I, like most proteins, is huge. So large that even with recent improvements to mass spectrometry that earned three scientists from the United States, Japan and Germany the Nobel Prize in Chemistry in 2002, Troponin remained off limits to mass spectrometry - until now.

"We figured out a technological breakthrough that enabled us to tackle

Troponin using mass spectrometry for the first time," Walker said.

"Troponin interacts with many other proteins in the heart muscle. You could say all those different and highly specialized proteins 'talk' to each other, attaching or removing portions of their chemical makeup, changing their shape and activating or inhibiting nearby proteins. We are only beginning to understand these highly complex interactions and how they influence the function of a healthy heart, let alone a heart fraught with damage of any sort.

"Right now, all the Troponin test tells doctors is whether the biomarker is there. It doesn't give any information as to exactly how much is there, nor does it reveal anything about the chemical structure of the protein. We are seeking to develop better tests that will tell doctors the full story, so they have an accurate idea of the particular situation of an individual patient and can choose the treatment that is best for that patient."

Unlike the available tests, which use antibodies to detect either the absence or presence of Troponin in a blood sample, mass spectrometry analyzes the exact molecular structure, revealing the smallest details, such as the state of activation.

However, the possibilities do not end here. Walker's group is about to embark on a clinical study that seeks to enable clinicians to estimate their patients' cardiovascular risk profiles. Using blood samples obtained from patients who underwent diagnostic testing, the researchers are planning to use their highly sensitive mass spectrometry to scan for and identify genetic variations that make an individual more or less susceptible to heart disease.

"Troponin-I controls the relaxation of the heart muscle after each contraction," Walker explained, "so it is easy to understand why a disruption in its molecular structure could result in cardiomyopathies -

heart malformations, or arrhythmias - abnormal heart beats."

Provided by University of Arizona (news : web)