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A change of heart: Probing how chronic alcoholism alters cellular signaling of heart muscle

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Beyond the personal tragedy of chronic alcoholism there is heartbreak in the biological sense, too. Scientists know severe alcoholism stresses the heart and that mitochondria, the cellular energy factories, are especially vulnerable to dysfunction. But they don't know the precise mechanism.

Now new experiments led by a team at the Wadsworth Center of the New York State Department of Health in Albany, and Thomas Jefferson University in Philadelphia, may provide insights into possible modes of heart damage from alcohol. The teams will present their findings at the 56th Annual Meeting of the Biophysical Society (BPS), held Feb. 25-29 in San Diego, Calif.

Using a technique called electron microscopic tomography, the Albany group produced the first 3D images of mitochondria and discovered tiny tethers linking mitochondria to another cell compartment, the endoplasmic reticulum (ER), where calcium is stored. A clue about the role of these tethers was provided by collaborative experiments with the Philadelphia group. Normally mitochondria take up very little calcium but, as mitochondria get closer to the ER, calcium uptake increases. Calcium overload damages mitochondria, shutting down energy production and leading to cell death.

The researchers looked at calcium regulation and cell structure in the pumping chambers of two groups of laboratory rats to find clues to how

hearts are damaged by alcohol consumption. One group of rats was healthy and one was fed alcohol for six months.

The 3D images the team produced clearly show that the mitochondria of alcohol-fed rats are disorganized. The primary focus of the team's ongoing analysis is the mitochondrial interface with the ER – in particular, characterization of the length, number, and distribution of tethers, which could explain the observed dysfunction of heart mitochondria.

"We're hoping our ongoing 3D analysis, coupled with the functional information provided by our colleagues at Thomas Jefferson, will help answer the question of how alcohol causes heart disease," says biophysicist and lead Albany researcher Carmen Mannella, Ph.D. "If we can understand how chronic alcoholism disrupts fundamental functions such as calcium signaling, then hopefully that information can be used to design preventive or corrective therapies to save hearts – and lives – of those suffering from the disease of alcoholism."

More information: The presentation, "SR-Mitochondrial ultrastructure in the heart of normal and ethanol-fed rats," is at 4:45 p.m. on Tuesday, Feb. 28, 2012, in the San Diego Convention Center, Room 31ABC. ABSTRACT: http://tinyurl.com/7s4gkls

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