



The structure of heart failure

Cardiac hypertrophy—the enlargement of the heart muscle—is a compensatory response to the body’s demand for circulating blood. It often progresses to heart failure, the inability to satisfy the hemodynamic demand. That progression is typically manifest in thickening heart walls, reduced cardiac efficiency, and reduced cardiac output. On the cellular level, numerous changes also occur, including the molecular and chemical environments and the pattern of gene expression.

Benjamin Prosser and colleagues at the University of Pennsylvania have looked particularly closely at how one set of cellular components, microtubules in the cytoskeleton, differ between healthy and failing hearts. This image shows a cage of microtubules (yellow) surrounding the nucleus (blue) of a nonfailing cardiac muscle cell. Using superresolution imaging, the Penn team found that cells from failing hearts exhibit

a denser microtubule network. Moreover, more of the microtubules in failing hearts have been chemically modified by a process called detyrosination.

That modification causes a heart cell’s microtubules to buckle each time it contracts. The team’s mechanical assays of single cells revealed that the increased detyrosination in failing heart cells increases the cells’ stiffness, limits the contraction, and reduces the contractile and relaxation speed. But reducing or suppressing the detyrosination in failing cells softens them and restores a significant fraction of the lost contractile function, a demonstration that suggests a new therapeutic target for improving cardiac function in people with heart failure. (C. Y. Chen et al., *Nat. Med.* **24**, 1225, 2018. Image courtesy of the Prosser Lab, Perelman School of Medicine, University of Pennsylvania.)

—RJF

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