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CYTOSKELETON

Microtubules set the beat

Whereas actomyosin has a well-established role in the generation of muscle contractile forces, how microtubules contribute to muscle contraction is poorly understood. Robison *et al*. now reveal that microtubule detyrosination (one of their post-translational modifications) promotes their buckling upon compressive deformation, and that this, in turn, is important for the mechanical properties of cardiomyocytes during heart muscle contraction.

To visualize microtubules during cardiomyocyte contraction *in vitro*, the authors used high-speed, sub-diffraction imaging, revealing that microtubules reproducibly buckled upon contraction, acquiring a sinusoid-like shape that was resolved during relaxation. Experimentally reducing microtubule detyrosination indicated that this modification is required for efficient buckling. Furthermore, when detyrosination was reduced, cardiomyocytes were less stiff, contracted more and their contraction was faster. On the contrary, excess detyrosination increased cardiomyocyte stiffness and impeded their contraction. These observations suggest that microtubule detyrosination defines the mechanical properties of cardiomyocytes, and that detyrosinated microtubules can absorb and resist the force of deformation through reversible buckling.

A mathematical model indicated that buckling relies on the interaction of microtubules with stiff anchors that reside at the boundaries of sarcomeres (muscle contractile units). Owing to its rigidity and localization to sarcomere boundaries, the intermediate filament protein desmin was proposed to be such an anchor. This was supported by experimental evidence, which revealed that desmin interacted with detyrosinated microtubules, and that in its absence, the mechanical properties of cardiomyocytes were no longer affected by reduced detyrosination.

> “detyrosinated microtubules can absorb and resist the force of deformation”

When analysing human cardiomyocytes isolated from patients with heart conditions that impair blood pumping efficiency, the authors found that microtubule detyrosination was higher, and that levels of detyrosination inversely correlated with a functional indicator of cardiac contractility in these patients. Thus, microtubule detyrosination is directly linked to heart functionality.

This study reports that in cardiomyocytes, detyrosinated microtubules act as a compression resistor, and that, consequently, microtubule detyrosination is important for the muscle contraction cycle, opening up possible avenues of controlling muscle contractility *in vivo*.

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ORIGINAL ARTICLE Robison, P. *et al.* Detyrosinated microtubules buckle and bear load in contracting cardiomyocytes. *Science* **352**, aaf0659 (2016)