

Molecular Mechanism of Contraction of Skeletal and Cardiac Muscles

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It is generally believed that the heart beats in synchrony with the periodic change in $[Ca^{2+}]$ stimulated by the action potential on cardiac myocytes. However, spontaneous sarcomeric oscillation of myocytes has been observed at constant $[Ca^{2+}]$. To understand the molecular dynamics of the oscillations, we analyzed sarcomere length with high spatiotemporal precision and simulated the oscillation with chemical reaction model [1,2]. Cardiomyocytes expressing α -actinin-GFP oscillate spontaneously at ~ 7 Hz. The simulation predicted that the oscillatory contraction was induced by triggering the reversal stroke of powered myosin [2]. The force reduced by the reversal stroke of myosin and then other myosin bound to actin need to generate larger force. The large force accelerated the rate of the reversal stroke of the other myosin. The presence of an inverse response made it easier for the heart to oscillate. To understand the role of the reversal stroke in the contraction of cardiac muscle, the force generated by the small number of purified myosin molecules was measured with optical tweezers[3,4]. The reversal motion observed by cardiac myosin was about 5 times higher than that of skeletal myosin, suggesting that cardiac myosin executes the reversal stroke more frequently than fast skeletal myosin [3]. These results suggest that myocardium is endowed with the ability to spontaneously oscillate by facilitating the reversal stroke of myosin. The ability to oscillate not only helps the heart to contract periodically, but also contributes to the efficiency of the pump.

References

- [1] S.A. Shintani, T. Washio and H. Higuchi. Sci. Rep. 10:20468, 1-12 (2020)
- [2] T. Washio, T. Hisada, S.A. Shintani and H. Higuchi. Physical Review E. 95, 022411(2017).
- [3] Y. Hwang, T. Washio, T. Hisada, H. Higuchi*, and M. Kaya*. Proc. Natl. Acad. Sci. USA 118, e2011659118, 1-11 (2021)
- [4] Motoshi Kaya, Yoshiaki Tani, Takumi Washio, Toshiaki Hisada and Hideo Higuchi. Nature Communications 8,16036 (2017)