

The Regulation of Mitochondrial Na⁺ and Ca²⁺ Concentration and Pathological Mechanism of Cardiovascular Diseases for Its Abnormality

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Summary

Cardiovascular disease including heart failure is a one of the most important health problem owing to its significant morbidity and mortality. One of the most important factor causing heart disease including cardiac hypertrophy and heart failure is dysregulation of Ca²⁺ signaling. Recently, mitochondrial calcium uniporter (MCU) and mitochondrial Na⁺/Ca²⁺ exchanger (NCLX) was identified, and possessed mitochondrial Ca²⁺ signaling study in many different cells and organs. However, physiological and pathological roles of mitochondrial Ca²⁺ signaling in cardiovascular function are still unclear. To study the functional role of mitochondrial Ca²⁺ signaling in cardiovascular diseases, we developed NCLX and MCU-knockout mice. We found that phenylephrine-induced contraction was reduced in isolated aorta from NCLX-knockout mice. Furthermore, we investigated phenylephrine-induced pressor response. Interestingly, phenylephrine-induced increased pressure response was reduced in NCLX-knockout mice. On the other hand, phenylephrine-induced contraction was not significantly changed in isolated aorta from NCU-knockout mice. These result suggested that the disruption of mitochondrial Ca²⁺ signaling contribute to the onset and progression of cardiovascular diseases. Further study will be required to define the pathological mechanisms of cardiovascular disease progression by mitochondrial Ca²⁺ signaling disruption.