Phospholamban is downregulated by parkin-mediated degradation in failing heart □

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The E3 ubiquitin ligase, parkin, regulates protein stability by promoting polyubiquitination and degradation. Although parkin is known to play an essential role in cardiac function after myocardial infarction (MI) by promoting degradation of damaged mitochondria via autophagy, its physiological significance in the other cardiac diseases such as dilated cardiomyopathy (DCM) remains unclear. Here, we found that the expression level of parkin was downregulated in cardiomyocytes from DCM mouse hearts. Conversely, the interaction between parkin and phospholamban (PLN), a potent inhibitor of sarco(endo)plasmic reticulum Ca^{2+}-ATPase, was increased in cardiomyocytes from DCM mouse hearts in the age-dependent manner. It was also shown that the interaction between PLN and PTEN-induced putative kinase 1 (PINK1), which has been shown to cooperate with parkin to promote polyubiquitination and degradation of mitochondrial proteins to regulate mitochondrial dynamics, was enhanced. These data indicate that the enhanced interaction of PLN with PINK1 as well as with parkin leads to the increased degradation of PLN in failing hearts. The degradation of PLN by parkin and PINK1 might be one of the compensating mechanism to maintain the cardiac function.