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Editorial Comment

An Endless Story in Cardiac Ischemia-Reperfusion Injury

Percutaneous coronary intervention (PCI) is effective to establish reperfusion of occluded coronary arteries in patients with myocardial infarction. Although restoration of coronary blood flow by PCI is mandatory, ischemic cardiomyocyte death followed by reperfusion eventually results in a detrimental cardiac ischemia-reperfusion (IR) injury.[1] Excess of intracellular calcium and reactive oxygen species (ROS) lead to uncoordinated contraction of myofibril, swollen mitochondria, and destruction of cytoskeleton and sarcolemma.[2] The injured myocardium is characterized by an enhanced expression of inflammatory cytokines, cardiomyocyte apoptosis, and infiltrating leukocytes.[2] These mentioned histological changes reflect myocardial necrosis that mostly becomes more manifest during reperfusion than that during ischemia. Taken together, cardiac IR injury contributes to expansion of infarct size, post-MI cardiac fibrosis, heart failure, and poor prognosis.[1,2] A variety of pharmacological treatment in reducing cardiac IR injury has been tried, however, the results are mostly disappointing.[2,3] For example, the use of adenosine,[4] mineralocorticoid receptor antagonist eplerenone,[5] erythropoietin,[6] intravenous nitrite nicorandil,[7] and protein kinase C inhibitor delcasertib[8] showed no benefits to reduce infarct size or improve clinical outcomes.

In this present issue of *International Journal of Gerontology*, Xue et al. reported that exenatide has protective effects on the cardiomyocytes during hypoxia-reoxygenation injury. Additionally, they also demonstrated that the GLP-1R/PI3K/AKT signaling pathway may be involved in the beneficial process of exenatide.[9] Despite the wok in this article has revealed an experimental method to investigate the effect of GLP-1R agonist on cardiomyocytes, the endless story of cardiac IR injury is still going because of the complexity of molecular mechanism. Further research should be encouraged to investigate the effect of other GLP-1R agonists, in which allow us to elucidate whether a class effect of drugs exists. Additionally, detail experiments *in vitro* using primary culture from animal cardiomyocytes and *in vivo* IR models are also necessary to figure out the underlying mechanisms.

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