expression of Sarcolipin Reticulum Calcium-transporting ATPase (SERCA2a) decrease in diabetes, leading to diastolic and systolic dysfunction of myocardium. It was recently reported that SUMOylation could elevate the activity and stability of SERCA2a. We assume that diabetes might affect the intensity of SUMOylation of SERCA2a after MI.

METHODS Diet-induced type 2 diabetic rats and controls were divided into six subgroups and divided into sham-operated groups or I/R groups. Primary cardiomyocytes were used to examine the effects of SUMOylation in I/R myocardium. The expression of SUMOylation in I/R myocardium was evaluated.

RESULTS Diabetes exacerbated diastolic and systolic dysfunction of myocardium after infarction. SUMOylation intensity of SERCA2a was enhanced in 1-week-post-MI non-diabetic rats and 6-hour-OD cardiomyocytes but not in 4-week-post-MI rats and 12-hour-OD cardiomyocytes. The expression of enzyme 2 of SUMOylation, namely Ubc9, was in accordance with the SUMOylation intensity, while SUMO1 and enzyme 1 were also not changed. Additionally, overexpression of Ubc9 with lentivirus neutralized the decreasing of SUMOylation intensity caused by glucose in vitro.

CONCLUSIONS SUMOylation intensity of SERCA2a was compensatory enhanced in post-MI non-diabetic rats, but not in diabetic rats. SUMOylation intensity of SERCA2a decreased in cardiomyocytes with addition of high glucose and insulin in vitro, which could be neutralized by overexpression of Ubc9. These observations provide evidence that Ubc9 and SUMOylation of SERCA2a is involved in diabetes-mediated exacerbation of left ventricular dysfunction after MI.

GW26-e3918 DCPIB Attenuates Myocardial Ischemia/Reperfusion Injury Through Inhibiting Autophagy in Rat Model

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OBJECTIVES Autophagy plays a contradictory role in myocardial ischemia/reperfusion (I/R) process, which acts as both beneficial cardioprotective during ischemia stress and myocardial injury in response to subsequent reperfusion. DCPIB (4-(2-Butoxy-6,7-dichloro-2-cyclopentyl-2,3-dihydro-1-oxo-1H-inden-5-yl)butanoic acid), a selective inhibitor of volume-sensitive outwardly rectifying (VSOR) chloride channel, has been determined to protect cardiomyocytes from reperfusion damage. However, the underlying mechanism remains unclear. The present study explored the possible mechanism of DCPIB in alleviating myocardial I/R injury.

METHODS Sprague-Dawley rats were randomly divided into three groups. DCPIB group, RAPA (1mg/kg) group, and RAPA+DCPIB group, 6 rats in each group. Rats were perfused with heparin for 30 minutes and then perfused with a buffer of 24 hours, DCPIB (1mg/kg), RAPA (1mg/kg), and 3MA (1mg/kg) were administrated as intraperitoneal injection 10 min before the onset of reperfusion, respectively. Serum myocardial enzymes were measured and heart microscopic study was performed. The myocardial LC3 was detected by immunohistochemistry, nuclear factor-κB (NF-κB) and tumor necrosis factor-α (TNF-α) were detected by enzyme-linked immunosorbent assay (ELISA).

RESULTS The expression of myocardial LC3, TNF-α and NF-κB were significantly increased (P<0.05), and cardiac function was declined in I/R group compared with that in sham-operated group (P<0.05). Additionally, myocardial LC3 were further increased in RAPA group, whereas these could be reversed through 3MA, a selective inhibitor of autophagy. Of note, DCPIB administration caused significant reduction of myocardial LC3, TNF-α and NF-κB (P<0.05), and significantly improved the cardiac functional recovery and reduced myocardial enzymes activity compared with that in I/R group and I/R+RAPA+DCPIB group (P<0.05).

CONCLUSIONS Our results demonstrated that DCPIB attenuated excessive autophagy to protect rat heart from I/R injury.