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**CALPAIN ACTIVATION CONTRIBUTES TO ISCHAEMIA/
REPERFUSION-INDUCED MYOCARDIAL APOPTOSIS**

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Objectives Calpains belong to a family of calcium-dependent intracellular cysteine proteases. Previous studies demonstrated that

calpain activation contributes substantially to ischaemia/reperfusion (I/R) injury. However, it remains unclear whether administration of calpain inhibitor ameliorates I/R-caused heart injury in vivo.

AIM The objective of this study was to investigate the role of calpain inhibitor PD150606 (PD) in I/R-induced cardiomyocyte apoptosis.

Methods Male C57BL/6 mice, 2–4 months of age, were randomly divided into sham, I/R, and PD+I/R group (1 mg/kg by IV injection 30 min before ischaemia). Mice were subjected to ischaemia by ligation of the left anterior descending coronary artery for 45 min, then reperfusion for 3 h. The risk and necrotic areas were assessed by Evans blue dye and triphenyltertrazolium chloride (TTC) staining, respectively. Myocardial apoptosis was assessed by using TUNEL staining, ELISAs for cytochrome c level, and fluorescence assays for the activity of calpain and caspase-3 activities.

Results Compared to I/R group, the ratio of infarct to risk size was significantly decreased in PD+I/R group ($38.26 \pm 1.91\%$ vs $29.53 \pm 1.64\%$). Compared to control, myocardial caspase-3 activity was significantly increased in I/R group, however, it was significantly decreased in PD+I/R group (2.47 ± 0.37 , 5.13 ± 0.50 and 3.40 ± 0.39 AMC cleaved pmol/mg protein, respectively). Calpain activity (1.15 ± 0.16 , 2.07 ± 0.15 and 1.55 ± 0.10 arbitrary units/mg protein, respectively), cytochrome c concentration (5.66 ± 0.54 , 8.38 ± 0.64 and 7.57 ± 0.56 ng/mg protein, respectively), and TUNEL-positive nuclei ($0.56 \pm 0.05\%$, $10.16 \pm 1.20\%$ and $4.60 \pm 0.50\%$, respectively) were significantly increased in I/R mouse compared with control, but were decreased by PD treatment.

Conclusions Calpain inhibitor PD treatment is an effective strategy to prevent I/R induced myocardial apoptosis in vivo.