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Protective role of neuregulin-1 toward doxorubicin-induced myocardial toxicity

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ABSTRACT. The aim of this study was to investigate the role of the rat neuregulin-1 (NRG-1) protein in reducing doxorubicin (DOX)-induced myocardial toxicity and its underlying mechanism. The prokaryotic expression of the NRG-1 protein and the CCK8-determined activity of rat primary myocardial cells were evaluated under different DOX concentrations. Myocardial cells were divided into three groups: the control group, the 5 μM DOX (DOX5) group, and the DOX5 + NRG-1 group. Western blotting was used to determine the Na^+-Ca^{2+} exchanger (NCX-1) and cardiac myosin light-chain kinase (cMLCK) protein expression levels and real-time quantitative polymerase chain reaction methods were used to determine the mRNA expression levels. The prokaryotic expression of NRG-1 in the DOX5 group produced

toxicity in the rat myocardial cells, and cell activity was significantly restored with the addition of NRG-1. The protective effect of NRG-1 was limited at higher DOX concentrations (DOX10), and the degree of cellular activity restoration was positively correlated with NRG-1 concentration. The addition of NRG-1 to DOX5 intervention inhibited NCX-1 protein and mRNA expression, and increased cMLCK protein and mRNA expression. In conclusion, DOX-induced toxicity in rat myocardial cells could be protected by NRG-1, and the mechanism may be related to the role of NRG-1 in up-regulating the cMLCK expression level and down-regulating the NCX-1 expression level.

Key words: Neuregulin; Doxorubicin; Myosin light-chain kinase; Cardiac myosin light-chain kinase; Na^{+}-Ca^{2+} exchanger

