



Exercise Biochemistry Review

Proceedings of IBEC 2018, Beijing, China, October 23-25

PL-027

Up-regulation of NRG1 improves cardiac repair in zebra fish and involved in the cardioprotective effects of exercise training in rats of myocardial infarction

Mengxin Cai¹, Shaojun Du², Zhenjun Tian¹

1. Institute of Sports and Exercise Biology, Shaanxi Normal University, Xi'an, Shaanxi 710119

2. Institute of Marine and Environmental Technology, Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, MD 21202 (USA)

Objective Myocardial infarction (MI) remains a leading cause of morbidity and mortality worldwide. Exercise training could improve cardiac function following MI. However, the mechanisms are still not well-known. Neuregulin 1 (NRG1) plays an important role in heart development and regeneration. In this study, we investigated the effect of NRG1 on cardiac regeneration in a zebrafish model, detected whether exercise could improve cardiac function through regulating NRG1 expression in infarcted heart and explore the possible role of up-regulation of NRG1 in skeletal muscle play in the cardioprotective effects in rats with MI.

Methods Transgenic zebrafish line, *cm1c2:CreER* and β -*act2:BSNrg1*, were used to study the effect of NRG1 on heart growth and regeneration after injury. PCNA was detected by immunofluorescence staining and mRNA expression of *gata4*, *nkx2.5*, *tbx5*, *smyd1b*, *hsp90 α* and *murf* were tested by RT-PCR. Sprague-Dawley rats were used to establish MI model and underwent four weeks of exercise training (ET) or pAAV-{dMCK promoter}-rNRG1-eGFP intervention. AG1478 was used as an inhibitor of NRG1/ErbBs signaling pathway. Cardiac function and structure, cardiomyocyte proliferation and NRG1 expression were detected in the heart or skeletal.

Results Cardiac-specific overexpression of NRG1 induced cardiac hypertrophy and cardiomyocyte proliferation, regulated the mRNA expression of *gata4*, *nkx2.5*, *tbx5*, *smyd1b*, *hsp90 α* and *murf* in uninjured zebrafish, and promote cardiac repair and regeneration after injury in the zebrafish. Exercise activated NRG1/ErbBs signaling pathway, improved cardiac remodeling and heart function, enhanced cardiomyocyte proliferation, reduced cardiomyocyte apoptosis, ROS level and MuRF1 protein expression in rats with MI. Blocking ErbB signaling attenuated the ET-induced cardioprotection effects in rat with MI. Up-regulation of NRG1 expression in skeletal muscle could increase the protein level of NRG1 in serum and infarcted heart, improve cardiomyocyte proliferation and reduce the level of cardiac fibrosis, finally promote cardiac function.

Conclusions Up-regulation of NRG1 expression in the heart or skeletal muscle may be one of the underlying mechanisms of the beneficial effects of exercise training following MI.