

## Sexual differences on effects of voluntary exercise on heart failure in DCM model mice.

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Nowadays, exercise is regarded as one of therapies for heart failure (HF). However, the effects of exercise on patients with dilated cardiomyopathy (DCM) have not been established. A knock-in mouse model of human inherited DCM, TNNT2  $\Delta$ K210, shows similar characteristics to DCM patients. We have recently found that voluntary exercise significantly improves cardiac function in DCM mice. In this study, we focus on differences in the effects of voluntary exercise due to sexual specificity in the DCM model mice.

Homozygous  $\Delta$ K210 (DCM) mice showed enlarged heart and frequent sudden death with t1/2 of  $\sim$ 70 days. Male and female DCM mice started running using wheels at 1 month of age. The non-exercise controls of both genders were housed without wheels. After running for a month and two months, mice were investigated with echocardiography. After sacrifice, weights of body, heart, lung, lower extremity muscles were measured. Gene expressions of HF- and arrhythmia-related genes in myocardium were quantified by qPCR analysis.

At 2 months of age, the ejection fraction (EF) were significantly improved in male exercise group compared with male control group (exercise group:  $36.9 \pm 10.0$  (n=5)%, control group:  $21.2 \pm 7.9$ % (n=7)) However, in females, the EF of both groups did not differ significantly (exercise group:  $27.5 \pm 10.1$ % (n=7), control group:  $23.1 \pm 9.6$ % (n=5)). We will also show the results of gene expression analysis and discuss reasons for the difference in effects of voluntary exercise.