

Effects of exercise training and antioxidant supplementation on endothelial cell gene expression

A. Matsumoto,¹ L.C. Ward,² P.A. Wilce,² S.A. Marsh,³ R.G. Fassett⁴ and J.S. Coombes,¹ ¹School of Human Movement Studies, The University of Queensland, St Lucia QLD 4072, Australia, ²School of Molecular & Microbial Science, The University of Queensland, St Lucia QLD 4072, Australia, ³Department of Nutrition and Exercise Metabolism, Washington State University, PO Box 1495 Spokane WA 99210-1495, USA and ⁴Royal Brisbane Women's Hospital, GPO Box 48, Brisbane QLD 4001, Australia.

Introduction. There are many studies to support that regular exercise is cardioprotective. It is established that exercise training has a beneficial effect on cardiovascular risk factors however these improvements do not explain all exercise-induced elements of cardioprotection. Additional molecular mechanisms by which exercise provides cardioprotection are poorly understood. Recent data suggests that exercise-induced alterations in myocardial and vascular endothelial cells may provide cardioprotection. Ras homolog gene family member A (RhoA) is a protein shown to regulate important cell functions, such as contraction, migration, proliferation, apoptosis and gene expression. Rho kinases (ROCKs) are the first downstream effector of RhoA, and studies have shown that RhoA/ROCK plays a significant role in arteriosclerotic disease as well as vascular smooth muscle cell hypercontraction. Specifically in endothelial cells, the RhoA/ROCK pathway induces endothelial dysfunction by decreasing the synthesis of the vasodilator, nitric oxide. This can also effect endothelial barrier disruption by increased permeability, enhance inflammation and atherothrombosis. These factors may explain the importance of this pathway in relation to cardiovascular disease. Little research has studied the effect of exercise on RhoA. The purpose of this study was to investigate the effects of exercise and/or antioxidant supplement on myocardial and vascular endothelium gene expression, specifically Ras homolog gene family member A.

Method. Male Wistar rats (N = 48) were divided into four groups: i) antioxidant; ii) exercise; iii) antioxidant and exercise; and iv) control. Exercise group underwent 14 weeks of endurance running on a motorised treadmill (90min/day, 4days/week, at 70% VO₂max). Animals in the supplement group received Vitamin E (1000 IU/kg diet) and α -lipoic acid (1.6g/kg diet) mixed with rat chow. After 14 weeks, rats were sacrificed and tissues were collected. Myocardial and coronary artery ECs were isolated from the hearts. The 27K rat genome oligo slides were used to conduct cDNA microarray analysis on those ECs.

Results. 2-Way ANOVA revealed that gene expression levels on 35, 40 and 40 were altered for the exercise, antioxidant supplementation and interaction of exercise and antioxidant supplementation respectively. Specifically, Ras homolog gene family member A (RhoA) was down-regulated by the effect of exercise (P < 0.02).

Conclusion. Inhibition of the RhoA/ROCK pathway might be one of the mechanisms to explain the positive effect of exercise on CVD. Future research on the effect of exercise on RhoA/ROCK may provide important information to further understand the molecular mechanism of exercise cardioprotection. Confirmation of these results by real-time RT-PCT and western blot will be conducted.