Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol16Issue1abst175P.pdf

Na+/H+ exchanger isoform 1-induced osteopontin expression facilitates cardiomyocyte hypertrophy through CD44

F. Mraiche[1], N. Abdulrahman[1], L. Fliegel[2], A. Gadeau[3]. [1]Qatar University, Doha, QATAR, [2]University of Alberta, Edmonton, CANADA, [3]INSERM, Bordeaux, FRANCE.

Introduction: Heart failure is a common fatal disease. One in three cases of heart failure is due to dilated cardiomyopathy. NHE1 expression and activity are increased in this cardiac defect. We have previously shown that elevated activity of NHE1 in the cardiomyocytes induced cardiac hypertrophy in transgenic mice. However, it protected the myocardium following ischemia/reperfusion. This overexpression of active NHE1 elicited modulation of gene expression in cardiomyocytes including an up regulation of myocardial osteopontin (OPN) expression and a decrease of peroxisome proliferator–activated receptor (PPAR)γ. To determine the role of OPN in inducing NHE1 cardiomyocyte hypertrophy, we created new transgenic mice that co-express active NHE1 and OPN knockout.

Method: We have evaluated by echocardiography the cardiac phenotypes and function of these mice. Then hearts were harvested and submitted to histological, immunohistological and QRT-PCR analysis.

Results:. Our data demonstrated that the NHE1 mice demonstrated heart remodeling identified by a significant decrease in diastolic interventricular septal (IVSd) and diastolic left ventricular posterior wall (LVPW) thickness and an increased diastolic left ventricular internal dimension (LVIDd). Moreover these hearts demonstrated impaired function with a decreased fractional shortening (<21 % vs 31% in wild type mouse) and ejection fraction. ANP and BNP up regulation confirmed the hypertrophic effect, an effect which was regressed in mice expressing active NHE1 and OPN knockout. Interestingly, CD44 was also upregulated in the transgenic mice expressing NHE1, an effect that was regressed in the presence of OPN knockout.

Conclusion: We have developed an interesting comparative model of active NHE1 transgenic mouse lines with express a dilated hypertrophic phenotype expressing CD44, an effect which is regressed in the presence of OPN knockout.

References:

1. *Xue J et al. (2010). Physiol Genomics***42:**374–383.

2. Mohamed IA et al. (2015). *J. Cell Physiol***230:** 2006-2018.