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The Sarcolemmal Membrane Associated Protein (SLMAP) Modulates AKT/ GLUT4 Expression in Cardiomyocytes.

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The glucose transporter 4 (GLUT4) is critical for glucose transport into cardiomyocytes and the regulation of its expression is essential to meet the metabolic demand of cardiac tissue. AKT is required for the insulin induced translocation of GLUT4 to the plasma membrane and its deficiency is linked to insulin resistance and diabetes. Previous work from our group has shown that the sarcolemmal membrane associated protein (SLMAP) is highly expressed in various muscle types, especially the myocardium (1). Further, the expression of SLMAP has been shown to be regulated in vascular and adipose tissue from diabetic animals and may potentially modulate glucose transport (2, 3). Here we have assessed the role of SLMAP *in vivo* in the myocardium of mice (B6C3F1) genetically engineered to over express a truncated SLMAP isoform with a focus on GLUT4 and AKT expression. The SLMAP-transgenic mice presented with dysfunctional myocardium exemplified by changes in membrane structure, depressed contractility and abnormal electrical properties (1). Both GLUT4 and AKT protein expression was markedly upregulated in cardiomyocytes from SLMAP transgenic mice compared with age matched wild type controls (Fig. 1). *GLUT 4 expression in transgenic cardiomyocytes was increased (167%* ± 32.4%, *n=4, P<0.05) and AKT expression was increased (102%* ± 34.7%, n=4, P<0.05) compared with cardiomyocytes from age-matched wildtype mice. Furthermore, glucose upregulated the expression of GLUT4 in a dose dependent manner incardiomyocytes with a maximal increase of 197% ± 7.7%, (n=3, P<0.01) noted at 30mM glucose. The myofibroblasts from SLMAP-transgenic hearts did not express GLUT4 and were not responsive to glucose treatment. Interestingly, AKT expression in myofibroblasts from SLMAP transgenic hearts was decreased by 65% ± 5.2% (n=5, P<0.05) compared with those isolated from wild type hearts. The data here further support a role for SLMAP in glucose metabolism in myocardium and implies that SLMAP may be a unique target in metabolic disease such as diabetes.

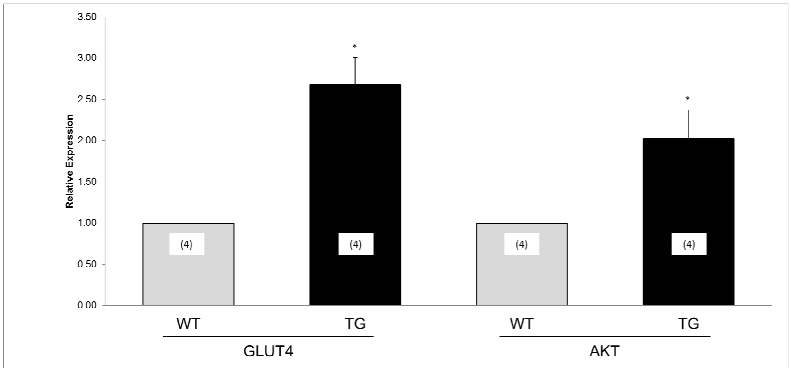

Fig. 1 SLMAP regulates GLUT4 and AKT expression in neonatal cardiomyocytes
*P<0.05 versus wildtype

1) Nader M et al, Am J Physiol Heart Circ Physiol 302:H1138-H1145, 2012

2) Chen X, Ding H,. Experimental Diabetes Research 10:421982, 2011

3) Ding H et al. Am J Physiol Heart Circ Physiol 289:H206-H211, 2005