



MEETING ABSTRACT

Open Access

Increased cardiac contractility by decreased HAX-1 expression

Wen Zhao

From 2012 Sino-American Symposium on Clinical and Translational Medicine (SAS-CTM) Shanghai, China. 27-29 June 2012

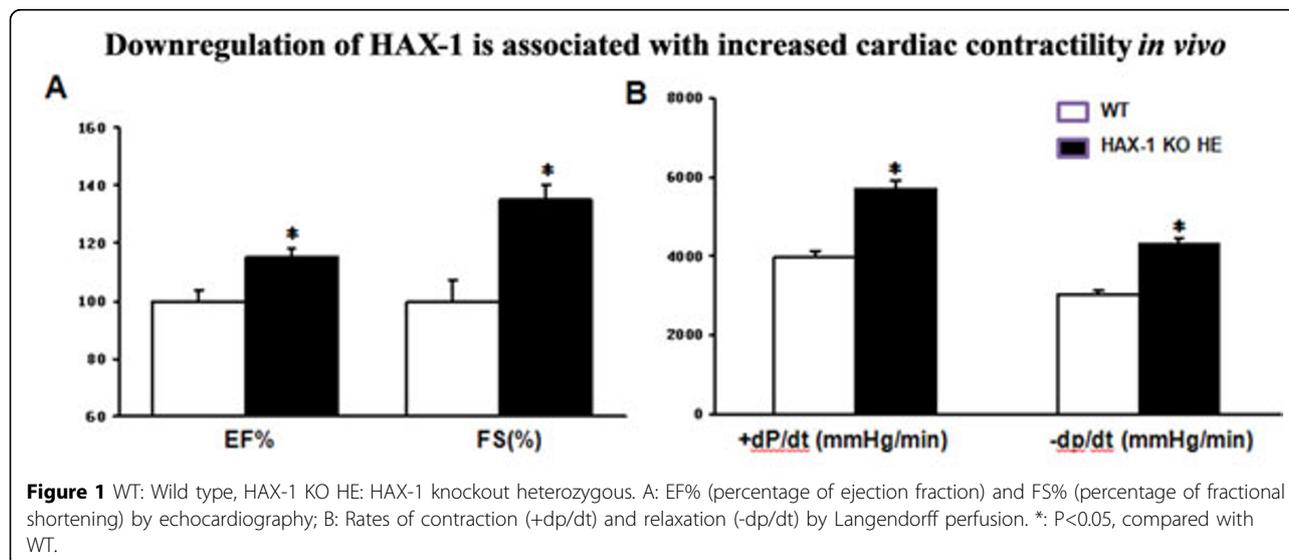
Background

The HS-1 associated protein X-1 (HAX-1) is a ubiquitously expressed protein that protects cardiomyocytes from programmed cell death. HAX-1 is mainly located in cardiac mitochondria and sarcoplasmic reticulum. Recently, it has been recognized that HAX-1 serves as a binding partner of phospholamban, which plays a fundamental role in controlling basal contractility and constitutes a key downstream effector of the β -adrenergic signaling cascade. However, the functional significance of HAX-1 in the heart remains unclear. Our previous studies have shown that overexpression of HAX-1 *in vitro* or *in vivo* by adenoviruses and transgenesis reduced cardiac myocyte contractility and calcium transients under basal

condition without significant alterations of isoproterenol response. Conversely, *in vitro* downregulation of HAX-1 enhanced calcium kinetics and mechanics under basal conditions.

Methods and results

To further investigate the role of the endogenous HAX-1 in the cardiac contractile function, HAX-1 heterozygous deficient mice with 36% of HAX-1 expression in the heart were characterized, since the homozygous mice are lethal at 5-12 weeks afterbirth. Interestingly, *in vivo* echocardiography showed that decreased HAX-1 expression was associated with significantly enhanced cardiac performance, including fractional shortening and ejection frac-



Correspondence: zhaowen100@gmail.com
School of Pharmaceutical Sciences, Zhengzhou University, 100 Kexue Avenue, Zhengzhou, Henan 450001, China

tion, when compared to age-matched wild types. *Ex-vivo* Langendorff perfusion suggested markedly increased rates of contraction and relaxation, compared to wild types (Figure 1). Furthermore, at the cardiomyocyte levels, we also found similar cardiac phenotype with elevated fractional shortening, rates of contraction and relaxation as well as calcium kinetics under basal conditions. The functional improvement in the heterozygous HAX-1 deficient mouse hearts does not play a role in the expressions of major SR calcium handling proteins, including: SERCA2a, calsequestrin and phospholamban. However, the affinity of SERCA2 for calcium was significantly increased without alteration of maximal velocity of this calcium pump. The enhanced cardiac contractility is not related to any significant cardiac remodeling and histology changes at the age of 10-12 weeks.

Conclusion

These results indicate that decreased HAX-1 expression in the heart is associated with increased cardiac contractility and calcium handling, suggesting that HAX-1 may be a novel regulator in cardiac contractile performance.

Acknowledgement

The author thanks Dr. Evangelia G. Kranias, who is from University of Cincinnati College of Medicine, for her constructive suggestion in the current study. This work was supported by the Starting Package of Zhengzhou University for Wen Zhao.

Published: 17 October 2012

doi:10.1186/1479-5876-10-S2-A65

Cite this article as: Zhao: Increased cardiac contractility by decreased HAX-1 expression. *Journal of Translational Medicine* 2012 **10**(Suppl 2):A65.

**Submit your next manuscript to BioMed Central
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

