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Vascular biomechanical properties in mice with smooth muscle specific deletion of Ndst1

Neeta Adhikari · Marie Billaud · Marjorie Carlson · Spencer P. Lake · Kim Ramil C. Montaniel · Rod Staggs · Weihua Guan · Dinesha Walek · Snider Desir · Brant E. Isakson · Victor H. Barocas · Jennifer L. Hall

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Abstract Heparan sulfate proteoglycans act as co-receptors for many chemokines and growth factors. The sulfation pattern of the heparan sulfate chains is a critical regulatory step affecting the binding of chemokines and growth factors. *N*-deacetylase-*N*-sulfotransferase1 (*Ndst1*) is one of the first enzymes to catalyze sulfation. Previously published work has shown that HSPGs alter tangent moduli and stiffness of tissues and cells. We hypothesized that loss of *Ndst1* in smooth muscle would lead to significant changes in heparan sulfate modification and the elastic properties of arteries. In line with this hypothesis, the axial tangent modulus was significantly decreased in aorta from mice lacking *Ndst1* in smooth muscle (SM22αcre^{+}Ndst1$^{-/-}$, $p < 0.05$, $n = 5$). The decrease in axial tangent modulus was associated with a significant switch in myosin and actin types and isoforms expressed in aorta and isolated aortic vascular smooth muscle cells. In contrast, no changes were found in the compliance of smaller thoracodorsal arteries of SM22αcre^{+}Ndst1$^{-/-}$ mice. In summary, the major findings of this study were that targeted ablation of *Ndst1* in smooth muscle cells results in altered biomechanical properties of aorta and differential expression of myosin and actin types and isoforms.

Keywords Ndst1 · Heparan sulfate proteoglycan · Arterial compliance · Tangent moduli · Biomechanics

Introduction

Heparan sulfate proteoglycans (HSPGs) are highly abundant molecules on the cell membrane and in the extracellular matrix [1]. HSPGs are composed of polysaccharide chains attached to a core protein [2, 3].The polysaccharide chains are composed of alternating disaccharide units of *N*-acetylglucosamine and glucuronic acid residues [4]. Biosynthesis of HSPG polysaccharide chains involves a series of enzymatic reactions. Post-translational modifications include *N*- and *O*-sulfations of the disaccharide subunits of the heparan sulfate side chains [5–7]. Sulfated domains

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N. Adhikari · M. Carlson · K. R. C. Montaniel · R. Staggs · S. Desir · J. L. Hall (✉)
Lillehei Heart Institute, Department of Medicine, University of Minnesota, 4-106 NHH, 312 Church St. SE, Minneapolis, MN 55455, USA
e-mail: jlhall@umn.edu

M. Billaud · B. E. Isakson
Robert M Berne Cardiovascular Research Center, School of Medicine, University of Virginia, Charlottesville, VA 22908, USA

S. P. Lake · V. H. Barocas
Department of Biomedical Engineering, University of Minnesota, Minneapolis, MN 55455, USA

W. Guan
Department of Biostatistics, University of Minnesota, Minneapolis, MN 55455, USA

D. Walek
Biomedical Genomics Center, University of Minnesota, Minneapolis, MN 55455, USA

J. L. Hall
Division of Cardiology, Department of Medicine, University of Minnesota, Minneapolis, MN 55455, USA