**LBX1 Modulates Muscle Function and Curve Progression in Adolescent Idiopathic Scoliosis**

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INTRODUCTION: Emerging evidence suggests that imbalanced paraspinal muscle (PSM) plays an important role in onset and/or progression of curve progression in adolescent idiopathic scoliosis (AIS) [1]. Targeting the imbalanced PSM metabolism has been proposed to minimize uneven mechanical loading between concave and convex side PSM, and thus a new therapeutic approach for AIS. Ladybird Homeobox 1 (LBX1) is the most promising candidate gene in the etiology of AIS, however, its role in AIS PSM phenotype and curve progression is still undetermined [2]. This study aimed to examine the relationship between LBX1 and AIS in clinical samples, and to determine its role in curve progression in an advanced three-dimensional (3D) mouse scoliosis model.

METHODS: PSM were collected from age-matched individuals with AIS (n = 12), congenital scoliosis (CS) (n = 7) and non-scoliosis (n = 12). Histological MyHC immunofluorescence was performed to test PSM phenotype. LBX1 expression was compared between concave and convex side PSM in AIS patients (n=6). To verify the link between LBX1 and curve progression, the mouse scoliosis model was induced by applying a 3D printed restrainer. Female wild-type C57BL/6 mice and same background transgenic mice with LBX1 overexpression (LBX1-OE) were used for comparing differences of LBX1 expression of concave and convex side PSM in AIS.

RESULTS SECTION: Muscle fiber type counting was imbalanced between concave and convex side PSM of AIS patients. LBX1 was down-regulated in concave side PSM compared to convex side PSM of AIS patients (Fig. 1B). Upregulation of polyamine biosynthesis metabolites was identified with metabolomic analysis in LBX1-OE cells. Further analysis showed key enzyme of polyamine biosynthesis pathway was upregulated with LBX1 overexpression (Fig. 1 C).

DISCUSSION: Our results provide new evidence that decreased LBX1 expression in concave side PSM may contribute to curve progression in AIS. LBX1 appears to modulate muscle function and curve progression via polyamine biosynthesis pathway. These results provide new insight into the etiology of curve progression in AIS.

SIGNIFICANCE/CLINICAL RELEVANCE: Further studies on the LBX1 or the polyamine biosynthesis pathway will shed light on the development of novel treatment for curve progression in AIS via targeting PSM.


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**Figure 1.** (A) The RNA expression of LBX1 in AIS PSM samples through qPCR analysis (n = 6). a-(apex-), d-(distal-). (B) X ray, viva CT of scoliosis model with AAV-control or AAV-cre virus. (C) The protein expression of key enzyme of polyamine biosynthesis pathway in wide type (LV-5) and LBX1 over-expressed (LBX1-OE) HSMM cells.