Monitoring Skeletal Muscle Changes in Dystrophin and Laminin-α2 Deficient Mice.

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Introduction

Defect in laminin- α2 (LAMA-2) gene causes congenital muscular dystrophy (MDC1A). It is the second most common form of congenital muscular dystrophies (CMD). Although several murine models have been developed to study the underlying mechanism and therapeutic interventions Lama2$^{Dy\text{-}w}$ mice closely resembles the pathophysiological changes that occur in MDC1A. Using histological methods, significant amount of apoptosis, fibrosis and inflammation have been observed in these mice[1, 2]. On the other hand, several therapeutic strategies have shown to alleviate muscle and nerve pathology in different mouse models of MDC1A[3]

Experimental

MR measurements were performed on *mdx* (n=5, 2-3 months; mean ± SD), LAMA^{Dyw} (n=8, 2-3 months; mean ± SD), C57BL10 (n=5, 2-3 months; mean ± SD), mice within the AMRIS Facility. All mice were imaged on a 4.7T Oxford Magnet with a Varian/Agilent operating system. T_2-weighted single spin–echo images of the hind-limb muscles were acquired (TR 2,000 ms; TE 14 and 40 ms; field of view, 20X20 mm^2; slice thickness, 1.0 mm; acquisition matrix size, 256 X 128; averages, 2) using a custom built solenoid coil (2 cm diameter). T_2 values were derived using average signal intensity from anterior and posterior hind-limb muscles of each TE using OsiriX software.

Results and Discussion

Hindlimb (anterior and posterior compartment) muscles *mdx* mice were significantly ($p<0.05$) greater than WT and LAMA^{Dyw} mice. Similarly, mean muscle T_2 of hind-limb muscles of *mdx* mice was significantly ($p<0.05$) higher than WT and LAMA^{Dyw} mice (Figure 1).

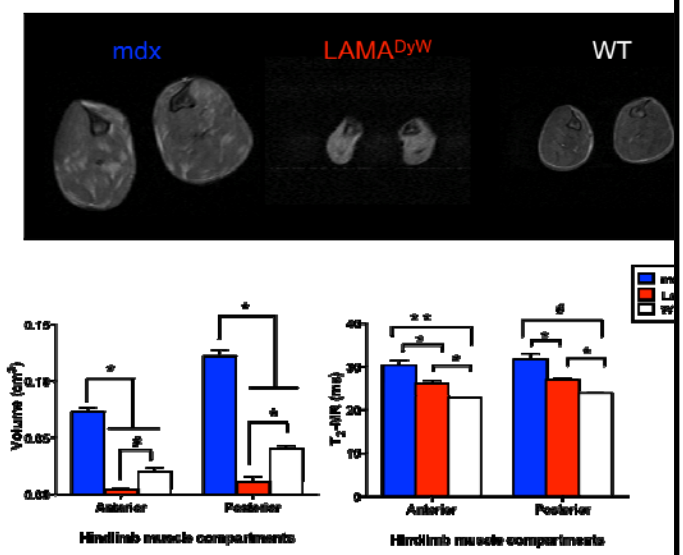

Figure.1. Example of axial hindlimb images and corresponding muscle volume and mean T_2 of anterior and posterior compartment of mdx, LAMA^{Dyw}, WT mice

Conclusions

The results of this study indicate that similar to subjects with CMD, the transgenic mouse model, LAMA^{Dyw}, of CMD demonstrates stark muscle atrophy and elevated water T_2 determined by MRI compared to control mice. In contrast, the *mdx* mouse was found to possess a greater muscle mass with T_2 elevations significantly higher than that for control and LAMA^{Dyw} mice.

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References

1. Gawlik, K.I. et al *Muscle Nerve* **42**, 30-7 (2010).
2. Girgenrath, M. et al *J Clin Invest* **114**, 1635-9 (2004).
3. Gawlik, K. et al *Hum Mol Genet* **13**, 1775-84 (2004).