

Mayank Verma

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Atsushi Asakura, Department of
Neurology

Partial amelioration of the muscular
dystrophy phenotypes through an
increase in vasculature in *mdx* mice

Duchenne Muscular Dystrophy (DMD) is an X-linked recessive genetic disease in which the gene coding for the protein dystrophin is missing. Dystrophin is a membrane stabilizing protein and absence of it leads to the damage of the muscle membrane resulting in degradation of the muscle fibers followed by replacement with adipose and fibrous connective tissue. A functional role of dystrophin has also been found in the smooth muscle of the vasculature and its deficiency leads to vascular deficiency and abnormal blood flow. Consequently, the decreased circulation may induce a state of functional ischemia increasing the muscular dystrophy pathogenesis. For an effective form of therapy of DMD, both the muscle and the vasculature need to be repaired. For this reason, *mdx* mice (a model animal for DMD) with increased vasculature were created by heterozygous Flt1 gene deficient mice, an inhibitory decoy receptor for a vascular endothelial growth factor (VEGF). Interestingly, the *mdx* mice with increased angiogenesis (*mdx:Flt1^{+/-}*) display an improved muscle histology compared to the *mdx* mice, including decreased fibrosis, calcification, membrane and permeability. In addition, *mdx:Flt1^{+/-}* mice are also shown to have an increase in muscle force production, compared to the *mdx* mice. Consequently, *Flt1^{+/-}* mice also display increased regenerative capacity after muscle injury, compared to the *wild-type* mice. These data strongly suggest that increasing the vasculature in DMD may be able to partially ameliorate the histological and functional phenotypes associated with this disease.

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