VEGF OVEREXPRESSION VIA ADENO-ASSOCIATED VIRUS GENE TRANSFER PROMOTES SKELETAL MUSCLE REGENERATION AND ENHANCES MUSCLE FUNCTION IN *MDX* MICE

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Vascular endothelial growth factor (VEGF) is a major regulator of physiological and pathological angiogenesis. Several studies support its role in myogenesis and in myoblast migration and survival. Recently it has been reported that the delivery of VEGF using recombinant adeno-associated-virus (rAAV) vectors reduces muscle damage and promotes muscle regeneration in different experimental models of muscle necrosis. Duchenne muscular dystrophy (DMD) is characterized by cycles of necrosis and inefficient regeneration at long term. We tested VEGF effect on muscle function, histopathology, immunohistochemistry and biochemical parameters in *mdx* mice, a model of DMD, and in wild type mice. We performed intramuscular administration into the biceps and tibialis anterior muscles of rAAV-VEGF or rAAV-LacZ as controls. One month after injection, rAAV-VEGF treated muscles showed augmented expression of VEGF and immunolocalization of VEGFR-2. VEGF treated *mdx* mice showed: 1) increased forelimb strength and strength normalized to weight; 2) reduced necrotic fibers area and increased regenerating fibers area; 3) increased number of cells positive for markers of early and late regeneration; 4) augmented capillary density in regenerating fibers area. We report the novel observation of a beneficial effect of VEGF in *mdx* mice exerted mainly by a pro-regenerative and angiogenic effect, opening a new therapeutic prospective in DMD and in other types of muscular disorders.