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Biodistribution of AAVpo1 and AAVpo1A1 in mice with myotubular myopathy

Edith Renaud-Gabardos, Paloma Navas-Navarro, Jihad Elandari, Louise Mangin, Karine Poulard, Samia Martin, Dirk Grimm, Ana Buj-Bello

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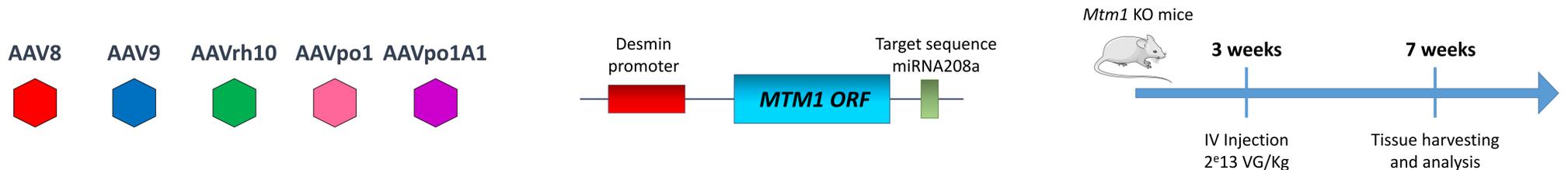
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INTRODUCTION:

Recombinant adeno-associated viral (AAV) vectors are powerful vehicles for *in vivo* delivery of therapeutic transgenes. Tissue tropism and consequently vector dosage for gene therapy can vary amongst naturally occurring and engineered AAV serotypes. We previously reported that serotype 8 AAV-mediated MTM1 gene delivery can correct the phenotype of murine and canine models of myotubular myopathy, a severe pediatric disorder leading to generalized muscle weakness and respiratory failure in patients.

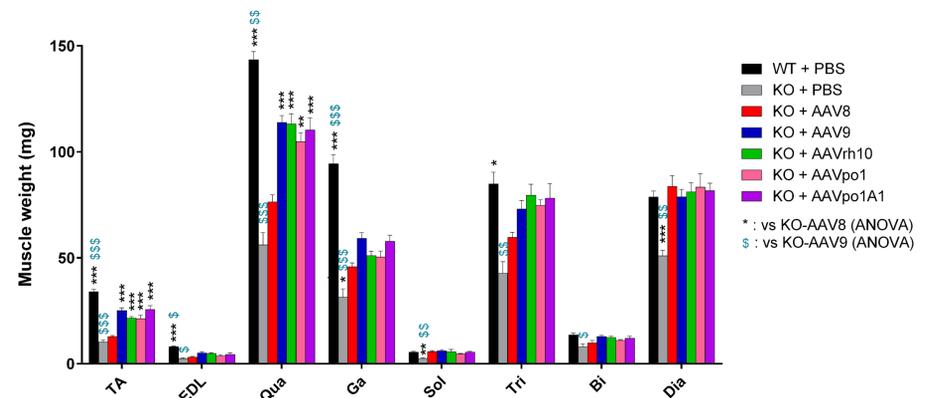
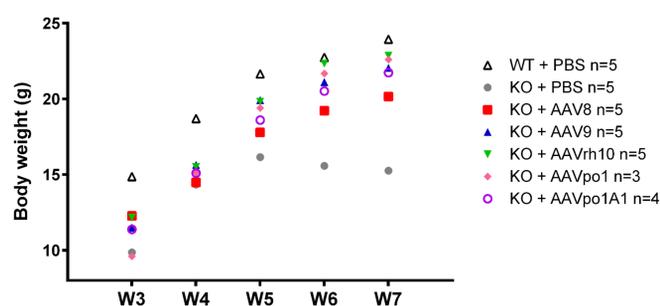
In order to identify AAV vectors with increased skeletal muscle potency in myotubularin deficient muscle, in the present study we compared the biodistribution and transgene expression of serotype 8, 9 and rh10 vectors with AAVpo1, and its derivative AAVpo1A1, of porcine origin that carry a MTM1 expression cassette.

METHODS:

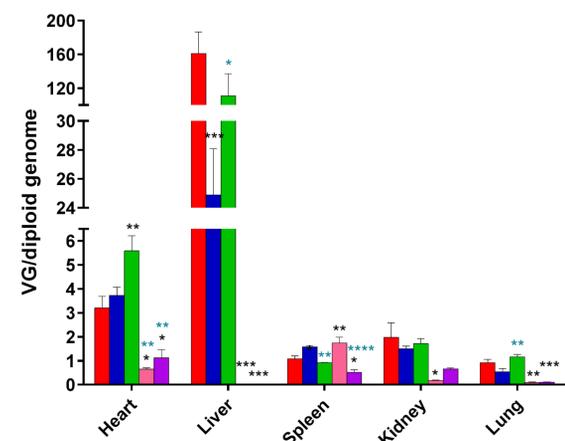
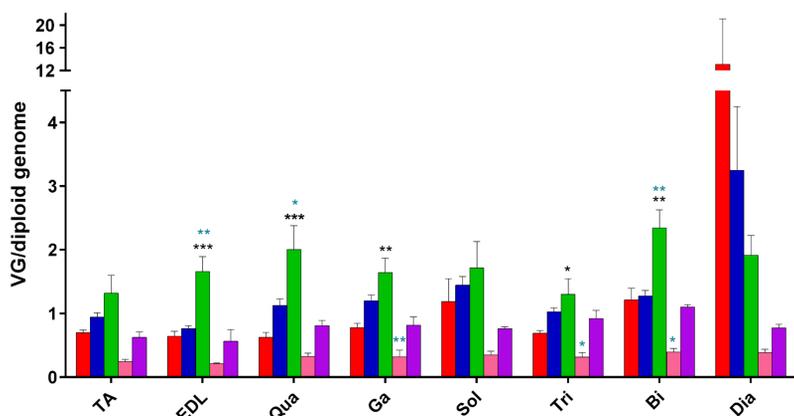


RESULTS:

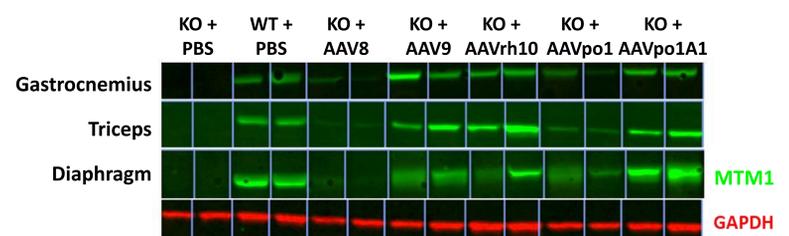
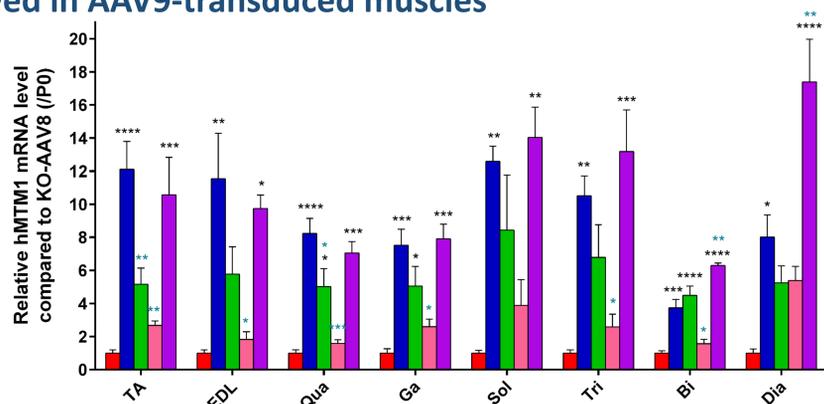
Intravenous administration of AAVpo1- and AAVpo1A1-MTM1 vectors resulted in higher body and muscle weight in myotubularin-deficient mice compared to AAV8-MTM1



The AAVpo1A1 vector transduced muscles as efficiently as the AAV8 vector but detargeted main organs, including liver



AAVpo1A1-MTM1 administration resulted in higher transgene expression in skeletal muscles compared to AAV8, reaching levels observed in AAV9-transduced muscles



CONCLUSIONS:

We found that administration of AAV9-, AAVrh10- and AAVpo1A1 vectors in *Mtm1*-KO mice resulted in higher myotubularin expression levels in skeletal muscles compared to AAV8- and AAVpo1 vectors. In addition, the AAVpo1A1 capsid detargeted liver transduction. These results indicate that AAVpo1A1 vectors may be suitable for gene transfer in myotubular myopathy, and other myopathies.