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Therapeutic approach based on GDF5 to counteract age-related muscle wasting

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Therapeutic approach based on GDF5 to counteract age-related muscle wasting

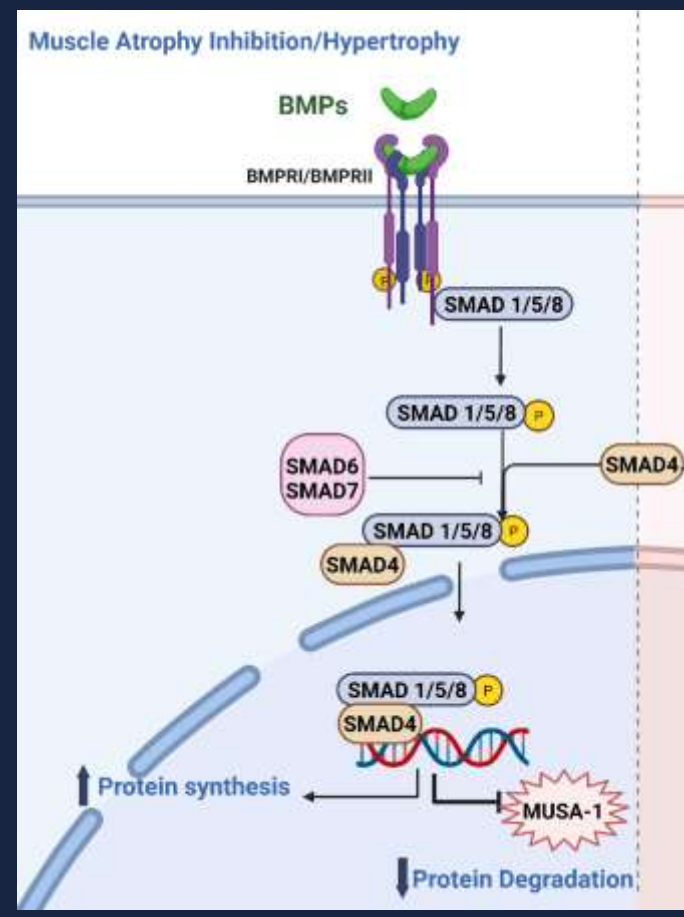
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Introduction

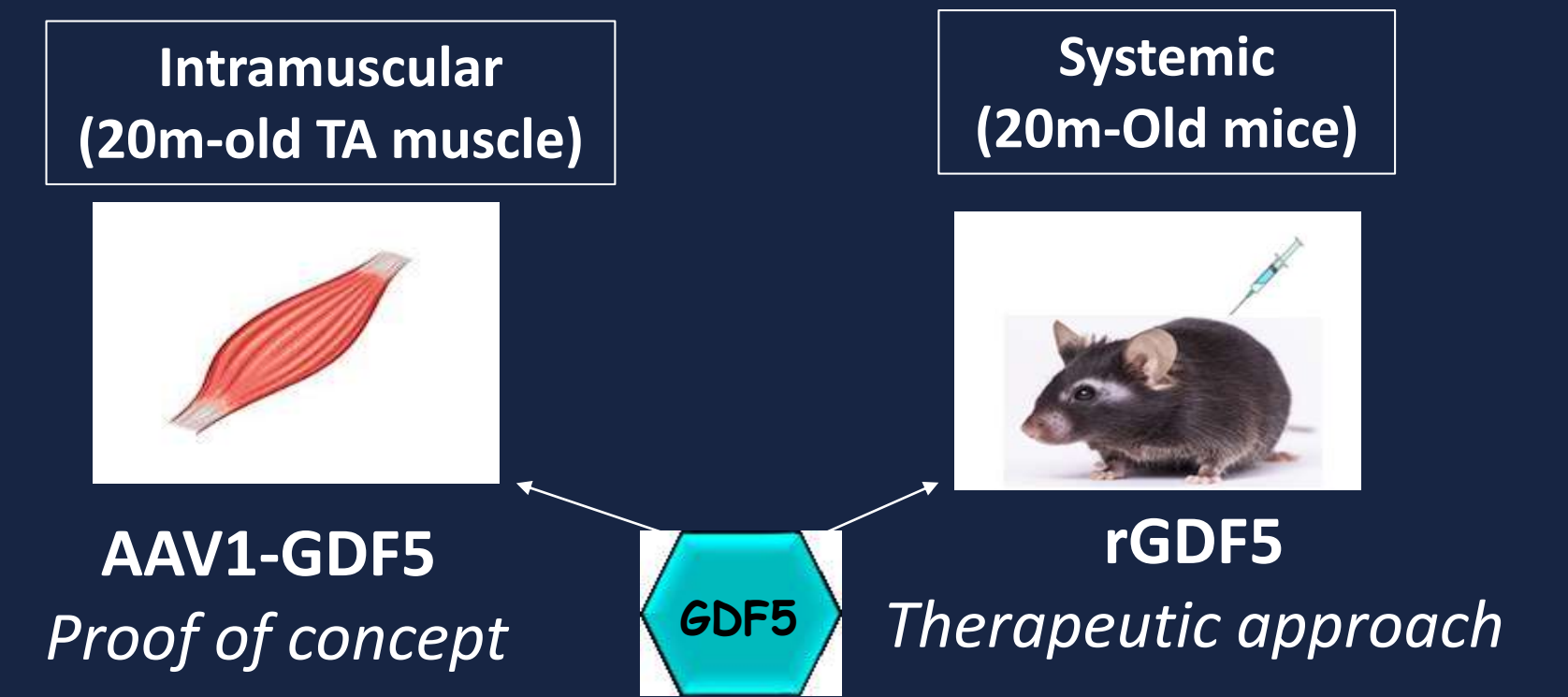
Age-related muscle wasting



GDF5 canonical signaling

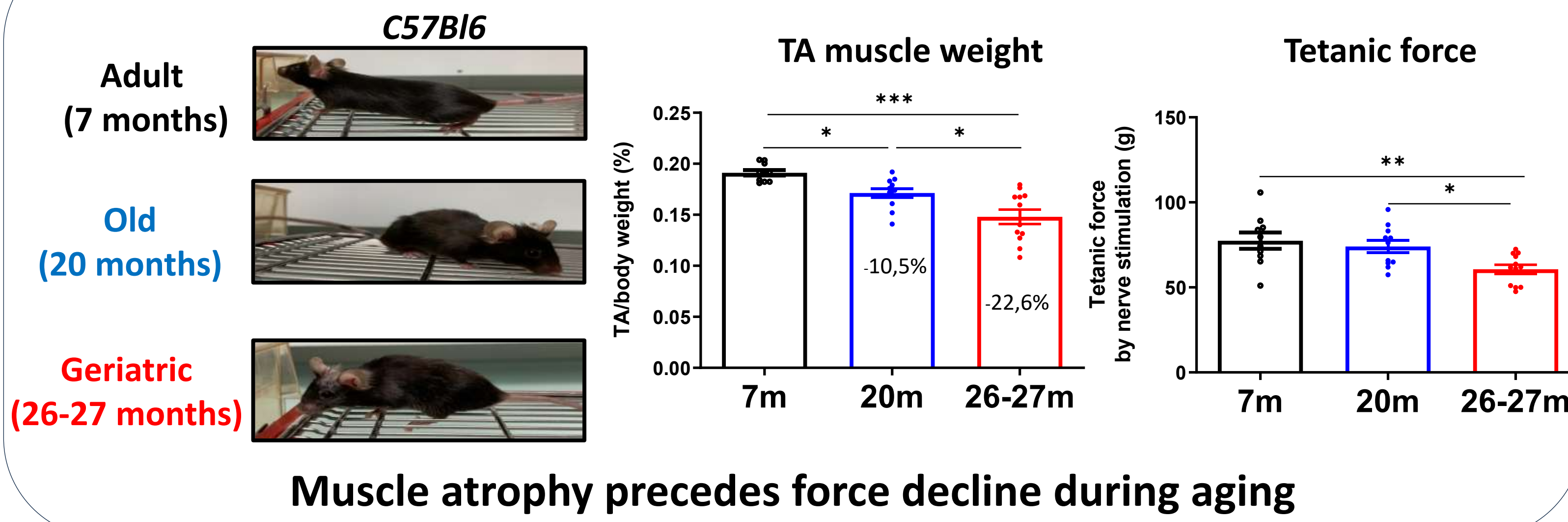


Evaluation of GDF5 effects in old mouse muscle

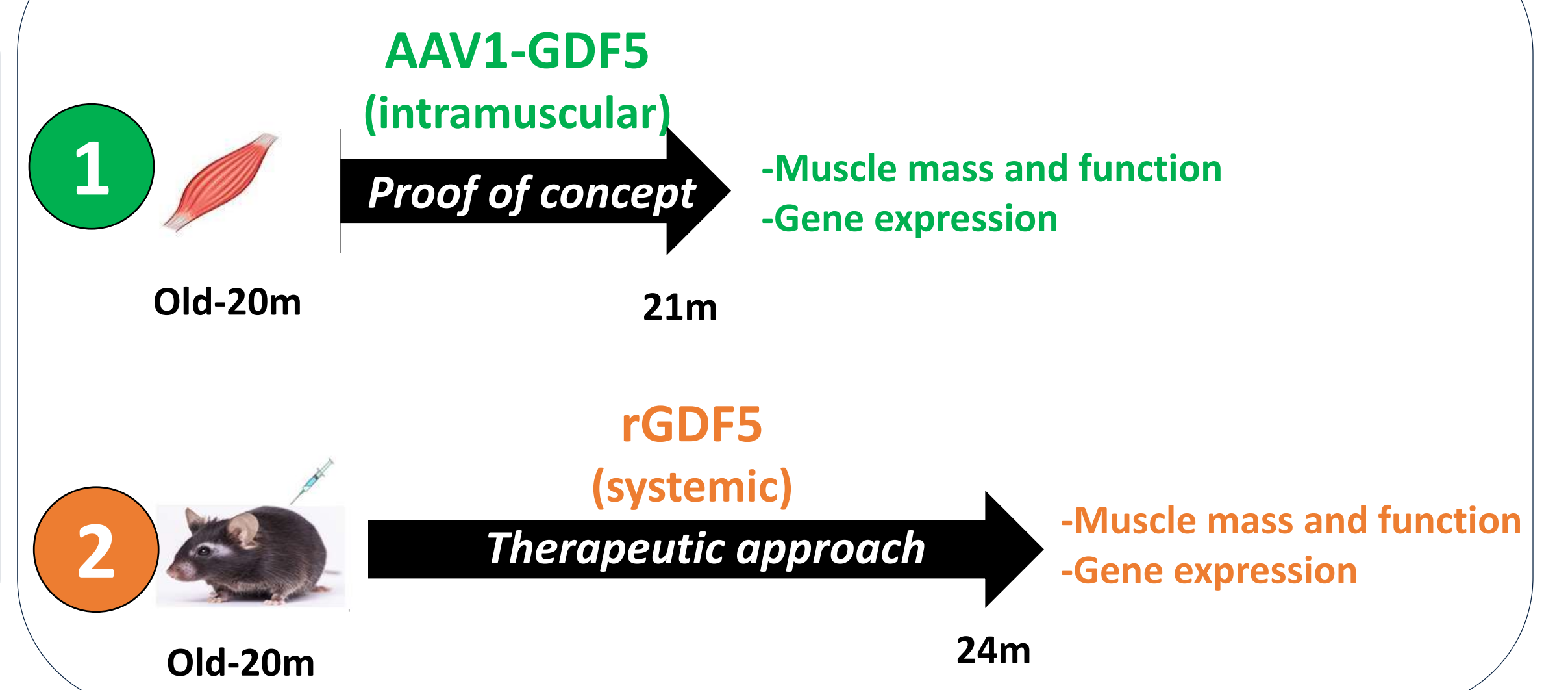


Sarcopenia is defined as a progressive age-related loss of muscle strength, quality and mass, which results in increased mortality. Some of its pathophysiological aspects are still not very well understood and no cure has been established to date. **GDF5 (Growth Differentiation Factor 5) is a blood circulating factor, expressed by skeletal muscle after nerve damage, playing a critical role in limiting muscle atrophy (Sartori et al., 2013).** The canonical GDF5 signaling includes the phosphorylation of intracellular SMAD1/5/8 complex, which translocates to the nuclei and controls gene transcription. Our previous work demonstrated that GDF5 overexpression prevents age-related muscle decline (Traoré et al., 2019). However, to decipher the molecular mechanisms behind the effects of GDF5 on muscle mass and function, we overexpressed the protein by intramuscular AAV gene transfer. Here we show a deeper report on the mechanisms and consequences of GDF5-based treatment on aged muscle. In addition, as potential therapeutic approach to prevent age-related muscle decline, we evaluated the benefits of a systemic supplementation of recombinant GDF5 protein (rGDF5) in aged mice.

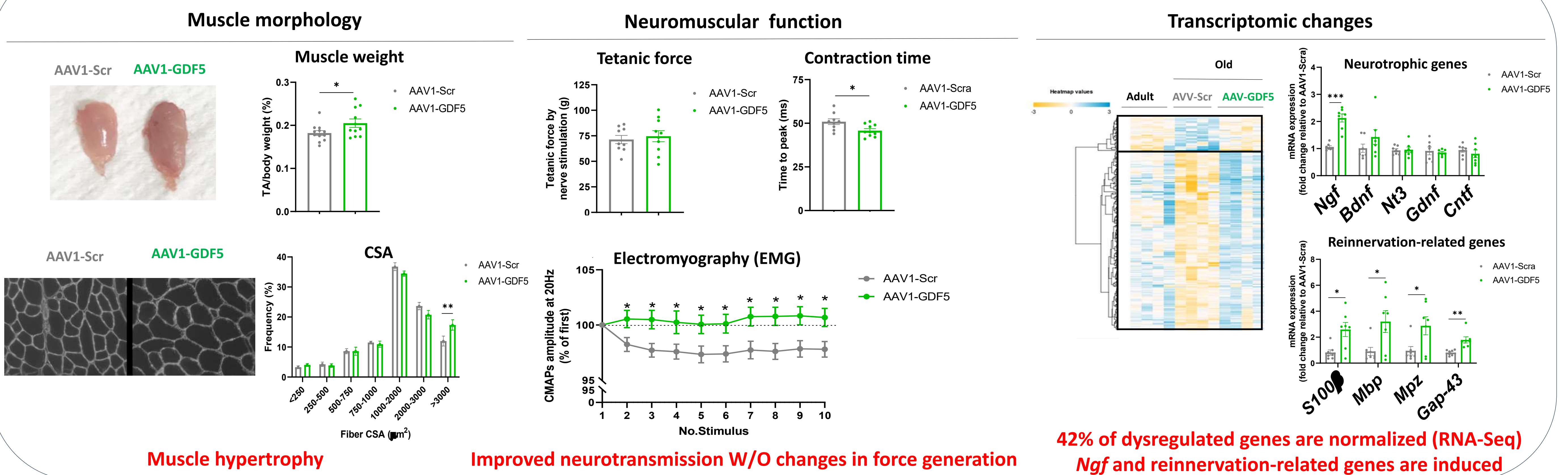
Characterization of age-related muscle wasting in mice



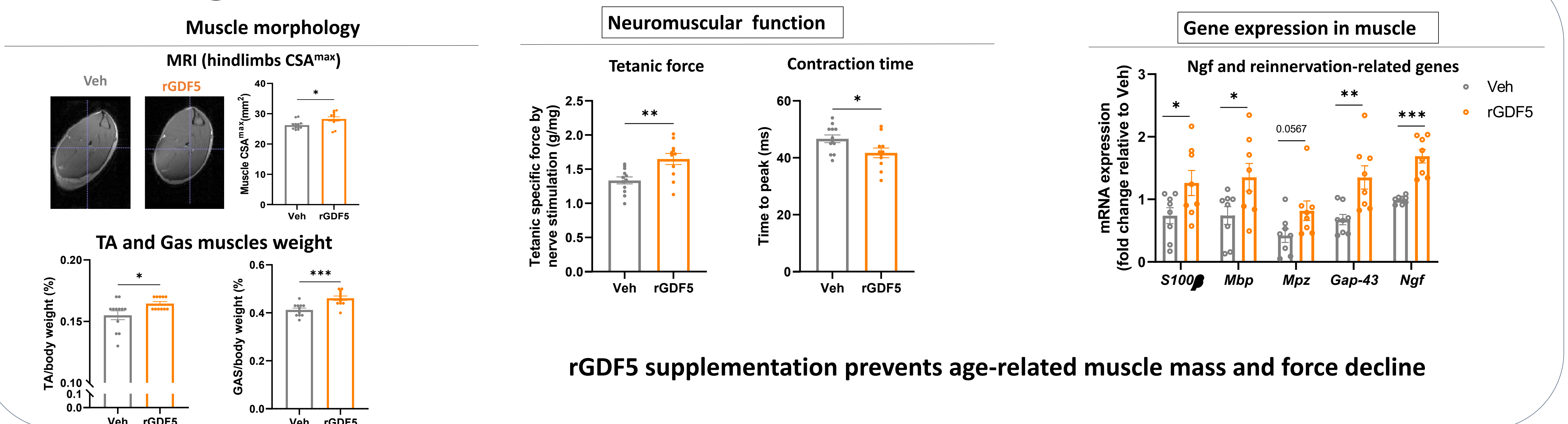
Study design



1 GDF5 overexpression in old mouse muscle



2 rGDF5 protein supplementation in old mice : a therapeutic approach



Conclusion and perspectives

-rGDF5 systemic administration represents a promising therapeutic strategy to improve age-related muscle decline in sarcopenia.
 -Possible applications in gene therapy optimization for muscular (DMD) and neuromuscular diseases.