Exploring the protective role of GDF5 against skeletal muscle disuse atrophy

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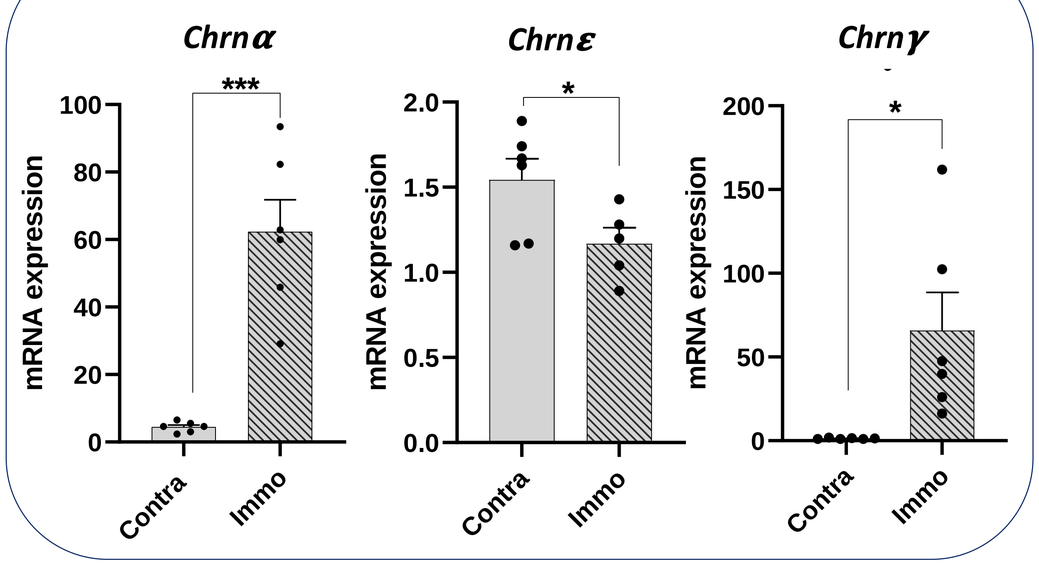
Skeletal muscle is a high plastic tissue able to change its mass upon different stimuli accordingly with environmental changes. Its adaptability depends on many factors and is based on complex mechanisms. Among the process that could alter muscle mass homeostasis, disuse and inactivity induce strong muscle mass and function decrease, having heavy impact on life quality and requiring long time to recover.

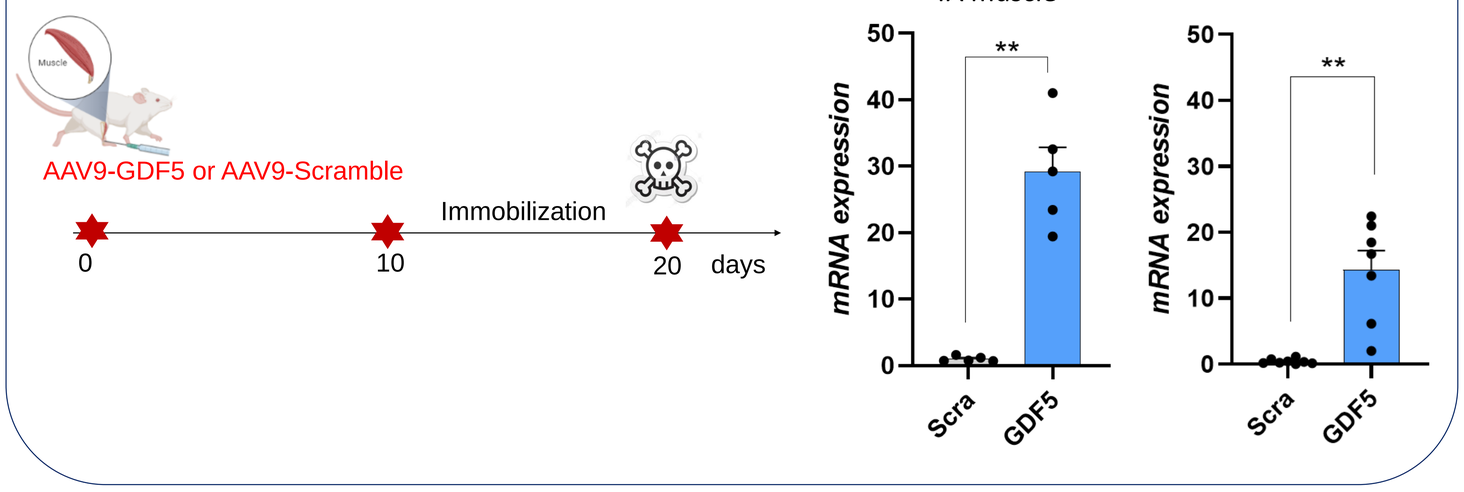
Growth Differentiation Factor 5 (GDF5) is a crucial player in muscle homeostasis, shown to counteract both denervation- and age-related muscle wasting by limiting the activation of catabolic signals. However, its effects on disuse atrophy following muscle immobilization has to be investigated.

Our aim is to better characterize the effect of GDF5 treatment on several morphological and functional parameters of skeletal muscle upon immobilization/release. In addition, we will assess its eventual benefits at shorter time points after release, in order to establish if GDF5-based treatment could be proposed to shorten the time-window needed for optimal muscle recovery after disuse.

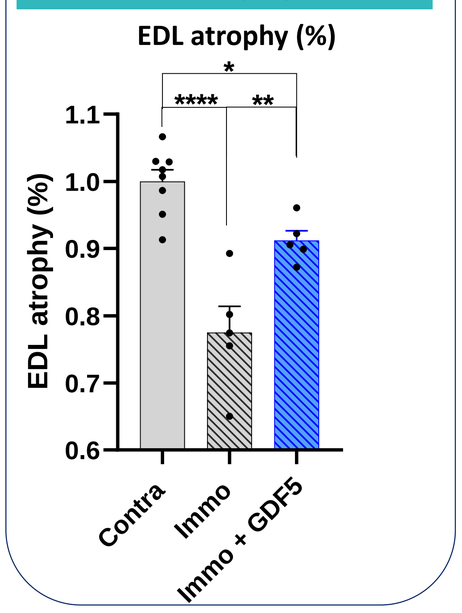
Immobilization induces AchR remodeling



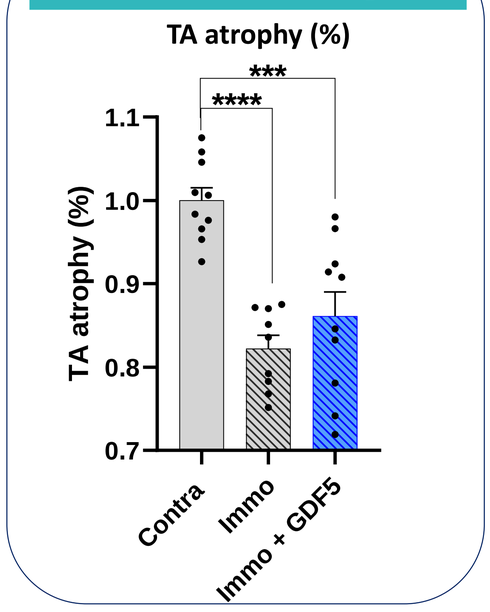
Protocol



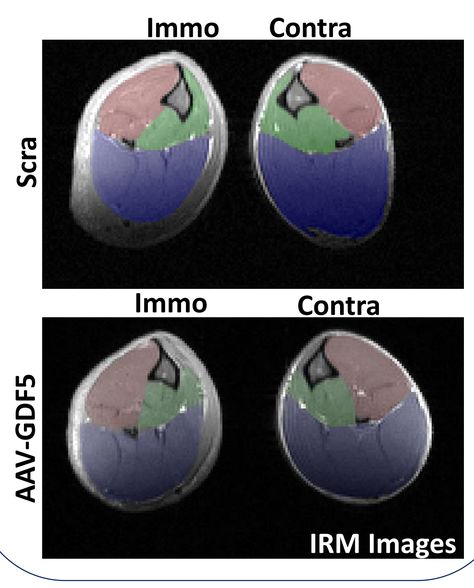
GDF5 OE rescues EDL atrophy



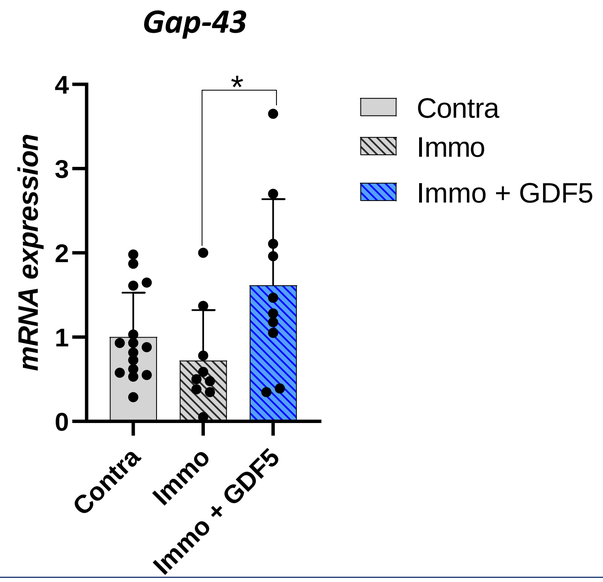
GDF5 OE has a mild effect on TA muscle weight



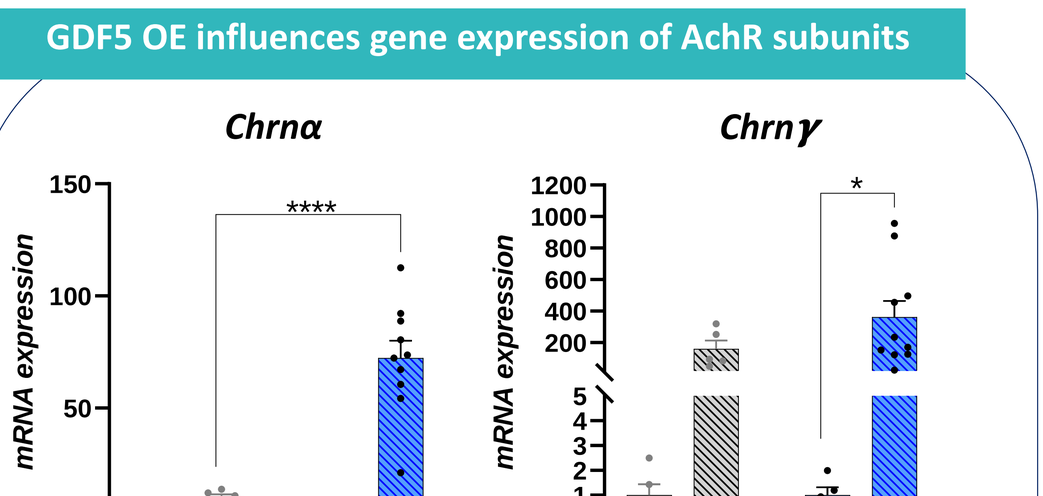
GDF5 OE slightly reduces hindlimb atrophy



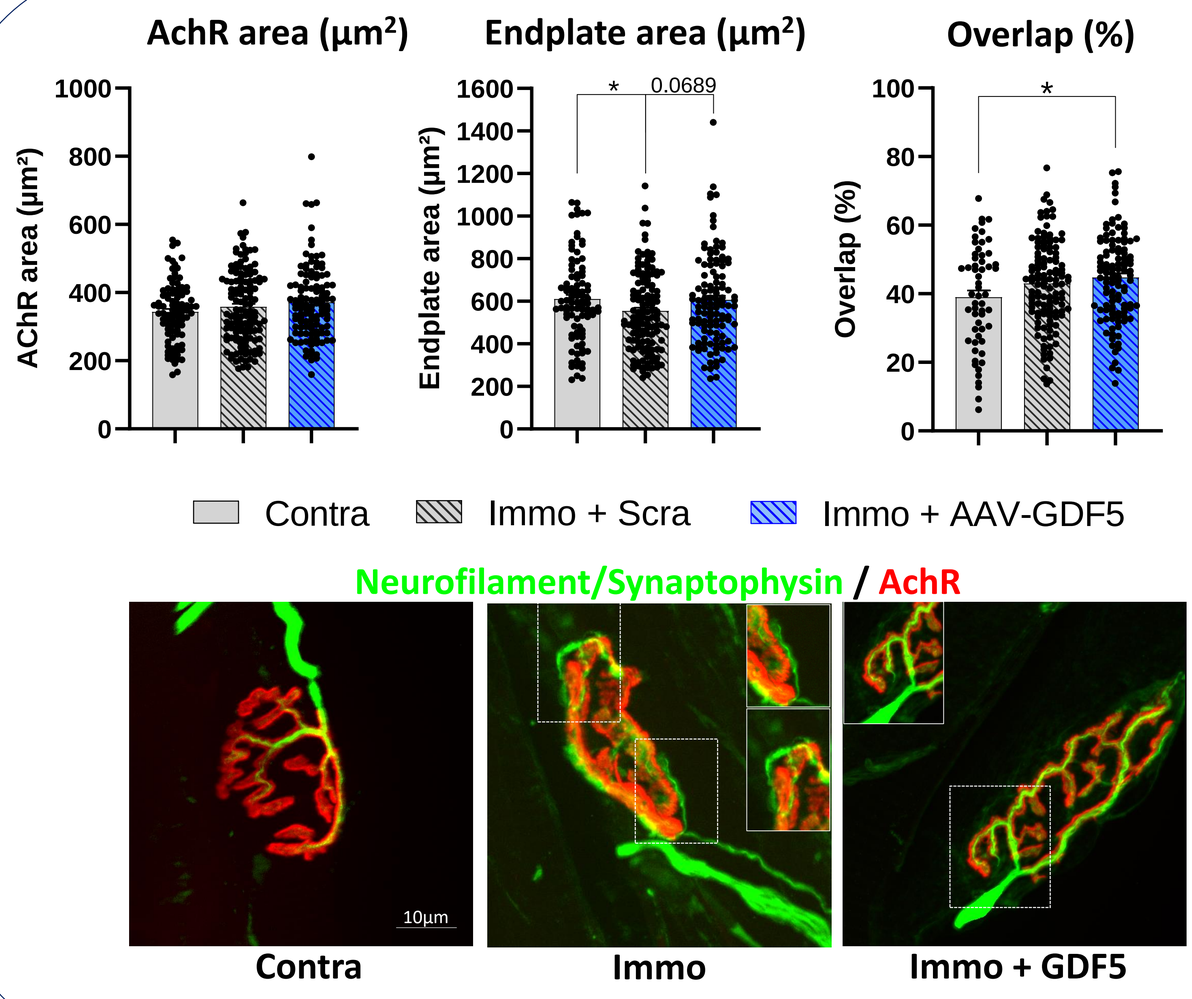
GDF5 OE increases the expression of gene responsible for nerve sprouting and axons regeneration



GDF5 OE influences gene expression of AchR subunits



GDF5 OE ameliorates NMJ connection



Conclusion

OE of GDF5 limits muscle atrophy caused by immobilization. In particular it has a positive effect on neuromuscular junction, increasing the expression of AchR subunits. These data suggest that GDF5 stimulates the formation of new receptors increasing the muscle sensibility to the immobilization. Moreover NMJ investigations shows that GDF5 OE ameliorates myofibers innervation.

Perspectives

In vitro studies are envisaged in order to understand the molecular mechanism influencing muscular cells in absence of gravity.

Future studies could consider GDF5 as a potential therapeutic tool to reduce the side effects caused by immobilization on neuromuscular system.