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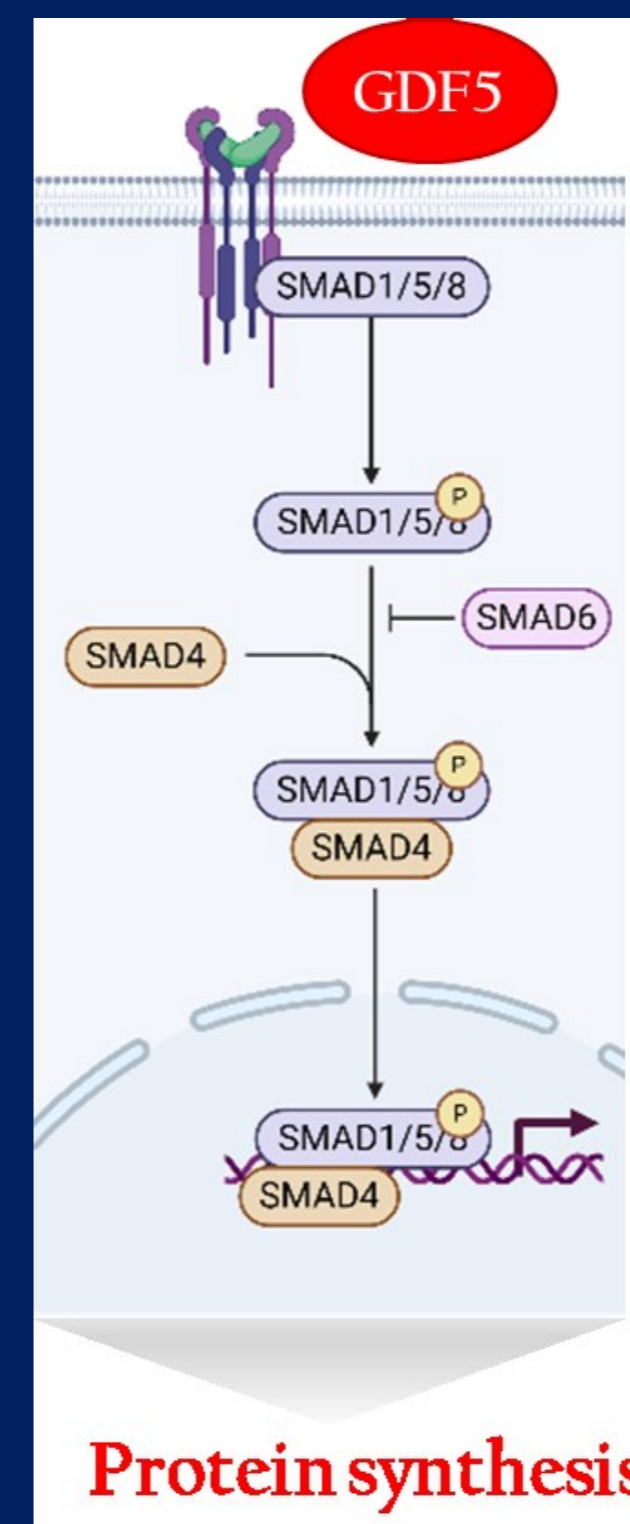
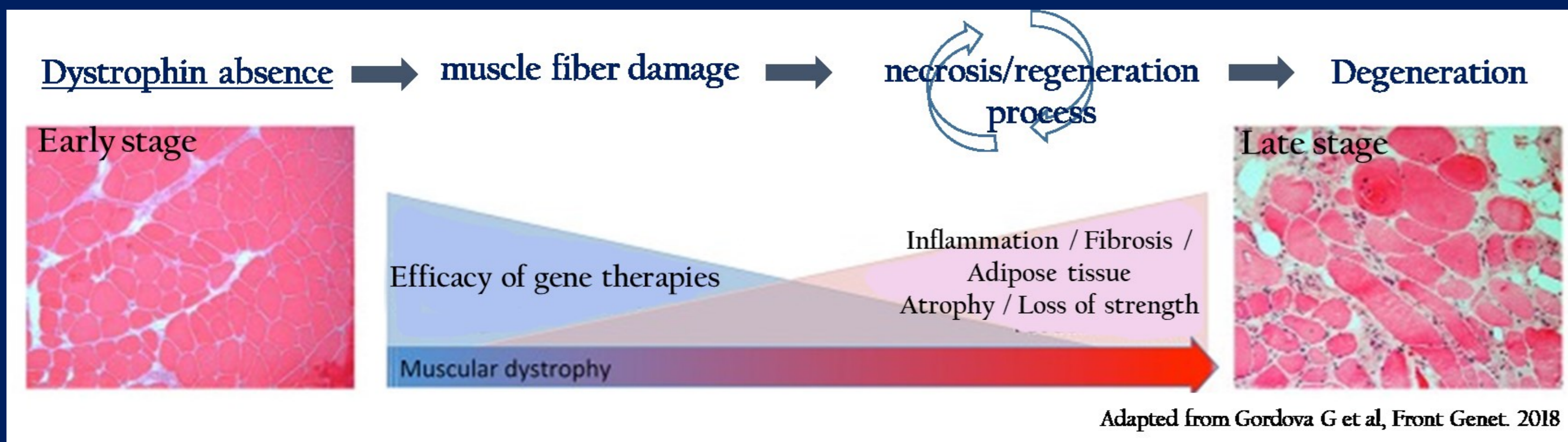
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GDF5 therapeutic potential for DMD

Christel Gentil¹, Lucile Saillard¹, Amélie Vergnol¹, Lorenzo Giordani¹, Bruno Cadot¹, Anne Forand¹, Sophie Moog¹, Chiara Novello¹, Pierre Meunier¹, Sestina Falcone¹ and France Piétri-Rouxel¹

¹Sorbonne Université, INSERM, Institut de Myologie, Centre de Recherche en Myologie, F-75013 Paris, France

Introduction



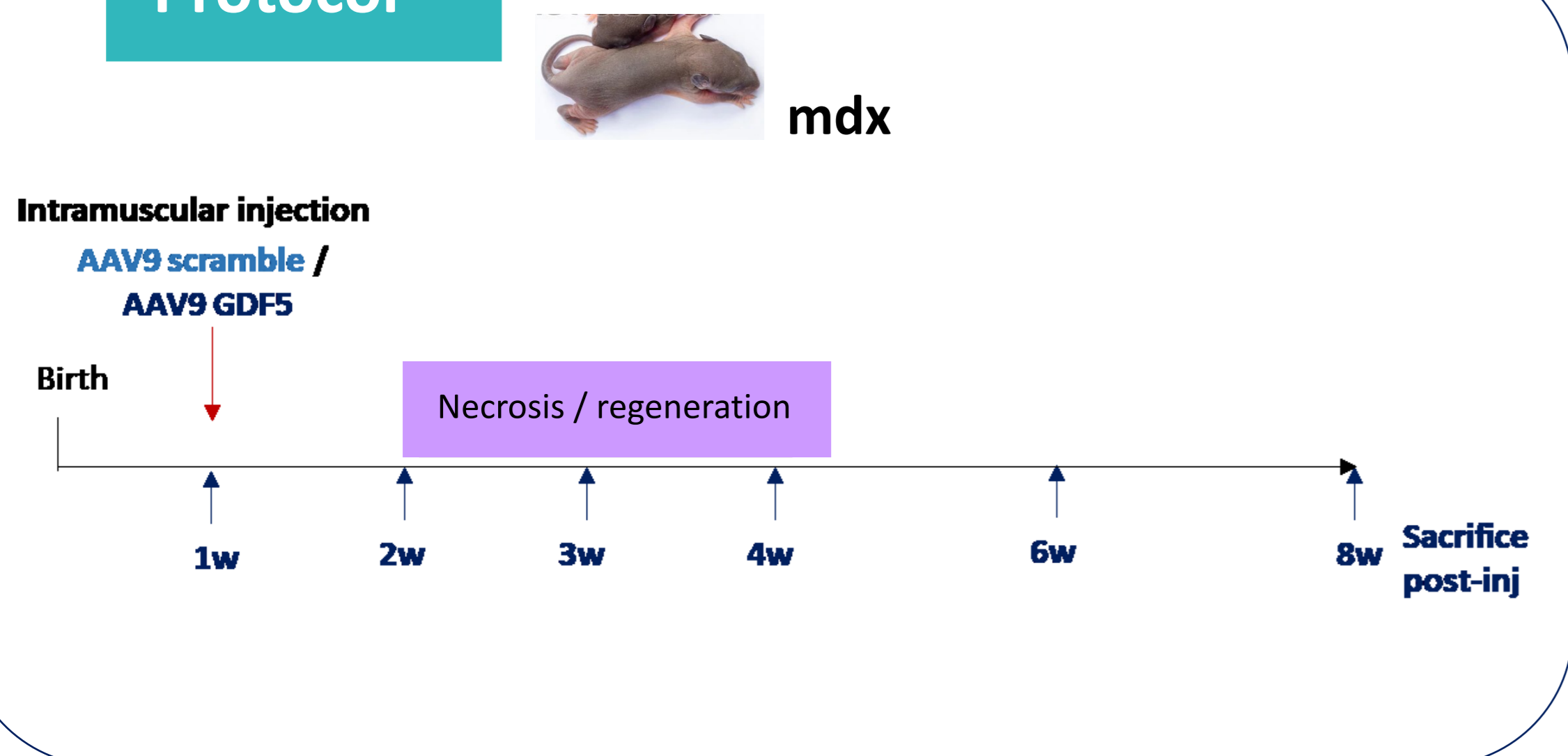
In terms of muscle tissue homeostasis, an emerging relevance is observed for components of Bone Morphogenetic Protein (BMP) family such as BMP14 also called Growth Differentiation Factor 5 (GDF5). GDF5 signaling includes the phosphorylation of intracellular SMAD1/5/8 complex, which translocate to the nuclei and controls gene transcription.

GDF5 has been shown to prevent both muscle mass loss and force decline during ageing (Traoré et al, 2019).

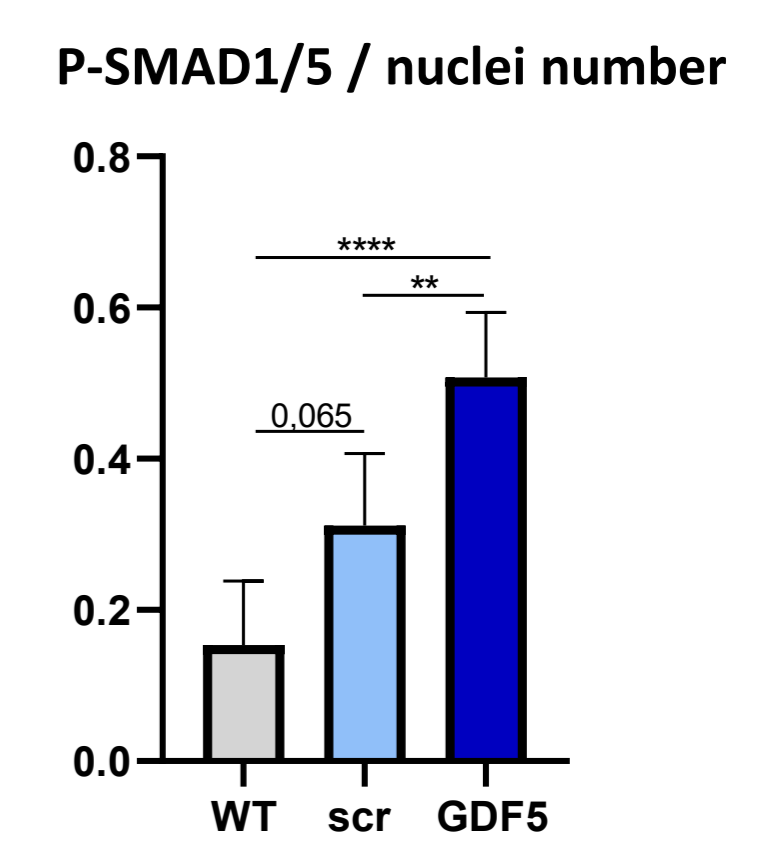
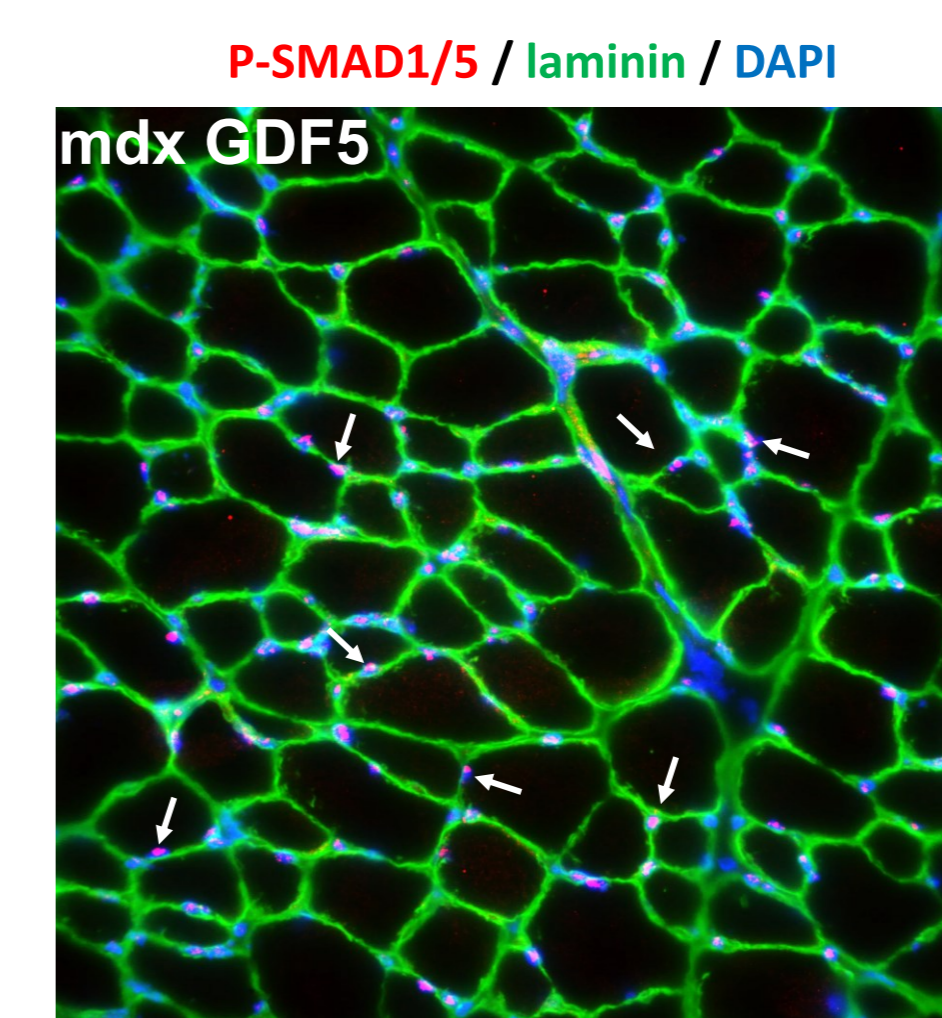
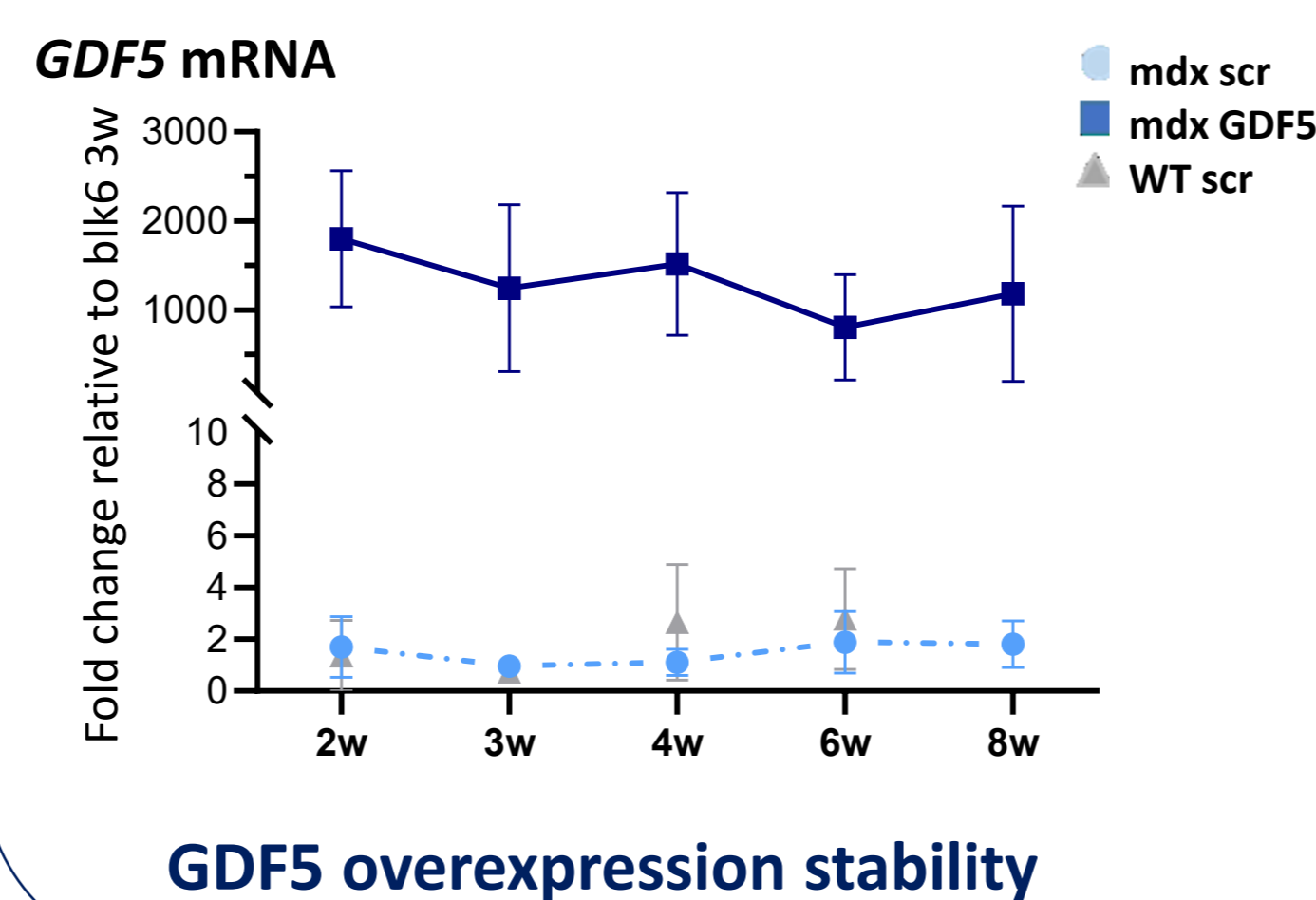
In addition, this factor has been described as a positive modulator of muscle mass homeostasis and a potential regulator of muscle repair (REF).

Here, we investigated the impact of GDF5 overexpression in the progression of DMD pathophysiology features in mdx mice (a DMD mouse model).

Protocol

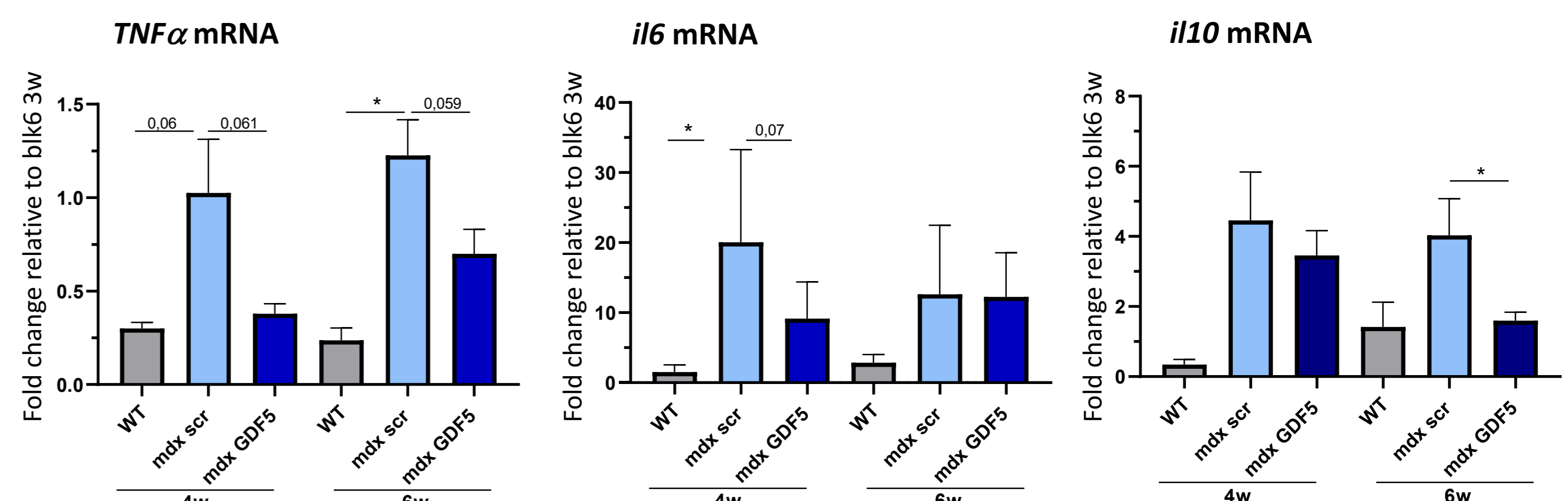
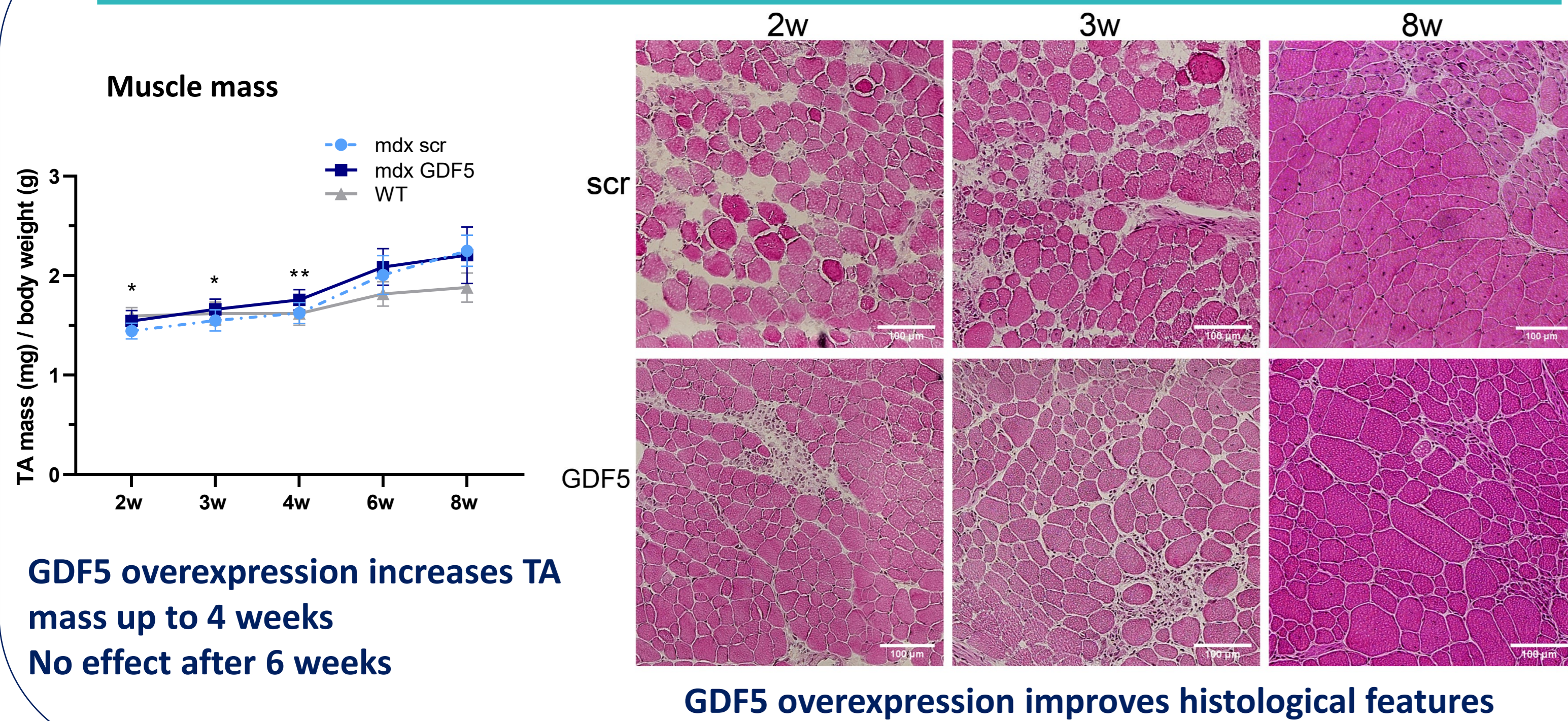


Activation of the GDF5 pathway

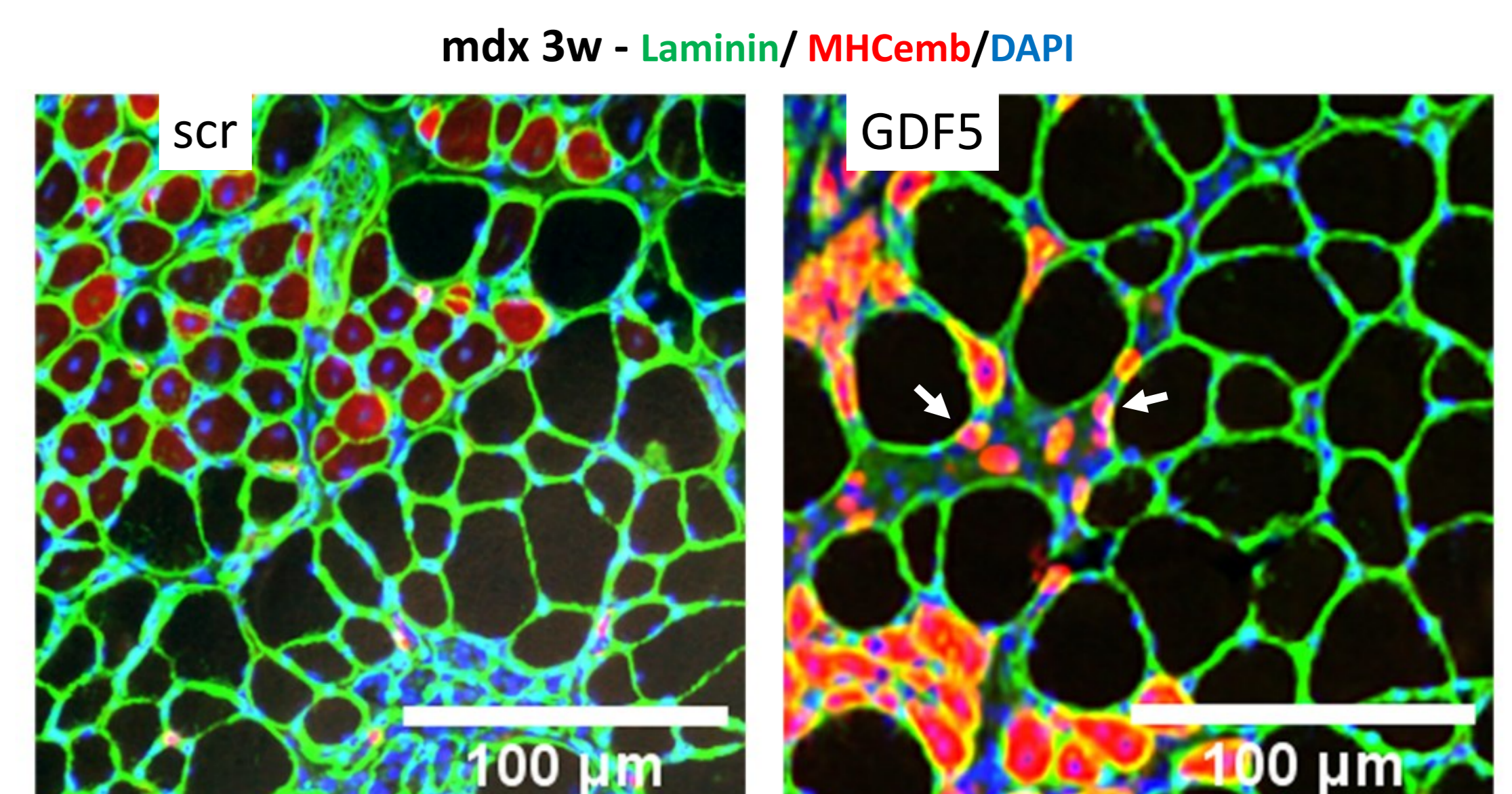
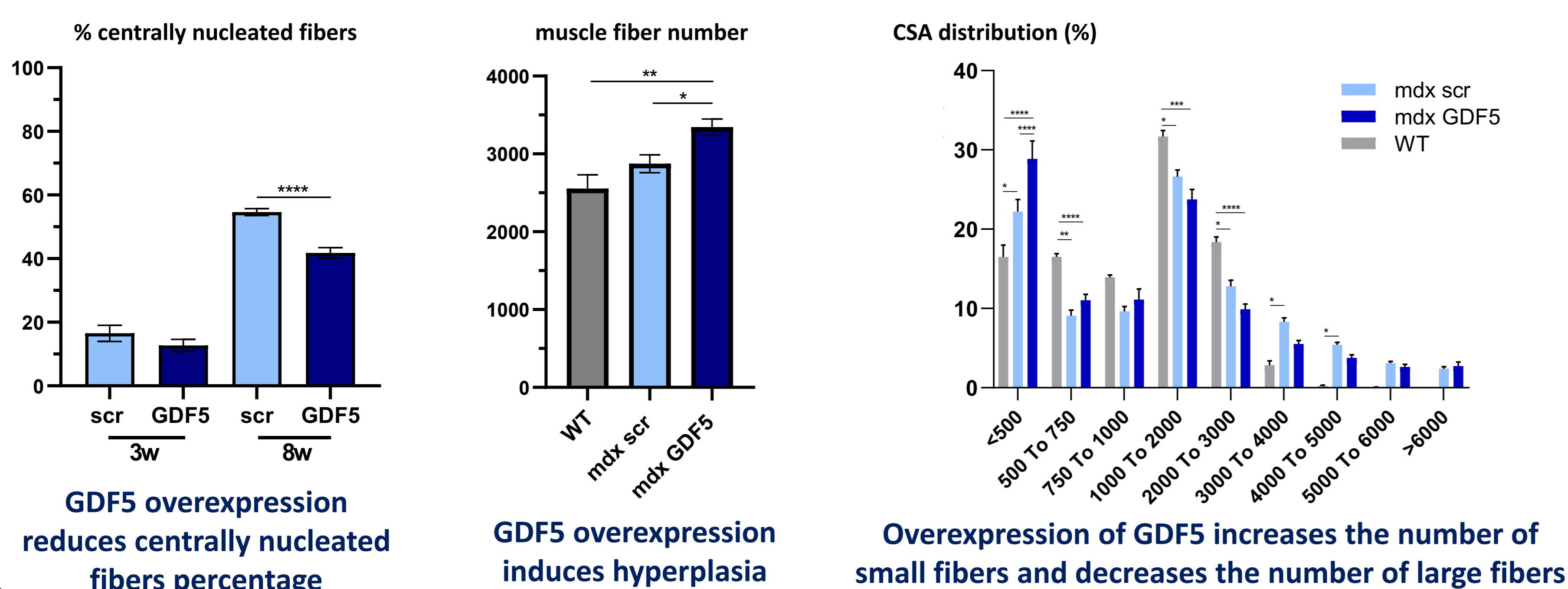


GDF5 overexpression induces SMAD1/5 phosphorylation

GDF5 overexpression effect on the DMD muscle pathophysiology



GDF5 overexpression on the differentiation / regeneration process



Presence of newly fused fibers in interstitial regions of GDF5 treated TAs

Conclusions

GDF5 overexpression seems to slow down the necrosis/regeneration process in mdx muscle

GDF5 overexpression promotes fiber formation in muscle interstitial regions

Perspectives

Identification of different cellular players underpinning the observed hyperplasia.

Does GDF5 activate muscular progenitors differentiation ?

Investigate potential benefits of AAV-GDF5 in DMD gene therapy