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Skeletal muscle atrophy and impaired myogenesis in spinal muscular atrophy

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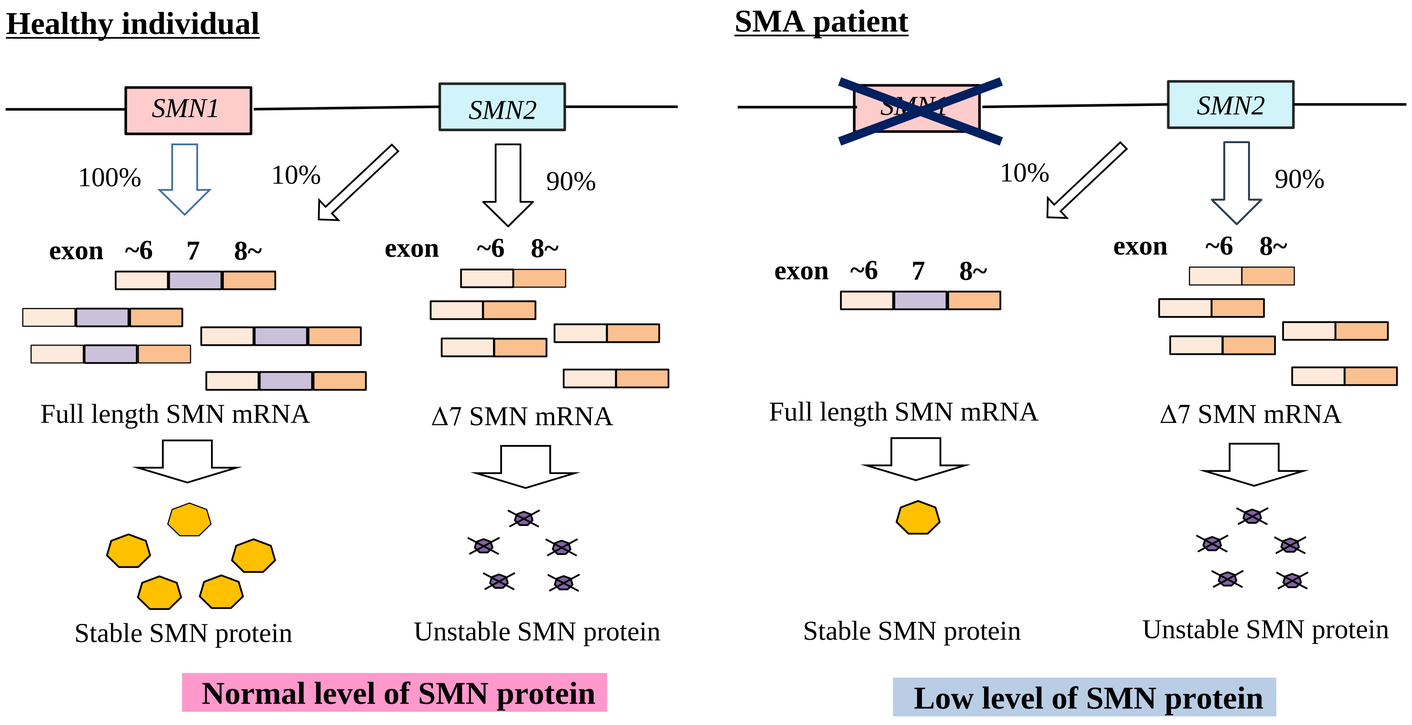
Background

Spinal muscular atrophy (SMA)

- Inherited disease with deletion or mutation of survival motor neuron (SMN) 1 gene. While SMN protein form derived from SMN1 gene is stable, SMN2 gene mainly produce unstable form of SMN protein, then the lack or mutation of SMN1 gene results in low expression level of SMN protein (1).
- The characterized symptoms of SMA are progressive motor neuron death and subsequent muscle weakness.
- Nusinersen, an antisense oligonucleotide that increase SMN protein level, has been approved as the first drug for SMA treatment (2). Nusinersen is administered intrathecally.



Purpose

The purpose of this study was to elucidate the mechanism underling muscle atrophy in SMA and propose a new therapeutic target to prevent skeletal muscle atrophy.

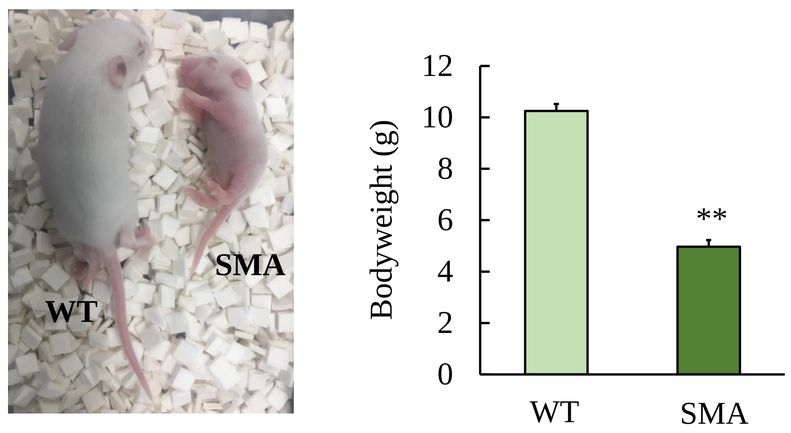
Animal

SMNΔ7$^{+/+}$; *SMN2*$^{+/+}$; *mSmn*$^{-/-}$ mouse (SMNΔ7 mouse)

- A severe mouse model for SMA
- Exhibit impaired motor function and normally live for 14 days (3)
- Gastrocnemius muscle of.SMNΔ7 mouse (SMNΔ7-GM) was isolated at P11.

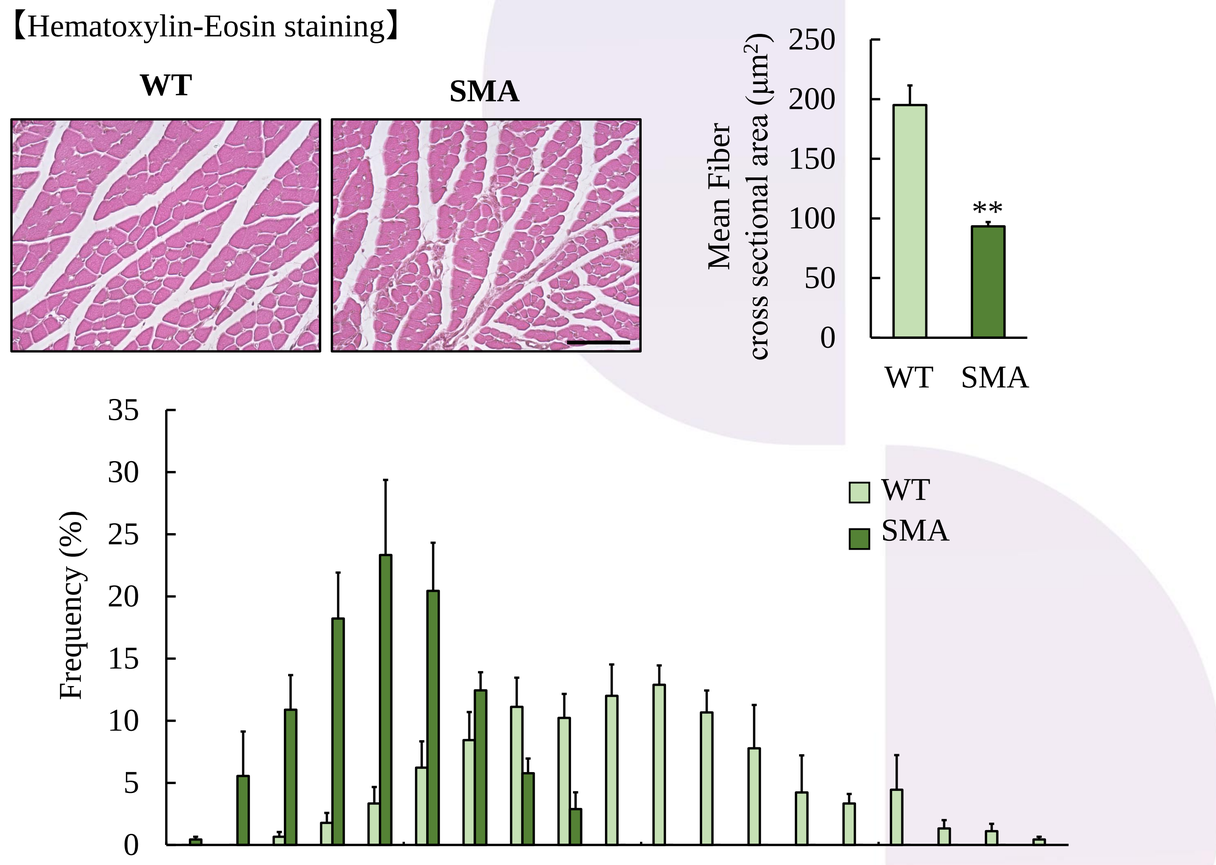
Results

Fig.1 SMNΔ7 mouse exhibits decreased body mass.



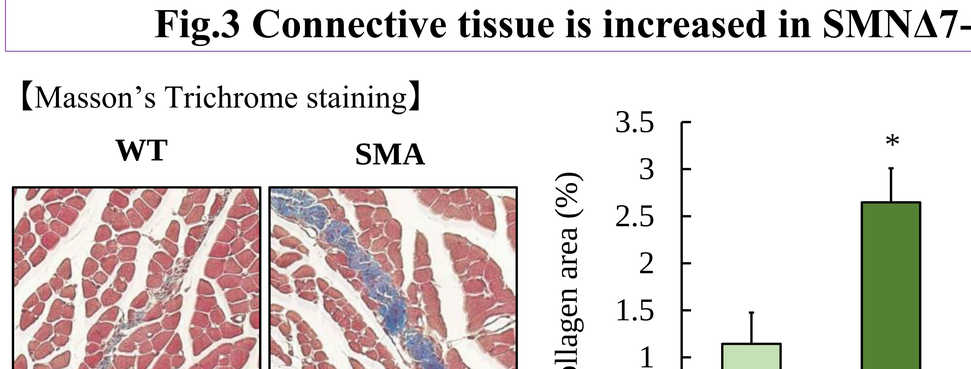
**P < 0.01 vs WT group.Data are expressed as mean ± SEM. (n = 3 or 4)

Fig.2 SMNΔ7 mouse exhibits impaired skeletal muscle growth.



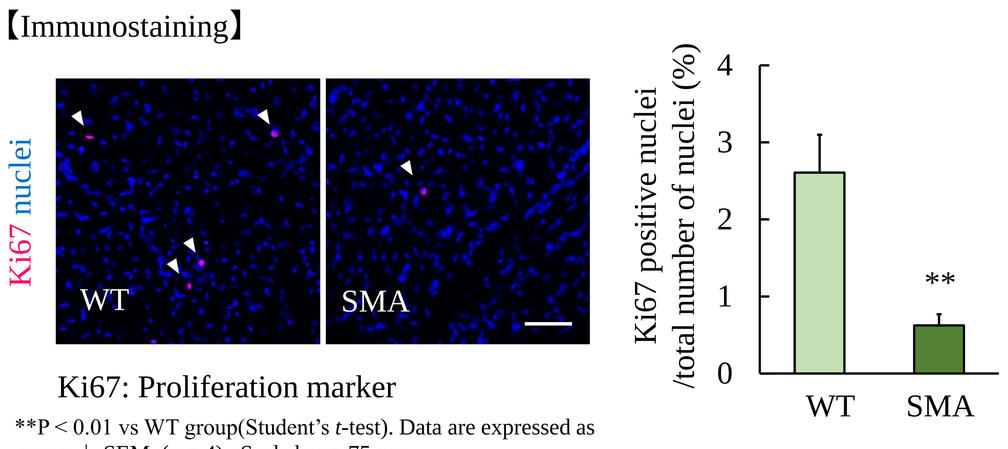
**P < 0.01 vs WT group.Data are expressed as mean ± SEM. (n = 3) Scale bar = 75 μm

Fig.3 Connective tissue is increased in SMNΔ7-GM.



*P < 0.05 vs WT group (Student's *t*-test). Data are expressed as mean ± SEM. (n = 3). Scale bar = 100 μm

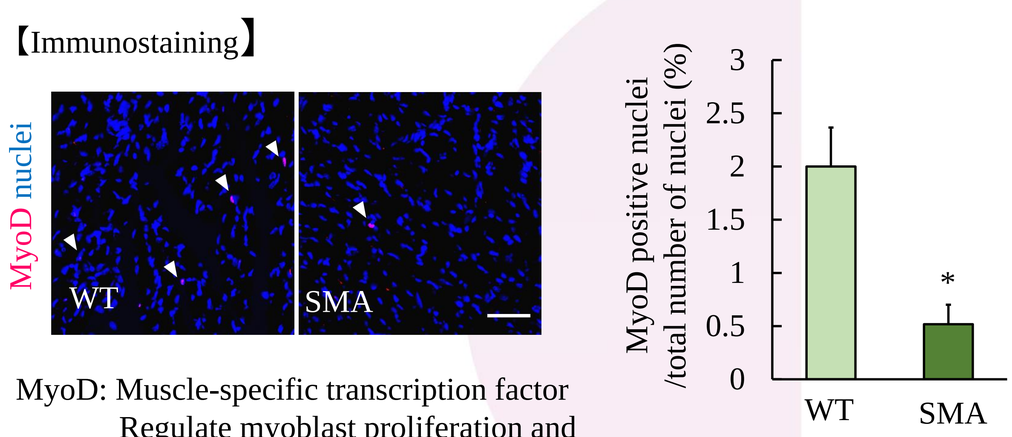
Fig.4 Proliferative cells are decreased in SMNΔ7-GM.



Ki67: Proliferation marker

**P < 0.01 vs WT group(Student's *t*-test). Data are expressed as mean ± SEM. (n = 4). Scale bar = 75 μm

Fig.5 Myogenesis related transcription factor, MyoD was decreased in SMNΔ7-GM.



MyoD: Muscle-specific transcription factor
Regulate myoblast proliferation and differentiation.

*P < 0.05 vs WT group (Student's *t*-test). Data are expressed as mean ± SEM. (n = 4). Scale bar = 100 μm

Conclusion

These results suggest myogenesis should be impaired in skeletal muscle under SMA pathology and impaired myogenesis contribute to skeletal muscle atrophy in SMA. Modulation of myogenesis in skeletal muscle may be an effective strategy for the SMA treatment.

Disclosure

The authors have no conflict of interest to disclose.

References

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