

Poster
25

Inhibition of JNK3 signaling pathway promotes spinal motor neurons survival and muscle improvement in a humanized cell model of neuromuscular junction of SMA

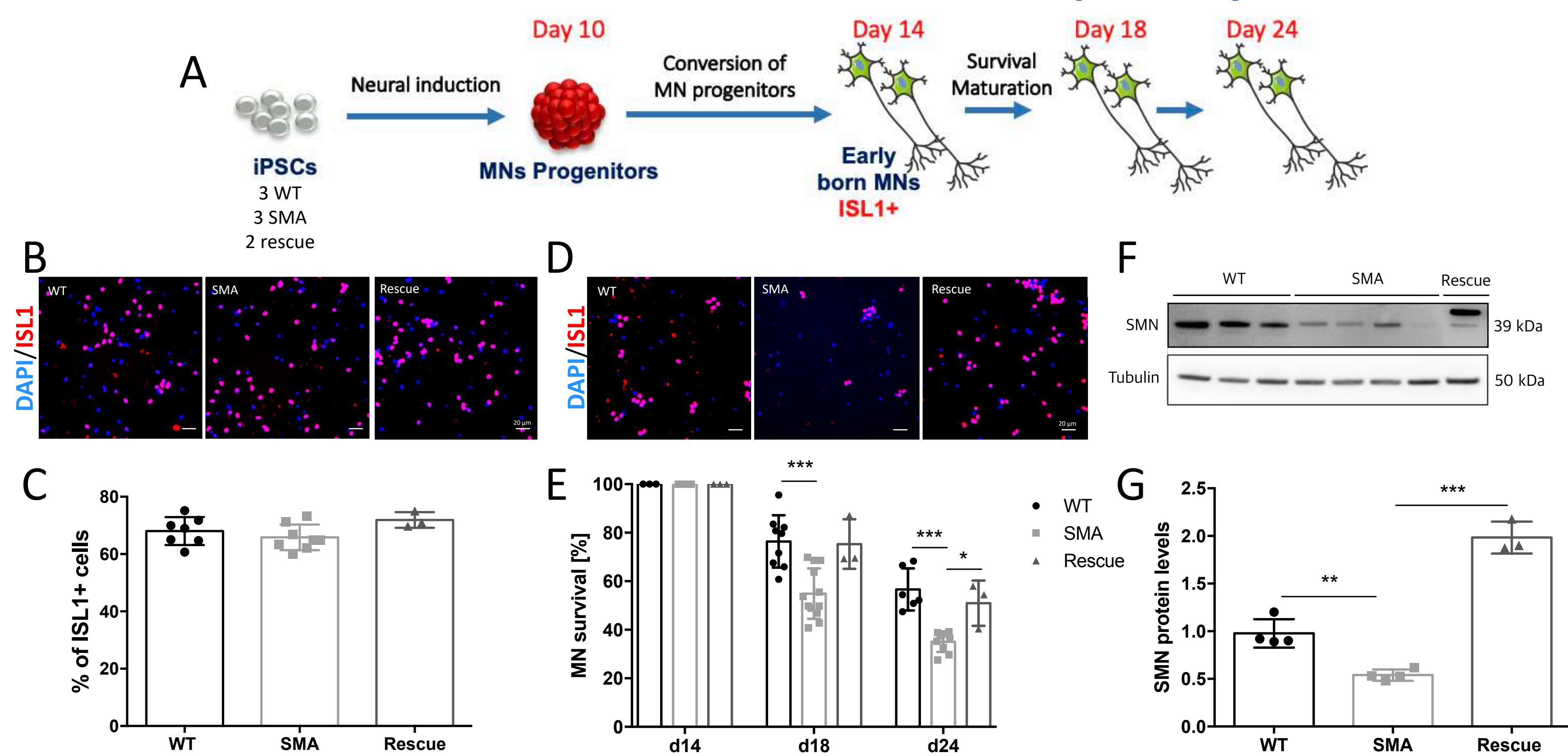
C. Januel¹, J. Tahraoui¹, J. Côme², L. Lesueur², L. Morizur², Céline Leteur², Jérôme Polentes², Vincent Mouly³,
M. Peschanski², C. Martinat¹

¹I-STEM, INSERM UEVE UMR861, Corbeil-Essonnes, France

²CECS/AFM, I-STEM, Corbeil-Essonnes, France.

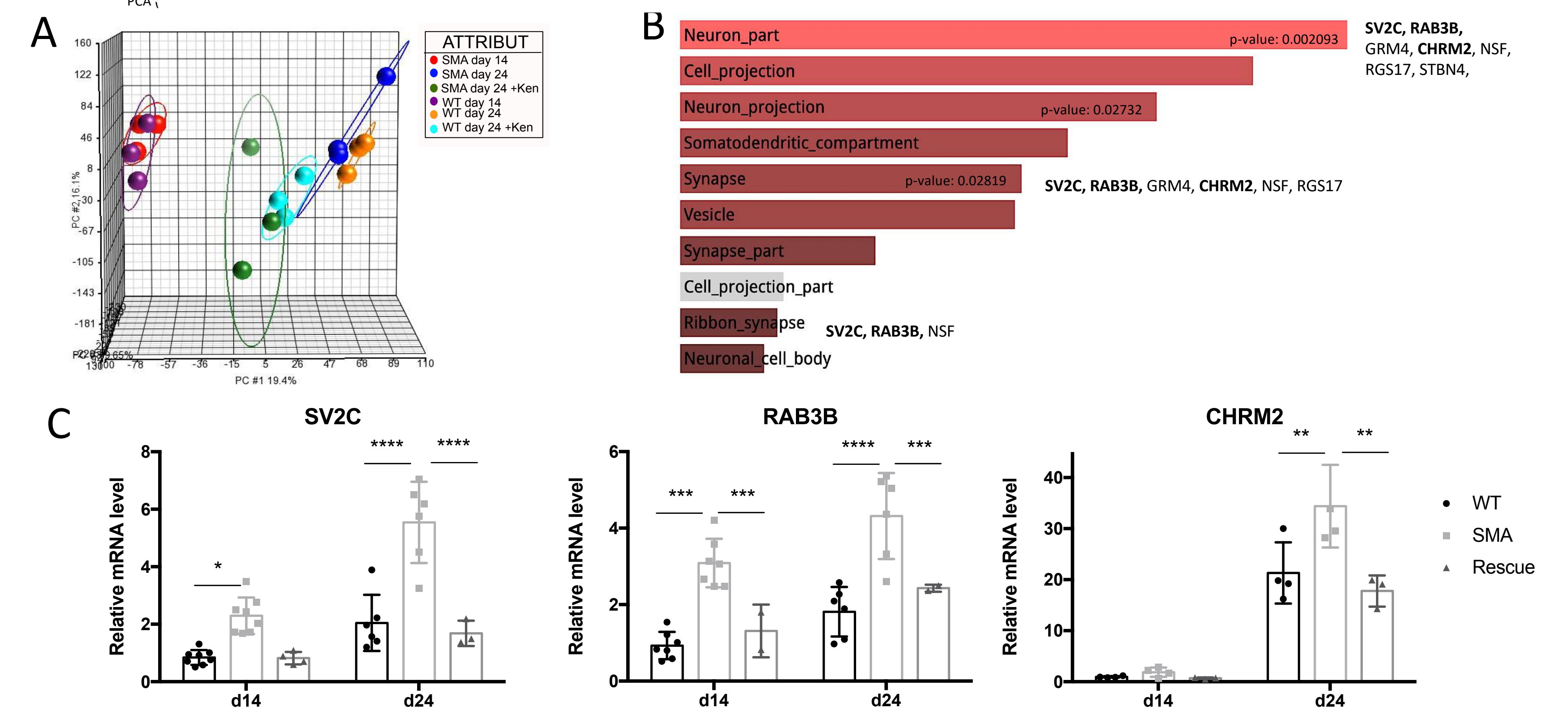
³Sorbonne Université, INSERM, Association Institut de Myologie, Centre de recherche en myologie, UMR-S 974, Paris, France.

1. SMA iPSC-derived MNs have increased susceptibility to MN death



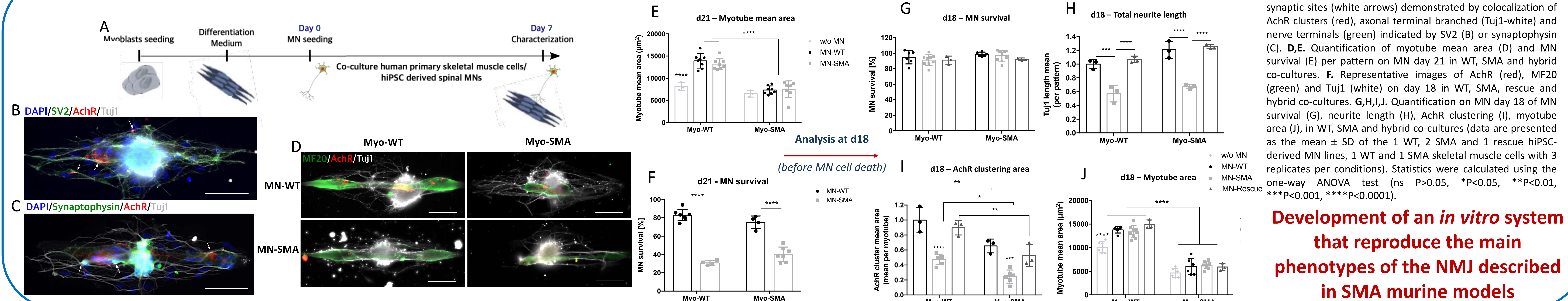
SMN reduction does not affect the early steps of MN specification but their survival

2. Dysregulation of synaptic markers in SMA spinal MN



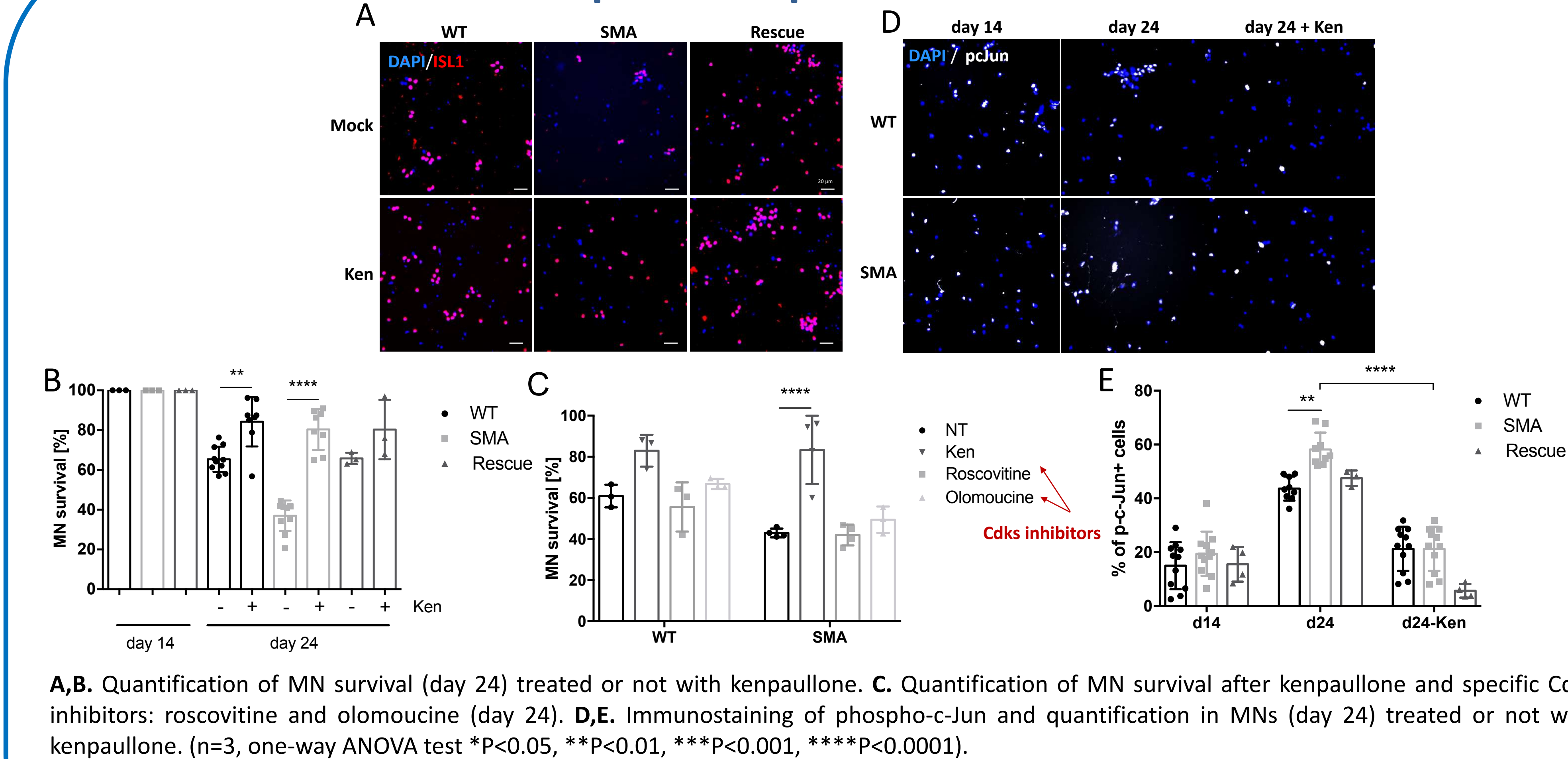
What are the functional consequences in term of connectivity?

3. Study the interaction between MN and its skeletal muscle target



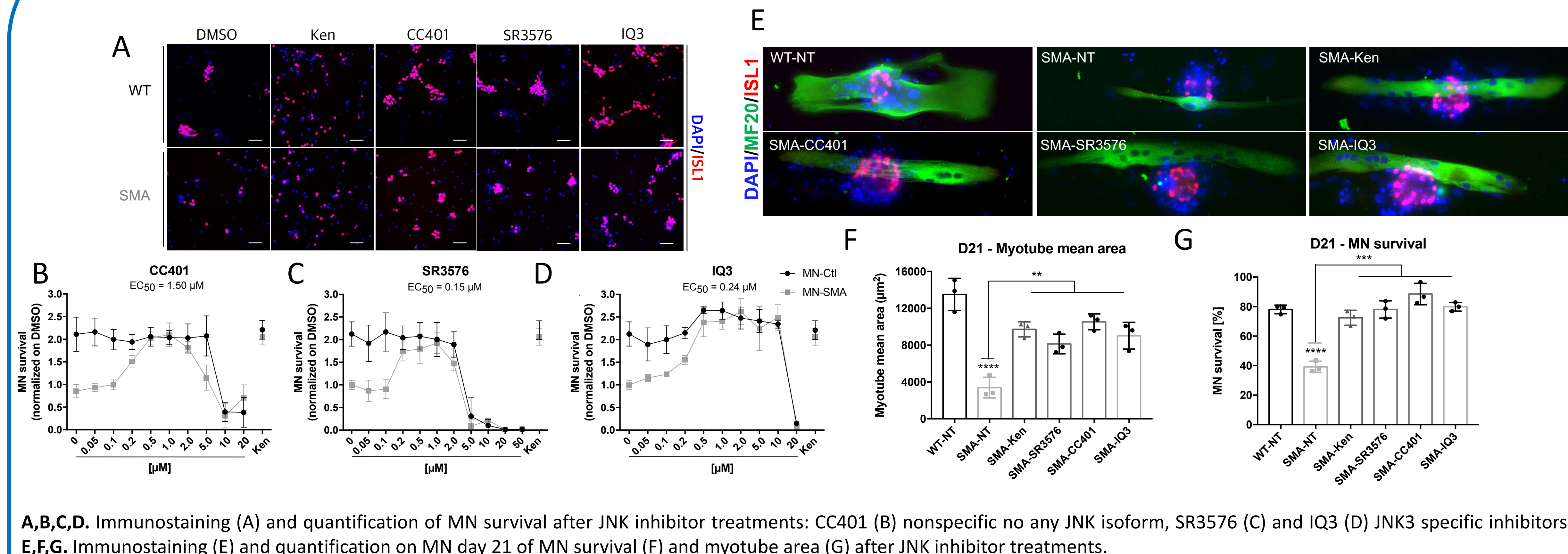
Development of an *in vitro* system that reproduce the main phenotypes of the NMJ described in SMA murine models

4. Kenpaullone promotes MN survival



Kenpaullone promotes MNs survival through a JNK signalling pathway inhibition

5. Correction of SMA-related neuronal and muscular phenotypes by the JNK inhibitors

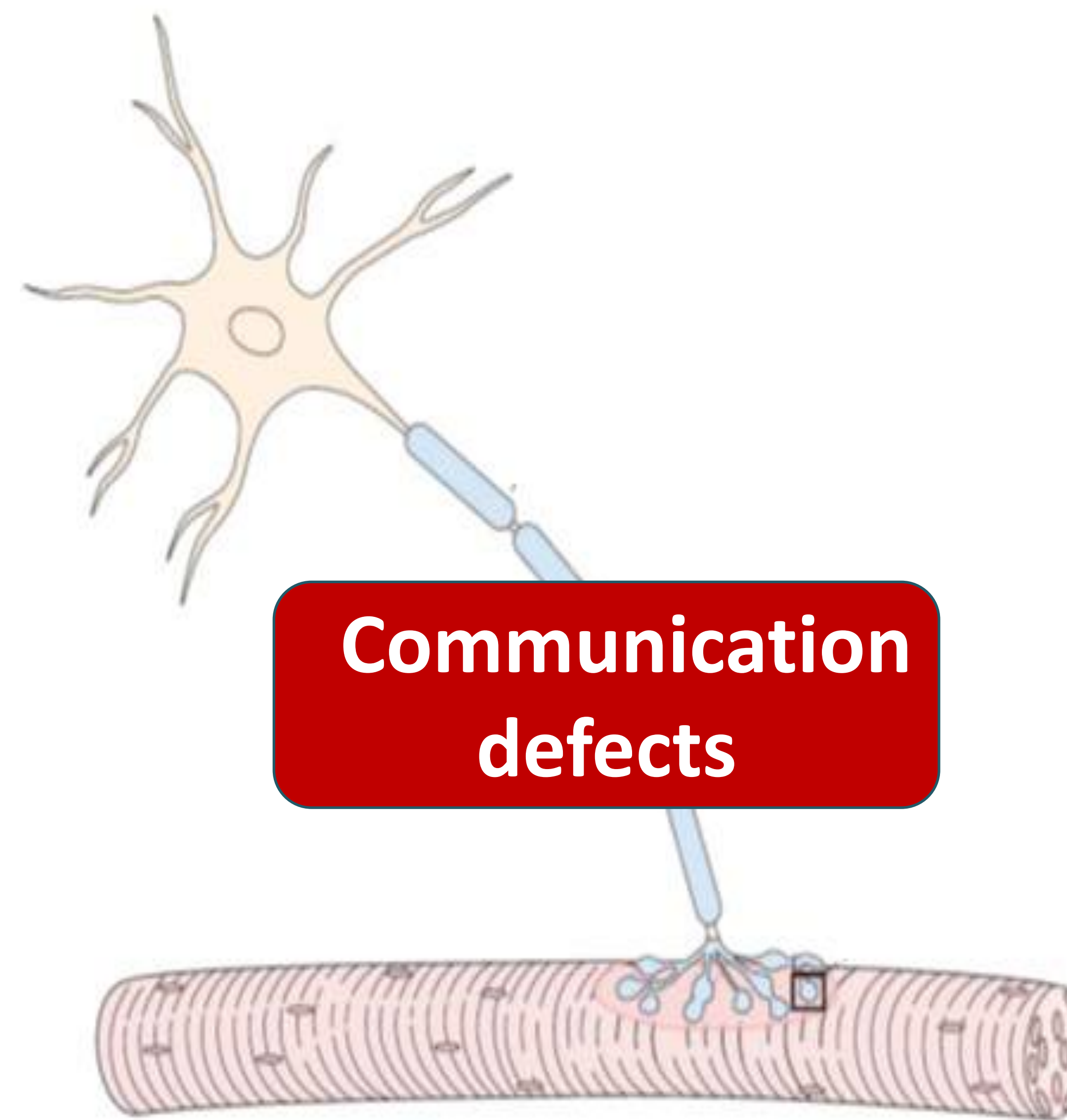


JNK3 inhibition might sufficient to promote the correction of SMA-related neuronal and muscular phenotypes

Conclusions & Perspectives

Conclusions

- ✓ iPSC-derived MNs as a solid and robust model to phenocopy the SMA disease
- ✓ Development of an *in vitro* system that reproduce the main phenotypes of the NMJ described in SMA murine models
- ✓ Correction of SMA-related neuronal and muscular phenotypes by the JNK inhibitors



Perspectives

- **Therapeutic target:** JNK signalling pathway: an emerging therapeutic target for SMA?
- **Functional consequences:** Analyse of the JNK inhibition effect on other and more functional NMJ phenotypes: neurite outgrowth, AChR clustering, calcium flux, synaptic markers...
Analyse of the JNK inhibition effect on SMN expression level