

YMTHE, Volume 30

## **Supplemental Information**

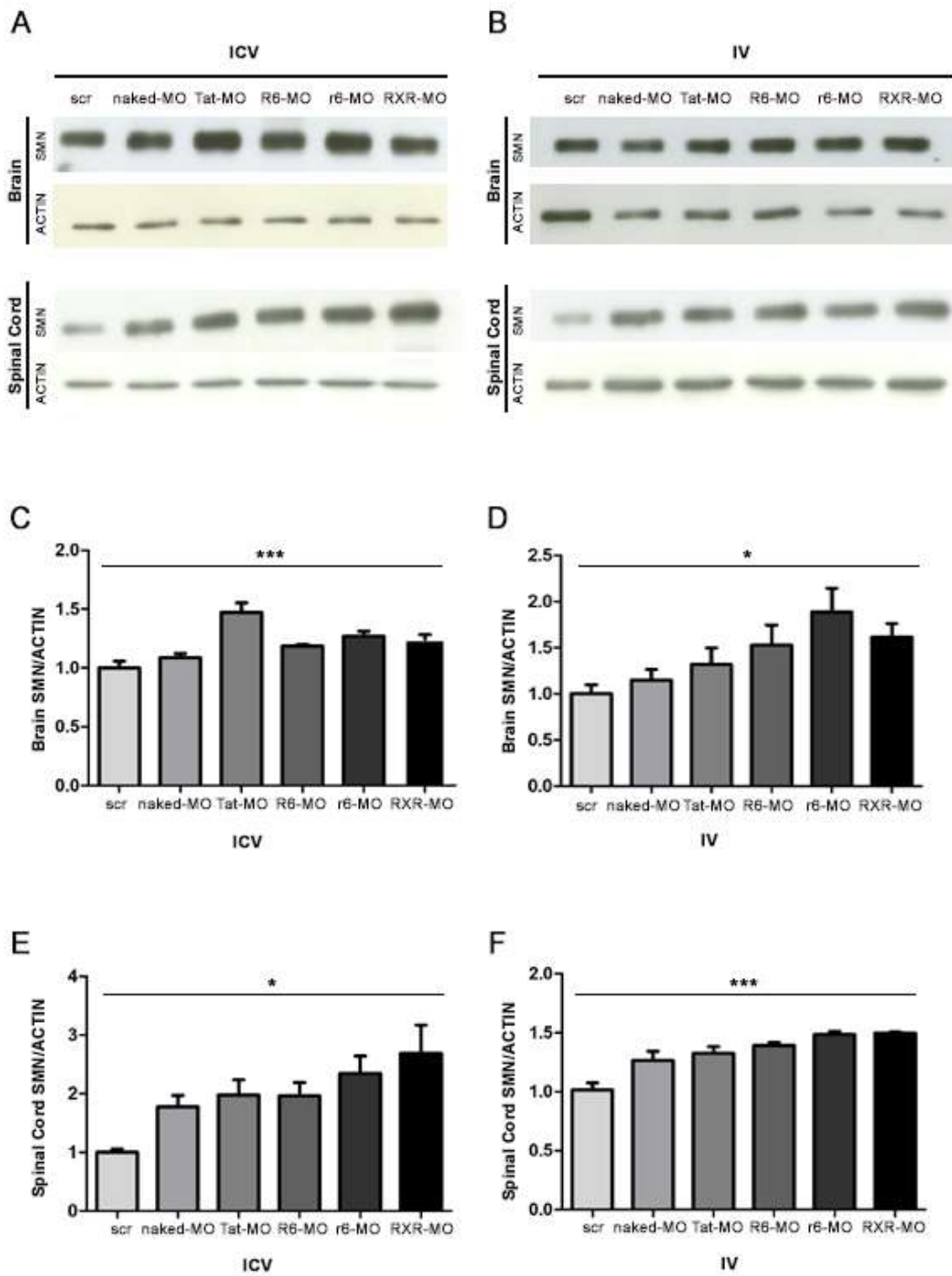
### **Cell-penetrating peptide-conjugated Morpholino rescues SMA in a symptomatic preclinical model**

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## Supplementary materials

### Supplementary Figures

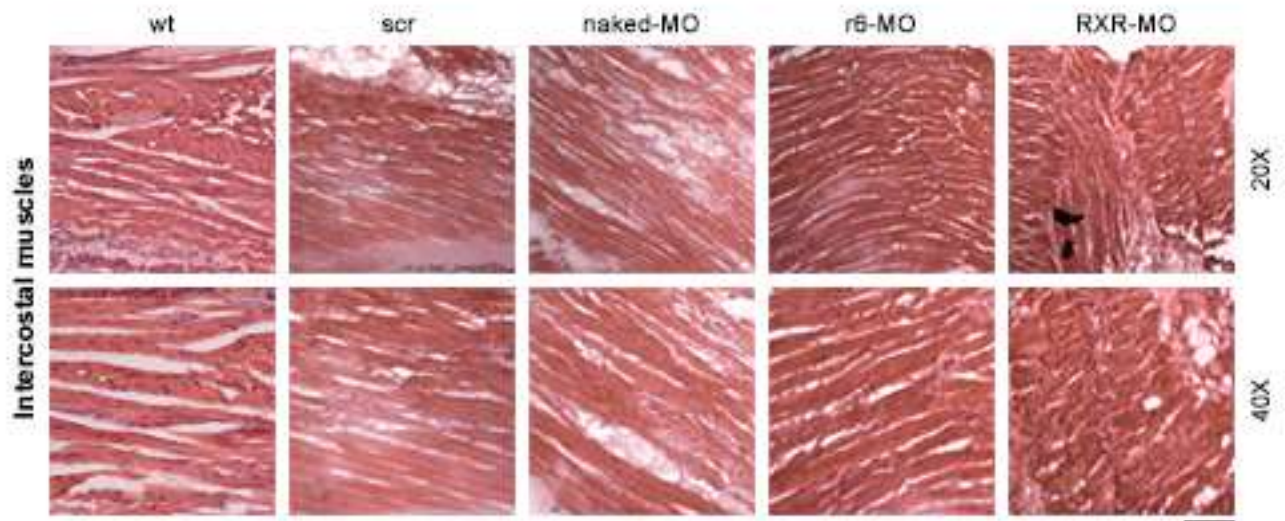
Figure S1



**Fig. S1. r6 and RXR peptides are the most efficient in carrying MO to CNS**

Representative image of WB for SMN and actin (A) and densitometric analysis of brain (B, D) and spinal cord (C, E) of heterozygous SMA mice treated ICV (B, C) and IV (D, E) at P1 with 12 nmoles/gr dose of naked MO, Tat-MO, R6-MO, r6-MO, RXR-MO, and sacrificed at P7. Scr-animals were used as controls. Relative amounts of SMN were normalized on the actin levels as mean value (n=6 mice/group). Statistical significance was determined using ANOVA (\* $P < 0.05$ , \*\*\* $P < 0.001$ ) and Student's *t* test for r6- and RXR- vs naked MO ( $P < 0.05$ ).

**Figure S2**



**Fig. S2. CPPs-MO ameliorate muscle fibers organization**

Representative image of haematoxylin/eosin staining of intercostal muscles from SMA mice treated with scr-MO, naked MO, r6-MO, or RXR-MO and wild type mice, sacrificed at P10. Magnification: 20X, 40X; scale bar: 90  $\mu$ m.

## **Supplementary Movies**

### **Movie S1. P5 SMAA7 mice failing righting test**

Representative video of SMAA7 mice showing first symptoms of the disease, like motor disability, at P5. When turned on their back, pups were not able to stand on four paws again.

### **Movie S2. CPP-MO SMAA7 mice maintain good motor skills**

Representative video of mice treated with 12 nmoles/gr CPPs-MO at P5 by IP injection maintaining motor ability after 1 month from the first treatment.

### **Movie S3. CPP-MO SMAA7 mice are able to perform righting test**

Representative video of mice treated with 12 nmoles/gr CPP-MO at P5 by IP injection successfully performing righting test at P14.

### **Movie S4. CPP-MO SMAA7 mice are able to complete rotarod test**

Mice treated with 12 nmoles/gr CPP-MO at P5 by IP injection were able to undergo and complete 300 seconds of rotarod test at P45, while scr and naked MO mice could not survive long enough to be tested.