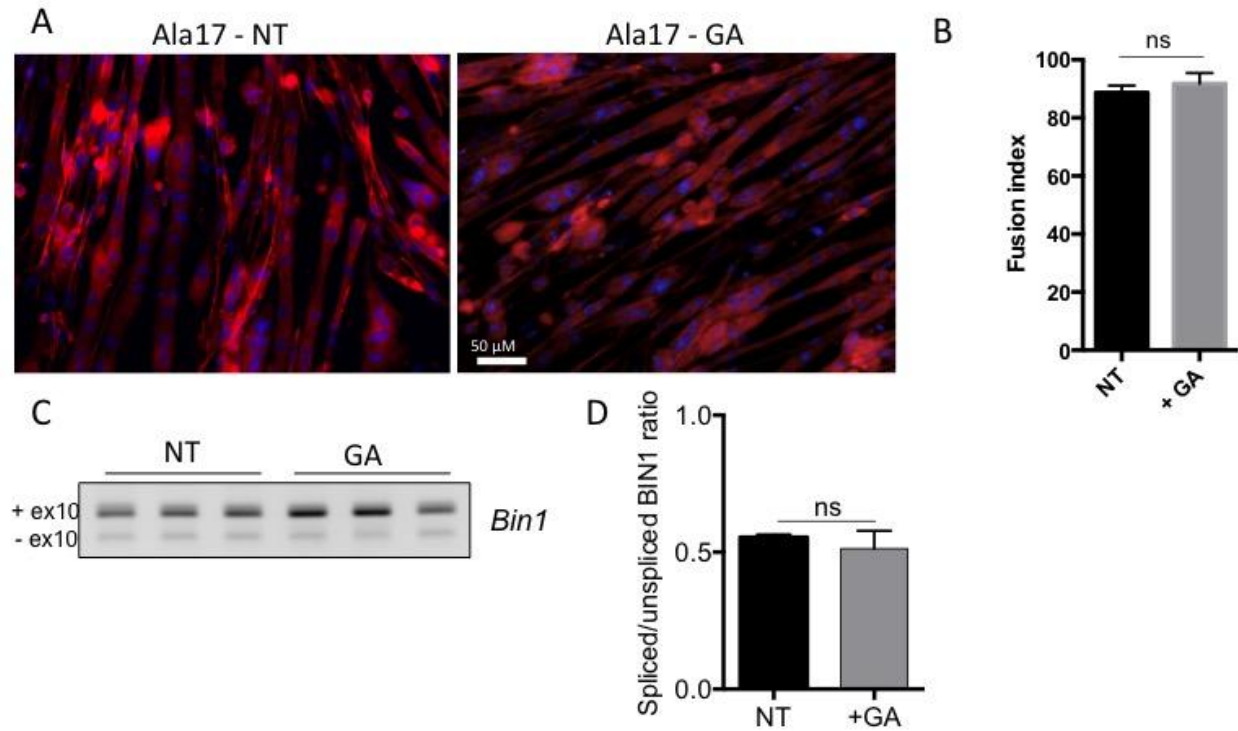
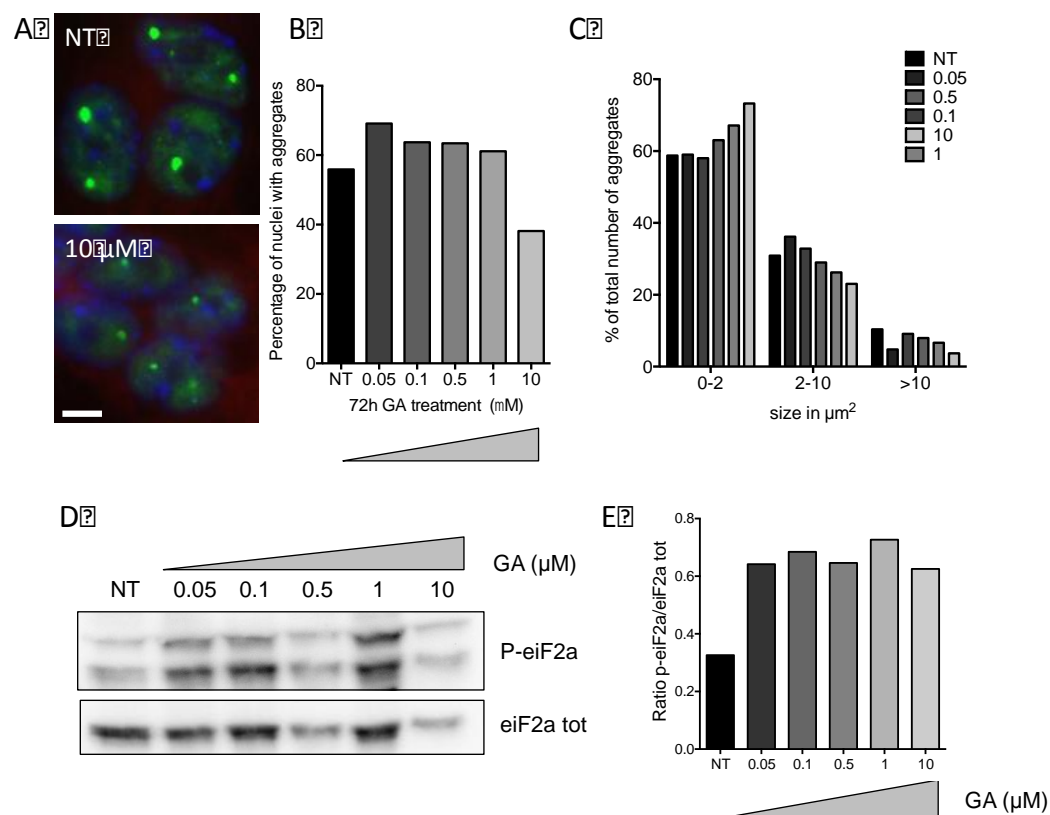


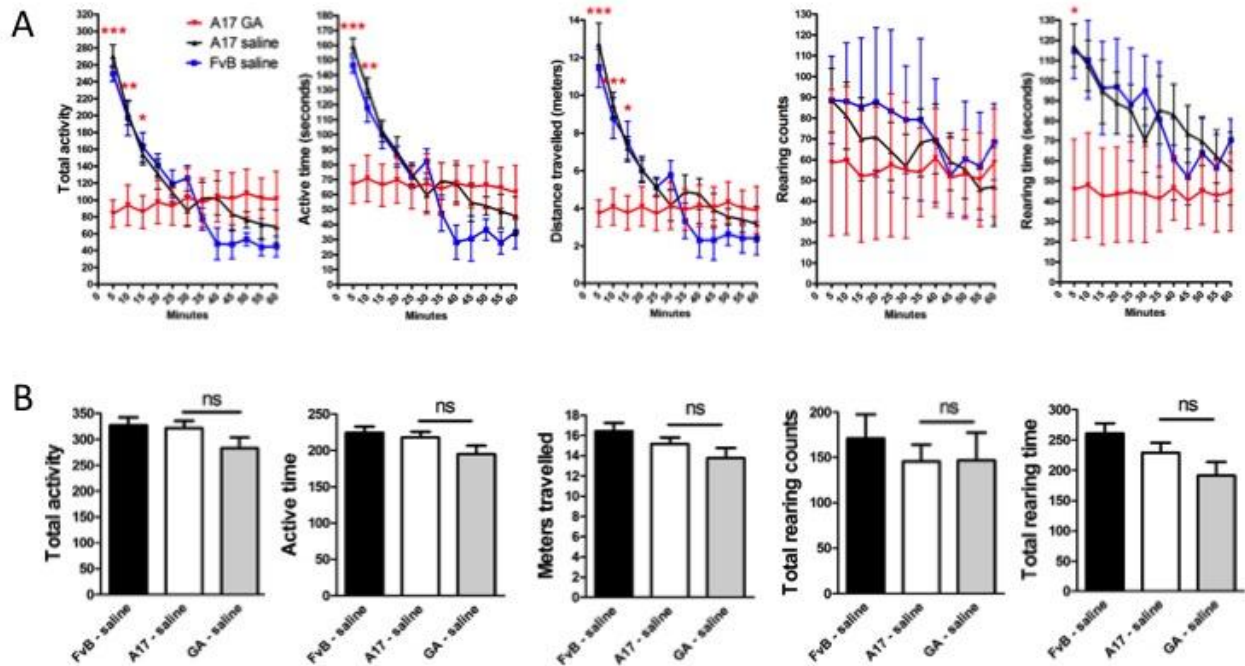
## Supplementary Information



**Supplementary figure 1: Muscle differentiation is not altered in Ala17 murine cell model of OPMD after GA treatment.** Ala17 cells were treated with 10  $\mu$ M GA at day 2 of differentiation for 3 additional days. **(A)** Muscle differentiation is similar in non-treated and treated Ala17 cells. Phalloidin staining (red) is used to visualize myotubes. Nuclei are stained with Hoechst (blue). **(B)** Fusion index was similar in non-treated (NT) and treated (+GA) Ala17 cells. Fusion index is calculated as the percentage of nuclei included in myotubes on the total percentage of nuclei. Unpaired t-test, ns: not significant; 1000 nuclei counted per condition. **(C-D)** The splicing inclusion of *Bin1* exon 10 (physiologically enhanced during myoblast differentiation) is comparable in Ala17 non-treated and GA-treated cells. Unpaired t-test, ns, not significant.

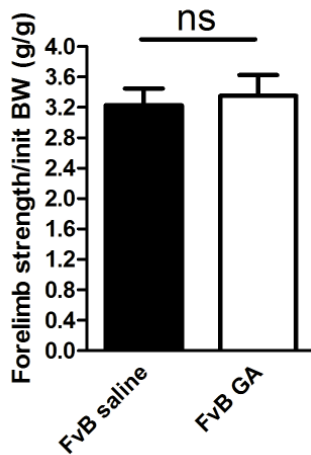


**Supplementary figure 2: PABPN1 nuclear aggregates are sensitive to GA treatment in a dose-dependent manner.** (A) Representative image of the size of nuclear aggregates in Ala17 cells treated with 10  $\mu$ M of GA compared with non-treated OPMD cells (NT). Nuclear aggregates are stained with PABPN1 antibody (green) and nuclei are counterstained with Hoechst (blue). Scale bar = 5  $\mu$ m. (B) Percentage of nuclei with aggregates decreased with 10  $\mu$ M GA treatment. Percentage of nuclear aggregates is calculated as the number of nuclei with aggregates on the number of nuclei in myotubes. NT=non treated (DMSO). (C) The size of nuclear aggregates is gradually impacted with increasing doses of GA ( $\mu$ M). Size of nuclear aggregates was determined using image J in an automatic manner. The sizes are arbitrary classified in 3 categories: small: 0-2  $\mu$ m<sup>2</sup>; medium: 2-10  $\mu$ m<sup>2</sup> and large: >10  $\mu$ m<sup>2</sup>. (D-E) Western blot and quantification showing an increase in phosphorylated eIF2 $\alpha$  (P-eIF2 $\alpha$ ) in Ala17 cells treated with a range of concentration of GA (0.05 to 10  $\mu$ M) compared to DMSO-treated cells (NT).

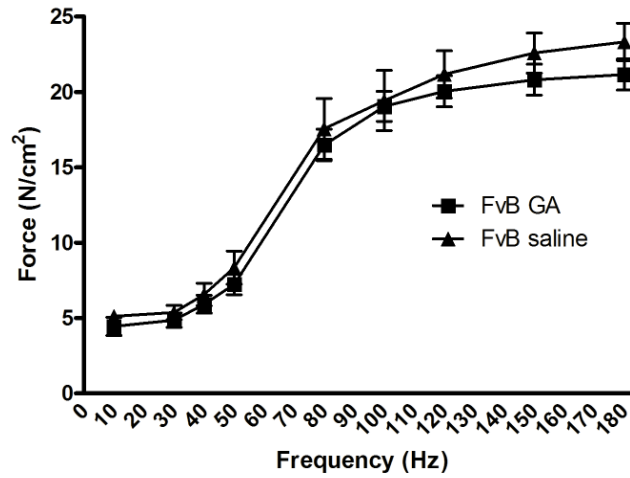


**Supplementary figure 3: GA administration affects locomotor behavior of A17 mice soon after a single injection but effects are transient.** After either the first or the last injections of the study mice were housed for 60 minutes in activity cages to monitor their locomotor behavior and 21 parameters were analyzed. **(A)** Data on total activity, active time, distance travelled, number of rearing and rearing time show that during the first 30 minutes of monitoring, mice treated with GA are less active than control mice treated with saline. One-way ANOVA test with Bonferroni post-hoc test, \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . Red stars refer to A17 GA vs A17 saline comparison. **(B)** The same parameters analyzed in mice at the end of the treatment (more than 24h after the last GA administration) show that mouse behavior is not significantly affected by the drug administration. One-way ANOVA test with Bonferroni post-hoc test. ns: not significant. Data are presented as mean  $\pm$  s.e.m.  $n=6$  per group.

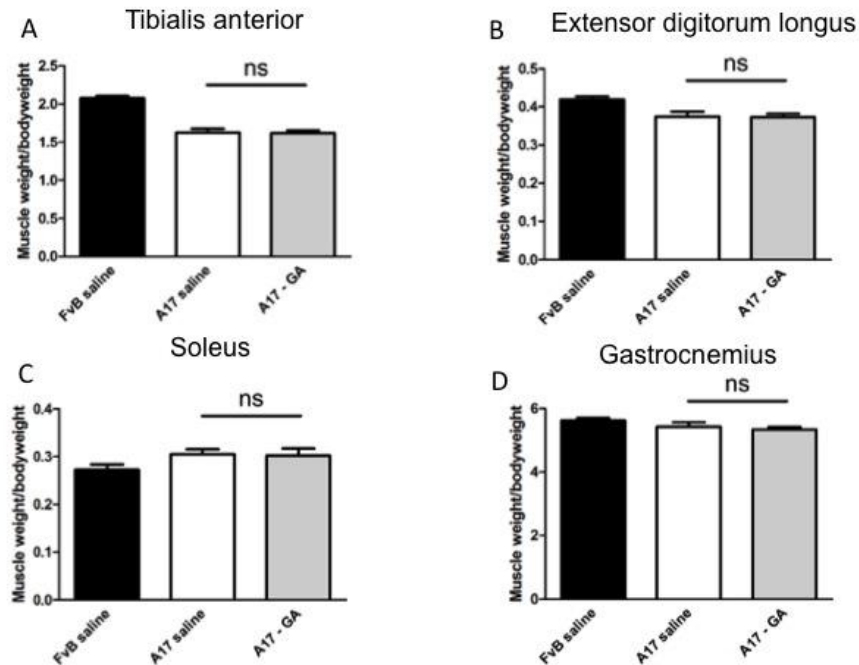
A?



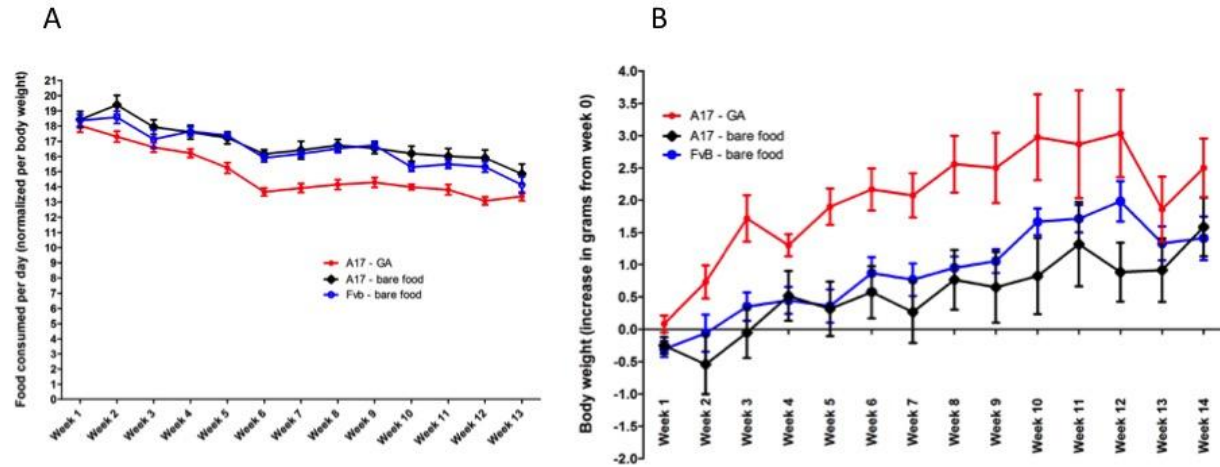
B?



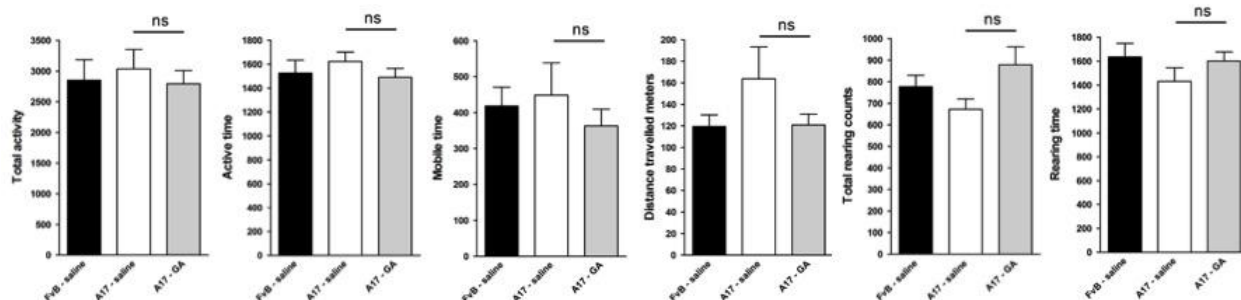
**Supplementary figure 4: GA administration has no effect on FvB mice.** (A) Grip-strength analysis performed in mice at the end of a 13-week long treatment shows that forelimbs of FvB mice treated with GA were indistinguishable from FvB mice treated with saline. Unpaired t-test, ns non significant. (B) *in situ* muscle physiology in muscles: force-frequency analysis of maximal force generated by TA muscles of treated mice shows that GA administration has no effect on the maximal force generated by TA muscles of FvB mice.



**Supplementary figure 5: Muscle weight is not affected by i.p. administration of GA.** Muscles from mice treated by i.p. injection of GA or saline were harvested and weighted: weight of Tibialis anterior, Extensor digitorum longus, Soleus and Gastrocnemius were normalized by the initial bodyweight of each treated mice. No statistical difference was present among groups for any muscle. One-way ANOVA test with Bonferroni post-hoc test. ns: not significant.



**Supplementary figure 6: Mice orally fed with chow supplemented with GA ate and grew similarly to mice fed with bare food.** n=6-8, 10-12 week old mice per group were fed with GA supplemented chow or bare food. Mice were caged individually and the pellets changed twice a week for 13 weeks until the end of the experiment. **(A)** During the experiment, food was weighted each time in order to assess the amount of food eaten by the mice. Mice treated with GA ate about 10% less food than mice supplemented with bare food. **(B)** Mice were weighted weekly. All mice grew similarly and consistently along the 13-week long experiment.



**Supplementary figure 7: GA administration does not affect locomotor behavior of A17 mice orally fed with GA supplemented food.** At the end of the study mice were housed for 60 minutes in activity cages to monitor their locomotor behavior and several parameters were analyzed. Data on total activity, active time, distance travelled, number of rearing and rearing time show that locomotor behavior of mice treated with GA is similar to the one of mice eating bare food. Data are presented as mean  $\pm$  s.e.m. One-way ANOVA test with Bonferroni post-hoc test. ns: not significant.

**Table S1: primers used for the study**

Name	Séquence 5'->3'
mXbp1-F	AGTTAAGAACACGCTTGGAAT
mXbp1-R	AAGATGTTCTGGGGAGGTGAC
mAtf4-F	GACCGAGATGAGCTTCCTGA
mAtf4-R	GCCAAGCCATCATCCATAGC
mGrp78-F	CTTTGATCAGCGGGTCATGG
mGrp78-R	AGCTCTTCAAATTTGGCCCCG
mDdit3-F	TCACTACTCTTGACCCTGCG
mDdit3-R	ACTGACCACTCTGTTTCCGT
mDnajc3-F	TAAGGATGAGAAGCCCGTGG
mDnajc3-R	TCCCGAATCTGCTGGTCATT
mGrp94-F	AGTCGGGAAGCAACAGAGAA
mGrp94-R	TCTCCATGTTGCCAGACCAT

**Table S2: Physical activity and behavior of mice** were analyzed using open-field behavioral cages where two levels of lasers were used to monitor the activity of mice. 6 parameters were evaluated.

<b>Parameters measured by activity cages</b>	
<b>Total Activity</b>	Total beam breaks
<b>Active Time</b>	This count is incremented every time an animal is active (breaking the same or different beams) in any given second
<b>Distance travelled in meters</b>	Calculation of meters travelled by the mice into the cage
<b>Mobile Time</b>	This count is incremented every time an animal is mobile (breaks different beams) in any given second
<b>Total Rearing Counts</b>	Count of second (higher) level beam breaks
<b>Rearing Time</b>	This count is incremented every time an animal is rearing in any given second