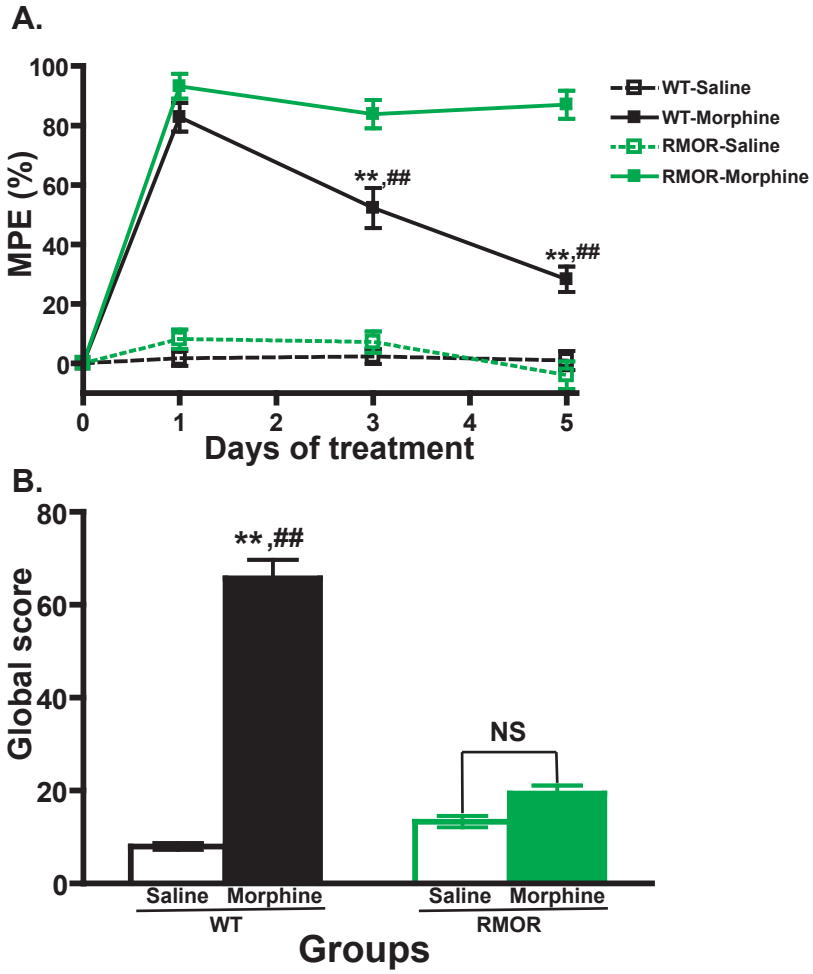
Supp. Fig. 1


A.
MPE (%)
100
80
60
40
20
0
0
1
2
3
4
5
Days of treatment
**,##
**,##
WT-Saline
WT-Morphine
RMOR-Saline
RMOR-Morphine
B.
Global score
80
60
40
20
0
**,##
NS
Saline
Morphine
WT
Saline
Morphine
RMOR
Groups

Supplemental Figure 1: Tolerance to and dependence on morphine in WT and RMOR mice. (A) Antinociceptive responses were measured with the hot-plate response latency test (56º C) 30 min after saline or morphine treatment (10 mg/kg, s.c.). A response endpoint was defined as latency to either lick the fore- or hindpaws or flick the hindpaws. Data are reported as the mean± SEM of percent maximum possible effect (MPE) by using the following formula: 100% 3 [(drug response time – basal response time) / (cut-off time – basal response time)]. WT mice developed substantial tolerance after 5 days of morphine treatment (n= 19), whereas RMOR mice, treated with the same protocol show no tolerance to morphine (n= 16), (****** $p < 0.01$: WT- morphine, day 3 and 5 vs day 1; ## $p < 0.01$**:** WT-morphine vs RMOR-morphine). **(B)** Mice from (A) were injected with naloxone (2 mg/kg, s.c.) after the hot-plate assay on day 5 and withdrawal signs were monitored. WT mice treated with chronic morphine showed significantly more withdrawal than RMOR mice (** $p < 0.01$: WT- morphine (n= 16) vs WT-saline (n= 9); ## $p < 0.01$: WT- morphine vs RMOR-morphine (n=16) by one way ANOVA followed by Newman-Keuls post-test).