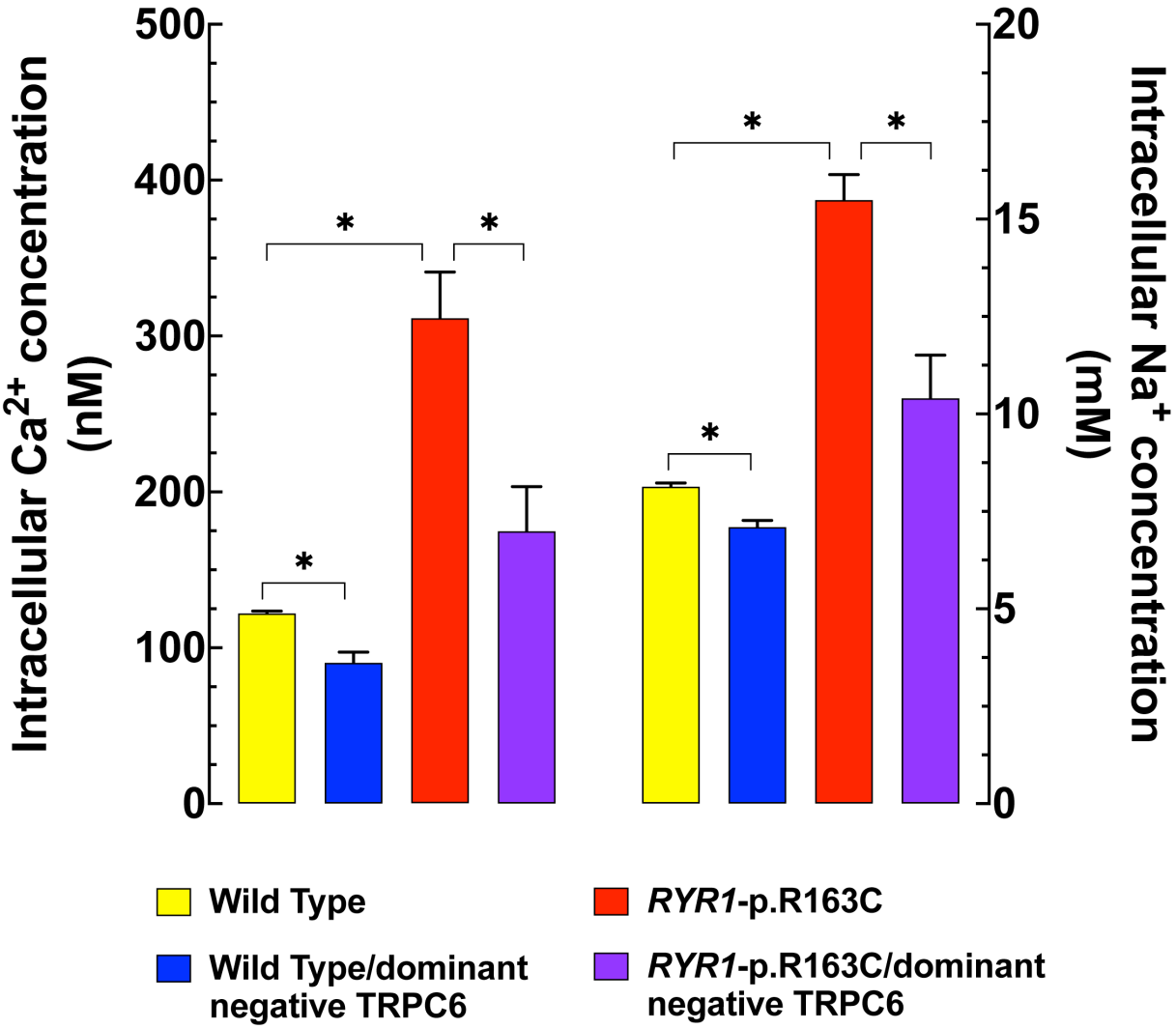
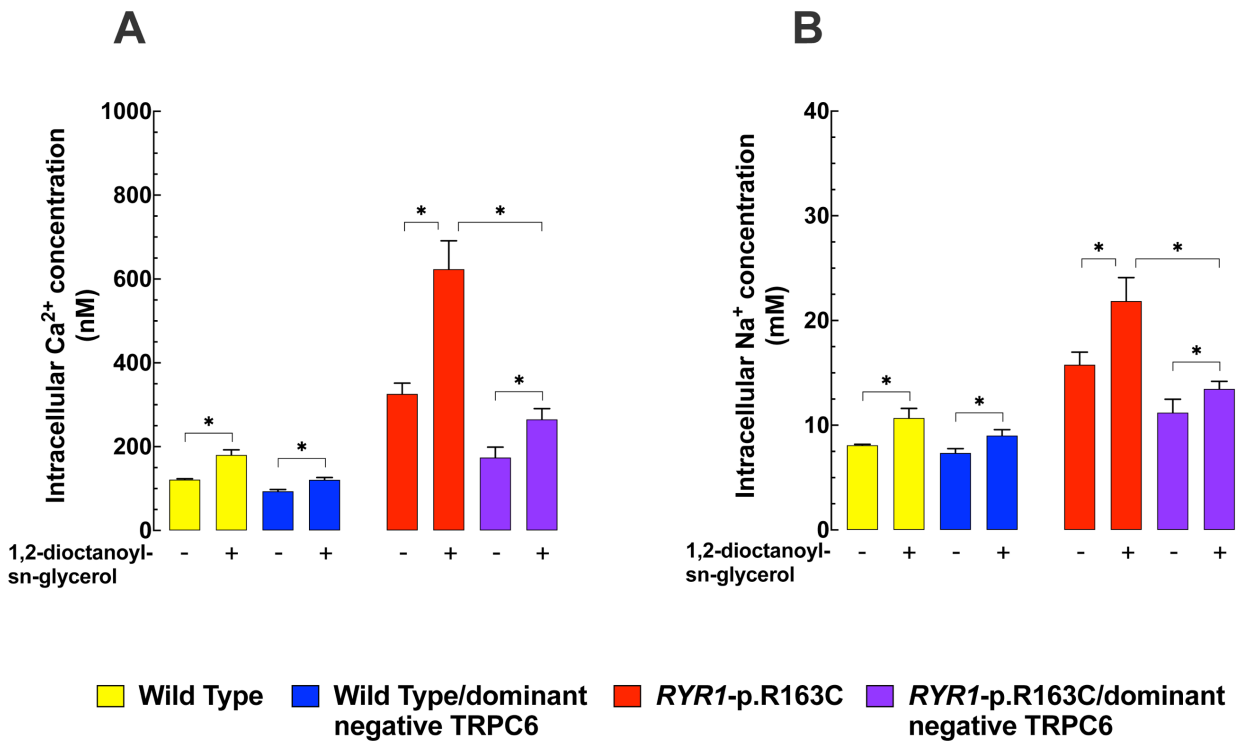


Supplementary Figure 1. ***Expression of dominant negative TRPC6 channels reduced intracellular Ca^{2+} and Na^{+} in isolated muscle fibers.*** Intracellular calcium or sodium concentrations were measured in quiescent isolated *flexor digitorum brevis* muscle fibers from wild type, wild type/dominant negative TRPC6, *RYR1*-p.R163C and *RYR1*-p.R163C /dominant negative TRPC6 mice using double-barreled ion-specific microelectrodes. Intracellular calcium and sodium were statistically significantly (p<0.0001) higher in *RYR1*-p.R163C than wild type. Expression of dominant negative TRPC6 reduced Intracellular calcium and sodium in all genotypes. For intracellular Ca^{2+} concentration measurements N_{mice}=3/genotype, Wild Type, n_{cells}=14; Wild Type dominant negative TRPC6, n=13; *RYR1*-p.R163C n_{cells}=16; *RYR1*-p.R163C/ dominant negative TRPC6 n_{cells}=15. For intracellular Na^{+} concentration measurements N_{mice}=3/genotype, Wild Type, n_{cells}=13; Wild Type dominant negative TRPC6, n_{cells}=12; *RYR1*-p.R163C n_{cells}=12; *RYR1*-p.R163C/ dominant negative TRPC6 n_{cells}=11. Values are expressed as means±SD. for each condition. Statistical analysis was done using a one-way ANOVA with Tukey's post-test, *$p\leq0.05$.



Supplementary Figure 2. ***The effect of 1,2-dioctanoyl-sn-glycerol on intracellular calcium and sodium concentration was inhibited by the expression dominant negative TRPC6 channel in single cells muscle fibers,*** Intracellular Ca^{2+} or Na^{+} concentration was measured *in vitro* in single FDB muscle fibers isolated from wild type, wild type/dominant negative TRPC6, *RYR1*-p.R163C, and *RYR1*-p.R163C dominant/negative TRPC6 before and after the incubation in 1,2-dioctanoyl-sn-glycerol 100 μM. 1,2-dioctanoyl-sn-glycerol induced elevation of intracellular Ca^{2+} and Na^{+} concentration in all genotypes. Expression of dominant negative TRPC6 abolished the robust elevation of intracellular Ca^{2+} or Na^{+} concentration upon incubation in 1,2-dioctanoyl-sn-glycerol. The experimental conditions used are indicated on the horizontal axis. N_{mice}=3/genotype, For intracellular Ca^{2+} concentration measurements Wild Type, n_{cells}=11; Wild Type-1-oleoyl-2-acetyl-sn-glycerol n_{cells}=13; Wild Type dominant negative TRPC6, n_{cells}=11; Wild Type dominant negative TRPC6-1-oleoyl-2-acetyl-sn-glycerol n_{cells}=13; *RYR1*-p.R163C n_{cells}=13; *RYR1*-p.R163C-1-oleoyl-2-acetyl-sn-glycerol n_{cells}=16 *RYR1*-p.R163C/ dominant negative TRPC6 n_{cells}=12; *RyR1*-p.R163C/ dominant negative TRPC6-1-oleoyl-2-acetyl-sn-glycerol n_{cells}=10. For intracellular Na^{+} concentration measurements N_{mice}=3/genotype, Wild Type, n_{cells}=10; Wild Type-1-oleoyl-2-acetyl-sn-glycerol n_{cells}=11; Wild Type dominant negative TRPC6, n_{cells}=11; Wild Type dominant negative TRPC6-1-oleoyl-2-acetyl-sn-glycerol n=12; *RYR1*-p.R163C n_{cells}=11; *RYR1*-p.R163C-1-oleoyl-2-acetyl-sn-glycerol n=12 *RYR1*-p.R163C/ dominant negative TRPC6 n_{cells}=11; *RYR1*-p.R163C/ dominant negative TRPC6-1-oleoyl-2-acetyl-sn-glycerol n_{cells}=12.Values are expressed as means ± S.D. for each condition. Statistical analysis was done using a one-way ANOVA with Tukey's post-test, *$p \leq 0.05$.