

Expanded View Figures

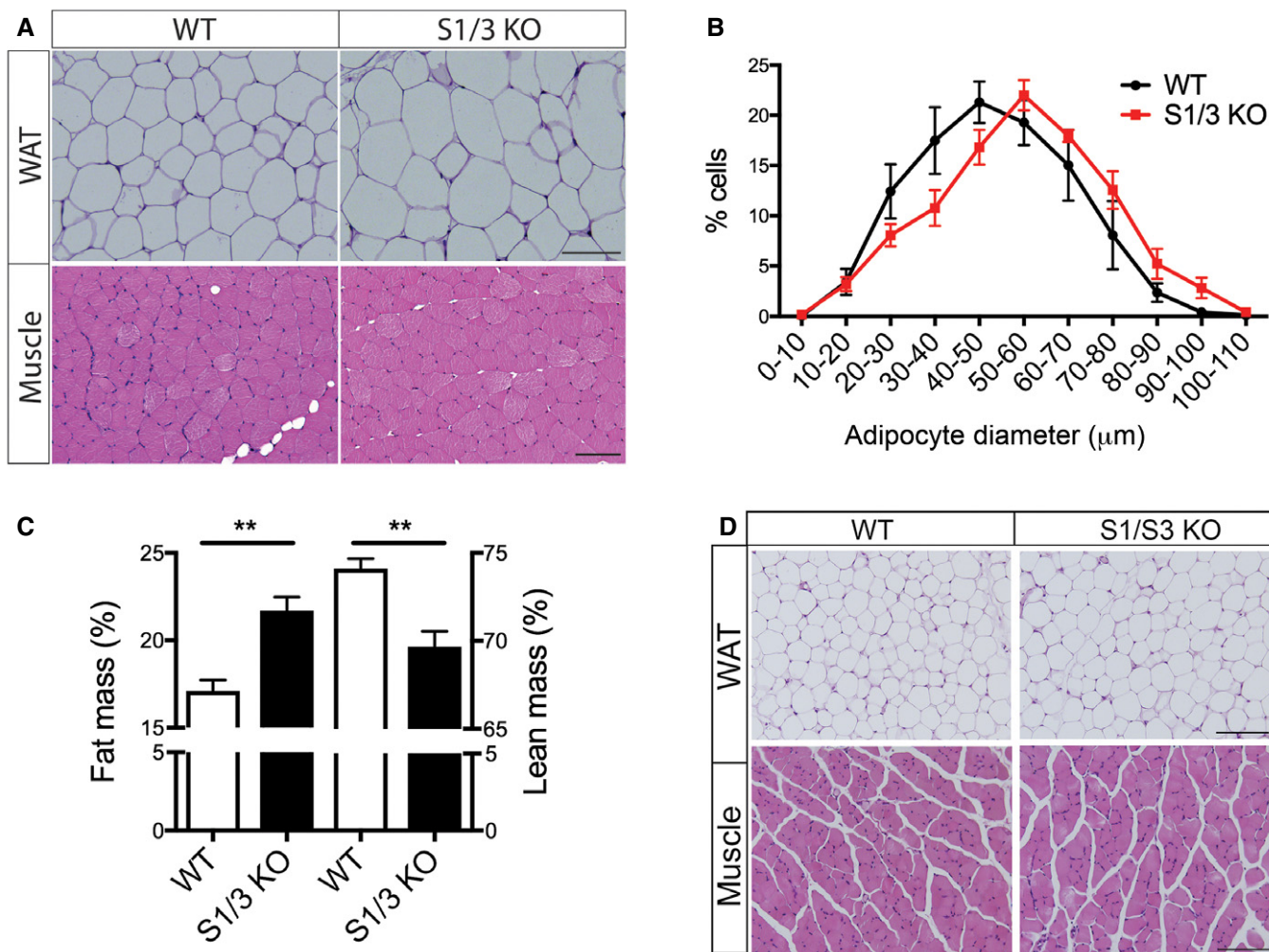


Figure EV1. Morphology of white adipose tissue and muscle in S1/3 KO mice of different ages.

A Representative hematoxylin and eosin (H&E)-stained sections of perigonadal white adipose tissue (WAT) and quadriceps muscle from 14- to 15-week-old WT and S1/3 KO mice. Scale bars: 100 μm.

B Adipocyte size distribution shows a decrease in the number of small cells and an increase in the number of large cells (% of total cell numbers) in perigonadal adipose tissue of S1/3 KO mice as compared to controls. For each mouse, 332–551 adipocytes across the tissue depot were analyzed on H&E-stained sections ($n = 4–5$ mice/group). Two-way ANOVA; $P = 0.0207$ for interaction between genotype and adipocyte size.

C Body composition as determined by NMR imaging in 6-week-old mice of the indicated genotypes. S1/3 KO mice show an increase in fat mass and a concomitant decrease in lean (fat-free) mass as compared to WT controls ($n = 5–6$ animals/group).

D Representative H&E-stained sections of perigonadal white adipose tissue (WAT) and quadriceps muscle from 6-week-old WT and S1/3 KO mice. Scale bars: 100 μm. $n = 3–5$ mice/genotype.

Data information: Data in (B and C) are shown as mean ± SEM and were analyzed using two-way ANOVA with Bonferroni post-test (B) or two-tailed unpaired t-test (C). ** $P < 0.01$.

Figure EV2. Impaired glucose tolerance in adult S1/3 KO mice on a normal chow.

- A Blood glucose and insulin levels after overnight fasting in 12-week-old WT and S1/3 KO mice ($n = 12\text{--}17$ animals/group).
- B Glucose tolerance test (GTT) in mice at 12 weeks of age. S1/3 KO mice show increased blood glucose levels after an i.p. bolus of glucose (2 g/kg body weight) as compared to WT controls ($n = 15\text{--}17$ mice/group).
- C Area under the curve (AUC) for GTT.
- D Plasma insulin levels in mice of the indicated genotype during GTT ($n = 9\text{--}10$ mice/group).
- E Insulin tolerance test (ITT) in mice at 13 weeks of age. Blood glucose levels after an i.p. injection of insulin (0.75 U/kg body weight) were not significantly different between the genotypes ($n = 8\text{--}9$ mice/group).
- F Pyruvate tolerance test (PTT) in mice of the indicated genotypes at 18 weeks of age. Blood glucose levels after an i.p. injection of sodium pyruvate (1 g/kg body weight) are shown ($n = 8\text{--}9$ mice/group).
- G Area under curve (AUC) for PTT.

Data information: Data are shown as mean \pm SEM and were analyzed using a two-tailed unpaired *t*-test (A, C, G) or two-way ANOVA with Bonferroni post-test (B, D–F). ** $P < 0.01$, *** $P < 0.001$.

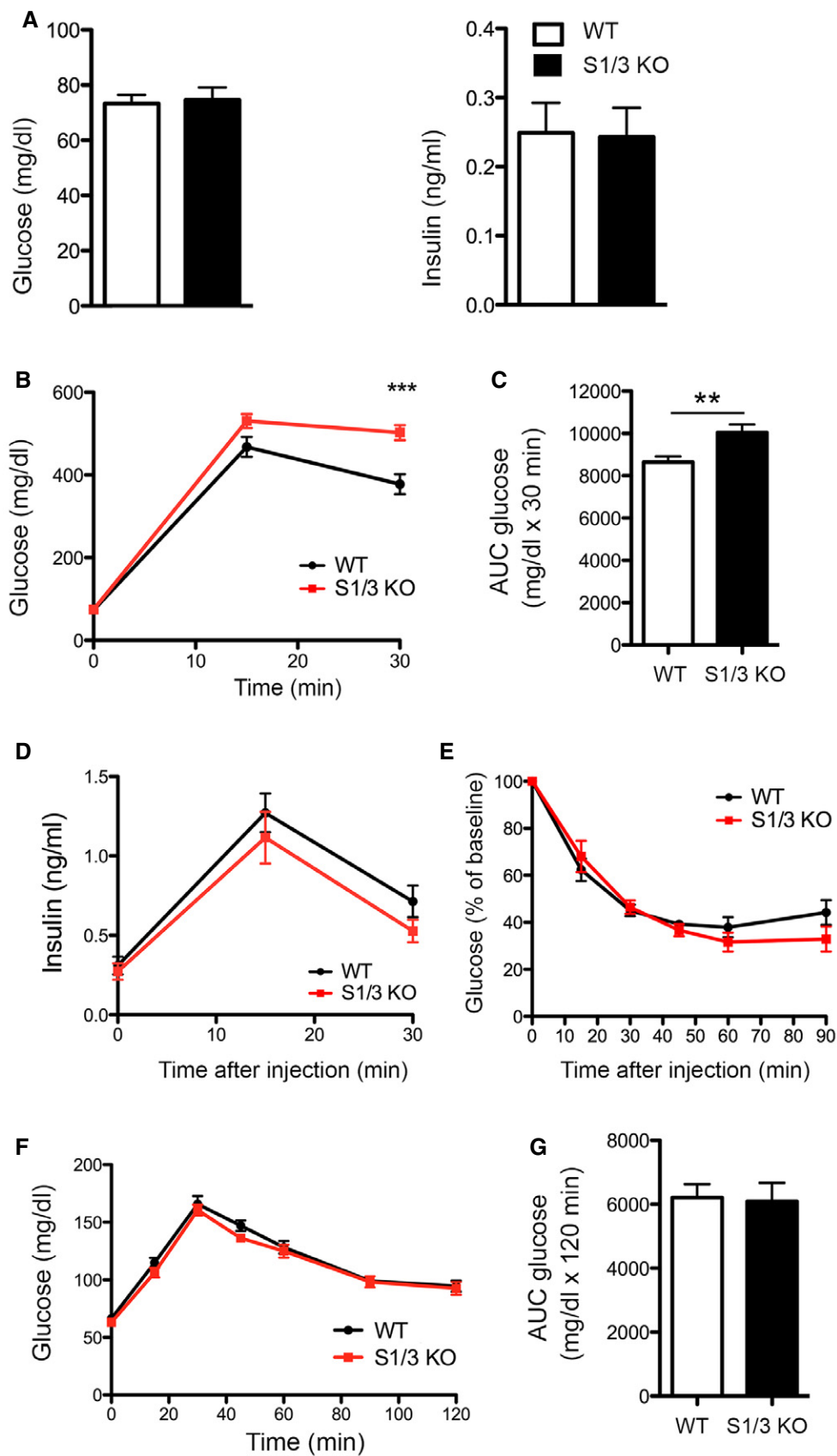


Figure EV2.

Figure EV3. Glucose homeostasis in aged S1/3 KO mice.

- A, B Blood glucose (A) and insulin (B) levels after overnight fasting in 9-month-old WT and S1/3 KO mice ($n = 6-9$ animals/group).
- C Plasma insulin levels before and after an i.p. bolus of glucose (2 g/kg body weight) in 9-month-old WT and S1/3 KO mice ($n = 6-9$ mice/group).
- D Insulin tolerance test at 9 months of age. Blood glucose levels were measured before and after an i.p. injection of insulin (0.75 U/kg body weight) ($n = 7-9$ mice/group).
- E Glucose tolerance test (GTT) at 8 months of age. Blood glucose levels were measured before and after an i.p. bolus of glucose (2 g/kg body weight) ($n = 6-8$ mice/group).
- F Area under curve (AUC) for GTT.

Data information: Data are shown as mean \pm SEM and were analyzed using a two-tailed unpaired t -test (A, B, F) or two-way ANOVA with Bonferroni post-test (C-E). * $P < 0.05$, ** $P < 0.01$.

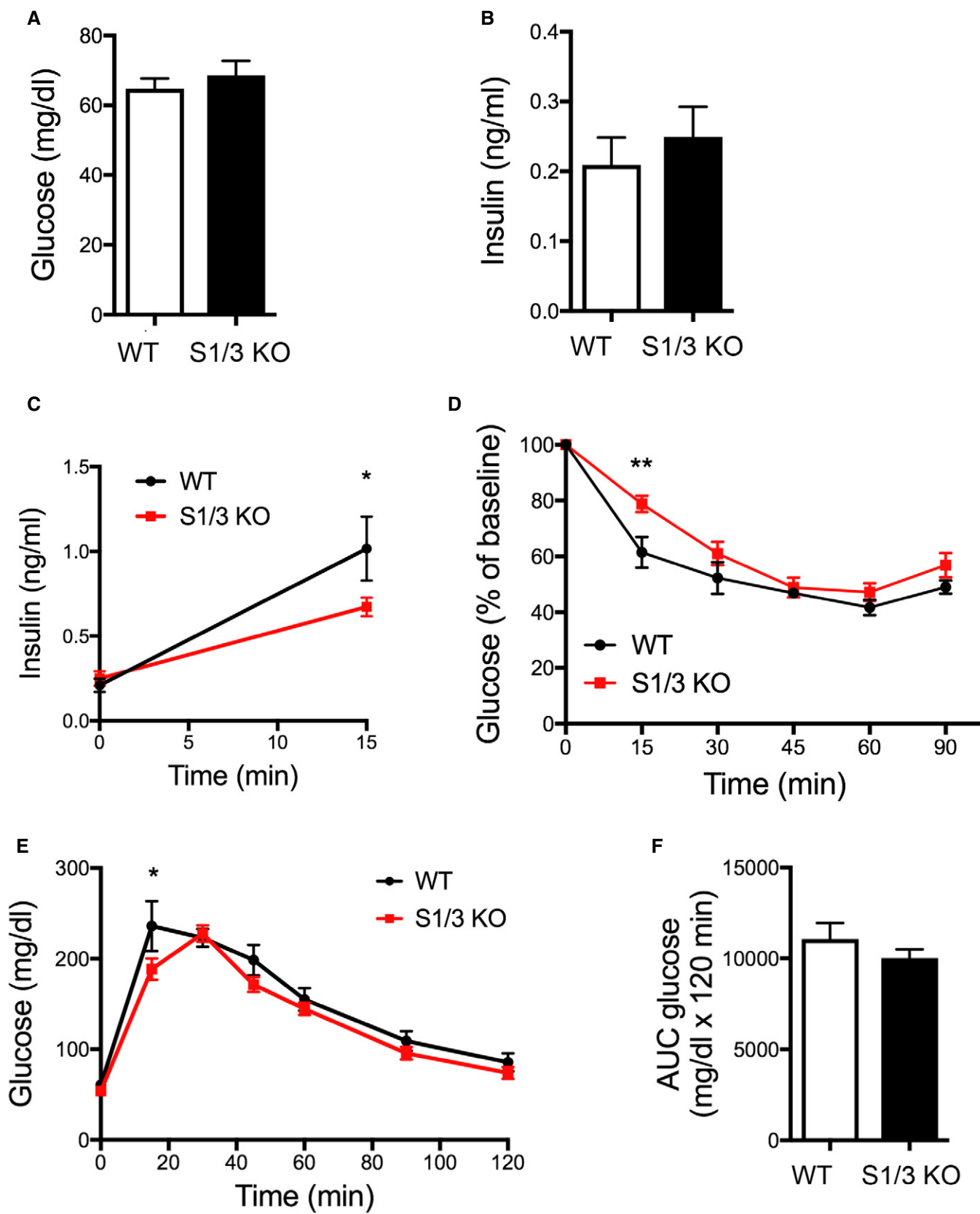


Figure EV3.

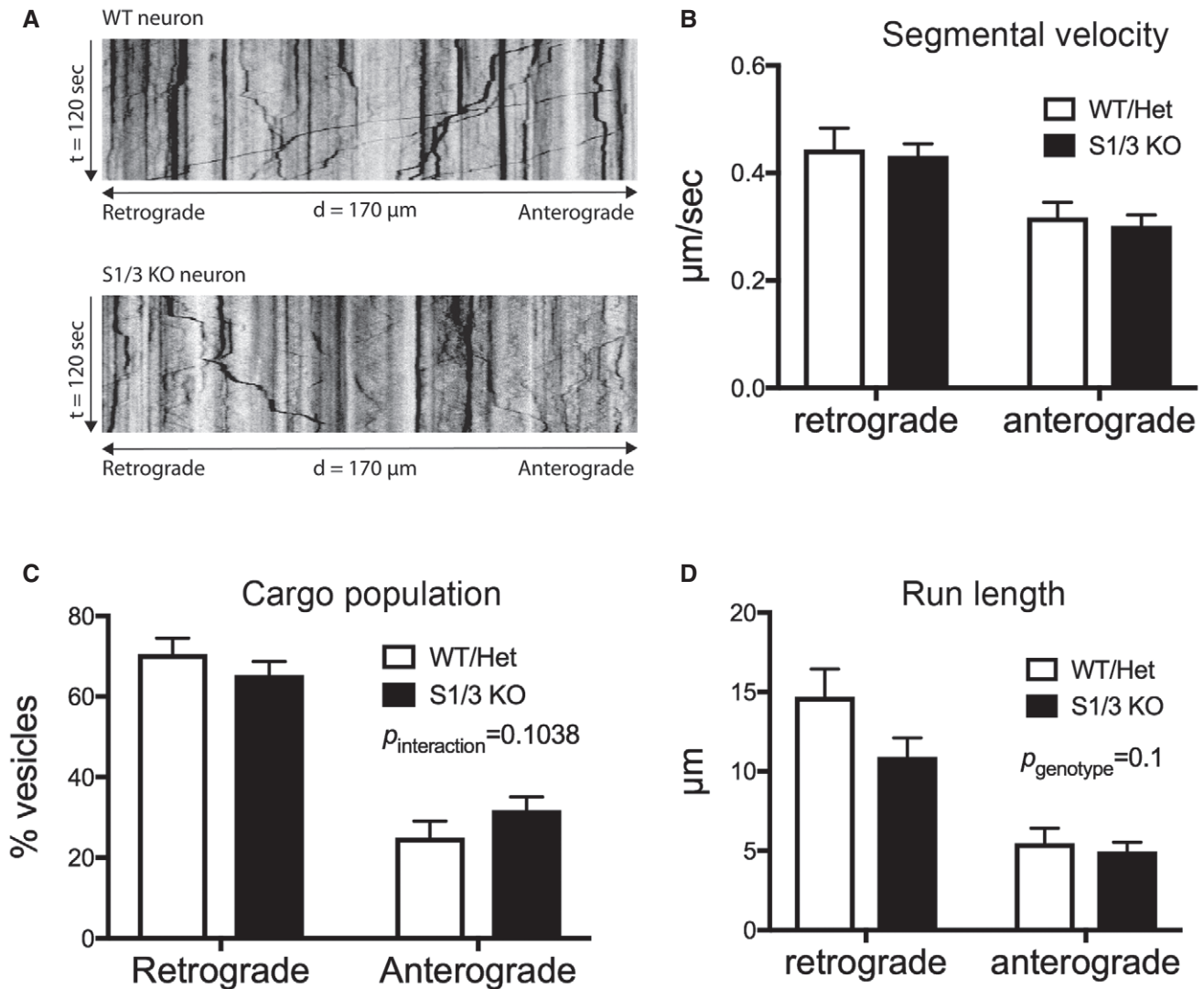


Figure EV4. Time-lapse imaging of GFP-TrkB trafficking in primary cortical neurons from WT and S1/3 KO mice.

- A Representative kymographs (time–space plots) generated from time-lapse movies visualizing trafficking of transiently overexpressed GFP-TrkB in DIV7 primary cortical neurons from WT and S1/3 KO mice.
- B Segmental velocity of GFP-TrkB vesicles uninterruptedly moving in retrograde or anterograde direction in axons from WT and S1/3 KO primary cortical neurons. ($n = 15\text{--}20$ neurons/genotype from two neuronal culture preparations each).
- C Population (% of total) of GFP-TrkB vesicles moving in retrograde and anterograde directions in axons from WT and S1/3 KO primary cortical neurons ($n = 28\text{--}29$ neurons/genotype from three neuronal culture preparations each).
- D Total distance covered by GFP-TrkB vesicles uninterruptedly moving in retrograde or anterograde directions in axons from WT and S1/3 KO primary cortical neurons. ($n = 15\text{--}20$ neurons/genotype from two neuronal culture preparations each).

Data information: Data in (B–D) are shown as mean \pm SEM and analyzed using two-way ANOVA with Bonferroni post-test.