



**Figure S2 – Normal Levels of Brain EVs in 2–3-month-old *Grn*<sup>-/-</sup> Mice**

**a, b**, Unlike older, *Grn*<sup>-/-</sup> mice, brains from 2–3-month-old *Grn*<sup>-/-</sup> mice did not contain more EVs than wild-type littermates based on nanoparticle tracking analysis (**a**, RM ANOVA effect of genotype,  $p = 0.4153$ , genotype x particle size interaction,  $p = 0.9983$ , **b**, ANOVA effect of genotype,  $p = 0.6413$ ). **c**, Fraction 2 from brains of 2–3-month-old *Grn*<sup>-/-</sup> mice did not contain more protein than wild-type littermates (ANOVA effect of genotype,  $p = 0.0053$ , but Dunnett's post-hoc test,  $p = 0.1556$ ). **d–f**, Levels of EV marker proteins also did not differ between 2–3-month-old *Grn*<sup>-/-</sup> and wild-type littermates (**d**, HSP-70, ANOVA effect of genotype,  $p = 0.3643$ , **e**, CD81, ANOVA effect of genotype,  $p = 0.9458$ , **f**, Flotillin-1, ANOVA effect of genotype,  $p = 0.3296$ ). All data are corrected for hemibrain weight except for the nanoparticle tracking profiles in **a**.  $n = 12–14$  mice per genotype.