



**Supplementary information, Figure S2** (A) Double immunofluorescence staining with a mixture of antibodies against DOR1<sup>3-17</sup> and CGRP antibodies shows co-localization of DOR1 and CGRP in LDCVs in a small DRG neuron of a wild-type mouse. In the DRG of *Oprd1* exon 1-deleted mouse, immunostaining of CGRP is found in LDCVs in small neurons, whereas DOR1-staining is absent. Scale bar, 8  $\mu$ m. (B) Percentage of immunogold particles for labeling of DOR1,  $\beta$ 2 AR, G<sub>αi2</sub>, PLCβ2, VGCC  $\alpha$ 2 $\delta$ 1, P2X<sub>2</sub>,  $\beta$ 1 AR, Fzd8 or Dvl1 in different subcellular locations. (C) Negative control (omission of primary antibodies) of immunogold labeling. Anti-rabbit, anti-mouse and anti-goat secondary antibodies were used without incubation with primary antibodies. Scale bar, 200 nm. (D) Double immunostaining shows the localization of  $\beta$ 1 AR, Fzd8 and Dvl1 (in green) in LDCVs in small DRG neurons of mice. These proteins are not co-localized with CGRP (in red) in LDCVs. Scale bar, 8  $\mu$ m.