



Supplementary information, Figure S1 (A) Immunoblotting with antibodies against DOR1¹⁻⁶⁰ shows specific immunoreactive band in the extract from the spinal cord of the wild-type mice but not in that from *Oprd1* exon 1-deleted mice. (B) An electron micrograph shows the presence of LDCVs in the LDCV-enriched fraction. Scale bar, 200 nm. (C) Immunoblotting of subcellular fractions shows the distribution profiles of indicated proteins, including low abundant GPCRs that are not detected by LC-MS and some proteins identified by LC-MS. H, homogenate; S1 and P1, the supernatant and pellet of homogenate centrifuged for 15 min at 10,500 g, and LDCV is concentrated in P1; S2 and P2, the non-LDCV- and LDCV-containing fractions respectively after first sucrose gradient centrifugation; LDCV, the LDCV-enriched fraction obtained by second sucrose gradient centrifugation. Three independent experiments are performed.