**Supplemental Figure Legends**

**Figure S1** (http://links.lww.com/PAIN/A612).Displacement of bound [3H]-DAMGO (4 nM) by fentanyl (Fen) (A, C, E) and NFEPP (B, D, F) at pH 7.4 (A and B), pH 6.5 (C and D) and pH 5.5 (E and F) in brain membranes. Inserts show the calculated IC50 values of each individual experiment. (G) Percentage of baseline [3H]-DAMGO (4 nM) bound protein (means ± SEM) for Fen and NFEPP at pH 5.5, 6.5 and 7.4; n = 6 independent experiments per group.

**Figure S2** (http://links.lww.com/PAIN/A613).Displacement of bound [3H]-DAMGO (4 nM) by fentanyl (Fen) (A) and NFEPP (B) in DRG membranes at pH 5.5, 6.5 or 7.4. Data are expressed as means ± SEM; n = 8 independent experiments per group.

**Figure S3** (http://links.lww.com/PAIN/A614). Displacement of bound [3H]-DAMGO (4 nM) by fentanyl (Fen) (A, C, E) and NFEPP (B, D, F) in DRG membranes at pH 7.4 (A and B), pH 6.5 (C and D) and pH 5.5 (E and F). Inserts show the calculated IC50 values of each individual experiment. (G) Percentage of baseline [3H]-DAMGO (4 nM) bound protein (means ± SEM) for Fen and NFEPP at pH 5.5, 6.5 and 7.4; n = 8 independent experiments per group.