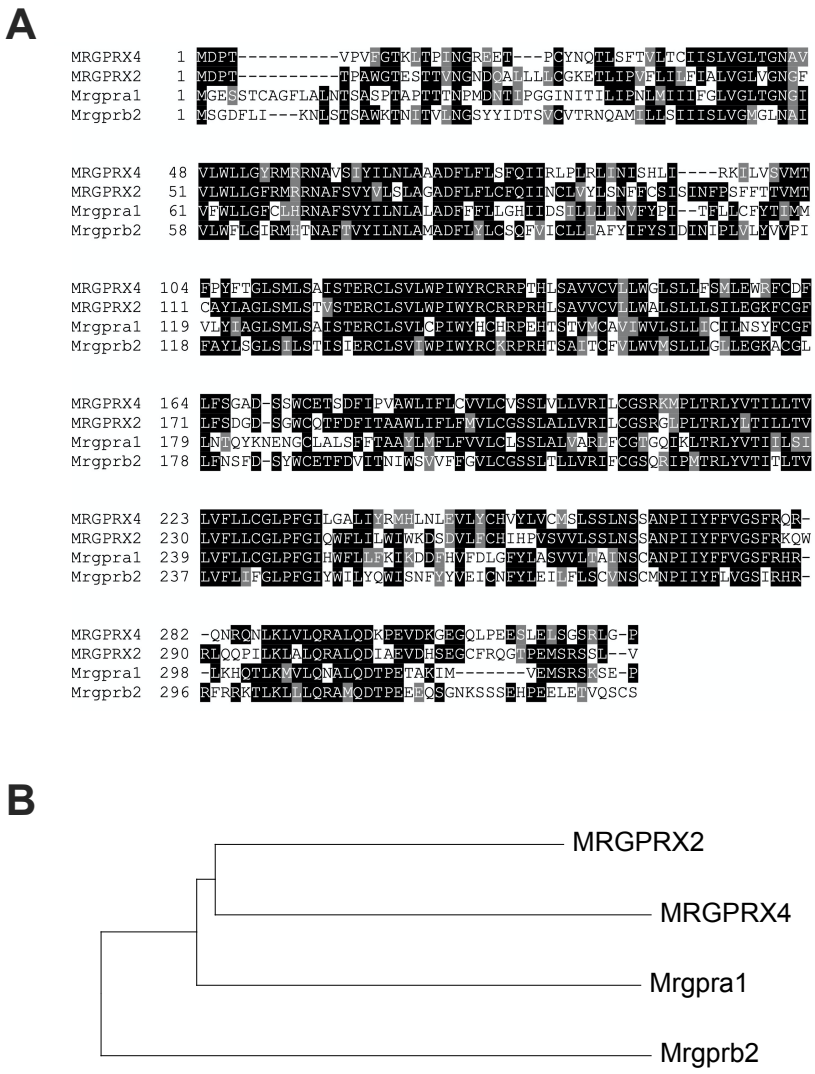
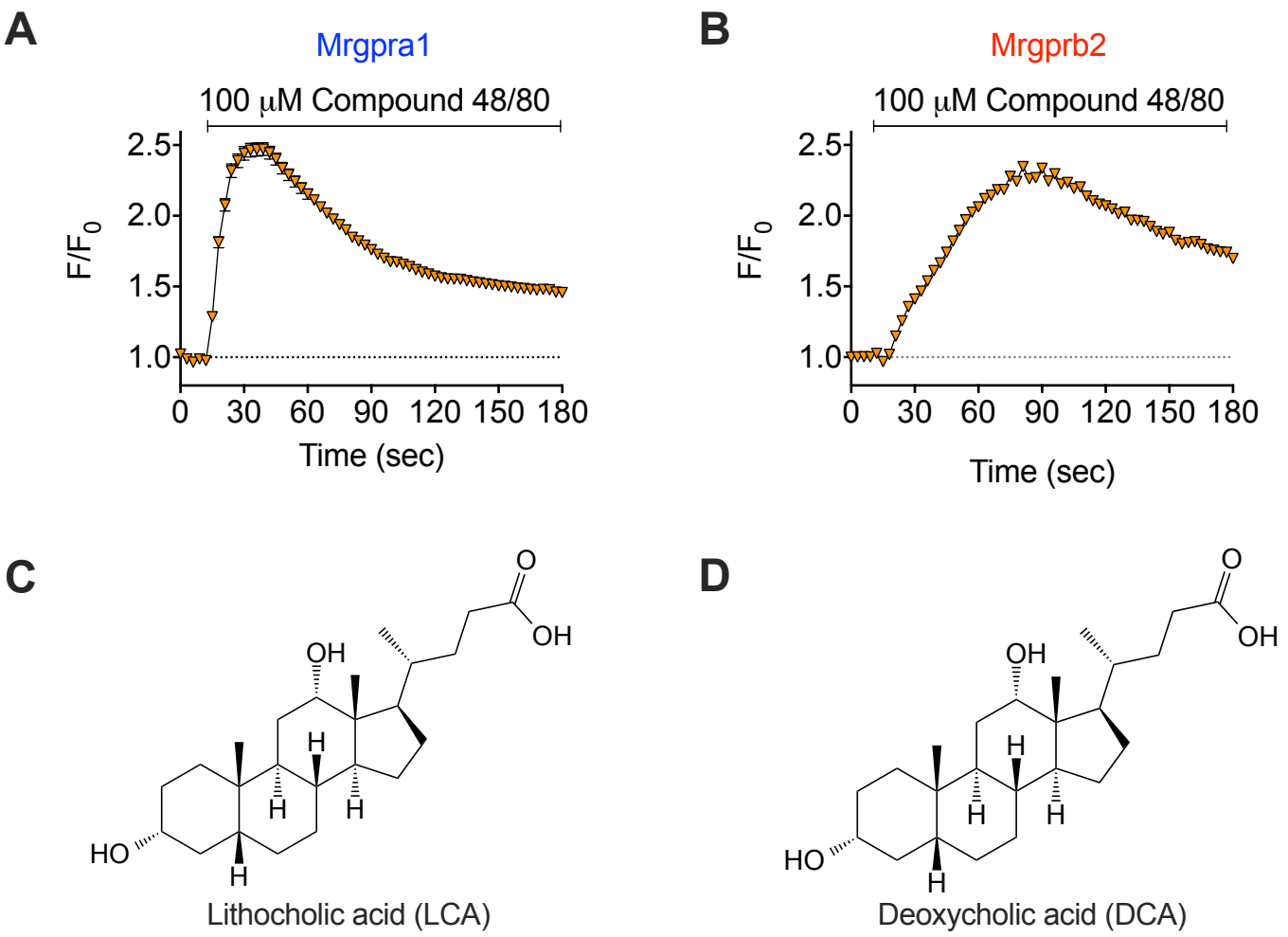
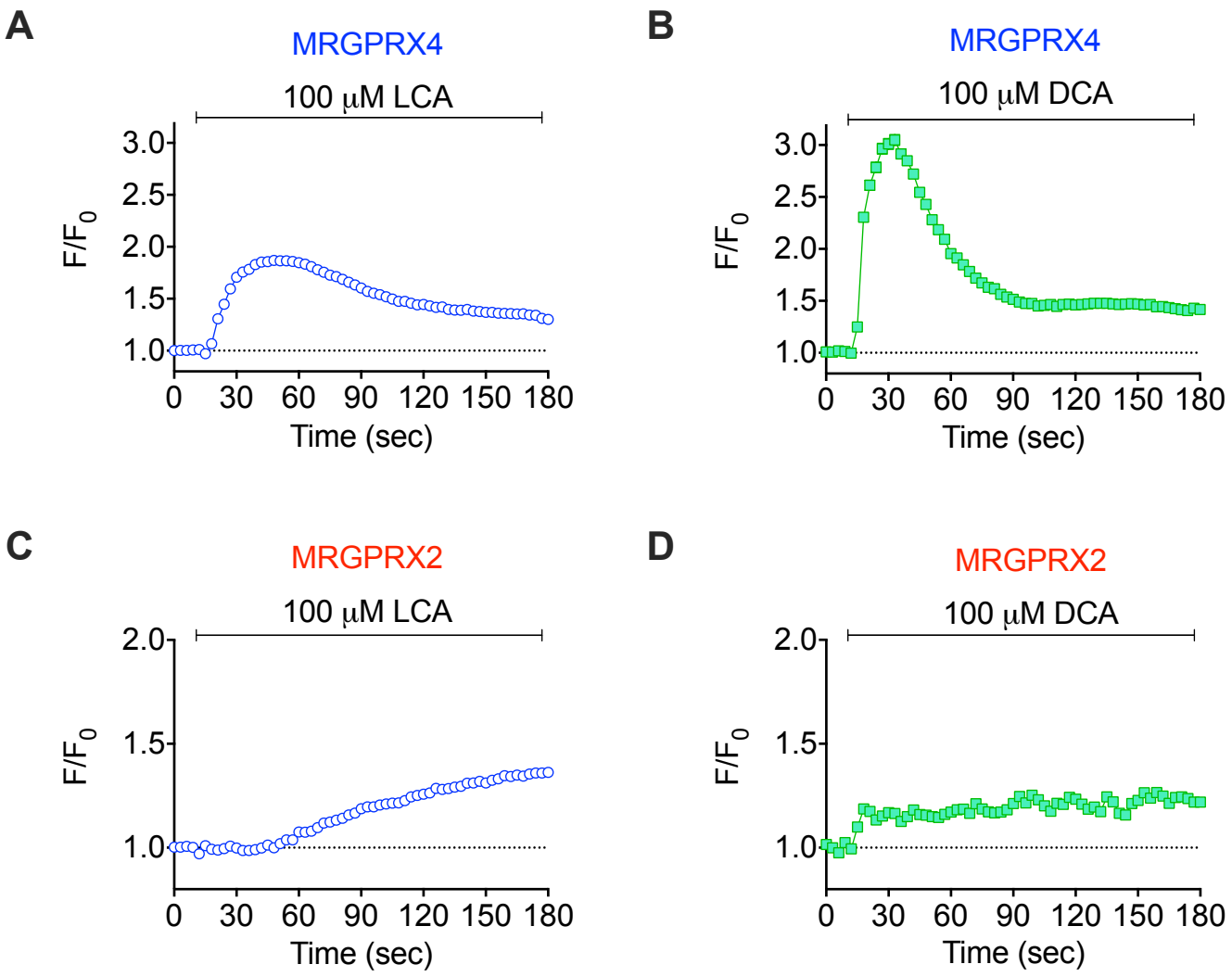


Supplementary Fig. 1. (A) Comparison of the amino acid sequences of human MRGPRX2, human MRGPRX4, mouse Mrgpra1, and mouse Mrgprb2. Identical residues are shaded in black, and conservative substitutions are colored in gray. (B) Phylogenetic tree showing the sequence similarity among human MRGPRX2, human MRGPRX4, mouse Mrgpra1, and mouse Mrgprb2. TM indicates transmembrane region predicted by TMHMM Server v. 2.0 (http://www.cbs.dtu.dk/services/TMHMM/)



Supplementary Fig. 2. (A) HEK293T cells transiently expressing Mrgpra1 were treated with compound 48/80 (100 μM), which led to an increase in intracellular calcium levels (n = 3794 cells). (B) HEK293T cells transiently expressing Mrgprb2 were treated with compound 48/80 (100 μM), which led to an increase in intracellular calcium levels. (n = 2216 cells) (C, D) The molecular stereochemical structure of lithocholic acid (LCA) and deoxycholic acid (DCA).



Supplementary Fig. 3. (A, B) HEK293T cells transiently expressing MRGPRX4 were treated with lithocholic acid (LCA; 100 μM, n = 1788 cells) and deoxycholic acid (DCA; 100 μM, n = 3331 cells) (C, D) HEK293T cells transiently expressing MRGPRX2 were treated with LCA (100 μM, n = 2491 cells) and DCA (100 μM, n = 3932 cells).