S1 Fig. Competitive binding and ERK activity assays: A. Binding competition between prokineticin-2 and $^{125}$I-MIT to PKR1 ($IC_{50}$: 36pM), indicating the same binding site of PKR1 as MIT. IS1 does not replace $^{125}$I-MIT, verifying that it has an allosteric binding site with the same binding site of PKR1 as MIT. B. IS1 at 1 nM concentration enhances the functional response (ERK kinase activity) of endogenous ligand PK2 (10nM) when the CHO-PKR1 cells were treated with these two ligands together, clearly indicating that IS1 acts as positive allosteric modulator.