



**Figure S1** GCY-4 and GCY-22 do not show chloride, bromide, or sodium activation upon ectopic expression in CHO cells. Membrane preparations from CHO cells were treated with 100 mM NaCl, NaBr, NaPO<sub>4</sub>, or NH<sub>4</sub>Ac. cGMP levels were measured as pmol cGMP per mg of total membrane proteins. Comparing with the control (NH<sub>4</sub>Ac), treatments with NaCl, NaBr or NaPO<sub>4</sub> did not produce a statistically significant stimulation of GC activity under the current experimental conditions. We also tested 100 mM NaI and observed no stimulation of GC activity. Protein expression was confirmed by Western Blotting, but we cannot be certain that proteins were transported to the cell surface.