

**P011** Comparison of glycine- and taurine-induced conformational changes in the glycine receptor M2-M3 domain

Nian-Lin R. Han<sup>1</sup>, John D. Clements<sup>2</sup>, Joseph W. Lynch<sup>1</sup>

<sup>1</sup>*School of Biomedical Sciences, University of Queensland, QLD, 4072, Australia*

<sup>2</sup>*JCSMR, Australian National University, Canberra, 2601, Australia*

In the glutamate receptor, partial and full agonists induce different conformational changes at the binding site and channel gate. However, in the nicotinic receptor family, the structural basis of partial agonism is not understood. This study sought to determine whether high and low efficacy agonists induce different conformational changes in the glycine receptor (GlyR). A substituted cysteine accessibility analysis previously demonstrated that glycine binding increased the surface accessibility of residues from R271 – K276 in the M2-M3 domain of the  $\alpha 1$  GlyR. The present study used the same approach to probe the conformational change induced by the lower efficacy agonist, taurine. In GlyRs incorporating the R271C or K276C mutations, taurine behaved as a particularly weak partial agonist. In these mutants, MTSET had no effect on saturating taurine-gated currents and thus, no conclusions can be drawn. However, in GlyRs incorporating the A272C, S273C, L274C or P275C mutation, the MTSET reaction rates were similar for taurine- and glycine-gated currents. Thus, the conformational changes experienced by these residues were agonist-independent, suggesting that high and low efficacy agonists impose similar conformational changes to the M2-M3 domain.