Computational Analysis of nAChR α4 and β2 Subunit Stability and NMR Study of Protein Anesthetic Interaction

Woodall, Logan; Tang, Pei; Bondarenko, Vasyl; Madura, Jeffry; Tillman, Tommy
Structural Biology
University of Pittsburgh

Abstract: Because the α4 and β2 subunits of the transmembrane domain of nAChRs are naturally unstable in solution suitable for NMR experimentation and structural determination, mutation of the subunit sequences has been performed to lower subunit pI. However, as α4 stability is much greater than β2 stability, further mutation of the β2 sequence at key residues has been attempted to increase β2 stability. Computer modeling and simulation of the α4 and β2 subunits provide a basis for assessing the mutant subunit stability. NMR experiments run both with and without anesthetic were performed to provide insight as to which specific residues within the α4 subunit interact with anesthetic based on observed differences in chemical shifts.