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Simulations of the Pore Structures for a M2GlyR Derived Channel Forming Peptide in Different Membrane Environments A. AL-RAWI, A. HERRERA, J. TOMICH, Kansas State Univ., T. RAHMAN, Univ. of Central Florida — As part of an effort to develop a peptide-based compound suitable for clinical use as a channel replacement therapeutic for treating channelopathies such as cystic fibrosis, we present a reductionist model that appears to grasp the characteristics of ion channeling peptides. In particular we present the observed changes in the functional characteristics of NK_4-M2GlyR p22 (KKKKPARVGLGITTVLTMTTQS), a M2 GlyR derived channel forming peptide. Starting with a structure determined by multidimensional NMR (800 MHz) in SDS, a potential from CHARMM force-field was used to relax the structure of NK_4-M2GlyR p22. Following the relaxation, numerous pore structures were generated for the symmetric five-helix assembly with geometries varying from cylindrical to conical. As it is difficult *a priori* to assign accurately the orientation of the hydrophilic portion of M2GlyR derived amphipath towards the inside of the pore, we tilted and rotated the helical structure by five different angles about the backbone axis before forming the pore. Energy minimization of the channel was performed in vacuum, in phosphotidylcholine (POPC) membrane, and 60% POPC 30% phosphotidylethanolamine (POPE) in order to determine the effect of the environment surrounding on the structure on its energy minimization. We will present the various pore assemblies, in the different membrane environments, used to predict the most probably membrane bound structure.

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