A single NaK channel conformation is not enough for non-selective ion conduction

Prof. Dr. Adam Lange

Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP), Berlin

NaK and other non-selective channels are able to conduct both sodium (Na^+) and potassium (K^+) with equally high efficiency. In contrast to previous crystallographic results, we show that the selectivity filter (SF) of NaK in native-like lipid membranes adopts two distinct conformations that are stabilized by either Na^+ or K^+ ions. The atomic differences of these conformations are resolved by solid-state NMR (ssNMR) spectroscopy and molecular dynamics (MD) simulations. Besides the canonical K^+ permeation pathway, we identify a side entry ion-conduction pathway for Na^+ permeation unique to NaK. Moreover, under otherwise identical conditions ssNMR spectra of the K^+ selective NaK mutant (NaK2K) reveal only a single conformational state. Therefore, we propose that structural plasticity within the SF and the selection of these conformations by different ions are key molecular determinants for highly efficient conduction of different ions in non-selective cation channels [1]. Furthermore, we will present proton-detected solid-state NMR data [2] that allow us to probe the presence of bound water molecules in the SF of NaK.

References

[1] Shi, C. et al. (2018) *Nature Communications*, 9, 717.
[2] Fricke, P. et al. (2017) *Nature Protocols*, 12, 764-782.