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Ion Binding to a Mammalian Sodium/proton Exchanger Membrane Protein from Molecular Dynamics Simulations CHENOU ZHANG, Arizona State University — The Na+/H+ exchangers (NHE) are a family of proteins that contribute to the control of the cell functions. However, despite their physiological importance, detailed molecular-level structural information for the NHE has been lacking. Although a number of prokaryotic structures of sodium/proton antiporters are known, it is not clear in how far the insights from these structures are applicable to the medically important mammalian homologs. Here we report molecular dynamics (MD) simulations at both atomic and coarse-grained (CG) level of detail based on the first atomic-resolution structure of a mammalian NHE9. We focus on the transporter-Na+ ion and transporter-lipid interactions. Multiple protonation states of the model were identified through heuristic pKa calculations. The atomic equilibrium MD simulations tested different combinations of those protonation states and identified a conserved aspartic acid residue as the likely ion-biding site. Based on the simulations we developed a detailed microscopic picture of events necessary for sodium. Because previous work suggested the membrane composition is critical for NHE activation and cell-volume regulation, we also investigated the interaction of the transporter with membrane lipids and cholesterol.

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