

Water structure in the intracellular osmosensor WNK1 E. J. Goldsmith*, Radha Akella, and Kamil Sekulski Department of Biophysics, UT Southwestern Medical Center at Dallas, Dallas, TX 75235-8816 (*Elizabeth.Goldsmith@UTSouthwestern.edu).

WNK1 is a protein kinase on pathway for the regulation of cation-chloride cotransporters (CCCs), important mediators of transepithelial transport and cell volume control. Knockout of WNK kinases causes low blood pressure; up-regulating leads to hypertension. WNK1 and WNK3 also mediate myogenic responses, immediate autonomic responses to pressure. They are both osmosensors. Structures of unphosphorylated and phosphorylated WNK1 reveal the osmosensing shifts the equilibrium from a water-filled inactive configuration to one which is auto-phosphorylation competent. WNKs 1 and 3 are intracellular osmosensors.