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Crystal Structures of the PhoQ Sensor Domain Suggest a Novel Mechanism for Signal Transduction Across Cell Membranes. U.S. Cho, M. W. Bader, M.F. Amaya, M.E. Daley, R.E. Klevit, S.I. Miller, W. Xu, Dept. of Biological Structure, Microbiology, Biochemistry, Medicine and Genome Sciences, Univ. of Washington, Seattle, WA 98195.

Many bacterial histidine kinases respond to environmental stimuli by transducing a signal from an extracytosolic domain to a cytosolic catalytic domain. PhoQ is a transmembrane sensor histidine kinase that functions to promote bacterial virulence for animals and plants by regulating resistance to antimicrobial peptides. PhoQ is repressed by divalent cations and activated by antimicrobial peptides. The crystal structure of *Salmonella* PhoQ sensor domain, in the Ca^{2+} -bound state, reveals a highly negatively charged surface of the PhoQ sensor domain that is in close proximity to the inner membrane. This surface binds at least three metal ions to neutralize charge repulsion between PhoQ and the membrane. The crystal structure of PhoQ sensor domain, in the Ca^{2+} -free state, exhibits a dramatic dimerization interface change. Our crystallographic, NMR and mutagenesis results suggest that charge repulsion from the membrane initiates a dimerization interface change which promotes signal transduction by bringing the transmembrane helices in closer proximity.

