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A Structural Genomics Analysis of Histidine Kinase Sensor Domains. J. Cheung, W. A. Hendrickson, Dept. of Biochemistry and Molecular Biophysics, Howard Hughes Medical Inst., Columbia Univ., New York NY, 10032, USA.

Two-component protein signaling systems in prokaryotes and lower eukaryotes relay external environmental signals to internal adaptive cellular responses. Signal transduction occurs via phosphotransfer between a histidine kinase sensor protein and a response regulator which interact in tandem. The sensor is usually a transmembrane protein that contains a conserved cytoplasmic histidine kinase transmitter domain and a modular periplasmic sensor domain. The response regulator is cytoplasmic protein that contains a receiver domain that interacts with the histidine kinase, and an output domain that interacts with regulators of transcription or chemotaxis. Our work focuses on the X-ray structure determination of a variety of bacterial histidine kinase sensor domains, guided by a structural genomics analysis of the entire sensor domain family. Structures of five sensor domains have been solved to atomic resolution, some in both ligand-bound and ligand-free states, revealing several distinct structural folds. An analysis of the structures reveals a possible mechanism of transmembrane signaling, and a comprehensive pan-genomic bio-informatics analysis of all sensor domain sequences allows fold prediction for over 350 sensor domains.