A universal signaling mechanism in bacterial chemoreceptors

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Bacterial chemoreceptors serve as a model system for understanding transmembrane signaling [1]. However, the mechanisms by which conformational signals move within and between receptors and how they control kinase activity remain unknown. Using all-atom, microsecond-range molecular dynamics simulations on a special-purpose supercomputer, we show that the kinase-activating cytoplasmic tip of the chemoreceptor fluctuates between two stable conformations in a signal-dependent manner. A specific residue, Phe396, appears to serve as the conformational switch, because flipping of the stacked aromatic rings of an interacting F396-F396' pair in the receptor homodimer took place concomitantly with the signal-related conformational changes [2]. Comparative genomic analysis reveals that F396 is the single most conserved residue in the entire chemoreceptor molecule: it is invariant in 99.8% of chemoreceptor sequences from all available genomes of bacteria and archaea. We conclude that despite substantial differences in the signaling domain between diverse bacterial species [3], the signaling mechanism is universally conserved.

1. G.L. Hazelbauer et al (2008) Bacterial chemoreceptors: high-performance signaling in networked arrays. *Trends Biochem Sci*, **33**:9-19.

2. D.R Ortega et al (2013) A phenylalanine rotameric switch for signal-state control in bacterial chemoreceptors, *Nat Commun*, **4:**2881.

3. R.P. Alexander and I.B. Zhulin (2007) Evolutionary genomics reveals conserved structural determinants of signaling and adaptation in microbial chemoreceptors. *Proc Natl Acad Sci USA*, **104**:2885-2890.