Structure and Function of Chemoreceptor Arrays- the Bacterial Brain that Controls Flagellar Motility

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Nearly all motile prokaryotic cells utilize a highly sensitive and adaptable sensory system to detect changes in nutrient concentrations in the environment and guide their movements towards attractants and away from repellents. This chemosensory system allows the cells to selectively colonize preferential environments and is also involved in host infection by some pathogenic bacteria.

The bacterial chemoreceptor array is a polar, highly organized sensory patch composed of thousands of transmembrane receptor proteins. Attractants and repellents bind to the sensory domains of these receptors, thereby regulating activity of the histidine kinase CheA, which phosphorylates a soluble messenger protein. This messenger protein in turn diffuses through the cytoplasm to the flagellar basal body, where it modulates the direction of flagellar rotation.

By combining 3D data from electron cryotomography (ECT) with high resolution structures derived from crystallography, we have determined that native chemoreceptor arrays are composed of trimers of receptor-dimers that are connected by rings of the histidine kinase and a linking protein, CheW. Analyses of receptor complexes assembled both in vitro and in vivo have yielded new insights into de novo array formation. Following commonly used in vitro protocols and comparing these assemblies with in vivo arrays, we have proposed a model for the formation of chemoreceptor arrays in which CheA and CheW cross-link the receptors into an extended hexagonal lattice.

To gain insight into how the activity of the kinase CheA is controlled in the native array, we used ECT to characterize a set of receptor mutants that lock the kinase in specific activation states. These studies revealed that kinase activity relies on the flexibility of two of the five kinase domains, and that inactivation occurs by the unproductive binding of these domains.

While the best-studied bacterial chemoreceptor arrays are membrane-bound, many motile bacteria and archaea contain one or more additional, purely cytoplasmic chemoreceptor systems. We have recently reported the architecture of the cytoplasmic chemoreceptor arrays and are currently investigating a novel, third chemoreceptor array that is associated with the membrane but lacks any detectable membrane-binding domain.