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**Discovering novel ligands for understanding molecular mechanism of bacteria chemotaxis**

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In order to understand the molecular mechanism of bacteria chemotaxis, we used a combined experimental and computational approach to discover novel chemoeffector molecules and compare their binding features, as well as the conformational changes they produce. We first used molecular docking to computationally screen a large chemical library and tested binding strengths of the top-ranking molecules for the E. coli chemoreceptor Tar. Chemotactic properties of the binding molecules were then studied using a specially designed microfluidic device. Novel attractant and antagonist molecules were identified that bind directly with the E. coli chemoreceptor Tar. Molecular dynamics simulations showed that attractant and antagonist binding result in distinct conformational changes in Tar. Differences of antagonist and attractant binding suggest that molecules lacking triggering interaction with the receptor behave as antagonist. For Tar, the triggering interaction is mediated by the hydrogen bonds formed between a donor group in the attractant and the main-chain carbonyls in the fourth helix of Tar. This ?bind-and-trigger? mechanism of receptor signaling is verified experimentally by converting an antagonist into an attractant when introducing an NH group into the antagonist compound. Similar conformational changes were also observed in the E. coli Tsr system.