

Allosteric Activation of Choanoflagellate Soluble Guanylate Cyclases

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Nitric oxide (NO) is a signaling molecule used by animals in key processes like vasodilation, neurotransmission, and host response to infection. Central to NO function in animal physiology is the metalloenzyme soluble guanylate cyclase (sGC), which generates the secondary messenger guanosine 3',5'-monophosphate (cGMP) in response to allosteric activation by NO. Because of its centrality to several physiological processes in humans, sGC is a current therapeutic target, and a complete structural and mechanistic understanding of the 3-stage activation of sGC by NO will inform continued development. Newly discovered sGCs from the single-celled colonial organism *Choanoeca flexa* have recently been shown to display regulation profiles similar to those of animals but with several conspicuous structural differences. Importantly, choanoflagellates like *C. flexa* are the closest single-celled relatives to animals, and their NO colonial signaling may represent a major step toward the evolution of multicellularity. Using structural techniques including small-angle X-ray scattering and cryo-EM, I characterize the unique properties of *C. flexa* sGC to better understand the allostery of sGCs and shed light on the evolution of NO signal transduction in animals.