Allosteric activation of choanoflagellate soluble guanylate cyclase and the evolution of NO signaling in animals

William Thomas[1]

[1]UC Berkeley

wcthomas@berkeley.edu

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. A newly discovered sGC from the single-celled colonial organism Choanoeca flexa has recently been shown to display NO-regulation behavior similar to that 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 a combination of mutagenic activity studies and structural techniques including small-angle X-ray scattering, 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.