

Publication

Activation mechanism of a small prototypic Rec-GGDEF diguanylate cyclase

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Diguanylate cyclases (DGCs) synthesising the bacterial second messenger c-di-GMP are found to be regulated by a variety of sensory input domains that control the activity of their catalytical GGDEF domain. As part of two-component systems, they are activated by cognate histidine kinases that phosphorylate their Rec input domains. DgcR from *Leptospira biflexa* is a constitutively dimeric prototype of this class of DGCs. Full-length crystal structures revealed that BeF₃ - pseudo-phosphorylation induces a relative rotation of two rigid halves in the Rec domain. This is coupled to a reorganisation of the dimeric structure with concomitant switching of the coiled-coil linker to an alternative heptad register. Finally, the activated register allows the two substrate-loaded GGDEF domains, which are linked to the end of the coiled-coil via a localised hinge, to move into a catalytically competent dimeric arrangement. Bioinformatic analyses suggest that the binary register switch mechanism is utilised by many DGCs with N-terminal coiled-coil linkers.

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