A Single-Domain Response Regulator Functions as an Integrating Hub To Coordinate General Stress Response and Development in Alphaproteobacteria

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4487439
Author(s) Lori, C.; Kaczmarczyk, A.; de Jong, I.; Jenal, U.
Author(s) at UniBasel Jenal, Urs ; Kaczmarczyk, Andreas ;
Year 2018
Title A Single-Domain Response Regulator Functions as an Integrating Hub To Coordinate General Stress Response and Development in Alphaproteobacteria
Journal mBio
Volume 9
Number 3
Pages / **Article-Number** e00809-18
Keywords Caulobacter; alpha-proteobacteria; bow-tie; general stress response; phosphorylation; regulation of gene expression; two-component system

The alphaproteobacterial general stress response is governed by a conserved partner-switching mechanism that is triggered by phosphorylation of the response regulator PhyR. In the model organism; Caulobacter crescentus; , PhyR was proposed to be phosphorylated by the histidine kinase PhyK, but biochemical evidence in support of such a role of PhyK is missing. Here, we identify a single-domain response regulator, MrrA, that is essential for general stress response activation in; C.ăcrescentus; We demonstrate that PhyK does not function as a kinase but accepts phosphoryl groups from MrrA and passes them on to PhyR, adopting the role of a histidine phosphotransferase. MrrA is phosphorylated by at least six histidine kinases that likely serve as stress sensors. MrrA also transfers phosphate to LovK, a histidine kinase involved in; C.ăcrescentus; holdfast production and attachment, which also negatively regulates the general stress response. We show that LovK together with the response regulator LovR acts as a phosphate sink to redirect phosphate flux away from the PhyKR branch. In agreement with the biochemical data, an; mrrA; mutant is unable to activate the general stress response and shows a hyperattachment phenotype, which is linked to decreased expression of the major holdfast inhibitory protein HfiA. We propose that MrrA serves as a central phosphorylation hub that coordinates the general stress response with; C.ăcrescentus; development and other adaptive behaviors. The characteristic bow-tie architecture of this phosphorylation network with MrrA as the central knot may expedite the evolvability and species-specific niche adaptation of this group of bacteria.; IMPORTANCE; Two-component systems (TCSs) consisting of a histidine kinase and a cognate response regulator are predominant signal transduction systems in bacteria. To avoid cross talk, TCSs are generally thought to be highly insulated from each other. However, this notion is based largely on studies of the HisKA subfamily of histidine kinases, while little information is available for the HWE and HisKA2 subfamilies. The latter have been implicated in the alphaproteobacterial general stress response. Here, we show that in the model organism; Caulobacter crescentus; an atypical FATGUY-type single-domain response regulator, MrrA, is highly promiscuous in accepting and transferring phosphoryl groups from and to multiple up- and downstream kinases, challenging the current view of strictly insulated TCSs. Instead, we propose that FATGUY response regulators have evolved in alphaproteobacteria as central phosphorylation hubs to broadly sample information and distribute phosphoryl groups between the general stress response pathway and other TCSs, thereby coordinating multiple cellular behaviors.

ISSN/ISBN 2150-7511
edoc-URL https://edoc.unibas.ch/66769/
Full Text on edoc No;
Digital Object Identifier DOI 10.1128/mBio.00809-18
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/29789370