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Abstract

Adaptive immune systems have recently been recognized in prokaryotic organisms. where, in response to viral infection, they incorporate short fragments of invacienderived DNA into loci called plustered regularly interspaced short palindromic repeats (CRISPRO In subsequent infections, the CRISPR loci are transcribed and processed into guide sequences for the neutralization of the invading RNA or CNA. The CRISPAassociated protein machinery (Cas) lies at the heart of this process, yet many of the molecular details of the CRISPIVCas system remain to be elucidated. Here, we report the first structure of Csa3, a CRISPR-associated protein from Sulfolybus solfabelous (Sso1445), which leveals a dimeric two domain protein. The Niterminal domain is a unique variation on the diructeotide binding domain that orchestrates dimer formation. In addition, it utilizes two conserved sequence motifs [Thr-h-Gly-Phe-(Ann/Asp.) Giu Xe Arg and Leu Xe Gly-h-Arg] to construct a 24bid symmetric pocket. on the dimer axis. This pocket is likely to represent a regulatory ligand-binding site. The N-terminal domain is fused to a C-terminal MerR-like wriged helix-turn-helix. domain that is expected to be involved in DNA recognition. Overall, the unique domain architecture of Cea3 suggests a transcriptional regulator under allosteric control of the N-terminal domain. Alternatively, Cso3 may function in a larger complex. with the conserved cleft participating in protein-protein or protein-nucleic acid interactions. A similar N-terminal domain is also identified in Cav1, a second CRISPRassociated protein family of unknown function.

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