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Mechanisms of long-range communication between DNA sites by NTP-dependent restriction endonucleases

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Nucleoside triphosphate (NTP)-dependent restriction endonucleases are one of the most prominent bacterial defenses against invading foreign DNA. These enzymes nucleolytically cleave foreign DNA and thus protect the host cell from bacteriophage infection and also control horizontal transfer of DNA, such as antibiotic resistant genes and pathogenicity islands. In general, DNA cleavage by these enzymes requires at least two sequence-specific target sites, which can be separated spatially by a few thousand base pairs. The nuclease activity of these enzymes is coupled to the hydrolysis of NTP by an inbuilt NTPase. Deciphering the mechanism of how these enzymes work has been hindered by a lack of structural information of them. We have been studying the mechanism of these enzymes by carrying out structural studies complemented by biochemical and biophysical studies. These studies have provided unprecedented insights into the molecular basis of the NTPases and their coupling to the nuclease, in addition to revealing varied mechanisms of long-range communication between the sites. I will present the mechanistic details that have emerged from them.