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Bacterial Effector Kinases

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Protein phosphorylation is one of the main signaling mechanisms in eukaryotic cells. Not surprisingly, pathogenic adopted this mechanism to interfere with signaling processes in the host cell. To this end pathogens evolved kinases that, in addition to other bacterial effector proteins, are injected into the host cell via a syringe-like type 3 (T3SS) or type 4 (T4SS) secretion systems. Kinases NleH1 and NleH2 from pathogenic E. coli, OspG from Shigella, SteC and SboH from Salmonella, LegK1-4 from Legionella and YspK and YpkA from Yersinia represent currently known effector kinases. Some of these kinases were likely derived from eukaryotes via horizontal gene transfer (SteC, LegK1-4, YpkA). Other kinases (NleH, OspG, SboH and YspK) have been so far identified only in the pathogenic bacteria. The structures of NleH and OspG proved that these kinases, which are half the size of an average human kinase, contain only a core kinase fold. These kinases lack the main regulatory element – the activation loop. The structure of NleH suggests that it has no activation mechanism since the apo-kinase domain adopts an active conformation and no change is observed on nucleotide binding. The OspG kinase, which also contains only the core kinase fold, is stimulated by its binding partner, the ubiquitin-conjugating enzyme E2-ubiquitin complex. The structure of OspG:UbcH7-Ub complex shows that OspG binds the E2 and ubiquitin (Ub) at two distinct sites on its surface. In this complex the OspG active site is unobstructed and primed for catalysis. However the mechanism of OspG activation remains presently unknown. Both NleH and OspG were found to inhibit the NF-kB pathway, however the substrates forOspG and NleH kinase activities are not yet known.

[1] *Grishin AM, Cherney M, Anderson DH, Phanse S, Babu M, Cygler M. NleH Defines a New Family of Bacterial Effector Kinases. Structure. 2014 Feb 4;22(2):250-9*

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