

MS03-P109 - LATE | HOW THE PARG PROTEIN MARK KEEPS THE STRESS RESPONSE KINASE MCSB UNDER CONTROL

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Protein arginine phosphorylation is an emerging post-translational modification found in gram-positive bacteria. Here, the phospho-arginine (pArg) mark serves as degradation signal directing aberrant proteins to the ClpC:ClpP protease. The chemically demanding phosphorylation of arginine residues is carried out by the protein arginine kinase McsB. Recent structural studies revealed the organizing of the McsB kinase, having an allosterically coupled dimer as basic functional unit. In vivo data suggest that the McsB's activity needs to be tightly controlled in the cell, most likely to keep the pArg death-marking function under control. However, molecular details of McsB regulation are still elusive.

Here, we present a comprehensive structural, biochemical and biophysical investigation of the *Bacillus subtilis* McsB kinase. Most importantly, single-molecule data reveal the presence of various functionally relevant oligomeric forms, which differ in their substrate-targeting activities. Moreover, we show that the change in oligomeric state depends on a phospho-arginine switch, allowing pArg effector proteins to modulate McsB activity. Delineating the molecular mechanism of the pArg-dependent oligomer conversion of McsB will help to better understand the bacterial stress-response system, which is one of the most critical assets underlying bacterial pathogenicity.