

Investigation of the structural basis for the inhibition of Histidine Kinase A by Sda in *Bacillus subtilis*

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The *Bacillus subtilis* histidine kinase A (KinA) regulates the activation of the transcription factor, Spo0A, that governs sporulation. In response to an as yet unidentified signal, KinA autophosphorylates at a conserved histidine residue. The phosphate is relayed via two other proteins to Spo0A, which becomes activated. The DNA-damage checkpoint inhibitor, Sda, halts the sporulation pathway by binding to KinA and inhibiting the autokinase reaction. The structure of Sda has been solved by NMR methods, and while the structure of KinA is unknown, there are homologous structures that provide a basis for modelling. It had been proposed that Sda sterically blocks the catalytic domains of KinA from accessing the target histidine. Small-angle X-ray scattering (SAXS) revealed low-resolution structural information on the KinA, Sda, and KinA variation was used to obtain details of the interaction between KinA and Sda. The scattering data show that upon Sda binding, KinA undergoes a conformational change, which results in a compaction of the structure. The SANS data revealed that two monomers of Sda bind KinA, and that the centres of these monomers are separated by a distance of ~ 45 Å. SANS also revealed that the centres of mass of KinA and Sda were separated by ~ 27 Å. Using these constraints and the available structural models for the components, we are using a rigid body refinement method to model the KinA₂:2Sda complex.