A Conserved PLPLRT/SD Motif within the C-terminal Tail of STING Mediates the Recruitment and Activation of TBK1

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The detection of nucleic acids is a central strategy of innate immunity. Cytosolic DNA is detected by cGAS, which catalyzes the synthesis of a cyclic dinucleotide cGAMP. The adaptor STING binds to cGAMP and mediates the activation of TBK1 and IRF-3. Together, this pathway regulates the induction of type-I interferons. The precise mechanisms governing STING activation by cGAMP and TBK1 activation by STING remain poorly understood. Here we identified a conserved PLPLRT/SD motif within the C-terminal tail of STING that is required for TBK1 recruitment. Crystal structures of TBK1 bound to STING revealed that the PLPLRT/SD motif binds to the dimer interface of TBK1. Cell-based studies confirmed that the direct interaction between TBK1 and STING is essential for IFN-β induction upon cGAMP stimulation. To further investigate the mechanism of STING activation, we expressed and purified full-length STING and observed via cryo-EM that STING oligomerizes in the presence of cGAMP.

Fig. 1. The crystal structure of TBK1 bound with STING CTD

Reference