Cryo-EM reveals that MuB is an AAA+ regulator of transposition that distorts target DNA

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Transposons are mobile genetic elements that drive genomic rearrangements and evolution. Many transposons, such as Tn7, CRISPR-Tn7-like, and Mu, depend on AAA+ proteins to enable target-site selection. MuB is an AAA+ protein, a component of the transposition system from bacteriophage Mu, that regulates the activity of the MuA transposase. It has been shown that MuB forms helical filaments in the presence of DNA and catalyzes the formation of the MuA strand transfer complex. Furthermore, in the absence of MuB the MuA transposase displays a distinct preference for mismatched DNA, and target DNA is sharply bent in the structure of the MuA transpososome. Despite decades of biochemical, genetic, and structural studies of the Mu system, a high-resolution structure of the MuB filament and a direct visualization of how MuB interacts with its DNA substrate have remained elusive. Here, we solved a cryo-EM structure of the MuB helical filament that reveals the mechanism of its association with DNA and gives context to existing data on how MuB interacts with MuA. We show that each MuB monomer interacts with DNA through a positively charged loop and that the DNA is distorted to match the helical parameters of the MuB filament. This structure further reveals the position of the MuA-MuB interaction motif on the exterior of the MuB filament, close to the ATP binding site. Additionally, comparison of this structure to the AAA+ regulator, TnsC, from the Type V-K CRISPR-Transposase family reveals a startling level of structural similarity. Our observations that MuB distorts DNA and, from prior research, that mismatched DNA are favored by MuA for transposition suggest that DNA deformation is a key prerequisite of transpososome assembly. All together, these results support a conserved manner of higher-order assembly for AAA+ regulators of transposition and a mechanistic model where DNA distortion by the AAA+ regulator primes the target DNA for subsequent transposition.