

1 Intrinsically Disordered C-terminal Tails of E. coli Single Stranded DNA Binding Protein Regulate Cooperative Binding to Single Stranded DNA.

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The authors provide a comprehensive analysis of the molecular mechanisms underlying peculiar multifunctionality and binding diversity of the homotetrameric Escherichia coli single-stranded DNA (ssDNA)-binding protein (SSB). SSB has several very different modes of interaction with ssDNA and is also known to be involved in specific interaction with a set of partner proteins (SSB-interacting proteins or SIPs). The authors show that the 56-residue-long intrinsically disordered linker (IDL) region, located between the N-terminal DNA-binding domain and the C-terminal 9-residue motif (the 'acid tip') needed for the SSB interaction with the SIPs, plays a crucial role in the highly cooperative binding of the tetrameric SSB to ssDNA. Curiously, the length of individual IDPs, their amino acid compositions, and the number of IDLs define the DNA-binding mode of this protein.

Disclosures

None declared

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Abstract:

ABSTRACT

The homotetrameric E. coli single stranded DNA binding (SSB) protein plays a central role in DNA replication, repair and recombination. E. coli SSB can bind to long single-stranded (ss) DNA in multiple binding modes using all four subunits ((SSB)65 mode) or only two subunits ((SSB)35 binding mode), with the binding mode preference regulated by salt concentration and SSB binding density. These binding modes display very different ssDNA binding properties with the (SSB)35 mode displaying highly cooperative binding to ssDNA. SSB tetramers also... [more »](#)

bind an array of partner proteins, recruiting them to their sites of action. This is achieved through interactions with the last 9 amino acids (acidic tip) of the intrinsically disordered linkers (IDLs) within the four C-terminal tails connected to the ssDNA binding domains. Here we show that the amino acid composition and length of the IDL affects the ssDNA binding mode preferences of SSB protein. Surprisingly the number of IDLs and the lengths of individual IDLs together with the acidic tip contribute to highly cooperative binding in the (SSB)35 binding mode. Hydrodynamic studies and atomistic simulations suggest that the E. coli SSB IDLs show a preference for forming an ensemble of globular conformations, whereas the IDL from Plasmodium falciparum SSB forms an ensemble of more extended random coils. The more globular conformations correlate with cooperative binding.

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