Structural basis for DNA unwinding at forked dsDNA by two coordinating Pif1 helicases

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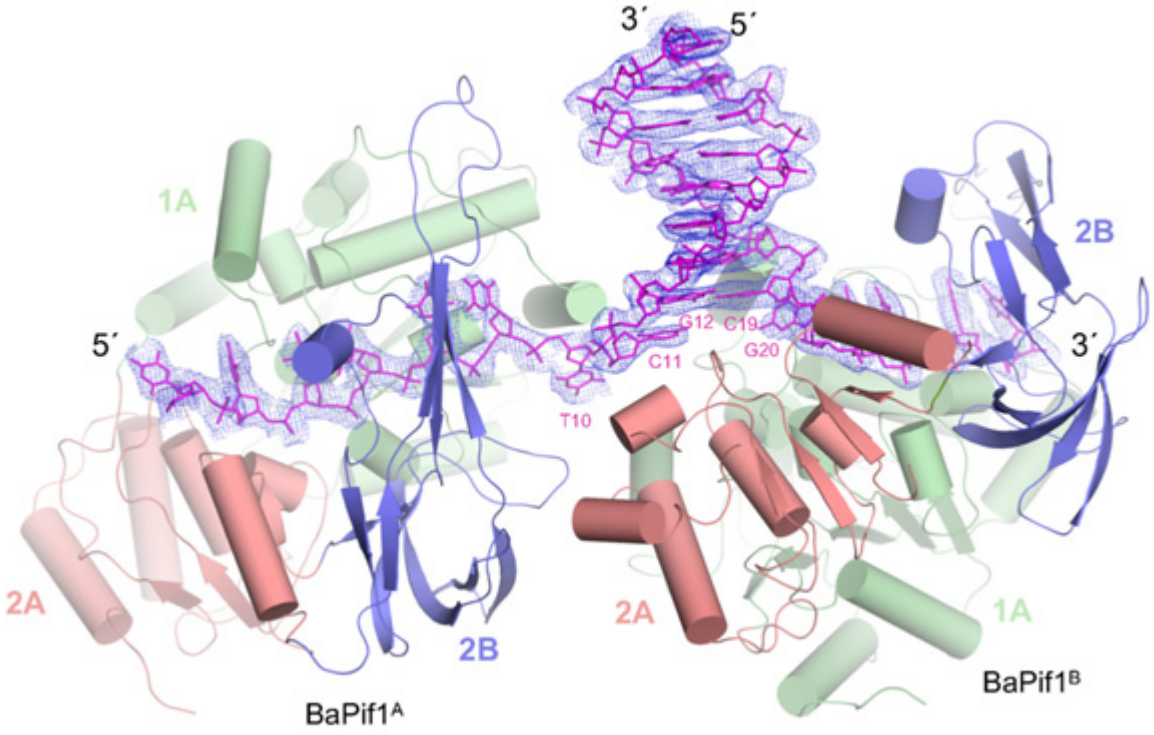
Abstract

Pif1 plays multiple roles in maintaining genome stability and preferentially unwinds forked dsDNA, but the mechanism by which Pif1 unwinds forked dsDNA remains elusive. Here we report the structure of Bacteroides sp Pif1 (BaPif1) in complex with a symmetrical double forked dsDNA. Two interacting BaPif1 molecules are bound to each fork of the partially unwound dsDNA, and interact with the 5′ arm and 3′ ss/dsDNA respectively. Each of the two BaPif1 molecules is an active helicase and their interaction may regulate their helicase activities. The binding of BaPif1 to the 5′ arm causes a sharp bend in the 5′ ss/dsDNA junction, consequently breaking the first base-pair. BaPif1 bound to the 3′ ss/dsDNA junction impacts duplex unwinding by stabilizing the unpaired first base-pair and engaging the second base-pair poised for breaking. Our results provide an unprecedented insight into how two BaPif1 coordinate with each other to unwind the forked dsDNA.

Figure



Legend for the Figure:

Two molecules of BaPif1 bind to a replication fork-like substrate: One of the BaPif1 molecules binds to the 5' ssDNA and unwinds the first base pair of the duplex; the other binds to the 3' arm of the fork on the leading strand template and stabilizes the ss/ds junction. Interactions between the two BaPif1 molecules occur at the junction and appear to limit the processivity of the individual BaPif1 molecules.