DCIA, THE ANCESTRAL REPLICATIVE HELICASE LOADER

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DNA replication is a crucial step for the proliferation of all organisms. Multi-subunits complex termed replisome carried out strand synthesis while controlling the fidelity of the replication. In front of the replisome, the replicative helicase unwinds DNA by its translocation on the lagging strand. One of the essential steps of the replication is the recruitment and the loading of the helicase at the initiation site of replication. In bacteria, the initiation protein DnaA localized at the unique origin of replication *oriC* recruits two helicases DnaB, but the loading depends on a protein loader. DnaB loading has been well described within the *Escherichia coli* model where DnaC ensures DnaB loading by cracking open the helicase. Yet, DnaC distribution is marginal in the bacterial domain. It was established phylogenetically that *dnaC* gene is a domesticated phage element that replaced several times through evolution the bacterial and ancestral gene, *dciA* (1). Despite the preponderance of *dciA* in bacteria, the loading mechanism of DnaB managed by DciA was not yet studied.

Our work focused on biochemical and structural characterization of DciA and DnaB from *Vibrio cholerae*. As other bacterial replicative helicases, *Vc*DnaB adopts a toroid-shaped homo-hexameric structure but with a slight opening (2). Performing helicase assays and SPR analyses, we showed that *Vc*DnaB can load itself on DNA and that *Vc*DciA stimulates this function, resulting in an increased DNA unwinding (2). We obtained a crystal structure of the *Vc*DnaB•*Vc*DciA complex, which we compared to the DnaB•DnaC complex from *E. coli*. Interestingly, both loaders target the same binding site. We determined that *Vc*DciA is composed of two structural domains: a globular NTD (structure solved by NMR), which binds to DNA, and an unstructured CTD, which can fold transitory into 2 small helices (3) and binds to *Vc*DnaB. We combined a multi-disciplinary approach to study the structural and functional interplay between the three partners of the *Vc*DnaB•*Vc*DciA•DNA complex in order to propose a loading mechanism of DnaB by DciA. We expect a completely different mechanism than the one known for DnaC.

(1) Brezellec P, et al (2016) doi: 10.1038/ncomms13271.

(2) Marsin S, et al (2021) doi: 10.1093/nar/gkab463.

(3) Chan-Yao-Chong M, et al (2020) doi: 10.1016/j.jsb.2020.107573.