Sliding mechanism of eukaryotic and prokaryotic DNA clamps

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To replicate genomic DNA with high fidelity and efficiency, several enzymes cooperate as a replication complex. Among those enzymes, the DNA clamp—beta-clamp for prokaryotes and proliferating cell nuclear antigen (PCNA) for eukaryotes—plays the central role. The DNA clamp is a ring-shaped protein complex that encircles DNA such that the clamp itself and other replication enzymes attached to the clamp stably slide along DNA. Ten years ago, the diffusion coefficients of both beta-clamp and PCNA were experimentally measured using the single-molecule techniques, revealing that PCNA diffuses about an order of magnitude faster than beta-clamp does. However, the general sliding mechanism still remains elusive and the factor that slows down beta-clamp remain unexplained. Here, we use the molecular dynamics (MD) simulation technique to answer the questions. For each of beta-clamp and PCNA systems, we generated a 10 microsecond-long continuous trajectory, in which the computed diffusion coefficient matched the experimental measurement. The MD trajectories revealed that the difference in the binding mode between DNA and clamps can explain the difference in the diffusion speed. For beta-clamp, arginine residue 24 (R24) was found to spontaneously binds to the minor groove of DNA, providing a breaking mechanism that slows down the diffusion. For PCNA, conversely, no basic residues were found to bind to the minor groove, resulting in a fast diffusion without a breaking mechanism.