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LS-4-P-5998 Single particle analysis of molecular architecture of DNA replication fork complex and switching mechanism of replication factors

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DNA replication in archaea and eukaryotes is executed by family B DNA polymerases, which exhibit full activity when complexed with the DNA clamp, proliferating cell nuclear antigen (PCNA). PCNA has a trimeric ring structure that encircles the DNA, and increases the processivity of the bound DNA polymerase by tethering it to the DNA. It is known now, that PCNA also interacts with multiple partners to control DNA replication, DNA repair, and cell cycle progression, and works not only as the platform, but also as the conductor for the recruitment and release of these factors. However, the molecular architectures as well as the mechanism of the regulation of these replication factors are not known in detail.
We have investigated the three-dimensional structure of the core components of the replisome, such as DNA polymerase B(PolB)-PCNA-DNA, and DNA ligase-PCNA-DNA ternary complexes [(1- 2)], by single particle analysis, and successfully could obtain atomic models of both complexes, by docking crystal structures of each components in the two maps . Both maps exhibited a novel contact between both polymerase-PCNA and ligase-PCNA, besides the authentic interaction through a PCNA-interacting protein box (PIP-box).
Mutant analysis showed that these contacts are involved in the regulation of the replication factors, such as the switching between the polymerizing and editing modes of the PolB. As we found similar multiple interactions in both complexes, we are now studying the structure of other complexes such as Hjm helicase-PCNA-DNA and FEN-PCNA-DNA, to check if such regulation mechanism can be also found in replication complex more generally.

References

(1) Mayanagi, *et al*., *PNAS*, **108**, 1845-1849 (2011)
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