“Structure informs function: What can we learn about DNA replication mechanisms from cryo-EM structures of its machines”

by

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Abstract

The assembly of DNA replicative helicase onto origin DNA is central to the regulation of replication initiation. A family of six homologous subunits, Mcm2, -3, -4, -5, -6 and -7, each with its own unique features, forms the catalytic core of the eukaryotic replicative helicase. The necessity of six similar but non-identical subunits has been a mystery since its initial discovery. Extrapolating from the simpler models, especially of the archaea which have homologs of Mcm, has been useful, especially with the early crystal structures of portions of these proteins. However, the simplified model exactly lacks the intricacies of eukaryotes that have puzzled researchers. The biochemistry and genetics of this subject accumulated throughout the years suggest that this process is much more complicated in eukaryotes.

High-resolution structures of the eukaryotic replication machinery are key to assembling this elaborate puzzle. Until only very recently, sub-nanometer high-resolution structures of the critical components of the DNA replication-initiation molecular assembly were rare. With the advent of the resolution revolution of cryo-electron microscopy (cryo-EM), we have solved the structures of the Mcm2-7 single hexamer (MCM-SH), the Cdt1-Mcm2-7 (CM) heptamer, and the Mcm2-7 double hexamer (MCM-DH). The information derived from these valuable structures provides significant insights into the unique roles of the Mcm2-7 subunits in orchestrating the assembly of the pre-replicative complex at origin DNA as well as the translocation mechanism of the helicase.

Date : 21 March 2018 (Wednesday)
Time : 4 p.m.
Venue : Room 1505 (near Lifts 25/26) - HKUST

(Host faculty: Prof. Mingjie Zhang)

ALL ARE WELCOME!!