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Cryo-EM visualization of the protein machine that replicates the chromosome

HUILIN LI, Van Andel Research Institute

Structural knowledge is key to understanding biological functions. Cryo-EM is a physical method that uses transmission electron microscopy to visualize biological molecules that are frozen in vitreous ice. Due to recent advances in direct electron detector and image processing algorithm, cryo-EM has become a high-resolution technique. Cryo-EM field is undergoing a rapid expansion and vast majority research institutions and research universities around the world are setting up cryo-EM research. Indeed, the method is revolutionizing structural and molecular biology. We have been using cryo-EM to study the structure and mechanism of eukaryotic chromosome replication. Despite an abundance of cartoon drawings found in review articles and biology textbooks, the structure of the eukaryotic helicase that unwinds the double stranded DNA has been unknown. It has also been unknown how the helicase works with DNA polymerases to accomplish the feat of duplicating the genome. In my presentation, I will show how we have used cryo-EM to derive at structures of the eukaryotic chromosome replication machinery and describe mechanistic insights we have gleaned from the structures.