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Selected Publication

Li, N.[*], Zhai, Y.[*#], Zhang, Y., Li, W., Yang, M., Lei, J., Tye, B.[#], and Gao, N.[#] (2015) Structure of the Eukaryotic Minichromosome Maintenance Complex at 3.8 Å. *Nature,* 524, 186–191 doi:10.1038/nature14685.

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Research Aims and Interests

Eukaryotic DNA replication is strictly regulated to maintain genome integrity and hence a faithful inheritance of genetic material during the cell division cycle. A central step in this regulation is the stepwise assembly of the eukaryotic helicase Mcm2-7 complexes onto the replication origins during early G1 phase to form inactive double hexamers. Subsequent activation of Mcm2-7 complexes takes place in S phase and requires two kinases, Dbf4-depende kinase (DDK) and cyclin-dependent kinase (CDK), and multiple factors, resulting in the formation of an active Cdc45-Mcm2-7-GINS (CMG) helicase. The detailed mechanism for the conversion of inactive Mcm2-7 double hexamers into active single hexamers remains largely unknown.

Our research aims at elucidating the regulatory mechanisms underlying the above mentioned process, both locally at individual replication origins at a molecular level and globally of the nuclear architecture at a genomic and organelle scale. We combine diverse approaches in genetics, biochemistry, molecular biology and imaging to achieve these goals.

Using advanced cryo-EM, we have solved the structure of the MCM2–7 double hexamer at 3.8 Å. Our structure reveals rich details for the organization of this large complex, and informs many functional aspects of this replicative helicase, particularly in the initial origin melting.

To explore the spatial organization of subcellular organelles at nanometer scale, we have successfully built up a user-friendly two-color super-resolution localization microscope (SRLM) at HKUST. By applying the SRLM techniques in yeast studies, we have been able to examine cellular structures at a resolution of 20 nm that is impossible for the conventional fluorescence microscopies. So far, we are the first to visualize replication origin clustering in the yeast nucleus using SRLM imaging. Based on this result, several derivative research directions are being developed to understand the organization and the role of origin clustering in the temporal regulation of replication initiation.