



Chromatin architecture defines eukaryotic origins of DNA replication



In the more than six decades since the discovery of the double helix, there has been tremendous progress in understanding the biochemical mechanisms responsible for the precise and accurate duplication of the genome. However, despite the remarkable conservation of proteins and protein functions required for DNA replication across both prokaryotic and eukaryotic systems, we know comparatively little about the functional elements that direct DNA replication in higher eukaryotes. Our research program is focused on understanding how the start sites of DNA replication are selected and regulated in the context of the local chromatin environment to maintain genomic stability and to ensure the accurate inheritance of genetic and epigenetic information. We utilize an interdisciplinary approach combining genetics, biochemistry, and cell biology with genomics and computational biology to systematically identify and dissect the regulatory elements and mechanisms that direct the DNA replication program. Using multiple model systems, including yeast and Drosophila, we have found that the local chromatin architecture is a primary determinant of eukaryotic origin selection and activation.

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