7 have more plasticity in its origin selection142.Data from these newer mapping approaches show that replication origins can be kilobase- sized zones in metazoans and were reported to fire stochastically with no sequence specificity82,109,158.Consistently, metazoan ORC was shown to bind DNA with no apparent sequence specificity in vitro159-161.Despite the lack of sequence specificity, G-rich sequences which have the potential to form G-quadruplex secondary structure have been found to be associated with sites of efficientIn metazoan species, it has been more difficult to locate replication origins and independent studies with different methods do not show high concordance of origin features and locations90,151, likely due to the large genome sizes, the existence of large replication initiation zones, analysis of different cell types, movement of Mcm2-7 double hexamers and technical limitations.Interestingly, bioinformatic analysis of some other fungi, such as Neurospora crassa and Aspergillus nidulans, suggest that AT-hooks at their Orc4 N-terminus might be used to specify replication origin location at AT-rich sequences in their genomes (N. Zali and B. Stillman, unpublished).One possibility is that ORC from S. cerevisiae has lysine-rich sequence in an intrinsically disordered region (IDR) of the Orc1 subunit that binds to a minor grove in the origin DNA and this amino acid sequence is conserved in other eukaryotes and has been shown in ORC from human cells to bind DNA, possibly a short sequence the ORC1 IDR139,143.Following the release of the first draft of the human genome, techniques such as quantitative mapping of RNA-capped short nascent strands (SNS) and 2-dimensional gel electrophoresis were employed to map replication origins84,153-157.They are organized into spatially and temporally regulated replication timing domains6.

Summarized by © lakhasly.com