IN BRIEF

DNA REPLICATION

DNA Pol θ controls replication timing

Although DNA polymerase θ (Pol θ) has been implicated in translesion synthesis and DNA repair, its physiological function remained elusive. Fernandez-Vidal *et al.* now report that DNA Pol θ has a role in the timing of DNA replication. They showed that in human cells DNA Pol θ is recruited to chromatin in early G1 and interacts with origin recognition complex subunit 2 (ORC2) and ORC4. siRNA-mediated depletion of DNA Pol θ led to increased chromatin loading of minichromosome maintenance (MCM) proteins, which assemble at ORC-binding sites, on chromatin in G1. Although DNA Pol θ depletion did not affect origin density, the authors found genome-wide changes in replication timing (both early to late and late to early) in a subset of replication domains, and overexpression of DNA Pol θ mostly delayed the replication of several domains. Together, these results suggest that DNA Pol θ controls human DNA replication timing by regulating MCM accumulation at pre-replication complexes.

ORIGINAL RESEARCH PAPER Fernandez-Vidal, A. *et al.* A role for DNA polymerase θ in the timing of DNA replication. *Nature Commun.* http://dx.doi.org/10.1038/ncomms5285 (2014)

RNA

Two classes of mRNA methylation sites

The modified base N^6-methyladenosine (m6A) is present in mammalian mRNA and might modulate mRNA function. Schwartz *et al.* used a proteomic approach to identify and validate components of the human m6A methyltransferase complex that associate with methyltransferase-like protein 3 (METTL3). Depletion of any of the complex components (WTAP, METTL3, METTL14 and KIAA1429) resulted in decreased m6A levels. Moreover, the authors generated high-resolution catalogues of the mouse and human m6A methylome. They identified two classes of mRNA methylation sites: WTAP-dependent sites are present at internal positions, topologically static and associated with decreased transcript stability, whereas WTAP-independent methylation sites are located at the 5′ cap structure and positively correlated with translation efficiency.

ORIGINAL RESEARCH PAPER Schwartz, S. *et al.* Perturbation of m6A writers reveals two distinct classes of mRNA methylation at internal and 5′ sites. *Cell Rep.* http://dx.doi.org/10.1016/j.celrep.2014.05.048 (2014)

CHROMOSOMES

Epigenetics of kinetochore assembly

Vertebrate centromeres are specified by the deposition of the histone H3 variant centromeric protein A (CENPA), but whether other epigenetic marks are important for centromeric chromatin function was unclear. Hori *et al.* now show that centromeric monomethylation of histone H4 at Lys20 (H4K20me1) is required for kinetochore assembly. H4K20me1, which is associated with transcribed regions throughout the genome, was enriched at centromeres in chicken and human cells. Moreover, immunoprecipitation data revealed that this modification occurs primarily on histone H4 of CENPA-containing nucleosomes after CENPA deposition into centromeres. Lastly, by targeting the H4K20me1 histone demethylase to centromeres, they showed that H4K20me1 is essential for the recruitment of CENPT, which is required for subsequent kinetochore assembly. Whether H4K20me1 has centromeric functions beyond CENPT recruitment remains to be determined.

ORIGINAL RESEARCH PAPER Hori, T. *et al.* Histone H4 Lys 20 monomethylation of CENP-A nucleosome is essential for kinetochore assembly. *Dev. Cell* **29**, 740–749 (2014)