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IN BRIEF

STEM CELLS

Nanog safeguards pluripotency and mediates germline development.

Chambers, I. *et al. Nature* **450**, 1230–1234 (2007)

The transcription factor NANOG is not essential for stem cell self-renewal, report Ian Chambers and colleagues. The presence of NANOG has long been considered a hallmark of pluripotency, and its absence has been regarded as a marker of differentiation. The team showed that NANOG expression fluctuates in mouse embryonic stem (ES) cells. A reduction or lack of NANOG predisposes ES cells to differentiate, but does not commit them to do so. Using genetic deletion and rescue experiments, Chambers *et al.* also showed that cells lacking NANOG can contribute to embryonic development *in vivo*, but fail to form mature germ cells. The authors propose that NANOG regulates the efficiency of self-renewal: the higher the expression level, the lower the likelihood of cell differentiation.

DNA REPLICATION

Regulation of replication fork progression through histone supply and demand.

Groth, A. *et al. Science* **318**, 1928–1931 (2007)

During eukaryotic DNA replication, the progression of the replication fork and the supply and demand of histones must be fine-tuned to ensure that nucleosomes are disrupted ahead of the moving fork and that new nucleosomes, composed of new and recycled histones, are assembled on the daughter DNA strands. What is the mechanism of fine-tuning? Now, Geneviève Almouzni and colleagues show that the histone H3–H4 chaperone anti-silencing function-1 (ASF1) facilitates DNA unwinding in coordination with nucleosome assembly on daughter strands. At the replication fork, ASF1 is connected to the putative replicative helicase MCM2–7 through a bridge of histone H3–H4 proteins, enabling ASF1 to handle parental and new histones. When the equilibrium between histone supply and demand is disrupted (by depletion of ASF1 or overproduction of new histone H3–H4), DNA unwinding is impaired. In the future, it will be important to investigate how histone modifications are inherited from the parent to the daughter strand.

CELL PROLIFERATION

c-IAP1 cooperates with Myc by acting as a ubiquitin ligase for Mad1.

Xu, L. *et al. Mol. Cell* **28**, 914–922 (2007)

The mechanism by which the E3 ubiquitin ligase c-IAP1 (a member of the inhibitor of apoptosis protein (IAP) family) promotes cell proliferation and tumorigenesis is poorly understood. A team led by Junying Yuan now shows that c-IAP1 catalyses the ubiquitylation of MAX-dimerization protein-1 (MAD1), an important cellular antagonist of the tumour-promoting factor MYC. Once ubiquitylated, MAD1 is targeted for degradation by the 26S proteasome pathway and the repression of its target genes is released. Knockdown of *c-IAP1* decreases the rate of cell proliferation and oncogenic phenotypes, whereas knockdown of *MAD1* promotes cell proliferation and transformation. The authors suggest that inhibition of the E3 ligase activity of c-IAP1 and stabilization of the MYC antagonist MAD1 could provide a powerful approach towards cancer treatment.