Nature Reviews Molecular Cell Biology | AOP, published online 18 November 2015; doi:10.1038/nrm4093/nrm4094/nrm4095

IN BRIEF

STEM CELLS

Histone mark of stemness

Asymmetric division of a stem cell generates another self-renewing stem cell and a differentiating daughter cell. How this differential acquisition of cell fates is established and regulated is so far poorly understood. In their previous study, Chen and colleagues reported that upon division of fly male germline stem cells, histone H3 was asymmetrically distributed, with the stem cell retaining the 'old' pool of these histones. Now, the group has demonstrated that this histone asymmetry is established by transient phosphorylation of 'old' histones, occurring upon mitotic entry. They also showed that perturbation of this phosphorylation had severe consequences. including infertility and tumorigenesis. Altogether, the authors revealed that histone H3 phosphorylation enables discrimination between sister chromatids destined for stem cells versus differentiating progeny, and this ensures proper functioning of the stem cell compartment.

ORIGINAL RESEARCH PAPER Xie, J. et al. Histone H3 threonine phosphorylation regulates asymmetric histone inheritance in the Drosophila male germline. Cell 163, 920–933 (2015)

CHROMATIN

R loops regulate chromatin remodelling

Interactions of chromatin-remodelling complexes with RNA are known; however, their significance is poorly understood. Chen et al. studied the chromatin-activating complex Tip60p400 (an acetyltransferase) and found that it was able to bind to nascent transcripts near their initiation start sites, and that this binding was enhanced by the presence of DNA:RNA hybrids (R loops) between the transcript and the DNA template. At the same time, binding of the Polycomb repressive complex 2 (PRC2) was found to be inhibited by the formation of R loops. Thus, the presence of R loops near the 5' ends of transcribed genes affects the recruitment of chromatin remodellers to these sites, thereby shaping chromatin structure and influencing transcription. Moreover, the authors provided evidence that the disruption of R loops perturbed stem cell differentiation, indicating that the absence of R loops can lead to global changes in gene expression.

ORIGINAL RESEARCH PAPER Chen, P. B. et al. R loops regulate promoter-proximal chromatin architecture and cellular differentiation. *Nat. Struct. Mol. Biol.* http://dx.doi.org/10.1038/nsmb.3122 (2015)

UBIQUITYLATION

Maintenance of nutrient homeostasis

Nutrients are the mediators of metabolism, thus their cytoplasmic levels need to be precisely controlled. Previous study by Emr and colleagues revealed that a yeast Lys transporter present on the vacuole (the yeast equivalent of the lysosome) membrane is ubiquitylated and degraded when Lys levels are low. Now, they provide evidence that this mechanism is more broadly utilized and also that vacuolar Zn²⁺ transporters are regulated by ubiquitylation in response to Zn²⁺ levels. In this case, however, a separate protein complex (known as the Dsc complex), together with a distinct, transmembrane ubiquitin ligase Tul1, was primarily responsible. These results demonstrate that cells can react to changes in nutrient availability by specific, ubiquitin-mediated degradation of vacuolar transporters, thus influencing the shuttling of nutrients between the cytoplasm and the lysosomal compartment.

ORIGINAL RESEARCH PAPER Li, M. et al. Membrane-anchored ubiquitin ligase complex is required for the turnover of lysosomal membrane proteins. J. Cell Biol. <u>http://dx.doi.</u> org/10.1083/icb.201505062 (2015)