Nature Reviews Molecular Cell Biology | Published online 21 Jan 2016

IN BRIEF

DNA REPLICATION

Rif1 times replication

Replication of DNA follows a highly reproducible temporal programme, in which some genomic regions are replicated early and others late during S phase. Replication timing has previously been linked to chromatin organization, but the molecular nature of this link has remained elusive. Foti *et al.* reveal that in mammalian cells, Rif1, an evolutionarily conserved regulator of replication timing, abundantly associates with late-replicating genomic regions, and that following Rif1 deletion, the timing of replication is perturbed, as evidenced by random switching from early to late replication and vice versa. It was further found that Rif1 functions in the G1 phase to regulate chromatin interactions between late-replicating genomic regions, so that such interactions are constrained to domains with the same replication timing. Altogether, the authors uncovered Rif1 as an important organizer of genome architecture and suggest that this function of Rif1 underlies its role in regulating replication timing, thus providing a molecular link between chromatin organization and the replication programme in mammalian cells.

ORIGINAL ARTICLE Foti, R *et al.* Nuclear architecture organized by Rif1 underpins the replication-timing program. *Mol. Cell* http://dx.doi.org/10.1016/j.molcel.2015.12.001 (2016)

STEM CELLS

Autophagy rescues muscle ageing

Mammalian muscle regeneration relies on the presence of muscle stem cells, known as satellite cells. The number and functionality of these cells decreases with age, as they progressively enter senescence. Using mice and mouse cells, García-Prat *et al.* show that satellite cell ageing and senescent state are associated with the impairment of autophagy. In line with this, the loss of autophagy was sufficient to deplete the pool of satellite cells and induce their senescence, whereas stimulating autophagy pharmacologically improved the functionality of aged satellite cells. Notably, this has also been confirmed in satellite cells derived from aged humans. The authors further demonstrated that both aged satellite cells and cells with experimental impairment of autophagy showed an increase in reactive oxygen species (ROS), and this was associated with derepression of the expression of the major senescence marker $p16^{INK4A}$. Accordingly, pharmacological inhibition of ROS could reinstate autophagy and prevent senescence. Collectively, this study opens up new possibilities for the treatment of geriatric muscle loss.

ORIGINAL ARTICLE García-Prat, L. *et al.* Autophagy maintains stemness by preventing senescence. *Nature* http://dx.doi.org/10.1038/nature16187 (2016)

GENE EXPRESSION

Nuclear mRNA retention buffers expression noise

Mature mRNAs have been thought to reside predominantly in the cytoplasm, where they serve as templates for protein translation. Bahar Halpern *et al.* analysed cytoplasmic versus nuclear mRNA pools in pancreas and liver cells and found that, in fact, fully mature mRNAs of a significant fraction of genes (including various metabolic genes) are found in higher amounts in the nucleus than in the cytoplasm. This was attributed to low mRNA export rates in comparison to cytoplasmic degradation rates. Computer modelling based on these data indicated that such a nuclear accumulation of mRNAs might dampen gene expression noise, which originates from the pulsatile nature of transcription. Thus, mRNA nuclear retention could confer robustness to the process of gene expression, without the need to alter the steady-state levels of mRNA.

ORIGINAL ARTICLE Bahar Halpern, K. *et al.* Nuclear retention of mRNA in mammalian tissues. *Cell Rep.* **13**, 2653–2662 (2015)