IN BRIEF

CELL SIGNALLING

When signals cross

TGF-β–SMAD signalling regulates growth and epithelial-to-mesenchymal (EMT) transition. Thien *et al.* now show that tuberous sclerosis protein TSC1, which in complex with TSC2 inhibits mTOR-dependent growth and proliferation, interacts with the TGF-β receptor complex and SMAD2/3, and mediates their association, thereby facilitating SMAD2/3 phosphorylation, nuclear translocation and target gene expression. TSC1 is also required for SMAD-dependent growth arrest and EMT induction. Finally, insulin–AKT signalling (which inhibits TSC1–TSC2 and thus activates mTOR signalling) promotes SMAD2/3 phosphorylation in a TSC1-dependent manner, and hyperactive AKT promotes SMAD2/3-mediated growth arrest. These findings suggest that AKT activity is coupled to TGF-β–SMAD signalling, possibly providing a mechanism to control cell growth and proliferation induced by aberrant AKT activity.

ORIGINAL RESEARCH PAPER Thien, A. *et al.* TSC1 activates TGF-β–Smad2/3 signaling in growth arrest and epithelial-to-mesenchymal transition. *Dev. Cell* **32**, 617–630 (2015)

RNA METABOLISM

m^{6}A modulates RNA structure

N^6-methyladenosine (m^{6}A) is an RNA modification that regulates transcript metabolism. Liu *et al.* now report that m^{6}A induces structural remodelling in RNAs and that this affects gene expression. They found that a m^{6}A in a hairpin at the human *MALAT1* non-coding RNA enhanced interactions with the RNA-binding protein hnRNP-C, by promoting a structural switch ('m^{6}A switch') in the hairpin that made the proximal hnRNP-C binding motif single-stranded and accessible. Transcriptome-wide analyses identified multiple m^{6}A residues proximal to hnRNP-C-bound sites, and RNA structure mapping of m^{6}A–hnRNP-C binding sites supported the global occurrence of m^{6}A switching. Moreover, the expression of >800 m^{6}A-switch-containing genes was affected similarly by knocking down *HNRNPC* or m^{6}A methylases, resulting in lower proliferation and aberrant splicing in the vicinity of m^{6}A switches. Thus, m^{6}A-mediated RNA structural remodelling alters RNA–protein interactions and gene expression.

ORIGINAL RESEARCH PAPER Liu, N. *et al.* N^6-methyladenosine-dependent RNA structural switches regulate RNA–protein interactions. *Nature* **518**, 560–564 (2015)

DNA REPLICATION

Double duty for ATR

Mec1, the yeast orthologue of human ATR, is an essential protein kinase that regulates the DNA damage response following replication stress to maintain genome integrity. In this study, de Oliveira *et al.* used a quantitative mass spectrometry approach to study Mec1 signalling *in vivo* and found that it is robustly activated during normal DNA replication. Interestingly, this action is partially uncoupled from Rad53 activity, which is an effector kinase in the DNA replication checkpoint, and the authors showed that Mec1 targets proteins involved in transcription, RNA processing and chromatin remodelling. The authors propose that in addition to regulating the replication stress response, which involves Rad53, Mec1 functions during normal replication to positively regulate ongoing DNA synthesis.

ORIGINAL RESEARCH PAPER de Oliveira, F. M. B. *et al.* Phosphoproteomics reveals distinct modes of Mec1/ATR signaling during DNA replication. *Mol. Cell* http://dx.doi.org/10.1016/j.molcel.2015.01.043 (2015)