IN BRIEF

TRANSCRIPTION

Histone crosstalk between H3S10ph and H4K16ac generates a histone code that mediates transcription elongation

Zippo, A. *et al. Cell* **138**, 1122–1136 (2009)

In this study, Zippo *et al.* reveal a mechanism by which phosphorylation of histone 3 (H3) triggers a cascade that activates stalled RNA polymerase II and leads to transcriptional elongation. They observed that phosphorylation at Ser10 of H3 (pre-acetylated at Lys9; H3K9acS10pho) at the serum-inducible FOS-like antigen 1 (*FOSL1*) enhancer leads to acetylation of H4 at Lys16 (H4K16ac). This modification is mediated by the recruitment of 14-3-3 proteins following phosphorylation of H3K9ac, which in turn recruit the acetyltransferase MOF (also known as MYST1) to H4K16. This histone code (H3K9acS10pho–H4K16ac) is preferentially recognized by bromodomain-containing protein 4 (BRD4), which associates with positive transcription elongation factor b (P-TEFb), ultimately leading to activation of RNA polymerase II and transcription elongation.

MOLECULAR MOTORS

Kinesin-8 motors act cooperatively to mediate length-dependent microtubule depolymerization

Varga, V. *et al. Cell* **138**, 1174–1183 (2009)

Kinesin 8 family members are motor proteins that depolymerize microtubules and control cell length, but the mechanism by which they achieve this was not fully understood. Varga *et al.* observed that the yeast kinesin 8 Kip3 bound to microtubule filaments and moved processively towards the plus ends. The presence of other Kip3 molecules reduced the plus end residence time of individual Kip3 molecules, and this correlated with increased depolymerization by the removal of one tubulin dimer for each dissociated Kip3. Interestingly, Kip3 paused on the microtubule plus ends until another Kip3 molecule attached, leading to dissociation of the original Kip3. They propose that depolymerization is achieved either by removal of a tubulin dimer when Kip3 reaches the plus end or through the dissociation of Kip3–tubulin when a second Kip3 binds the microtubule.

ION TRANSPORTERS

Genome-wide RNAi screen identifies Letm1 as a mitochondrial Ca^{2+}/H^{+} antiporter

Jiang, D., Zhao, L. & Clapham, D.E. *Science* **326**, 144–147 (2009)

A genome-wide RNA interference screen has identified LETM1 (leucine zipper EF hand-containing transmembrane protein 1) as essential for the regulation of mitochondrial Ca^{2+} and H^{+} concentration. Knockdown of the LETM1 *Drosophila melanogaster* homologue, CG4589, markedly reduced mitochondrial Ca^{2+} uptake and H^{+} extrusion at submicromolar cytoplasmic Ca^{2+} concentrations. Furthermore, low pH in the cytoplasm induced Ca^{2+} extrusion and H^{+} influx, but this effect was reduced by CG4589 knockdown. These findings were reflected in mammalian cells: LETM1 knockdown abolished Ca^{2+}–H^{+} exchange, and LETM1 overexpression increased pH-driven Ca^{2+} uptake and H^{+} extrusion. Finally, incorporating LETM1 into liposomes led to the accumulation of high levels of Ca^{2+}, confirming that it is an active transporter. These data suggest that LETM1 is a Ca^{2+}–H^{+} antiporter, which mediates the uptake of Ca^{2+} when mitochondrial Ca^{2+} levels are low or when pH is high, and triggers the exchange of Ca^{2+} for H^{+} during the reverse conditions.