IN BRIEF

CELL SIGNALLING

PARP-1 attenuates Smad-mediated transcription

Lönn, P. *et al. Mol. Cell* **40**, 521–532 (2010)

Transforming growth factor-β (TGFβ) activates receptors to phosphorylate SMAD2 and SMAD3, enabling them to form a complex with SMAD4. This complex coordinates SMAD-activated transcription until transcription is terminated by the dephosphorylation, nuclear export or degradation of SMADs. Lönn *et al.* now show that poly(ADP-ribose) polymerase 1 (PARP1) — which covalently attaches ADP-ribose to substrates during poly(ADP-ribosyl)ation (PARylation) — can also terminate SMAD-activated transcription. PARP1 interacts with SMAD2, SMAD3 and SMAD4 in the nucleus, in response to TGFβ, and induces the PARylation of SMAD3 and SMAD4 *in vitro* and *in vivo*. This reduces the amount of SMAD3–SMAD4 bound to DNA, and attenuates the effects of SMADs on transcription. Depletion of PARP1 enhances the TGFβ-induced transdifferentiation of epithelial cells to mesenchymal cells, suggesting that PARylation can regulate SMADs in physiological settings. Thus, SMAD PARylation can also terminate SMAD-mediated transcription.

POST-TRANSLATIONAL MODIFICATION

β-*N*-acetylglucosamine (O-GlcNAc) is part of the histone code

Sakabe, K., Wang, Z. & Hart, G. W. *Proc. Natl Acad. Sci. USA* **107**, 19915–19920 (2010)

The dynamic post-translational modification of proteins on Ser and Thr by β-*N*-acetylglucosamine (O-GlcNAc) can regulate processes such as transcription and cell signalling. This study identifies histones as novel substrates of O-GlcNAcylation. The authors show that histones are modified by O-GlcNAc *in vitro* and *in vivo*; histone 2A (H2A), H2B and H4 are modified on Thr101, Ser36 and Ser47, respectively. To determine whether histone O-GlcNAcylation is dynamic, and thus might have a biological role, the authors assessed histone O-GlcNAc levels during mitosis and recovery after heat shock — two processes in which O-GlcNAc and histone modifications change dramatically. Histone O-GlcNAcylation decreases during mitosis and increases during the recovery after heat shock. Thus, the authors conclude that "O-GlcNAc cycles dynamically on histones and can be considered part of the histone code."

UBIQUITYLATION

c-IAP1 and UbcH5 promote K11-linked polyubiquitination of RIP1 in TNF signalling

Dynek, J. N. *et al. EMBO J.* 26 Nov 2010 (doi:10.1038/emboj.2010.300)

This study shows that, in addition to their role in degrading cell cycle proteins, atypical Lys11-linked ubiquitin chains might function in cell signalling. Receptor-interacting protein 1 (RIP1), which is involved in the tumour necrosis factor (TNF)-mediated activation of nuclear factor-κB (NF-κB) signalling, was modified with Lys11-linked chains by the E2 enzyme inhibitor of apoptosis 1 (IAP1); this is in addition to the known IAP-mediated ubiquitylation of RIP1 with canonical Lys43- and Lys68-linked chains. Canonical chains on RIP1 are crucial for recruiting NF-κB essential modulator (NEMO) to the TNF receptor complex, which is required for TNF-induced activation of NF-κB signalling. Interestingly, NEMO was found to bind Lys11-linked chains on RIP1 with similar affinity to canonical chains, indicating that Lys11-linked chains might have a role in NEMO recruitment and, consequently, in TNF-mediated signalling.