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IN BRIEF

CYTOSKELETON

Capping protein increases the rate of actin-based motility by promoting filament nucleation by the Arp2/3 complex.

Akin, O. & Mullins, R. D. *Cell* **133**, 841–851 (2008)

Capping protein (CP), which caps barbed ends of actin filaments and terminates actin filament elongation, actually promotes actin-based motility. To investigate this apparent paradox, the authors used an actin-based motility system that was reconstituted using purified components, including CP and the actin-related protein-2/3 (ARP2/3) complex. CP does not increase the rate of motility by increasing the rate of elongation of uncapped actin filaments as previously thought, but instead promotes actin filament nucleation by the ARP2/3 complex. This also implies that the rate of motility can be uncoupled from the rate of actin network assembly.

STEM CELLS

The ground state of embryonic stem cell self-renewal.

Ying, Q.-L. *et al. Nature* **453,** 519–523 (2008)

Embryonic stem cell (ESC) self-renewal is thought to require a number of external stimuli, including cytokines (which activate STAT3) and growth factors. However, Ying *et al.* now demonstrate that both wild-type and *Stat3*$^{-/-}$ mouse ESCs show robust self-renewal in the presence of inhibitors that eliminate differentiation-inducing signalling from mitogen-activated protein kinase and glycogen synthase kinase-3. These findings suggest that external stimuli shield the pluripotent ESC state from differentiation and that ESCs have an intrinsic ability to self-renew, which is also reflected by their tumorigenic potential.

CHROMATIN

Chemically ubiquitylated histone H2B stimulates hDot1L-mediated intranucleosomal methylation.

McGinty. R. K. *et al. Nature* **453**, 812–816 (2008)

Nonprocessive methylation by Dot1 leads to functional redundancy of histone H3K79 methylation states.

Frederiks, F. *et al. Nature Struct. Mol. Biol.* **15**, 550–557 (2008)

Ubiquitylation of histone H2B on K120 in humans (K123 in yeast) has been correlated with enhanced H3K79 methylation by histone methyltransferase DOT1. McGinty *et al.* used a novel chemical-ligation approach to synthesize human H2B ubiquitylated on K120 and subsequently assemble nucleosomes *in vitro* from recombinant histones. DOT1 methylates H3K79 only on ubiquitylated nucleosomes, yet the enzyme binds equally well to non-ubiquitylated nucleosomes. The authors therefore propose that ubiquitylation induces a conformational change that increases the catalytic activity of DOT1. Frederiks *et al.* showed by mutagenesis studies that the putative ubiquitin-binding domain of yeast Dot1 is not required for H3K79 methylation, suggesting that the effect of ubiquitylation is probably indirect. The authors further demonstrated that yeast Dot1 catalyses H3K79 mono-, di- and trimethylation using a distributive mechanism; the enzyme generates monomethylated nucleosomes over a wide chromosomal area before they are dimethylated and eventually trimethylated. This mechanism is consistent with the high frequency of H3K79 methylation across the genome and with its primary role in blocking the binding of the silencing protein Sir3 — irrespective of the specific (mono-, di- or tri-) methylation status.