IN BRIEF

UBIQUITYLATION

K11-linked polyubiquitination in cell cycle control revealed by a K11 linkage-specific antibody

Mutsumoto, M. L. *et al. Mol. Cell* 22 Jul 2010 (10.1016/j.molcel.2010.07.001)

Although the roles of Lys48- and Lys63-linked ubiquitylation are well known, the function of Lys11-linked ubiquitylation is not clear. To investigate this, Mutsumoto *et al.* used a phage display strategy to develop a Lys11-linked polyubiquitin-specific antibody, which they termed 2A3/2E6. The specificity of 2A3/2E6 was confirmed using western blots and immunoprecipitation assays. Previous studies had suggested that Lys11-linked chains are involved in the degradation of anaphase-promoting complex (APC) substrates during cell division. Using 2A3/2E6, the authors find that Lys11-linked chains are upregulated in cells following exit from mitosis (which corresponds to APC substrate degradation) and that inhibition of the E2 enzymes UBCH10 (also known as UBE2C) and UBE2S — which abrogates APC activity — blocks Lys11-linked chain formation. This suggests that APC assembles Lys11-linked chains on its substrates during mitosis by working together with UBCH10 and UBE2S.

CELL CYCLE

An overlapping kinase and phosphatase docking site regulates activity of the retinoblastoma protein

Hirschi, A. *et al. Nature Struct. Mol. Biol.* 8 Aug 2010 (doi:10.1038/nsmb.1868)

Hypophosphorylated retinoblastoma (RB) sequesters transcription factors required for cell cycle progression, which are released when RB is phosphorylated by cyclin-dependent kinases (CDKs) such as CDK2–cyclin A. To further understand RB dephosphorylation, Hirschi *et al.* solved the crystal structure of a carboxy-terminal RB domain (residues 870–882) in complex with the protein phosphatase 1 (PP1; the RB phosphatase) catalytic subunit, PP1c. They identify an RB docking site containing Leu875 and Phe877 that is essential for RB's interaction with PP1c and that overlaps with the docking site for CDK2–cyclin A. PP1c can inhibit CDK2–cyclin A-mediated RB phosphorylation and cell cycle progression independently of its phosphatase activity, which suggests that, in addition to catalysis, these enzymes affect RB phosphorylation by competing for the same docking site.

CELL DIVISION

γ-Tubulin regulates the anaphase-promoting complex/cyclosome during interphase

Nayak, T. *et al. J. Cell. Biol.* **190**, 317–330 (2010)

γ-tubulin is classically known for its key role in microtubule nucleation. Now Nayak *et al.* find that, in the fungus *Aspergillus nidulans*, γ-tubulin has a unique interphase role in inhibiting the anaphase-promoting complex (APC), the ubiquitin ligase that normally targets cell-cycle factors for degradation to allow mitosis. They characterize a cold-sensitive γ-tubulin allele, *mip*AD159, that shows specific defects in synchronous divisions of multinucleated cells. Although microtubule arrays are unaffected in this mutant, time-lapse analysis showed that cyclin B, cyclin-dependent kinase 1 and the phosphatase Cdc14 no longer accumulate in a subset of nuclei, and this prevents subsequent cell cycle re-entry. They go on to show that this occurs because APC is not inactivated during interphase in the mutants, and, importantly, that perturbation of APC function is sufficient to allow some nuclei to resume cell division.

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