ISWI extends the Ran repertoire

The RanGTP gradient surrounding chromosomes drives mitotic spindle assembly by allowing the local release of several factors from the importin–α/β heterodimer, including microtubule regulators. Eric Karsenti and colleagues (*J. Cell Biol.* **187,** 813–829; 2009) now identify the ATPase ISWI as a new RanGTP-dependent microtubule-associated protein (MAP) that is needed after the spindle is established, to maintain spindle microtubule stability in anaphase and allow proper chromosome segregation.

ISWI is better known for its role in chromatin remodelling. It has been reported, however, to bind microtubules, and Karsenti and colleagues identified ISWI as a potential Ran-regulated MAP through sequential affinity purification for proteins containing nuclear localization sequences (NLSs) and showing microtubule association. They then showed that recombinant ISWI can trigger microtubule assembly *in vitro*, independently of its ATPase activity. In *Xenopus* cells and egg extracts, ISWI localized to spindle microtubules during mitosis, and was required for RanGTP-dependent stabilization of spindle microtubules and for anaphase chromosome segregation. This role of ISWI was conserved in *Drosophila* S2 cells. Importantly, the effects of ISWI on anaphase were independent of its effects on chromosomes.

Thus, the RanGTP gradient drives not only the assembly of spindles, but also their subsequent stabilization to ensure chromosome segregation at anaphase. No doubt further insights into the breadth of Ran's remit will be gained by characterization of the other factors isolated by this purification method. AS

TORC2 regulates dendritic branching through Trc

The mammalian target of rapamycin (mTOR) forms two distinct multi-protein signalling complexes: TORC1 and TORC2. TORC1 has a defined role in several neurobiological processes, but the function of TORC2 in neurons is less well understood. Emoto and colleagues now show that TORC2 regulates dendritic arborisation to ensure that dendrites of the same sensory neuron subtype completely and with little overlap cover an entire sensory field — a process known as dendritic tiling (*EMBO J.* **28,** 3879–3892; 2009).

The authors found that loss of Sin1 and Rictor, two components of the TORC2 complex, caused tiling defects of *Drosophila* class IV neurons. Previous studies have shown that the NDR family kinase tricornered (Trc) regulates sensory neuron tiling, and in the present work Trc was detected in complexes with Sin1, Rictor and mTOR. TORC2 kinase activity was essential for Trc phosphorylation at Thr 449 and its subsequent activation, suggesting that TORC2-mediated activation of Trc regulates dendritic tiling. Indeed, a dominant-active Trc mutant rescued the dendritic tiling phenotype elicited by Sin1 and Rictor deficiency.

This study defines a previously unappreciated function of TORC2 complexes in sensory neurons. As these proteins are well conserved in vertebrates, it will be important to determine the extent to which TORC2–Trc signalling regulates dendritic tiling in other species. EJC

Mitotic control of Wnt signalling

The transmembrane Wnt receptors of the low density lipoprotein receptor-related protein (LRP) family are activated via phosphorylation of multiple conserved motifs within their intracellular domain. Niehrs and colleagues now show that the cyclin-dependent kinase CDK14/PFTK1 and its membrane-tethered Cyclin Y, promote Wnt activation in mitosis (*Dev. Cell* **17,** 788–799; 2009).The authors identified *Drosophila* Cdk14, called L63, through a kinase RNAi silencing screen for effectors of LRP6 phosphorylation and Wnt activation. Cyclin Y was previously found to interact with L63/PFTK1in a yeast two-hybrid screen; the authors confirmed this interaction biochemically and showed that purified cyclin Y/PFTK1 mediates LRP6 phosphorylation at PPPS/TP motifs *in vitro* and that co-expression of cyclin Y and PFTK1 in cells enhances LRP6 phosphorylation. Knockdown of cyclin Y reduces endogenous LRP6 phosphorylation in *Drosophila* and mammalian cells as well as in *Xenopus*. In *Xenopus* embryos, Cyclin Y reduction mimics Wnt loss-of-function anteriorization defects. The authors observed that Wnt activation is higher during mitosis and showed that arresting cells in G2/M by silencing CDC25 phosphatases also increases LRP6 phosphorylation and Wnt activation in *Drosophila* cells and *Xenopus* embryos.

Although it's unclear why Wnt signalling should be increased in mitosis, these studies reveal an unexpected layer of control of Wnt activation. NLB

Kinetochore proteomics identifies PP1 regulator

Faithful chromosome segregation depends on the microtubule attachment and biorientation of kinetochores, a process monitored by the spindle checkpoint. Aurora B and protein phosphatase 1 (PP1) have opposing roles in regulating the checkpoint. Biggins and colleagues (*Genes Dev.* **23,** 2887–2899; 2009) have now used a new kinetochore purification method in combination with quantitative proteomics to identify Fin1 as a regulatory subunit of PP1.

The authors enriched for kinetochores by isolating yeast minichromosomes, and then analysed them by quantitative mass spectrometry. Among the identified kinetochore-associated proteins was Fin1, a cell-cycle-regulated protein without known chromosomal function. Known interactions of Fin1 with yeast PP1 (Glc7) and 14-3-3 proteins were confirmed, and the kinetochore association of PP1/Glc7 was found to be partly dependent on Fin1. Biggins and colleagues found that mislocalization of Fin1 to spindle microtubules prevented bipolar spindle formation and caused mislocalization of PP1/Glc7. PP1 was recently found to have a role in spindle checkpoint silencing and here Fin1 mislocalization prematurely inactivated the spindle checkpoint in a manner dependent on the interaction with Glc7. Fin1/Glc7 mislocalization was found to antagonize the function of Aurora B (Ipl1) in genetic experiments, suggesting that the mislocalized complex alters the kinase/phosphatase balance. Additional work is required to identify the substrates of Fin1/Glc7 relevant for checkpoint regulation. CKR

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