

cycle. Xic1 is not thought to be abundant at this stage of development, but levels build up at the mid-blastula transition⁵. So, does the mechanism described by Furstenthal *et al.* only operate at later stages of development, or is there another Xic1-like target for SCF in the early embryo? The latter idea is supported by the observation that the Cdc34 component of SCF is essential for DNA replication and cyclin E/Cdk2 activation in the early embryo⁶. Another problem is whether the known behaviour of the Cdc6 origin protein matches the demands made on it by the Xic1 results. Previous work has shown that Cdc6 is found associated with chromatin at two different stages in the early embryonic cell cycle: one peak in late mitosis and early G1 and another peak in mid-to-late S phase^{13,14}. However, if

recruitment of cyclin E/Cdk2 to Cdc6 is necessary for the initiation of replication, Cdc6 would be expected to be seen on chromatin during late G1 and early S phase. This problem is underlined by the observation that once origin licensing has occurred in the *Xenopus* system, neither ORC nor Cdc6 are subsequently required for the initiation of DNA replication to occur¹³. We can look forward to further work resolving these apparent discrepancies. Whatever the outcome, the recent work of Furstenthal *et al.*¹ provides an important new model to broaden our imagination about how Cip/Kip degradation and CDK activity can potentially be regulated. □

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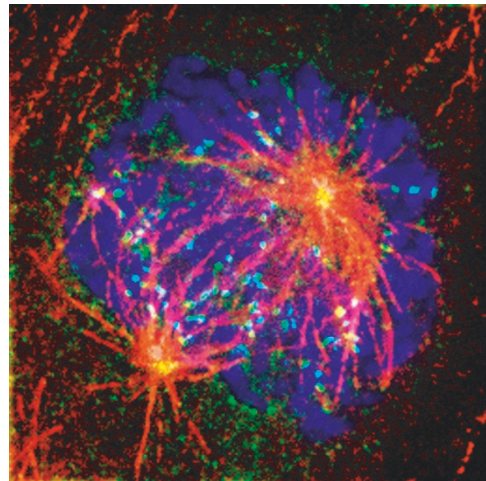
All for one and one for all

How does one become two? And how is two reduced back to a pair of ones? The answers to these questions are especially important during cell division, when the genome and the centrosome must be precisely duplicated to ensure cells progress correctly through mitosis. New work has indicated that the vertebrate homologue of yeast Mps1 acts to control both centrosome duplication and the mitotic checkpoint, which ensures that division can proceed.

Centrosomes act as microtubule-organizing centres and are segregated to daughter cells during cell division. This segregation involves the mitotic spindle, which attaches to the centrosomes by means of the kinetochore. Vertebrate centrosomes are the functional equivalent of the yeast spindle-pole body (SPB) and many components are conserved between the two structures. Mps1 is an essential protein kinase that regulates SPB duplication and the spindle assembly checkpoint in the yeast *Saccharomyces cerevisiae*. The spindle checkpoint determines whether or not all kinetochores are attached to the spindle, and halts cell division if this is not the case. Like SPBs, the checkpoint pathway has components conserved between yeast and vertebrates.

In 1992 Douville and colleagues identified Esk, a protein which later work indicated could be a mouse Mps1 homologue. However, it was unclear whether this was the only mouse homologue, and if it was whether or not it was a functional homologue. Fisk and Winey (*Cell*, **106**, 95–104; 2001) now show that Esk is indeed a functional homologue of Mps1 and have renamed the gene as *mMps1*. mMps1 localizes to centrosomes and kinetochores (see figure; GFP-mMps1 (green), α -tubulin (red) and DNA (blue)), and causes centrosome reduplication when overexpressed in cells arrested in S phase.

In a comparable study, Abrieu *et al.* (*Cell*, **106**, 83–93; 2001) identified the *Xenopus* Mps1 homologue, which is also a functional kinase localized to kinetochores. *Xenopus* extracts that are depleted of xMps1 do not activate the normal spindle checkpoint, a process that can be rescued with the addition of Mad2 (a downstream component of the checkpoint machinery). Extracts depleted of xMps1 have no Mad1, Mad2 or CENP-E (a microtubule motor protein of the kinesin family) localized to the kinetochores. Loss of xMps1 in extracts where



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the spindle checkpoint has deliberately been activated also prevents kinetochore association of Mad2 and CENP-E.

It seems, therefore, that the vertebrate homologues of Mps1 have a similar role to their yeast counterpart. They are present to ensure the centrosome is duplicated, in a process that also involves the cyclin-dependent kinase Cdk2, and they are essential for activation of the mitotic checkpoint in a process that places Mps1 upstream of Mad1/Mad2. Even though Mps1 is a functional kinase, localization of the protein to the centrosome or the kinetochore does not require any kinase activity, but the kinase activity is required for centrosome duplication and the spindle checkpoint. It will be very interesting to determine the precise regulation of Mps1 in these processes and the consequences for downstream events.

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