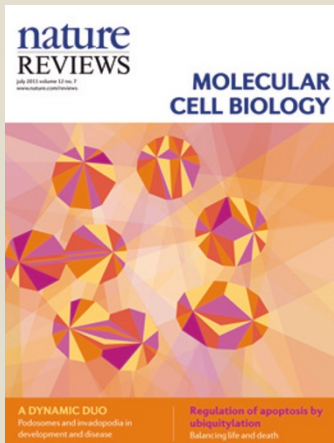




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► **COVER:** 'Cubist cell cycle' by Vicky Summersby, inspired by the Review on p427.



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To ensure viability of itself and/or of the organism, each cell needs to accurately distribute its genomic content to its two daughter cells during cell division. This is facilitated by kinetochores — proteinaceous structures assembled on centromeric chromatin that bind spindle microtubules to mediate sister chromatid segregation. On page 407 of this issue, Fabienne Lampert and Stefan Westermann highlight recent progress in our understanding of the structure and organization of kinetochores, with particular emphasis on the NDC80 complex, the interactions of which with microtubules have emerged as essential for mediating chromosome movement.

The correct attachment of kinetochores to spindle microtubules 'satisfies' the spindle assembly checkpoint (SAC), allowing the cell cycle to progress. One of the targets of SAC proteins is the APC/C (anaphase-promoting complex, also known as the cyclosome). This E3 ubiquitin ligase imposes temporal order to the cell cycle by recognizing cell cycle regulators at specific time points and targeting them for degradation. On page 427, Jonathon Pines discusses how the APC/C recognizes different substrates at distinct time points and how it is itself regulated by its co-activators, CDC20 and CDC20 homologue 1 (CDH1), and the SAC.

In addition to its roles in cell cycle regulation, ubiquitin signalling affects a broad range of cellular processes. As part of our series on post-translational modifications, Domagoj Vucic, Vishva Dixit and Ingrid Wertz (page 439) review how ubiquitin signalling regulates apoptosis. Several E3 ubiquitin ligases and deubiquitylating enzymes (DUBs) have important roles in this process by affecting the stability of key apoptosis proteins. These ligases and DUBs are frequently dysregulated in diseases such as cancer and could be targeted for therapeutic intervention.

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