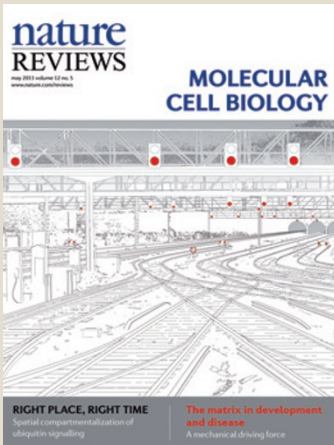




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► **COVER:** 'Knowing when to stop' by Vicky Summersby, inspired by the Review on p283.



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Cellular processes must be correctly organized in space and time to ensure the health of a cell. Perhaps the archetypal example of such a process is the cell cycle, which requires correct assembly of cellular components at defined time points. On page 320, Verdaasdonk and Bloom describe the crucial role that local chromatin at the centromere has in the organization of the kinetochore and, ultimately, on proper chromosome segregation and cell division.

One way to ensure correct spatial and temporal organization is through post-translational modifications such as ubiquitylation. As part of our 10-year anniversary series (<http://www.nature.com/nrm/series/10-anniversary/index.html>), Dikic and colleagues (page 295) discuss advances in our understanding of ubiquitin networks, and describe how components of the ubiquitin machinery depend on strict spatiotemporal control to regulate multiple biological processes.

Underpinning our current understanding of cellular organization is the idea that a protein can be made in one cellular compartment and targeted to another. However, this idea only properly developed in the 1970s, when Blobel and Sabatini formulated the 'signal hypothesis', which stated that a peptide sequence at the amino terminus of the nascent polypeptide targets it to the endoplasmic reticulum. The discoveries that led up to this influential hypothesis, as well as later findings that developed it to include 'topogenic signals', are described by Matlin in a Timeline article on page 333.

Also in this issue, Moore and colleagues (page 283) discuss the mechanisms of transcriptional termination, and describe new insights into the specificity of RNA polymerase II termination at different classes of RNAs, and Weaver and colleagues (page 308) explain how the cell can sense and interpret mechanical signals to regulate cell behaviour.

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