# HIGHLIGHTS



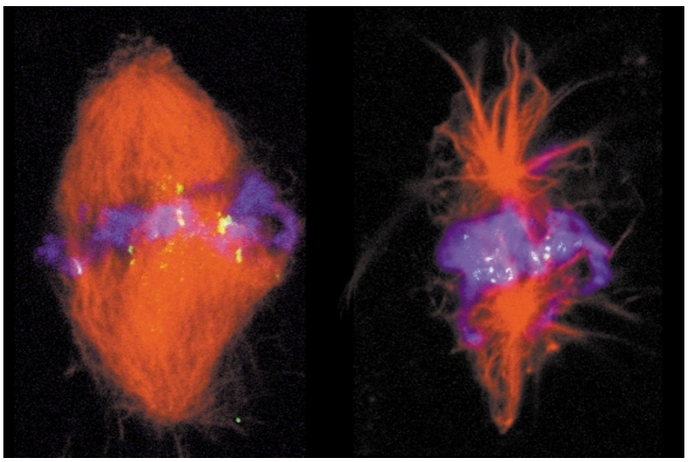
CELL DIVISION

## Location, location, location

About two years ago, the small GTPase Ran, well known as the regulator of nuclear transport, surprised many scientists by also taking centre stage in mitotic spindle assembly. Several groups have now independently discovered part of the molecular mechanism through which Ran might regulate this process.

Two papers in *Nature Cell Biology* discuss which particular aspect of spindle assembly is controlled by Ran. Carazo-Salas and colleagues report that Ran regulates the frequency of transition from shrinkage to growth of microtubules, as well as the capacity of centrosomes to nucleate microtubules. Wilde and co-workers confirm the first finding, and add that Ran might also be able to regulate the balance of microtubule-motor activities, in particular that of Eg5.

Two papers in *Cell* and one in *Science* go into more mechanistic detail, showing that Ran–GTP acts by releasing some microtubule-associated proteins (MAPs) from sequestration by importins (cargo receptors involved in nuclear transport), thereby allowing MAPs to carry out their functions in spindle assembly. Although the three groups attacked the problem from different angles, their conclusions are remarkably similar. The Karsenti/Mattaj task force find that importin-β sequesters the MAP TPX2, which they propose to be the Ran effector for spindle assembly. The Zheng and the Heald/Weis groups, on the other hand, show that importin-β sequesters the MAP NuMA, but both agree that importins probably sequester more than one factor involved in spindle assembly. The Karsenti/Mattaj and the Heald/Weis groups show that importin-β binds the respective MAPs indirectly, through importin-α, but the Zheng and the Heald/Weis groups suggest that importin-β might also be able to interact directly with some MAPs.



Mitotic spindle in the presence (left) and absence (right) of functional Ran–GTP.
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The emerging model is that Ran–GTP probably acts just as it does during nuclear transport, by promoting the release of proteins from importins at a specific cellular location. During interphase, Ran–GTP dissociates cargo from importins only in the nucleus, conferring directionality to nuclear transport. In mitosis, Ran–GTP is concentrated around chromatin owing to the tight association of RCC1 (its nucleotide exchange factor) to chromatin. So Ran–GTP only dissociates spindle assembly effectors from importins in a small perimeter around chromatin, thereby ensuring that they build the spindle in the right place.

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### References and links

**ORIGINAL RESEARCH PAPERS** Carazo-Salas, R. E. *et al.* Ran–GTP coordinates regulation of microtubule nucleation and dynamics during mitotic-spindle assembly. *Nature Cell Biol.* **3**, 228–234 (2001) | Wilde, A. *et al.* Ran stimulates spindle assembly by altering microtubule dynamics and the balance of motor activities. *Nature Cell Biol.* **3**, 221–227 (2001) | Gruss, O. J. *et al*. Ran induces spindle assembly by reversing the inhibitory effect of importin α on TPX2 activity. *Cell* **104**, 83–93 (2001) | Nachury, M. V. *et al*. Importin β is a mitotic target of the small GTPase Ran in spindle assembly. *Cell* **104**, 95–106 (2001) | Wiese, C. *et al*. Role of importin-β in coupling Ran to downstream targets in microtubule assembly. *Science* **291**, 653–656 (2001)
**FURTHER READING** Dasso, M. Running on Ran: nuclear transport and the mitotic spindle. *Cell* **104**, 321–324 (2001)