significance of the new work[7] is in shifting our attention first to a docking step on the pore fibrils, which does not require importin β or other factors, and then to an unexpected role for nuclear histone H1 and importin β–importin 7 in capsid disassembly and DNA entry. Discrepancies between these studies[7,12] could be explained if the requirement for importin β in the permeabilized-cell study[12] actually reflects a requirement for importin β downstream of the docking step, or if it reflects differences between the *in vivo*[7] and permeabilized cell[12] systems. Future work is likely to reveal requirements for additional cytosolic factors, as well as additional steps that can be experimentally inhibited.

The use of importins in capsid disassembly[7] has certain parallels with the recent exciting discovery that importins, in addition to acting as import receptors, can act as cellular switches that spatially control microtubule and spindle assembly (reviewed in refs 5, 13–14). In mitotic cells, for example, free importins α and β bind to and inhibit proteins required for spindle assembly. This inhibition of spindle assembly is, however, turned off in the vicinity of the mitotic chromosomes. There, Ran–GTP (produced by chromosomally bound Ran guanine-nucleotide exchange factor) locally disrupts the inhibitory complexes and allows spindle assembly. Thus, the adenovirus study of Greber and colleagues[7] is impressive not only for revealing a distinct viral entry pathway, but also as a novel example of how the highly abundant importins (~2 μM in *Xenopus* eggs) can be used to control different cellular activities. □

Amnon Harel and Douglass J. Forbes are in the Section of Cell and Developmental Biology, Division of Biology 0347, University of California, San Diego, La Jolla, California 92093-0347, USA
e-mail: dforbes@ucsd.edu

1. Whittaker, G. R., Kann, M. & Helenius, A. *Annu. Rev. Cell Dev. Biol.* **16,** 627–651 (2000).
2. Ribbeck, K. & Gorlich, D. *EMBO J.* **20,** 1320–1330 (2001).
3. Jenkins, Y., McEntee, M., Weis, K. & Greene, W. C. *J. Cell Biol.* **143,** 875–885 (1998).
4. Vodicka, M. A., Koepp, D. M., Silver, P. A. & Emerman, M. *Genes Dev.* **12,** 175–185 (1998).
5. Vasu, S. K. & Forbes, D. J. *Curr. Opin. Cell Biol.* **13,** 363–375 (2001).
6. Greber, U. F., Suomalainen, M., Stidwill, R. P., Boucke, K., Ebersold, M. W. & Helenius, A. *EMBO J.* **16,** 5998–6007 (1997).
7. Trotman, L. C., Mosberger, N., Fornerod, M., Stidwill, R. P. & Greber, U. F. *Nature Cell Biol.*, **3,** 1092-1100.
8. Ben-Efraim, I. & Gerace, L. *J. Cell Biol.* **152,** 411–417 (2001).
9. Matsubayashi, Y., Fukuda, M. & Nishida, E. *J. Biol. Chem.* **276,** 41755–41760 (2001).
10. Jakel, S. *et al. EMBO J.* **18,** 2411–2423 (1999).
11. Salman, H., Zbaida, D., Rabin, Y., Chatenay, D. & Elbaum, M. *Proc. Natl Acad. Sci. USA* **98,** 7247–7252 (2001).
12. Saphire, A. C., Guan, T., Schirmer, E. C., Nemerow, G. R. & Gerace, L. *J. Biol. Chem.* **275,** 4298–4304 (2000).
13. Dasso, M. *Cell* **104,** 321–324 (2001).
14. Kahana, J. A. & Cleveland, D. W. *Science* **291,** 1718–1719 (2001).

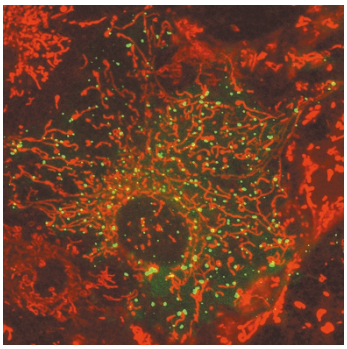
Mitochondrial fission in life and death

Mitochondria must replicate during cell division to ensure that daughter cells inherit roughly as many mitochondria as their mother cell. This is achieved through fission prior to cell division and subsequent mitochondrial enlargement in the daughter cells. Intriguingly, a similar mitochondrial fission phenomenon is observed in apoptotic cell death, where apoptosis is accompanied by fragmentation of subcellular organelles, including mitochondria, and eventually of the cell itself. Now Youle and colleagues shed light on the mechanism of mitochondrial fission in apoptosis, and find that it is indeed similar to the process of mitochondrial division (*Dev. Cell* **1**, 515–525 (2001)). They find that the dynamin-related protein Drp1 translocates from the cytosol to mitochondria after induction of apoptosis (see figure, Drp1 is stained in green and mitochondria in red).

Dynamin proteins function in membrane constriction by virtue of their mechanochemical properties. When Youle and colleagues overexpressed a dominant-negative mutant form of Drp1 (DN Drp1), it inhibited mitochondrial fragmentation in apoptotic cells. Interestingly, a protein homologous to Drp1, Dnm1, has been implicated in mitochondrial division in yeast.

In contrast to DN Drp1, overexpression of Bax, a protein that acts to induce apoptosis in a mitochondria-dependent manner, increases mitochondrial fragmentation. The BH3 domain of Bax is required for this fragmentation; BH3 is also essential for the pro-apoptotic activity of Bax. The Youle laboratory found that DN Drp1 blocked Bax-induced mitochondrial fission; and in cells expressing both Bax and DN Drp1, mitochondria seem to be swollen. So it is possible that Drp1 relocalization from the cytosol to mitochondria in apoptotic cells could limit the extent of mitochondrial swelling.

DN Drp1 also prevents the loss of mitochondrial membrane potential and release of cytochrome *c* from the mitochondrial intermembrane space, and indeed cell death itself (as assessed by DNA fragmentation, one of the hallmarks of apoptosis). Mitochondrial swelling, loss of mitochondrial membrane potential, and Bax-like proteins have all been proposed to regulate the release of cytochrome *c* and other death-promoting molecules from mitochondria in apoptotic cells, so it seems that the function of Drp1 could be central to the regulation of cell death. Youle and colleagues even speculate that Drp1 could mediate the formation of vesicles at the outer mitochondrial membrane, which could contribute to the release of pro-apoptotic proteins from the mitochondrial intermembrane space to the cytosol after induction of apoptosis, but that remains to be tested. It also remains to be confirmed whether the function of Drp1 is due to its mechanochemical properties.



Richard Youle

VALERIE FERRIER