IN THE NEWS

What next for students?
"British scientists say they may have invented themselves out of a job" was the opening to a story on *CNN.com* (15 January 2004), reporting on a paper published in *Nature*. Other media outlets took up a similar refrain in response to the news that Stephen Oliver and colleagues have developed a 'robot scientist', which "plans its experiments, reaches for the pipette, dispenses and mixes liquids and observes the results" (*The Guardian*, 15 January 2004).

The team had set their robot the task of determining the genes involved in a well-known metabolic pathway in budding yeast, by observing the growth of knockout strains on different media. The authors compared the results with those obtained by graduate students, and found that, "Not only were the results just as accurate, but the system did not need to perform as many experiments because its hypothesis generator found solutions more quickly, so its costs were about two-thirds lower" (*NewScientist.com*, 14 January 2004).

There was plenty of philosophical musing. "Some scientists questioned whether the system … deserved the title of scientist", said *The Boston Globe* (15 January 2004). They also quoted Stuart Schreiber: "For human scientists, some of the most interesting discoveries happen when researchers notice something they weren't looking for and suddenly change course".

The authors suggest, however, that the robot could improve things for graduate students. "It's a simple area of science. In that restricted world the computers compete well with scientists", co-author Ross King told *BBC News Online* (14 January 2004). "I think this frees students up to do more interesting work", King added (*The Globe and Mail*, 17 January 2004).

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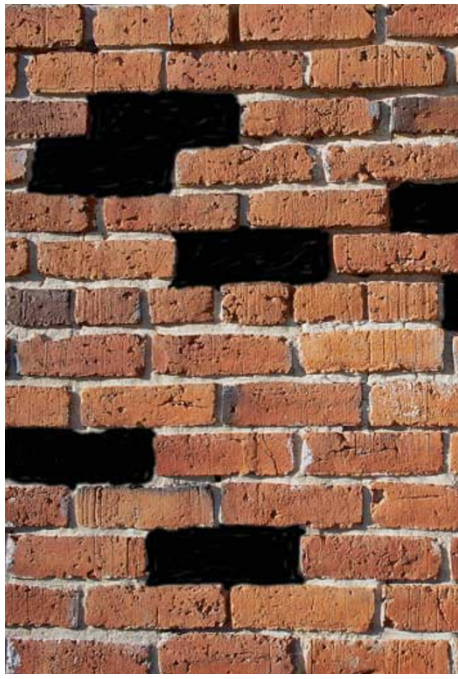
NUCLEAR TRANSPORT

The reductionist pore



'Better safe than sorry' is a recurring theme in cell biology — to ensure that cells are equipped to drive critical processes efficiently, more than one enzyme is recruited for the job, or more than one transport mechanism is in place. The nuclear pore complex turns out to be no exception. In the March issue of *Nature Cell Biology*, Susan Wente and colleagues define the minimal requirements for a functioning pore and, strikingly, they find that a large number of its key domains can be deleted with little apparent consequence.

Transport of cargo between the nucleus and the cytoplasm occurs through the nuclear pore complex and is mediated by transport receptors that interact with particular domains within the pore's nucleoporin protein scaffold. More than a hundred of these domains, which consist of FG (phenylalanine-glycine) repeats and polar spacer sequences, populate the pore and are thought to provide potential binding sites to help transport receptors on their way through.

Wente and colleagues set out to ask which FG domains are important for transport and to what extent there is redundancy in the system. In this way, they hoped to shed light on the mechanisms that direct nuclear transport. The approach they took was to systematically delete particular FG domains from nucleoporin genes in the budding yeast *Saccharomyces cerevisiae*. They initially generated single deletions, and then combined these in all possible double, triple and multiple mutant combinations until lethality or transport defects were observed.

Several surprising results emerge. First, all of the nucleoporin FG domains that localize to only one side of the pore can be removed with little consequence for nuclear transport. Second, more than half of the total number of FG domains can be deleted without affecting pore function, and there seems to be no direct correlation between the number of deleted FG domains and the severity of the phenotypes observed. Rather, specific combinations of FG repeats seem to provide key determinants for transport.

CELLULAR MICROBIOLOGY

Two types of tail

Cossart and colleagues, reporting in *Nature*, now describe a bacterial protein that is a unique activator of the Arp2/3 complex. RickA of *Rickettsia conorii* can induce Arp2/3 to polymerize actin at the bacterial cell surface, which results in pathogen movement. However, because the actin tail that is produced is different from those made by other bacteria, such as *Listeria* sp, and actually resembles the actin filaments that are found in filopodia, this work could help us to further understand how these long, thin cellular protrusions are formed.

Arp2/3 nucleates and polymerizes actin filaments to form the networks of short and highly branched filaments that are found both in lamellipodia (flattened, sheet-like structures that project from cells) and in the actin tails of bacteria such as *Listeria* sp. However, it is less clear how the long and unbranched filaments that are generated during filopodia formation are made. In this study, Cossart and co-workers focused their attention on *R. conorii*, which produces an actin tail that is reminiscent of the actin filaments of filopodia.

They searched the genome sequence of *R. conorii* and identified a protein — RickA — that is structurally similar to known Arp2/3-activating proteins. Although RickA lacks a membrane anchor, the authors found that it is highly expressed on the bacterial cell surface. In addition, they showed that, although RickA alone cannot polymerize actin *in vitro*, it can activate the Arp2/3 complex to do so.

But does Arp2/3 function in *R. conorii* actin polymerization *in vivo*? Cossart and colleagues showed that sequestering the Arp2/3 complex *in vivo* greatly reduces the recruitment of actin by *R. conorii*. Furthermore, they showed that Arp2/3 is abundantly localized to the *R. conorii* cell surface, but that it is apparently absent from the tail. This Arp2/3 localization differs to that seen for *Listeria* sp, which indicates that these pathogenic bacteria have evolved to manipulate the Arp2/3 complex of their hosts to produce different effects.

In the final part of this study, Cossart and co-workers showed that expressing RickA at the plasma membrane of mammalian cells results in the formation of filopodia-like structures. Further studies of RickA-induced actin polymerization might, therefore, help to clarify how filopodia are formed.

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References and links

ORIGINAL RESEARCH PAPER Gouin, E. *et al.* The RickA protein of *Rickettsia conorii* activates the Arp2/3 complex. *Nature* **427**, 457–461 (2004)
FURTHER READING Frischknecht, F. & Way, M. Surfing pathogens and the lessons learned for actin polymerization. *Trends Cell Biol.* **11**, 30–38 (2001)