CELL MOTILITY

Networks from mutants

Dennis Bray and Juri Vasiliev

THOSE of us who earn a living from the cytoskeleton feel a little threatened. We had always asserted (rather too dogmatically, as it now seems) that actin and actin-binding proteins were the motor by which animal cells crawl from one location to another. And yet André *et al.* now describe in the current issue of the *Journal of Cell Biology*[1] the third mutant strain of *Dictyostelium* which lacks a major actin-binding protein and nevertheless shows normal motility and chemotaxis. The ground begins to shake beneath our feet! Could it be that, like those primitive people who believed that when the wind blows it is because the trees are stirring the air, we have the wrong end of the stick? Is it possible that cell locomotion is driven not by the cytoskeleton but by lipids, or something equally improbable?

The amoeboid form of *Dictyostelium discoideum* crawls in a very similar fashion to other animal cells and also shows a chemotactic response to distant sources of cyclic AMP. Unlike neutrophils and fibroblasts, however, these cells are haploid and therefore particularly suitable for genetic manipulation. Gerisch and his colleagues[2] at the Max Planck Institute in Martinsried in 1986 took advantage of this combination of virtues by isolating a mutant deficient in the actin crosslinking protein α-actinin. The group's more recent study[3] of this mutant, using four monoclonal antibodies, confirms that α-actinin is almost completely absent; nevertheless, the mutant's movements, chemotaxis and ability to 'cap' and 'patch' surface proteins are unimpaired.

An indication that this might be a general phenomenon came in two papers[4,5] published in the same issue of *Science* last year describing life without myosin. As related in a News and Views article at the time[6], strains of *D. discoideum* were generated that lacked normal high-molecular-weight myosin (myosin-2). In one case, expression of the myosin gene was severely depressed through the introduction of antisense RNA; in the other, homologous recombination was used to substitute a myosin lacking most of its tail for the normal myosin. It is something of a relief to relate that these myosin-less cells are not entirely normal: they have an altered morphology and are severely defective in their ability to carry out cytokinesis. But they can crawl and they can direct their locomotion up a gradient of cyclic AMP.

The point has now been driven home in the new work of Gerisch's group[1], in which André *et al.* describe a mutant strain of *Dictyostelium* lacking severin — an actin-filament fragmenting protein related to gelsolin and villin. The cells grow at the usual rate, forming normal fruiting bodies and viable spores. By many criteria, such as speed of movement, rate of turning and precision of chemotactic orientation, their motility is unimpaired.

A literal interpretation of these findings, based on conventional genetic arguments, would be that α-actinin, myosin and severin are not involved in cell locomotion. But this conclusion is at variance with much circumstantial evidence linking actin-based systems to the generation of motile structures in the cell. An alternative explanation is that these proteins could be involved in cell locomotion but their function could be duplicated or 'guaranteed' (as Schleicher *et al.* put it[3]) by more than a single protein. There is indeed substantial overlap in the activity of actin-binding proteins *in vitro* and more than one way to crosslink, fragment or even to move actin filaments. But why should there be such extensive 'fail-safe' guarantees for cell locomotion when other, more essential cellular functions such as DNA synthesis are not thus underwritten?

The explanation that we favour — which, if correct, has implications that extend beyond the area of cell motility — is that actin-based motility has some of the properties of the parallel distributed processes used in artificial intelligence (see Anderson's News and Views article[7]).

That is, at every stage between the detection of environmental cues by receptors on the cell surface to the generation of cell movement, there is extensive overlapping redundancy. Cell surface receptors change the levels of second messengers such as calcium ions and phosphatidyl inositol bisphosphate; second messengers influence the activity of actin-binding proteins, either directly or through protein kinases. At each successive stage, the 'signal' generated by a specific agonist becomes distributed more widely; it spreads down parallel pathways and converges with various combinations of signals from other receptors on to different target proteins.

The ten or more actin-binding proteins in a cell would form one layer of this net-

Paternity of dunnocks by DNA fingerprinting

W. B. Carr

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THE hedge sparrow or dunnock (*Prunella modularis*) is a small, insect-feeding passerine bird belonging to the accentor family. It is common throughout the British Isles, inhabiting bushy places where nesting sites are plentiful and is a common sight in suburban parks and gardens. The species is unusual in having a variable mating system, a fact which has attracted considerable attention from behavioural ecologists. Mating may involve monogamy (one male, one female), polygyny (a male with two females), co-operative polyandry, where two males mate with a single female and may help to feed her young, and polygynandry, where two males share two or more females. On page 249 of this issue, T. Burke and collaborators report the successful application of the technique of DNA fingerprinting to link observations of mating behaviour and parental care of dunnocks in a well-studied population in a botanical garden in Cambridge, UK with precise measurements of reproductive success. They conclude that males do not discriminate between their own young and those of another male in multiply-sired broods, but feed offspring in relation to their access to the female during the mating period, which is a good predictor of paternity. Rory Howlett