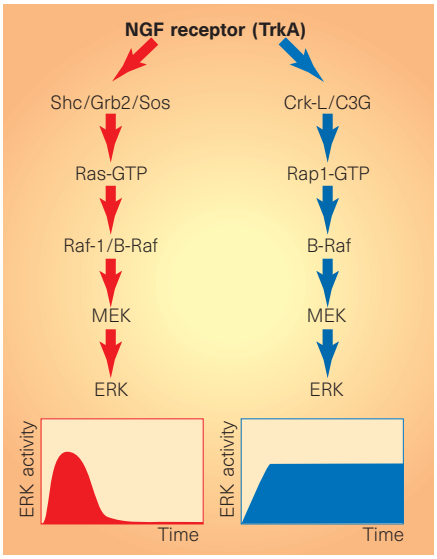

Figure 1 **Different pathways activated by nerve growth factor (NGF). York *et al.*[1] have found that sustained activation of extracellular-signal-regulated kinases (ERKs) occurs through a hitherto unknown pathway that involves the small GTPase Rap1 — all pathways were previously thought to act through another small GTPase, Ras. In the Ras pathway, Shc and Grb2 are the adaptor proteins that link Sos — the Ras guanine-nucleotide-exchange factor — to the NGF receptor (TrkA). In the Rap1 pathway, however, the Crk-l protein links C3G, the Rap guanine-nucleotide-exchange factor, to TrkA.**

phosphorylates Mek1 or Mek2 (Fig. 1). In mammalian cells, the Meks can also be activated by, among other proteins, A-Raf and B-Raf. York *et al.*[1] present a new twist to the pathway that leads to activation of ERK because they argue that, after NGF stimulation, the early phase of ERK activation is mediated by Ras, but sustained activation of the pathway is due to activation of Rap1. Furthermore, Rap1 is not acting through Raf-1, but through B-Raf. To study the relationship between the initial and sustained phases of activation, the authors expressed a mutant form of Ras that blocks activation of the endogenous protein, and a Rap1 mutant that may act in the same way. They found that the Ras- and Rap-dependent phases of ERK activation seem to be independent.

The idea that Rap1 may be responsible for the sustained activation of ERKs is intriguing. Relatively little has been done to examine the signalling pathways that are responsible for sustained activation of these kinases. Moreover, the compelling evidence that Ras must be activated for the initial phase of ERK activation, together with the fact that, in PC12 cells, NGF produces sustained activation of Ras–GTP whereas EGF produces transient activation of Ras and ERKs[7], may have led to the false assumption that everything is due to Ras. It would now be nice to know whether EGF also gives a transient activation of Rap1.

Rap1 was discovered through an expression cloning strategy for suppressors of Ras transformation. The mechanism by which Rap1 suppresses oncogenic Ras-driven transformation is still a puzzle — Rap1 could sequester effectors away from Ras, or, alternatively, Rap1 may activate a signalling pathway that suppresses the action of Ras. Rap1 is about 50% similar to Ras in primary sequence and, although it binds Raf-1 with a lower affinity than does Ras[8], interactions between B-Raf and Rap1 have not been characterized.

A number of issues need to be addressed from the work of York *et al.*[1]. The sustained activation of ERK seems to result from activation of Rap1, yet expression of a mutant Rap that blocks sustained ERK activation does not block outgrowth of PC12 neurites. It is clear from previous studies[5], however, that inhibition of ERK activation does block NGF-stimulated differentiation of PC12. Further inhibition of Ras function by microinjecting a Ras-neutralizing antibody blocks differentiation of PC12 cells[2] — clearly indicating a role for Ras-dependent signalling.

In other cell systems, Rap1-mediated signalling seems to impair activation of ERKs[9,10], and it will be interesting to find out whether the responses of different cells to Rap1 signalling depend on the isoforms of B-Raf that they express. B-Raf was originally thought to be expressed only in neuronal tissue, but different isoforms are now known to be expressed in many cell types[11], and B-Raf is essential for embryonic development of blood vessels[12]. To complicate interpretation further, at least one isoform of B-Raf can be activated by Ras[13]. But the work of York *et al.* points to new directions for the analysis of Rap1 function, and this, together with the simpler ways[14] for measuring activation of Rap1, suggests that there will be increased interest in these enigmatic proteins. □

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Daedalus

The eye of mercury

A big telescope mirror never gives a perfect image. Atmospheric fluctuations, and the distortion of the mirror under its own weight as the telescope tracks its stellar target, degrade its focusing. The answer is adaptive optics. An array of fast-acting piezoelectric elements on the back of the mirror can distort it in just the right way to correct the aberrations as they arise. A computer control system, looking at a specific star in the field or a laser beam traversing the optics, drives the elements so as to tweak the mirror continuously into optimum adjustment.

Daedalus is now taking this idea to extremes. A really adaptive mirror would need no optical figuring at all; any random piece of silvered glass could in principle be bent into the perfect shape for the task in hand. Sadly, glass or ceramic cannot be bent very far. But a liquid mirror could be made into any shape whatever, by imposing the right forces on it.

The obvious liquid is mercury. Imagine, says Daedalus, a large dish of mercury with an array of electrodes distributed through it, and a set of coils by which a complex magnetic field can be imposed on it. A current in a magnetic field produces a force, which will appear as hydrostatic pressure in the mercury. So instead of having a flat surface imposed purely by gravity, it will develop some subtle shape determined by the interaction of the field with the currents. Great mathematical cunning would be needed to deform the mercury into a focusing surface, and even greater cunning to superimpose whatever second-order deviations were needed to cancel the effects of atmospheric 'twinkling'; but the thing seems feasible. Such a telescope would need no tilting or steering. Sufficiently strong currents could tilt and shape its mercury surface into just the right form to focus light from any given target onto a fixed CCD retina; and could change its form continuously so as to track that target across the sky.

But this is an ultimate design. Daedalus's pilot scheme lets the mirror gaze vertically upwards, and steers its scrutiny around the sky by means of a big plane mirror or prism above it. These, of course, can be very cheap and crude; the infinitely adaptive optics will correct for their imperfections. Only the chromatic aberration of the prism will defeat it — but even this will be useful. Every object seen by the telescope will be drawn out into a perfect line spectrum.

David Jones

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