second messengers cyclic AMP, calcium and diacylglycerol (Fig. 1). These second messengers then activate GEFs for Rap1 directly[4,5]. For instance, cAMP directly regulates a protein called Epac, ('exchange protein activated by cAMP'), a result that is interesting in itself because it represents a protein-kinase-A-independent cAMP pathway[5].

Mochizuki *et al.*[1] and Jordan *et al.*[2] now show that the α-subunits of two other G proteins — $G_i$ and $G_o$, respectively — can form a complex with Rap1GAP. The authors detected this interaction by yeast two-hybrid analysis and by co-immunoprecipitation. There are, however, striking differences between the two papers. For example, Mochizuki *et al.* show that only an amino-terminally extended isoform of Rap1GAP, called Rap1GAPII, can interact with the active, GTP-bound form of $G\alpha_i$. The interaction leads to a decrease in the GTP-bound form of Rap1, indicating that the Rap1GAP is activated by the interaction with $G\alpha_i$. Jordan and colleagues, on the other hand, find that inactive $G\alpha_o$ interacts with chicken Rap1GAP, resulting in the activation of Rap1. This implies that $G\alpha_i$ and $G\alpha_o$ use different molecular mechanisms to modulate GAP activity.

Mochizuki *et al.* further show that receptor-induced activation of $G\alpha_i$ results in translocation of Rap1GAPII to the plasma membrane, and inactivation of Rap1. They also find that a mutant Rap1GAPII inhibits the receptor-induced inactivation of Rap1. Ever since GAPs were discovered, researchers have wondered whether, and how, they are regulated. Last year, Jiang *et al.*[6] reported that stimulation of the Gα12 subunit via the thromboxane $A_2$ receptor leads to direct binding and activation of $GAP1^m$ and inactivation of Ras. Mochizuki *et al.* now propose a similar mechanism for Rap1. Indeed, inactivation of GTPases by GAPs directly bound to the α-subunit of heterotrimeric G proteins may turn out to be a general phenomenon.

A frequently measured downstream effect of Rap1 is inactivation of ERK. This kinase is activated by many extracellular stimuli via the small GTPase Ras and the protein kinases Raf and MEK. Mochizuki *et al.*[1] show that when certain cells are stimulated with lysophosphatidic acid (LPA) — a growth factor in blood serum — Rap1 is inactivated, leading to activation of ERK and its downstream target, the transcription factor Elk-1. Both inactivation of Rap1 and activation of Elk-1 can be inhibited by a mutant Rap1GAPII, indicating that Rap1GAPII mediates the LPA-induced effects on ERK signalling.

This result was unexpected because LPA activates ERK through the βγ-subunit of $G_i$, which, through a still-debated pathway, activates Ras[7]. The $G_i$-coupled receptors seem to activate ERK in two ways — by inducing a positive pathway (βγ-mediated activation of Ras), and by inhibiting a negative pathway ($G\alpha_i$-mediated inactivation of Rap1; Fig. 1). To add to the complexity, LPA (presumably through $G\alpha_q$) also activates Rap1. So, the overall effect on ERK may depend on the cellular and/or subcellular context. Indeed, activation of endogenous Rap1 does not always have an observable effect on the activity of ERK[3].

Jordan *et al.*[2] used a different cell system in which Rap1 activates ERK. They show that introduction of $G\alpha_o$ — but not an active mutant of this protein — can activate ERK. But it is not clear whether this activation is indeed mediated by Rap1GAP and Rap1.

Modulation of ERK activity may be just one function of Rap1, and other functions have been implicated. For instance, during development in the fruitfly *Drosophila melanogaster*, Rap1 is critical for regulating normal morphogenesis. This function, although ill-defined, is independent of Ras signalling[8]. Rap1 activity is, in fact, rapidly regulated by a variety of activated receptors, suggesting that it may act in a common process in receptor signalling[3]. One intriguing possibility arises from analysis of Bud1, the homologue of Rap1 in budding yeast. Bud1 is involved in recognizing a positional cue, and it recruits polarity factors (such as the Rho-like small GTPase CDC42) to position the actin cytoskeleton for the formation of a new bud. Bud2 — a GAP for Bud1 — may play a role in positioning Bud1, as well as in the essential cycling of Bud1 between the GTP- and GDP-bound states[9].

So, maybe Mochizuki *et al.*[1] and Jordan *et al.*[2] witness the formation of a complex in which $G\alpha_i$ or $G\alpha_o$ is the positional cue to assemble a Rap1GAP–Rap1•GTP complex. This complex could perhaps, in turn, recruit polarity factors for the actin cytoskeleton. Such a function is not incompatible with the observed effects of Rap1 on cell morphology[10] or with the inhibitory effect of SPA-1 (which is another Rap1-specific GAP) on receptor-induced cell adhesion[11]. And it would not be the first time that yeast has set the stage for a molecular mechanism in mammalian cells. □

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**Daedalus**

## Sharp snow

**Abrasives are an important but rather traditional technology. Grinding wheels, abrasive papers and loose powders all exploit tiny particles of grit made by crushing larger chunks of the material. These grains tend to be roughly spherical; few have any acute, sharp cutting edges. Worse, their orientation in use is entirely random. Only a tiny minority do anything to shape the workpiece at all.**

**Daedalus now wants to make sharp and spiky abrasive particles directly. He points out that gases conduct heat very badly. Thus a snowflake growing in air cannot readily get rid of its latent heat of condensation. Its points and edges are much better cooled, and therefore grow much faster, than its core. Hence the highly branched, dendritic form of snowflakes. Accordingly, to make an ideal sharp and spiky abrasive powder, condense it from vapour in a large mass of air or inert gas. Indeed, when some metals (such as zinc) burn in air, the resulting smoke consists of fine, highly branched and pointed single crystals of metal oxide.**

**DREADCO chemists are now exploring these ideas. Abrasives such as aluminium oxide might be made by burning the parent metal in carefully controlled conditions. But others, such as silicon and tungsten carbides, cannot. So the team is burning derivatives such as aluminium trimethyl, silicon tetramethyl, and so on, in limited concentrations of strongly preheated oxygen. The desired abrasive should form by reaction in the intensely hot flame. Its vapour will cool into a micro-snow of tiny, dendritic, sharp-edged, ferociously abrasive single crystals.**

**DREADCO's dendritic abrasives will transform the technology. No matter what its orientation, each particle will present one or more cutting edges to the workpiece; and lacking grain boundaries, the single crystals will be immensely strong. Grinding wheels formed from them will carve effortlessly through metal and masonry. Machinists, production engineers and even burglars will rush to exploit their irresistible cutting power. Dendritic abrasives will even make headway through modern engineering ceramics, many of which are so hard that at present they are almost useless. Taking his vision to its limit, Daedalus even dreams of striking a carbon arc in ultrahigh-pressure xenon. Formed under extremes of pressure and temperature, the resulting carbon vapour should condense into the most abrasive snow of all — dendritic diamond dust.**

**David Jones**