	WINTER COVER OF ALPINE LAKES	ANTARCTIC LAKE ICE
Where	High mountain lakes (Alps, Pyrenees); annual precipitation: 1000 to >2000 mm	Lakes in the Dry Valley, Antarctica; annual precipitation: <200 mm
Duration	8–10 months: from November/December through June/July/August	Permanent; liquid water only in summer (5 months)
Thickness	1.5–3 m	3–6 m
Formation	Lake water penetrates through the ice cover, which is pushed downward by snow, forming slush and white ice layers; rain and melting water trickles down	Freeze-out of lake water: balance of ice formation from beneath and ablation to the atmosphere
Liquid water	10–30%, consisting of lake water, snowmelt water and rain	Up to 40% during Austral summer, consisting of ice meltwater
Temperature	Constantly 0°C, from formation to melting	0°C in summer; <0°C during winter
Radiation	Strong light gradient, from nearly 100 to <0.1%; ultraviolet-B radiation ~50% higher than at sea level	Strong light gradient; constant radiation in summer, low ultraviolet-B except during ozone hole events
Origin of organisms	Lake water, airborne (snow and rain), littoral sediment	Ini-blown from surrounding soils, and long-range transport
Main feature	Intermittent (~6 months) but constantly at 0°	Permanent, but most times frozen: liquid water and microbial activity only in summer
	Sandwich-like structure: "sediment" of snow-ice particles	Patchy distribution of sediment of terrestrial origin; activity restricted water pockets
	Microbial world, LIMCO (prokaryotes and eukaryotes) origination from different sources; no metazoa	Microbial world consisting of cyanobacteria and heterotrophic bacteria with some eukaryotic algae; no predation
	High bacterial production compared with lake water but reduced predation pressure	

and diversity of freshwater systems hosting active organisms at or below 0°C may grow greater in the near future (*7*).

What is the attraction of studying life in the cold? It may be the beauty of simplicity, which—especially in the case of the Antarctic lake ice—promises that sooner or later we may be able to understand and model ecosystems with simple structures and frozen dynamics. In addition, the origin of life in hot springs and vents has been debated for a long time (*8*). The vision of a cold origin of life—supported for instance by prebiotic researchers such as Lazcano from the University of Mexico (*9*)—may lay the foundation for a model of past conditions on Mars and of present-day conditions on Europa.

There are still many unsolved questions regarding the buildup and the fate of microbial assemblages in the ice cover of freshwater lakes and the role they may play as inocula to the pelagic system during thawing or after migration through the ice column. Also, their role in nutrient cycling and element fluxes is still an open question, as well as their responses to climate warming or increased ultraviolet-B radiation. Whatever the answers to these questions may be, Priscu and co-workers have shown that the icy life is more diverse and more exciting than could have been imagined.

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SIGNAL TRANSDUCTION

G Proteins and Small GTPases: Distant Relatives Keep in Touch

Alan Hall

Cells use all sorts of tricks to make the signal transduction pathways that tailor the cells' physiology to the changing environment. One feature used repeatedly is the protein switch, flicked on and off by the nucleotide guanosine 5′-triphosphate (GTP). When GTP is bound, two families of proteins—heterotrimeric guanine nucleotide–binding proteins (G proteins) and their distant relatives, the small molecular weight guanosine triphosphatases (GTPases)—are "on" and can activate the element immediately downstream to send a signal further down the line. But each of these proteins is also a GTPase, containing within the molecule itself the ability to hydrolyze GTP to guanosine diphosphate (GDP) and so turn off the switch.

Small GTPases control fundamental cell properties—polarity, shape, and the commitment to divide or differentiate. The larger G proteins usually regulate more specialized signals—the production of second messengers like cyclic AMP and calcium. Two members of the G protein family, G_{12} and G_{13}, are unusual in that they promote cell cycle progression and reorganization of the actin cytoskeleton, changes that are typically associated with the small GTPases. Now an impressive piece of detective work, described on pages 2109 and 2112 of this issue, unites the two distantly related families through these unique G proteins. Kozasa *et al.* and Hart *et al.* show that G_{13} directly activates a guanine nucleotide exchange factor, which in turn promotes GDP dissociation from the small GTPase Rho, allowing it to be activated again by GTP (*1*, *2*). At least in this instance, a G protein triggers action in its distant cousin, the small GTPase Rho.

Small, monomeric GTPases of the Rho-Rac family control the assembly of filamentous actin structures in response to signals from outside the cell (*3*). Rho, the founder member of this family, interacts with effector (downstream) proteins to cause the assembly of contractile actin:myosin filaments. Although the most clearly visible of these filaments are the stress fibers seen in fibroblasts adhering to a surface, actin:myosin structures actually play a fundamental role in all cell types. Consequently, Rho

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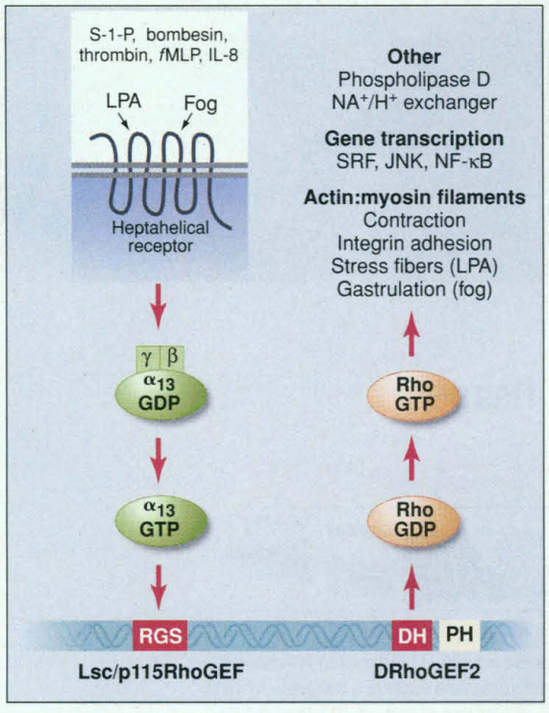
controls such diverse processes as smooth muscle contraction, growth cone collapse, embryonic wound healing, and cell shape changes during morphogenesis (*4*, *5*). Rho is activated by some members of a large family of guanine nucleotide exchange factors (RhoGEFs), each of which has a Dbl homology (DH) domain followed immediately by a pleckstrin homology (PH) domain (*6*). In addition, RhoGEFs have a variety of other motifs and domains unique to each member—one of these, an RGS (regulators of G protein signaling) domain in Lsc/p115RhoGEF, a GEF specific for Rho, is identified in the two reports in this issue.

The RGS domain was first detected in a yeast protein, Sst2p, which stimulates the intrinsic GTPase activity of the single G protein present in *Saccharomyces cerevisiae* (*7*). Since then a family of mammalian RGS-containing proteins (with over 19 members) has been identified and, as predicted from the yeast results, most stimulate the GTPase activity of mammalian G proteins. The RGS sequence therefore defines a family of GTPase-activating proteins (GAPs) capable of downregulating heterotrimeric G proteins. Kozasa *et al.*, using a database search, observed an RGS domain in mammalian Lsc/p115RhoGEF and in *Drosophila* DRhoGEF2 (*1*). By screening various G proteins, they found unexpectedly that the RGS in Lsc/p115RhoGEF interacts specifically with the GTP-bound α subunits of G_{12} and G_{13} and that it acts as an activating protein (a GAP) for both GTPases.

In 1992, phospholipase C β was reported to be both a specific GAP and an effector for the heterotrimeric G protein, G_q, raising the possibility that GAPs might in general also be targets of G proteins (*8*). Now it seems that in addition to acting as GAPs for G proteins, some RGS-containing proteins might also be effectors. Hart *et al.* therefore examined whether the RGS-containing Lsc/p115RhoGEF could be a target of G_{12} or G_{13} (*2*). Indeed, the ability of Lsc/p115RhoGEF to stimulate GDP/GTP exchange on Rho is significantly greater in the presence of the GTP-bound α subunit of G_{13}, but not G_{12}, demonstrating that Lsc/p115RhoGEF is both a GAP and a target for G_{13} (see the figure).

The new results point to the Rho exchange factor as a target for G_{13}. They also offer a mechanism for the observation that both G_{12} and G_{13} can induce Rho-dependent stress fiber formation. Because Rho appears to be activated exclusively by ligands that act through heptahelical receptors (see the figure), it seems likely that these receptors activate Rho through G_{12} or G_{13} (*6*, *9*). Kozasa *et al.* and Hart *et al.* illuminate how this might work: Activated $G\alpha_{13}$ interacts with and stimulates the catalytic activity of Lsc/p115RhoGEF. The new work also meshes well with the genetic analysis of gastrulation in *Drosophila*, which is driven by an extracellular ligand, fog, that activates a G protein, concertina. Two other components of this pathway are a *Drosophila* GEF (DRhoGEF2) and *Drosophila* Rho. Fog-mediated activation of Rho leads to an actin:myosin-dependent constriction at the apical surface of epithelial cells to drive this morphogenetic process (*5*). It now seems likely that concertina, which belongs to the $G_{12/13}$ family, interacts directly with DRhoGEF2 through an RGS domain.



Family reunion. Interaction of Lsc/p115RhoGEF with $G\alpha_{13}$-GTP, but not $G\alpha_{12}$-GTP, stimulates its ability to catalyze guanine nucleotide exchange on Rho, thereby providing a direct biochemical link between the heterotrimeric G protein and the small GTPase. The RGS domain of Lsc/p115RhoGEF functions as a GAP toward both $G\alpha_{12}$ and $G\alpha_{13}$, but its preferred substrate is $G\alpha_{13}$. Extracellular ligands activate Rho–lysophosphatidic acid (LPA), sphingosine-1-phosphate (S-1-P), bombesin, thrombin, and the chemotactic agents formyl-methionyl-leucyl-phenylalanine (fMLP) and interleukin-8 (IL-8). All act through heptahelical receptors and therefore activate G proteins. Once activated, Rho-GTP interacts with effectors leading to the assembly of contractile actin:myosin filaments and integrin-containing focal adhesion complexes. It may also control other cellular activities such as the transcription factors SRF and NF-κB, the JNK MAP kinase pathway, phospholipase D, and the sodium/proton exchanger.

Is this the only way Rho can be activated? Almost certainly not; other GEFs for Rho (for example, Lbc) lack an RGS domain, and it is still unclear how G_{12} activates Rho. Even for Lsc/p115RhoGEF, there is likely more to the story. First, the PH domain is essential for full activity of many GEFs, although it is not known why. Some PH domains interact with phosphoinositides, but so far the only lipids implicated in Rho activation are derivatives of arachidonic acid (*10*, *11*). Interestingly, however, activation of the yeast RhoGEF, ROM2, is mediated by TOR2, a phosphatidylinositol kinase–related protein (*12*). Second, G_{13}- but not G_{12}-induced activation of Rho is inhibited by tyrosine kinase inhibitors and so perhaps phosphorylation of Lsc/p115RhoGEF is required for exchange activity, as has been reported for another RhoGEF, Vav (*13*). Alternatively, phosphorylation of another protein might be required to initiate Rho signaling. Whatever the explanation, the analysis of gastrulation in *Drosophila* provides further support for an additional signal contributing to exchange factor activation, because deletion of DRhoGEF2 produces a more severe phenotype than deletion of concertina (*5*).

Kozasa *et al.* and Hart *et al.* have identified the first target for the $G_{12/13}$ family of G proteins and in so doing provide a biochemical link between heptahelical receptors and activation of the small GTPase Rho. Actin:myosin filament assembly underlies many fundamental biological processes, and this work is an important step in understanding its control.

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