exciting because it challenges us to explore previously unanticipated possibilities.

A possible rationale for linking a G_s-specific RGS domain to a sorting nexin derives from the unusual biology of G_s. Inactive GDP-bound G_s is associated with the inner leaflet of the plasma membrane by a covalently attached palmitoyl moiety and by binding to membrane-anchored β and γ subunits. Upon activation by an appropriate GPCR, the GTP-bound α subunit of G_s dissociates from the βγ subcomplex; a fraction of the activated α subunit then becomes depalmitoylated and moves away from the plasma membrane and into the peripheral cytoplasm. In contrast, α subunits from other heterotrimeric G proteins contain a stably attached myristoyl modification and remain attached to membranes after activation (*8*). The association of a G_s-selective RGS protein with endosomal membranes could provide a way to limit the range (or duration) of signaling induced by liberated G_s α subunits to a cytoplasmic region delineated by RGS-PX1–associated endosomes (see the figure). By superimposing on this model of G protein cycling the itinerary of certain G_s-coupled GPCRs (such as the β_2 adrenergic receptor), which cycle through endosomes after ligand-induced activation (*9*), one can envisage that localizing RGS activity could physically separate distinct signals. Thus, signals initiated by receptors at the plasma membrane and mediated by activation of G_s could be separated from signals emanating from internalized receptors and mediated by endosome-associated kinases (*7*). It is also conceivable that localized inactivation of α subunits near endosomes could facilitate regeneration of G_s heterotrimers in the vicinity of recycling GPCRs. This would help in the reassembly of receptor-G_s complexes in the plasma membrane (or perhaps on endosomes that later recycle to the plasma membrane), thereby rendering the receptor-G_s signaling system competent to be retriggered by a subsequent round of ligand-induced activation at the cell surface (see the figure).

Of course, these and other hypotheses about RGS-PX1 remain to be tested, and many questions relating to the structure and function of this G_s-selective RGS protein remain to be addressed. The Zheng *et al.* study should stimulate efforts to define additional molecular threads in the complex web linking signaling and membrane-trafficking events, and to investigate the functional significance of the connections thus revealed.

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PERSPECTIVES: ECOLOGY

Dammed Experiments!

Jared Diamond

Fragmentation of large expanses of habitat into many smaller patches is a problem of both scientific and practical interest. From a scientific perspective, habitat fragmentation is the way in which much of the modern world was formed. At the end of the last Ice Age 13,000 years ago, melting glaciers raised sea levels, drowned low-lying land bridges, and carved off edges of continents into islands such as Britain and Japan. But fragmentation is not just a feature of the last Ice Age, it is also the fate befalling most natural habitats today—hence the practical interest. In either case, fragmentation causes loss of animal and plant populations by a process termed faunal relaxation. How fast does relaxation occur, and which species are most likely to survive?

A report by Terborgh, Rao, and their colleagues (*1*) on page 1923 of this issue describes a grand natural experiment in habitat fragmentation. In 1986, construction of a dam in Venezuela created the 4300-km^2 Lake Guri, flooding valleys and turning hundreds of former hilltops into islands ranging in area from less than 0.1 ha to 150 ha. Barely 4 years later, surveys of many groups of plants and animals began (*2*–*5*). The Lake Guri study reminds us of two other famous fragmentation studies: the surveys of Barro Colorado Island and other islands in Panama's Lake Gatun, created by damming in 1913 during construction of the Panama Canal (*6*); and the Minimum Area Project in the Brazilian Amazon near Manaus, involving forest tracts isolated from each other by forest clearance since around 1980 (*7*). These three studies complement each other. For instance, relaxation has been proceeding much longer in Lake Gatun (88 years) than in Lake Guri (15 years), but detailed faunal surveys began much sooner in Lake Guri than in Lake Gatun.

CREDIT: ANIMALS ANIMALS

Many generalizations emerge about the biotas of Lake Guri islands of different sizes. The smallest islands (<1 ha) quickly lost 75% of their original species, and most species that persisted fell into just three ecological groups: canopy herbivores (howler monkeys, an iguana, and leaf-cutter ants); ground-dwelling insectivores (birds, lizards, frogs, and tarantulas); and seed consumers (small rodents and parrots). Medium-sized islands (4 to 12 ha) possessed in addition armadillos, agoutis, and phorid fly parasitoids of ants. Large islands (150 ha) retained most of their original species, including army ants, big frugivorous birds, anteaters, and big herbivorous and omnivorous mammals (deer, peccaries, tapir, and monkeys). But,

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within 4 years, all islands had lost their top predators: the jaguar, puma, and harpy eagle. Thus, as habitat area shrinks, predators are lost before their prey, and parasitoids are lost before their hosts—just as one would expect from the decrease in population densities as one ascends the trophic ladder, and from the inverse relation between extinction probability and population size.

Those species that do manage to persist on small islands tend to become far more abundant than populations of the same species on larger, more species-rich islands. The increase in abundance is by a factor of 2 for birds, 10 for iguanas and capuchin monkeys, 30 for howler monkeys, 35 for rodents, 100 for leaf-cutter ants, and a large but unmeasured factor for tarantulas. Part of the explanation for increased abundance is ecological release from competition: When competing species are removed, the resources that would have gone to them become available to the persisting species. The other part of the explanation is escape of prey from control by predators or parasitoids that limit their abundance on larger islands. For instance, on small islands leaf-cutter ants escape control by armadillos, army ants, and phorid flies, and birds escape control by monkeys, but on medium-sized islands the armadillos themselves escape control by jaguars, and the monkeys escape control by harpy eagles. The superabundance of small herbivorous animals on small islands acts through a trophic cascade to weed out palatable plant species and to convert the landscape into a forest of "herbivore-proof" plants. This mirrors the way in which goats convert islands into landscapes of goat-proof plants, and the exploding deer population—following the decline of wolves, bears, and human hunters in the eastern United States—has eliminated dozens of palatable woodland plant species.

Although this issue's report by Terborgh *et al*. emphasizes control of prey by their predators, and of plants by their herbivores, there is far more to the Lake Guri Project than those two conclusions. The project reminds me of a kaleidoscope that gets shaken up hundreds of times, with some general tendencies emerging among the resulting patterns, but with fascinating differences of detail because of effects of chance, yielding bizarre communities that would never exist at equilibrium. For instance, a herd of capybaras, trapped on one island too remote for them to escape by swimming, has converted that island's understory into bare ground covered with capybara dung. Howler monkeys similarly trapped on remote islands have soared in abundance and proceeded to shut down their per capita output of baby howlers fourfold. Capuchin monkeys survived on only two medium-sized islands, where they have gone on to clean out 90% of bird population densities. The forest on two islands with agoutis is turning into a forest of plant species whose seeds agoutis like to bury. Leaf-cutter ants forage mainly just at night on islands plagued with phorid flies that parasitize them, but the ants run around boldly in daylight on an island with few flies.

Perhaps the most important message of Lake Guri concerns the virtues of unplanned natural experiments. Professors of field biology urge their students to avoid "bird watching" not driven by hypotheses formulated in advance, and to go into the field only after designing a well-controlled experiment to discriminate between competing hypotheses. All too often, the sad result is that the student succeeds in answering that original question, and thereby fails to notice some much more interesting question at the same field site. Unplanned natural experiments create ecological communities that we would never have dreamed of creating, or that laws, moral scruples, or practical obstacles would have prevented us from creating even if we had dreamed of them. Who would or could locally exterminate jaguars, armadillos, or army ants, or make populations of capybaras or tarantulas explode in numbers? Nowhere else can one find such bold, large-scale experiments as on habitat fragments created by nature.

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PERSPECTIVES: IMMUNOLOGY

A Molecular Gut Reaction

Florence Lambolez and Benedita Rocha

The mucosal surfaces of the body are the regions where individuals and the environment meet. For example, the gut mucosa is in continuous contact with food antigens, the enteric commensal bacteria that constitute the gut flora, and potential pathogens that enter the host through the intestine. The gut epithelium and its mucous layer form a major barrier, trapping invading pathogens, which are then eliminated when the gut epithelium is shed. Maintaining the integrity of gut epithelium as well as ensuring its continuous turnover are essential for local defense. In the gut, local defense depends in part on T lymphocytes called intraepithelial lymphocytes (IELs) that are nestled among gut epithelial cells. These T cells modulate homeostasis of the gut epithelium through local production of cytokines (*1*), but exactly how they do this is unclear. On page 1936 of this issue, Leishman *et al*. (*2*) reveal the two molecules that enable IELs both to maintain the gut epithelium and to regulate its turnover.

IELs have unique properties. First, although they are T cells, they include a major subpopulation that is generated locally rather than within the thymus (*3*). During maturation of the thymus, T lymphocytes that recognize self antigens are eliminated. The "locally generated" IELs include T lymphocytes that express self-reactive T cell receptors (TCRs) (*4, 5*). Second, unlike thymus-derived naïve T cells, IELs are not in a "resting" state. Instead, they more closely resemble "effector" T cells, the lymphocytes present in other organs that are activated during acute immune responses. Before naïve T cells undergo division and differentiation into effector lymphocytes, they must be stimulated by antigen. In contrast, both effector T cells and IELs do not need this "priming" and, upon encounter with antigen, immediately produce cytokines that result in killing of infected target cells (*6*). Yet there must be some way that these effector cells are controlled locally. If antigen stimulation induces T cell division, what prevents IELs from dividing extensively and disrupting the gut epithelium? If self-reactive IELs have the potential to kill gut epithelial cells, what prevents them from doing so? According to Leishman and colleagues, unique local characteristics appear to modulate IEL behavior.

T lymphocytes recognize antigenic peptides through their TCRs. Thymus-derived T cells also express CD8, a corecep-

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