ing financial responsibility for their national malaria control programs. The international financial crisis and redirection of political and financial attention to other pressing global health problems such as malnutrition and family planning are potential threats to the investment needed to sustain and expand malaria control and research. Past experience shows the disastrous consequences of letting up on effective malaria control. It’s time to reap the benefits of the mosquito and parasite genomes to aggressively tackle this disease. Otherwise, this highly adaptable parasite and its vector will continue to outwit us and continue to kill millions.

References

The presence or absence of particular herbivore species influences which plant genotypes are favored by natural selection.

**How Insect Herbivores Drive the Evolution of Plants**

J. Daniel Hare

The most common biological interaction among species on Earth is that between plants and the insects that feed on them (1). Insect herbivores are thought to impose natural selection, which favors resistant plant genotypes and drives the evolutionary diversification of plant species. Two reports in this issue—by Züst et al. on page 116 (2) and Agrawal et al. on page 113 (3)—independently provide strong empirical evidence for the rapid evolution of plant traits that confer resistance to herbivores when herbivores are present but for the evolution of traits that confer increased competitive ability when herbivores are absent.

If resistance to insects benefits plants, then why are not all plants now resistant? Several answers to this long-standing question have been proposed. One is based on the assumptions that plant defenses are costly, that resistant genotypes are favored when the probability of insect damage is high, but that these genotypes pay a cost for resistance and are disfavored when the probability of herbivore attack is low. In its simplest form, this hypothesis states that chemical resources obtained by plants can be allocated maximally either to growth and reproduction or to defense, but allocation to both processes cannot be maximized simultaneously (4). A second hypothesis is that defense polymorphisms are the result of variation in selection regimes due to variation in the size and membership of herbivore communities at different locations (5). The two studies in this issue find strong evidence for variation in plant defense traits in response to particular herbivore species, but only partial support for the allocation hypothesis.

Züst et al. studied natural populations of *Arabidopsis thaliana* in Europe. They compared the geographic variation in the profiles of glucosinolates [a class of defensive chemical compounds in the plant family Brassicaceae (6)] with the distribution of two aphid species that feed only on brassicaceous plants. The frequency of the *GS-ELONG* gene, which determines the length of the carbon side chain on glucosinolate molecules, varied both with latitude and longitude. The aphid *Brevicoryne brassicae* predominated in areas where the plants produced glucosinolates with four-carbon side chains, whereas the aphid *Lipaphis erysimi* predominated in areas where plants produced glucosinolates with three-carbon side chains.

The authors next used a synthetic plant population consisting of genotypes that produce several different combinations of glucosinolates. After only five generations of selection, feeding by each aphid species selected for plant genotypes with glucosinolate profiles identical to those in the field locations where each aphid species predominated. By contrast, the plant genotype that predominated after five generations in a “no aphid” treatment produced relatively low levels of glucosinolates. This genotype was, however, eliminated from populations exposed to all aphid treatments (see the figure).

In a related but independent study, Agrawal et al. conducted a four-generation
Intestinal Wound Healing Requires a Wnt Balancing Act

Terrence A. Barrett

Inflammatory bowel disease (IBD) encompasses a group of disorders of the colon and small intestine including Crohn’s disease and ulcerative colitis. It affects roughly 396 per 100,000 persons worldwide (1) and in the United States is responsible for more than $1.7 billion in overall health care costs. The chronic or recurrent inflammation associated with this disease causes severe damage to the epithelial lining of the intestine. On page 108 of this issue, Miyoshi et al. (2) present a model for wound healing in the intestinal tract that may have clinical relevance to mucosal repair in disorders of intestinal ulceration.

Within the epithelial lining of the small intestine and colon is a gland composed of subunits called intestinal crypts or crypts of Lieberkhün. After mucosal wounding, channels of epithelial cells move under exposed surfaces to begin to recreate normal crypt architecture. Epithelial proliferation at wound edges is driven by the Wnt signaling pathway, particularly the canonical Wnts, which signal through β-catenin.

Miyoshi et al. have found that creation of new crypts requires release of noncanonical (β-catenin–independent) Wnt5a. Mesenchymal Wnt5a-secreting cells are derived from serosal mesothelial (WT1) stem cells and appear to migrate into areas to participate in tissue repair. Wnt5a lowers epithelial proliferation rates and induces epithelial channel clefting and epithelial channel clefting under the wounded surface. Miyoshi et al. suggest that Wnt5a potentiates transforming growth factor–β (TGF-β) signaling (via Serpine1 and Smad3) to reduce epithelial proliferation and cause clefting of epithelial channels. Clefting alters the polarization of highly proliferative crypt structures at wound margins, allowing them to branch into new crypt units. The authors did not detect Wnt5a-mediated inhibition of canonical Wnt signaling as reported by others (3). This inhibition, when observed, is context dependent (3), suggesting that noncanonical Wnt5a may affect canonical Wnt signaling in other mucosal healing processes in the intestine.

Wnt5a is needed for wound healing. Image of transmural ulcer from a Crohn’s disease resection specimen showing an area of hyperproliferative branching crypts producing an epithelial monolayer (EM). An area of epithelial channel clefing is highlighted (dark arrow).

References