

corresponding 2,3-*cis*-flavan-3-ols (4). These results indicate that BANYULS is an anthocyanidin reductase and is required for the biosynthesis of condensed tannins. This finding implies that the previous enzyme in the pathway, anthocyanidin synthase, should be needed not only for anthocyanin synthesis but also for condensed tannin synthesis. As predicted, the *Arabidopsis transparent testa* mutant defective in anthocyanidin synthase (*tt18*) exhibits a decrease in both anthocyanins (1) and condensed tannins (4), further supporting the placement of BANYULS in the condensed tannin biosynthetic pathway.

The new work clarifies a major problem regarding the stereochemistry of condensed tannin biosynthesis. Condensed tannins contain both 2,3-*cis*- and 2,3-*trans*-flavanol units, but leucoanthocyanidin is in the 2,3-*trans* configuration. The observation that BANYULS acts on anthocyanidins rather than leucoanthocyanidins pro-

vides a mechanism to establish *cis* stereochemistry. Leucoanthocyanidins have three chiral centers, all of which are destroyed during their aromatization to form the anthocyanidins. BANYULS then delivers two hydride equivalents to the top face of the anthocyanidins to generate both the 2*R* and the 3*R* stereocenters in 2,3-*cis*-flavanols. In principle, there could exist related enzymes that reduce anthocyanidins to similar but stereochemically distinct structures by delivering hydride to different faces of the common anthocyanidin precursors. Alternatively, a leucoanthocyanidin reductase could supply these *trans* isomers for condensation. This missing enzyme may be among the remaining uncharacterized DFR-like enzymes encoded in the *Arabidopsis* genome.

Thus, BANYULS is a branchpoint enzyme that regulates the relative amounts of two flavonoid families, the anthocyanins and the condensed tannins. BANYULS

activity is limiting for condensed tannin production, making this enzyme an attractive target for overexpression in forage plants, such as alfalfa (*Medicago sativa*), with the goal of inducing condensed tannin production. When present at moderate levels in animal feed, these compounds increase protein usage and decrease the risk of bloating in ruminants, thus increasing agricultural efficiency and reducing the need for antibloating drugs (3). As the beneficial effects of condensed tannins on human health are elucidated, modification of BANYULS in food products consumed by humans may become desirable.

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PARASITOLOGY

A Game of Cat and Mouth

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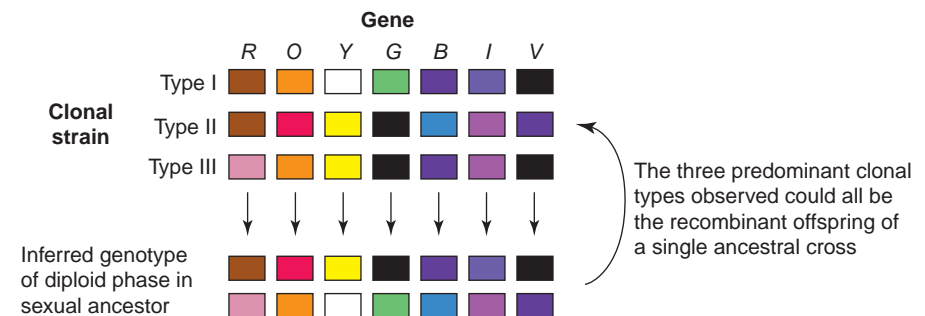
Every genome contains within itself a record of its origin and evolutionary history. This record often can be deciphered with the help of the rich repertoire of molecular evolutionary theory. For infectious diseases, evolutionary changes that affect virulence, drug resistance, and evasion of the host immune system have major implications for public health. This issue of *Science* includes a remarkable example of evolutionary change in the life history strategy of a pathogenic parasite, *Toxoplasma gondii* (1). The three predominant and most widespread genotypes of *T. gondii* are known to have originated as the offspring of a single cross between two parental strains (2). On page 414 of this issue, Su, Evans, and collaborators (1) provide evidence that this cross took place only about 10,000 years ago. The progeny were evidently so successful because they acquired an efficient means of oral transmission that promoted their asexual dissemination from one vertebrate host to the next without the need for a detour through the sexual phase.

T. gondii is an apicomplexan protozoan parasite whose life cycle alternates between an intermediate host, in which the

organism reproduces asexually, and a definitive host, in which the organism undergoes sexual reproduction. They are designated apicomplexans because of a characteristic cone-shaped configuration of microtubules at the tapering apical end of the cell. In the case of *T. gondii*, the intermediate host consists of a wide variety of warm-blooded vertebrates, whereas the definitive host is confined narrowly to the cat family *Felidae*. For transmission to humans, the most important definitive host is the domestic cat. Transmission occurs by handling soil or other materials contaminated with feces containing sporulated oocysts that infected animals excrete in great numbers for 2 to 3 weeks after infec-

tion. Transmission can also occur through contaminated water or by eating raw or insufficiently cooked meat that contains the organism in an encysted form.

Estimates based on the presence of antibodies to *T. gondii* suggest that 30 to 50% of the human population have been exposed to this organism. In the United States alone, this amounts to 90 to 150 million people. Fortunately, most infected people are asymptomatic and are also nontransmitters. However, the consequences of *T. gondii* infection can be severe among individuals who are extremely immunocompromised because of AIDS, chemotherapy, or immunosuppressive drug therapy. The clinical manifestations include enlargement of the lymph nodes, respiratory distress and heart disease, and disturbances of the central nervous system affecting vision and hearing. The second high-risk group are fetuses, which can be affected congenitally when the mother becomes infected during



Sibling unity. Proposed origin of the three predominant types of *T. gondii*, types I, II, and III, which are sibling progeny of a single cross between two parental strains that took place 10,000 years ago (1, 2). The three strains, which are clonal and show little genetic variation, have only one of two possible alleles for genes at many different loci (depicted as two shades of the same color). From the alleles present in the three strains, the genotype of the diploid ancestor can be inferred.

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PERSPECTIVES

pregnancy. Annually more than 3000 newborns in the United States have congenital *T. gondii* infections, but fortunately most cases are asymptomatic.

About 95% of *T. gondii* infections are due to one of three strains designated types I, II, and III. Each strain type comprises an asexually propagated clonal lineage whose members are virtually identical in DNA sequence. Although types I, II, and III are genetically distinct, each strain carries one or the other of only two alleles at a large number of polymorphic gene loci (see the figure) (2). This observation suggests that the three strains are siblings—the recombinant offspring of a single mating that brought each pair of alleles together briefly in the diploid sexual phase.

Su *et al.* (1) reasoned that the clonality of the predominant types may result from successive oral transmission through intermediate hosts, bypassing the sexual phase of the life cycle. To test this hypothesis, they examined the ability of the predominant strains of *T. gondii* to be transmitted orally as compared with exotic strains. Exotic strains are genetically diverse and contain many unique polymorphisms, but they account for less than 1% of infections. When mice were fed tissue cysts of the predominant strains, 50 to 100% of the animals became infected. In contrast, two of three exotic strains showed inefficient oral transmission (0 to 10%). Taken at face value, these data suggest that

as many as one-third of exotic strains may also show efficient oral transmission.

The authors argue that the fateful cross producing the three predominant clonal lineages may have brought together genes promoting efficient transmission by the oral route and perhaps other necessary adaptations as well. In almost all genetically diverse organisms, recombination can produce progeny with traits differing significantly from those of either parent. For example, a laboratory cross between type II and type III strains of *T. gondii* produced some progeny that were 1000 times as virulent as either parent (2). (A few percent of natural isolates of *T. gondii* are in fact recombinants between the clonal lineages.)

When did the fateful cross take place? To address this issue, Su *et al.* studied polymorphisms in noncoding DNA sequences (primarily introns) in 10 isolates of the predominant strains from diverse geographical locations. On the assumption that nucleotide mutations in noncoding DNA are selectively neutral (or nearly so), the number of unique polymorphisms that have arisen in each lineage since the time of the original cross is expected to increase in proportion to the mutation rate. Across 4067 base pairs in each of the 10 strains, the authors found only two new mutations. If the mutation rate in *T. gondii* is similar to that in the apicomplexan malaria parasite *Plasmodium falciparum*, then this result implies that the pre-

dominant clonal lineages diverged about 10,000 years ago. This estimate contrasts sharply with the time of divergence for exotic lineages (about 1 million years ago).

About 10,000 years ago, human society was undergoing one of its epochal transitions, from hunting and gathering to slash-and-burn agriculture. The population density was increasing, creating new opportunities for endemic or epidemic transmission of many kinds of parasites, and the cat was adopted as a companion animal. These conditions could well have favored strains of *T. gondii* that traded frequent sex in favor of rapid and efficient oral dissemination.

The finding of little genetic variation in each of the three predominant clonal lineages has important implications for public health. It means that drug resistance or immune evasion in these lineages must be acquired through the occurrence of new mutations, rather than through the selection of rare mutations that already exist. The waiting time for such mutations to occur may be substantial. On the other hand, the large amount of genetic variation present in the exotic strains, as well as in the recombinants between the predominant strains, implies that any sudden increase in the frequency of these strains should be viewed with alarm.

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GEOMORPHOLOGY

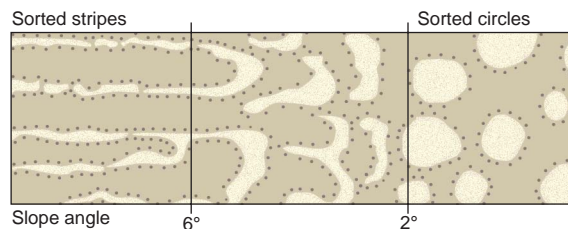
On Patterned Ground

Daniel Mann

Intricate patterns of stones and mud (see the figure) decorate the ground in many cold landscapes. Part of the beauty of this patterned ground comes from the contrast between its stony geometry and the disorder of its bleak surroundings. On page 380 of this issue, Kessler and Werner (1) venture an explanation for how the patterns form and maintain themselves. Building on their earlier research on landforms as diverse as sand dunes and beach cusps (2–5), they use computer simulations to model patterned ground as a self-organizing system. The approach may help to understand the origins of the bewildering variety of patterned ground in alpine and polar regions (6, 7).

Geomorphologists have long been preoccupied with how patterned ground develops in cold regions (8). Nordenskjöld (9)

suggested that the patterns resulted from aqueous convection currents in the ground caused by temperature differences, whereas Nansen (10) thought that they arose from the ejection of stones by freezing. Explorers, geologists, botanists, and native peoples all had their favored explanations. Laboratory and field studies have validated some mechanisms (11–13), but no general explanation has emerged.



Patterns on the ground. In polar and alpine environments, stones and mud often form patterns such as stripes and polygons, depending on the ground slope.

Washburn (6) predicted almost 50 years ago that a general explanation of patterned ground would involve two mechanisms: the compression of the stone domains by expansion of the adjacent soil during freezing, and the upfreezing of stones. But it has remained unclear how these mechanisms interact to create the often highly ordered, three-dimensional (3D) phenomena of patterned ground. Kessler and Werner now add a third mechanism, the gravitational redistribution of heaved stones. They show that acting over centuries, these three processes can together cause the development of self-maintaining landforms wherever the ground repeatedly freezes and thaws.

Although the physics of these mechanisms are simple, two obstacles have prevented us from understanding how they create patterned ground. The first is a problem of approach: At what spatial scale should we look for an explanation? Most researchers have looked for explanations in the physics affecting the individual grains of silt, sand, and pebbles that form the patterns. Unfortunately, this

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