third parties and would assign the task to a centralized facility, which would take responsibility for providing the cells to interested laboratories in a timely fashion. This could provide a solution to the dilemma faced by U.S. researchers.

The registry would include a Web-based database available to university and private-sector researchers where all the data about HESCs and human embryos would be collected. The registry would collect and distribute information pertinent to a number of areas, including results of microarray analysis (raw data) or other high-throughput methodologies, growth and culture conditions of the cell lines, differentiation potential of the cell lines, and number of passages the cell lines can sustain.

Two aspects of this endeavor will require special attention. First, quality control of the deposited information (for example, raw microarray data) must be stringent, defined and imposed by a committee, which we suggest be composed of scientists with expertise in molecular embryology, high-throughput data analysis, and bioinformatics. Second, the maintenance and upgrade of the information will require a committed, long-term effort.

This document provides a starting point, which we anticipate will be refined and strengthened as our knowledge of HESCs and human embryology expands.

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1. A workshop sponsored by the New York Academy of Sciences and The Rockefeller University, New York City, 13 November 2002. R. McKay (NIH) also participated in this workshop.
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ECOLOGY

Cryptic Herbivores of the Rainforest Canopy

James H. Hunt

For decades, Edward O. Wilson has been telling the world that ants are the ecologically dominant animals of tropical rainforests. This assertion is a centerpiece of Wilson's message that ants are fascinating, that "little things" are important (*1*), and that tropical rainforests should be preserved. Since the 1970s, quantitative field studies have documented that ants constitute about 20 to 40% of the arthropod biomass in tropical rainforest canopies (*2*). Tobin (*3*, *4*) has questioned the ecological foundation that supports so many ants. Conventional wisdom holds that ants are primarily predators or scavengers, yet thermodynamic principles mandate that the greatest animal biomass in terrestrial communities must be the herbivores at the second level of the trophic pyramid. Thus, Tobin recognized a paradox and inferred that many ants in rainforest canopies must be herbivorous. A preliminary study provided provisional support for this fascinating hypothesis (*5*). Now, on page 969 of this issue, Davidson and colleagues (*6*) demonstrate that many rainforest ant species do, in fact, feed primarily or in part as herbivores. Cryptic herbivory may be the answer to Tobin's paradox.

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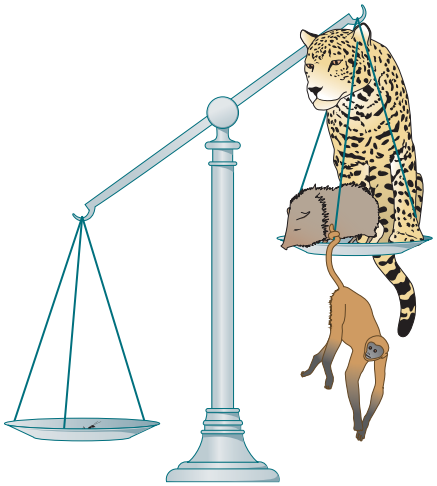
Protein is the principal currency of animal growth, with nitrogen as the essential element. The lighter of two stable isotopes of nitrogen is more readily lost in metabolic waste products, which causes the isotopic ratio of nitrogen in organisms to vary with ecological distance from the base of a food chain. Davidson and colleagues applied this analytical technique to ants, other insects, and plants from a Neotropical rainforest in Peru and a Paleotropical rainforest on the island of Borneo. Although the new data reveal that many rainforest ant species are predators or scavengers, many others have nitrogen isotope ratios in the same range as those of leaf-chewing insects, sap-feeding insects, and plants themselves. Overtly herbivorous rainforest ants feed on extrafloral nectar or the specialized food bodies of plants, or, in the case of Neotropical leaf cutter ants, on sap from the leaves that they cut. Unlike caterpillars and other leaf-chewing insects, no ants feed directly on leaf tissue. Ants that practice cryptic herbivory feed primarily on the liquid exudates of sap-feeding insects such as aphids, membracids, or scale insects (collectively called "trophobionts" when tended by ants). In addition, they may feed on pollen, fungal spores and hyphae, and leaf surface microflora (epiphylls). The ecological and evolutionary impact of ant herbivores, especially those that feed on the exudates of trophobionts, may be far-reaching.



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Tipping the scales of the rainforest carbon economy. The total biomass of ants in tropical rainforests exceeds that of mammals (*1*). Such abundance is hard to reconcile with the proposition that ants are primarily predators or scavengers and thus are two or more levels above plants in an ecological trophic pyramid. New research (*6*) shows that many rainforest canopy ants obtain nourishment primarily or substantially as herbivores. Herbivorous ants may be major players in the carbon economy of rainforests.

Close and sometimes complex ecological interactions between ants and plants drew attention primarily from myrmecologists (ant entomologists) until Janzen (*7*) elevated ant-plant symbioses (*8*) into the ecological mainstream. Most students of tropical ecology now confidently assert that ants provide a service to plants by acting as patrollers, keeping leaf-

chewing insects at bay. It is clear that sap-feeding insects must drain a plant of nutrients. Yet logic suggests that the cost extracted by trophobionts must be less than the potential cost of leaf herbivory that would take place if the ants that tend trophobionts were not on patrol against leaf herbivores (*9*). The evidence provided by Davidson *et al*. that much of the large biomass of rainforest canopy ants is maintained by plant products suggests that the total costs of herbivory to rainforest plants may be much greater than previously believed. Lowman (*10*) has suggested that "sap-suckers" may be important rainforest canopy herbivores, and now this seems likely to be true. By feeding on extrafloral nectar or the exudates of sap-sucking trophobionts (*11*), ants make a substantial contribution to herbivory in the rainforest canopy.

Predacious ants act as agents of natural selection on their prey, whereas scavenging ants are the garbage collectors of the rainforest—ecologically useful but with little evolutionary impact on the species that they scavenge. However, if rainforest canopy ants are herbivores, then, like predators, they would be agents of natural selection on their prey, rainforest canopy plants. The energy and nutrient budgets of affected plants may strongly reflect the impact of ant and ant-mediated herbivory. A possible ramification of considerable consequence is that as global climate change pushes tropical trees toward the limits of their physiological abilities (*12*), plants that pay high costs to herbivory may face constraints on both short-term and adaptive responses to the stress of rising temperatures. Ants as herbivores could be major players in the ecological dynamics of tropical rainforest trees and, thereby, in the carbon balance of Earth. "Little things" really do matter. Rainforests should be preserved.

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BIOMEDICINE

A View from the Top—Prion Diseases from 10,000 Feet

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The causative agent of the transmissible spongiform encephalopathies (TSE) or prion diseases, which include sheep scrapie, mad cow disease, and human variant Creutzfeldt-Jakob disease (vCJD), is still hotly debated. The "protein only" hypothesis postulates that the TSE agent is an infectious, self-replicating prion protein called PrP^{Sc}. This abnormal protein is considered to be an insoluble, partially protease-resistant isoform of a normal cellular protein, PrP^{C}, which is both soluble and protease-sensitive (see the figure). The biochemical differences between these two PrP isoforms are due to a change in conformation whereby the primarily α-helical and loop structure of PrP^{C} is refolded into the predominantly β-sheet structure of PrP^{Sc}. The conformational switch from PrP^{C} to PrP^{Sc} is "seeded" by PrP^{Sc} (most likely in the form of aggregates), which induces PrP^{C} to take on the aberrant form. This conversion process is undoubtedly a key event in TSE pathogenesis. However, questions remain as to how or even whether PrP controls replication of the TSE agent and its strain phenotype, contributes to TSE neurodegeneration, and causes heritable forms of human TSE disease. It is certainly a tall order for any single protein to encode all of these different properties, and researchers in the often combative prion field have differing opinions about whether, in fact, PrP^{Sc} does it all. At a recent meeting (*1*), participants discussed how the normal mammalian protein PrP^{C} and its subverted counterpart PrP^{Sc} contribute to the pathogenesis of TSE diseases. Perhaps it was the spectacular setting, maybe it was the great skiing, or maybe it was oxygen deprivation due to the altitude, but some common threads began to emerge detailing how PrP influences TSE pathogenesis.

Strains of TSE agent are distinguished in part by differences in disease-associated pathology in the brain. These pathological changes include spongiosis, neuronal vacuolation, gliosis, and diffuse versus plaque-like PrP^{Sc} deposits. Several groups investigated the relation between PrP^{Sc} and brain pathology. Formation of PrP^{Sc} takes place at the cell surface and/or at some point in the endocytic pathway that shuttles surface proteins into intracellular lysosomes for recycling or degradation (see the figure). Studies in sheep infected with scrapie or bovine spongiform encephalopathy (BSE or mad cow disease) illustrated not only that different sheep scrapie strains could target different cells in the brain, but also that the deposition and size of PrP^{Sc} in BSE- versus scrapie-infected sheep were different. This suggested that different strains of PrP^{Sc} become localized in different cellular compartments (Martin Jeffrey, Lasswade Veterinary Laboratory, Edinburgh). These differences were especially exciting because they could be used to distinguish BSE-infected sheep from scrapie-infected sheep. Interest in such discriminations was heightened by data demonstrating that many sheep genotypes are susceptible to BSE infection (Fiona Houston, Institute for Animal Health, Compton, UK).

In humans, the strain of the agent causing CJD also appeared to influence the extent of pathological changes in the brain: gliosis, spongiform changes, and the pattern of PrP^{Sc} deposition (Fabrizio Tagliavini, Carlo Besta National Neurological Institute, Milan). In transgenic mice, a single mutation in PrP^{C} changed not only the degree of susceptibility of the mice to infection but also targeting of CNS pathology in vCJD infection. This suggested that host cell PrP^{C} is a potent susceptibility factor capable of distinguishing among different TSE strains (Jean Manson, Institute for Animal Health, Edinburgh). In vitro studies also provided evidence that strain-specific differences in PrP^{Sc} may depend on host cell PrP^{C} as well as on the strain of injected PrP^{Sc} (Suzette Priola, Rocky Mountain Laboratories, Hamilton, MT). Thus, it is beginning to appear that strain-specific phenotypes are not necessarily encoded by the PrP^{Sc} molecule alone but can also be determined by the type of cell expressing PrP^{C} and the cellular location where PrP^{Sc} is formed (see the figure).

Studies of the association of PrP^{C} with membranes revealed that both glycosylphosphatidylinositol (GPI) anchor–dependent and anchor-independent modes of attachment may influence PrP^{Sc} formation and propagation between cells. When GPI-anchored in the plasma

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