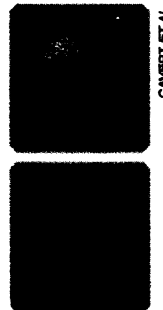


LETTERS

Hard questions

Convergent evolution at the molecular level is said to be one source of some "misleading phylogenetic analyses." Researchers discuss the "sanctuary problem," in which HIV persists in the brain even after it has been eradicated in other organs [yellow indicates concentration of HIV RNA in lymph nodes before (upper) and after (lower) treatment]. The challenge of designing studies to "test" the efficacy of prayer is reconsidered. And the relation between "economic consumption" and "environmental quality," and how these might be defined, is addressed.



"Misleading" Molecules?

In the article "Morphologists learn to live with molecular upstarts" by Michael Balter (Research News, 16 May, p. 1032), one section entitled "Misleading molecules" quotes Colin Patterson as saying that Gavin Naylor's presentation (demonstrating that "wrong" phylogenetic trees can be derived from molecular sequence data) received "the closest thing to a standing ovation." This demonstration, and others like it [for example (1)], should bring only cold comfort to detractors of molecular data, as the emerging message is not that molecular data are invalid in some way. Rather, phylogenetic analyses can be misleading if they do not incorporate our growing knowledge of the variable constraints on evolutionary change at the molecular level. Thus, the section might more appropriately have been entitled, "Misleading phylogenetic analyses in which all characters are given equal weight," as the molecules themselves do not mislead. We see instead human error in the failure to discriminate between character similarity among taxa due to convergence and that due to common descent.

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Treating AIDS Dementia

I read with interest the elegant report by Ashley T. Haase's group (W. Cavert *et al.*,

Reports, 9 May, p. 960) and the accompanying News article by Jon Cohen (9 May, p. 898) concerning the vulnerability of reservoirs of human immunodeficiency virus (HIV) stubborn to new treatments. The work by Haase and his colleagues, as well as related works (1), are crucial to the systemic treatment of AIDS. However, an important issue not dealt with is the reservoir of virus within macrophages and microglia in the brain. HIV-1 enters the brain very early after initial infection (2). The newer triple-drug combination therapies, which include protease inhibitors, are, in general, not capable of crossing the blood-brain barrier and eradicating infection in the central nervous system. Among these drugs, AZT alone may penetrate the brain to some degree, but its effects on the dramatic cognitive decline are manifest in about one-third of patients, who develop so-called AIDS dementia, level off, or fail after about 3 months of treatment (3).

For this reason, the Neurology Core Committee of the AIDS Clinical Trials Group (ACTG), of which I am a member, has designed adjunctive drug strategies to be piggybacked onto the best antiretroviral therapy in an effort to abort or even prevent AIDS dementia. Currently held models of HIV-induced neuronal damage are predominantly focused on neurotoxins that emanate from infected or immune-stimulated brain macrophages and astrocytes, which in turn overstimulate the N-methyl-D-glutamate (NMDA) subtype of glutamate receptor in the brain (2). This leads to excessive Ca^{2+} influx, free radical formation, and neuronal injury or apoptosis. One clinically tolerated NMDA antagonist, memantine, has recently entered a phase-II/III ACTG study, and it is hoped that this form of adjunctive therapy will prove useful to AIDS patients with cognitive decline. After all, who wants to live longer because of

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successful systemic treatment of the disease and yet be demented?

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2. S. A. Lipton and H. E. Gendelman, *N. Engl. J. Med.* **332**, 934 (1995).
3. S. A. Lipton and K. D. Kiebertz, in *The Neurology of AIDS*, H. E. Gendelman, S. A. Lipton, L. G. Epstein, S. Swindells, Eds. (Chapman Hall, New York, in press).

Response: Lipton rightly points out that, quite aside from the question of whether an AIDS sanctuary such as the brain will thwart attempts to eradicate HIV-1, it would be tragic indeed for an individual to suffer neurological complications of infection while antiretroviral therapy successfully controls viral replication in the periphery. We agree that it is important and prudent to continue efforts to develop antiviral agents that cross the blood-brain barrier and to pursue other

strategies that target neuropathological processes in AIDS patients. We also think it is worthwhile to commit coordinated efforts to supplement current tissue repositories with specimens from the nervous system and other potential viral refuges by collecting specimens at appropriate opportunities from persons with HIV infection who are on potent antiretroviral drug regimens. Assay of viral load in these samples would provide considerable insight into the scope of the sanctuary problem.

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Testing the Power of Prayer

J. S. Heilig and Dalmen Mayer (Letters, 9 May, p. 891), commenting on the profile of cardiologist Herbert Benson (W. Roush, *Research News*, 18 Apr., p. 357), discuss earlier approaches to establish objectively the efficacy of prayer in healing but do not mention a double-blind clinical trial using a sequential analysis protocol conducted by the British psychopharma-

cologist C. R. B. Joyce and R. M. C. Welldon (1). Forty-eight patients being treated for chronic psychological or rheumatic disease at two outpatient clinics at the London Hospital were matched in pairs by age, sex, and primary clinical diagnosis. One member of each pair was then assigned by the spin of a coin to the "treatment" group. Prayer groups received a brief abstract outlining the clinical conditions of patients in the "treatment" group (identifying them only by first name and an initial) and were asked to pray over a 6-month period for these patients. Other treatments were continued or given as necessary to all patients. After completion of the 6-month period, the clinical state of each pair of patients was reassessed, and the treatment group (prayer or control) associated with the better clinical outcome in the pair was noted. Joyce and Welldon concluded at the end of their study that there was no significant difference (at a 95% probability level) in the clinical state of patients in the "treatment" and control groups. However, they noted problems in the design and implementation of the protocol that might have influenced the results. The discussion section of the paper provides an interesting overview of the problems of designing and

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