

SCIENCE'S COMPASS

(and frequency) of the *A1* allele to be significantly higher in alcoholics than in people serving as controls. The most recent such analysis of about 1000 alcoholics and 1000 controls had a statistical level of significance of $P < 10^{-7}$ (1).

DRD2 has also been implicated in the abuse of other drugs [see a review (2)] and in nicotine addiction [recently, (3)], with about 50% of smokers carrying the *DRD2 A1* allele (4). Thus, *DRD2* is not an "alcoholism gene" per se, but is likely a reinforcement or reward gene involved in reactions to a variety of abused substances (5).

In any experiment designed to study alcoholism, control subjects should be carefully screened to exclude individuals who use other drugs—and those who show signs of possible alcohol abuse, if not addiction. Otherwise, the inflated *A1* allele in the comparative group could obscure significant association with alcoholism in the study group (6, 7). The "unaffecteds" in the COGA study (8) did not exclude smokers and other drug abusers, common in families with alcoholics. Furthermore, when alcohol-related problems were examined, only 6% of the "unaffecteds" actually showed no symptoms of alcoholism (9). Because of this limited group size, the

COGA authors decided to broaden the definition of "unaffecteds" by including subjects with as many as eight (of a total of nine) "sporadic" symptoms of alcoholism. Because three or more symptoms are required for defining alcohol dependence and a minimum of one symptom for that of alcohol abuse, a large majority of these "unaffecteds" could have contained not only smokers and other drug abusers, but also individuals experiencing significant alcohol problems.

Two studies of sibling pairs, one by a British group (10) and another by Americans (11), found significant linkage of *DRD2* with alcoholism and heavy drinking. In the same journal issue in which the COGA study was published, a quantitative trait loci (QTL) study of mice (12) found linkage between the *DRD2* locus and alcohol consumption, replicating two previous QTL studies of animal models of alcoholism. Mutations in *DRD2* also appear to have other measurable behavioral and physiological correlates [see reviews (1, 13)].

In sum, there is strong evidence, derived from association and other types of studies, that the *DRD2* is an important gene in substance use disorders and neural functioning.

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Testing for Alzheimer's

In his article "Allen Roses: From 'street fighter' to corporate insider" (News & Comment, 15 May, p. 1001), Eliot Marshall notes (p. 1004) that Roses disagreed with a group of experts at Stanford who had concluded that widespread

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An, Z. et al. *Clinical and Experimental Metastasis*, **15**, 184-195, 1997.

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molecular testing for late-onset Alzheimer's disease (AD) is not clinically justified. It is not mentioned that Roses is named as an inventor on a patent (1) claiming exclusive rights to the detection of the *APOE4* allele. The patent, resulting from research funded in part by the U.S. National Institutes of Health, has been licensed by Duke University (where Roses did the research) exclusively to AthenaDiagnostics, Inc. Athena has taken clinical AD testing in-house nationwide and has written to clinical laboratories to stop them from performing *APOE* genotyping for the purpose of diagnosing AD (2).

Like most universities, Duke routinely pays its faculty inventors a healthy share (up to 50% after expenses) of the royalties of licensed patents (3). This situation raises ethical concerns, not the least of which is that those who benefit financially from the performance of genetic testing and screening could be said to have a conflict of interest that might lead to aggressive promotion of those tests (4).

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Haeckel's Embryos, Continued

I am concerned to find that I may have helped perpetuate a Creationist myth, as described by K. Sander and R. Bender (Letters, 17 July, p. 349). The claim that Ernst Haeckel was convicted of fraud was made in *The Times* (1). I relied on that statement in a subsequent publication (2) without seeking a primary source—clearly a mistake on my part. Nonetheless, the core scientific issue remains unchanged: Haeckel's drawings of 1874 (3) are substantially fabricated. In support of this view, I note that his oldest "fish" image is made up of bits and pieces from different animals—some of them mythical. It is not unreasonable to characterize this as "faking." Later editions of Haeckel's drawings were somewhat more accurate, and showed

significant variations among embryos of different species. Sadly, it is the discredited 1874 drawings that are used in so many British and American biology textbooks today.

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CORRECTIONS AND CLARIFICATIONS

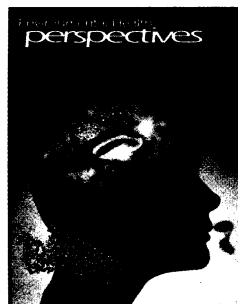
Marcia Barinaga's article "First images show monkey brains at work" (News of the Week, 10 July, p. 149) erroneously stated that Carl Olson of Carnegie Mellon University is working to develop a vertical magnet for monkey research. Olson is using an animal-dedicated magnet that is horizontal, not vertical.

In the Research News article "New clues to alcoholism risk" by Constance Holden (29 May, p. 1348), the affiliation of Ernest P. Noble should have been given as the University of California at Los Angeles.

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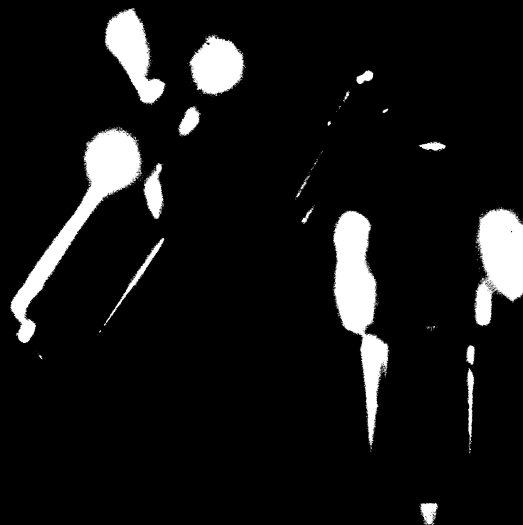
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