LETTERS

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted through the Web (www.letter2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

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A Plea for DNA Banking

FIFTY YEARS ON FROM THE DISCOVERY of the DNA double helix, species and, by extension, global genetic resources are becoming increasingly impoverished. On a large scale, little has been done to consolidate collections of genetic material, and even the vast amount of DNA sequence information collected and available in international depositories encompasses only a tiny proportion of extant biodiversity, largely concentrated around a few model species (*1*).

With predicted climate change and no immediate and drastic change in human behavior, the biosphere will be drastically modified within just a few decades (*2*), with the number of species facing extinction being estimated at a staggering one million by 2050 (*3*). Most current museum taxonomic collections are inadequate for long-term high-quality DNA preservation and extraction, and most curated collections do not organize their programs to address this issue and to house appropriate samples of DNA extracts. An accurate knowledge of Earth's genetic resources will soon be made impossible unless a concerted effort is made to store DNA extracts. Most biodiversity-rich countries are poor in resources, and thus these issues are unlikely to be made priorities at a national level. Nevertheless, we propose that the banking of genetic material be pursued with urgency.

Very few DNA banks have been established. The most comprehensive DNA bank for plants, in terms of phylogenetic coverage, is housed at the Royal Botanic Gardens, Kew, UK, and encompasses to date 20,000 species [(about 6% of all known angiosperms) (*4*)]. No such broad DNA banking program yet exists for animals, and only two nations are actively banking their in-country floras, namely the UK and South Africa, the latter under partnerships funded by the UK government's Darwin Initiative in response to the Rio Summit (*5*).

Implementation of conservation plans is time-consuming, and difficult decisions are made daily regarding those species that should receive priority. We propose here that following the Darwin Initiative's model, funding agencies make it a priority to support DNA banking programs around the world. This is not a solution per se to the disappearance of species, but genetic resources should still be archived for future scientific endeavor and in the process contribute across the planet to much-needed capacity building.

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4. See www.kew.org/data/dnaBank.
5. See www.defra.gov.uk/environment/darwin.

Setting Priorities for Genomic Research

IN THEIR VIEWPOINT "GENOMIC PRIORITIES AND public health" (Special Section on Genomic Medicine, 24 Oct., p. 599), K. R. Merikangas and N. Risch propose that diseases appearing to be "highly amenable to environmental modification" should take low priority in genomic research. Their conclusions ignore the large public health burden of complex genetic diseases like alcohol, nicotine, and other substance abuse disorders, which cost society over $500 billion per year (*1*). Furthermore, addiction is not easily malleable (*2*); approximately 90% of smokers who try to quit relapse within a year, with the majority relapsing within a week (*3*). Twin studies (*4*–*6*) consistently show that genetic contributions for substance dependence account for half the disease variance. Other studies show replication and convergence of genomic data, suggesting association between specific loci and substance dependence (*7*). Potential therapeutic interventions are also emerging from genetic studies. The A118G μ-opioid receptor polymorphism (*8*) shows a preliminary association with therapeutic response to naltrexone treatment for alcoholism, implicating targeted treatment for alcoholics carrying 118G (*9*). These findings justify priority for continued genetic investigation for these prevalent diseases.

Studying drug addiction involves understanding the genetic influences on the intractable behaviors that make treatment and prevention difficult. Studies of behavioral disorders addressing both genes and environment show that genetic information is critical in identifying environmental influences, especially when genetic vulnerability may only manifest under certain environmental exposures (*10*, *11*). Understanding the interplay of genes with environment will best inform us about behavior in general, as well as about the way abused substances target the central nervous system, affect the neural processes responsible for addictions, and associate with co-morbid disorders. Employing the power of genetic studies in understanding the underlying biological, behavioral, and environmental factors will enhance research on etiology, treatment, and prevention for these complex diseases.

The diseases given low priority by Merikangas and Risch affect about 30% of the U.S. population; those affected cannot afford to wait when advances in genetics will have a significant public health impact.

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Response

WE AGREE WITH VOLKOW *ET AL.* THAT substance abuse is a major public health problem; however, their arguments regarding translation of basic research into policy do not reflect the perspectives of epidemiology or public health (*1*). The major source of disagreement between our positions is the importance that they place on the identification of "susceptibility genes" as a basis for prevention and intervention in reducing the public health burden of substance abuse (*2*). Small but powerful and surprisingly rapid shifts in the risk factor distributions of entire populations have been shown to be far more cost-effective than knowledge or modification of either individual-level environmental or genetic factors (*3*).

The two arguments cited to justify gene hunting for substance abuse do not incorporate the multifactorial nature or the obvious environmental influences on substance abuse. It is likely that literally thousands of genes will be involved in the neurobiological, cognitive, emotional, and behavioral effects of drugs. Current strategies to identify genes are unlikely to yield replicable findings or have significant impact on substance dependence if the complexity of this phenotype is not addressed, despite the numerous claims that genes have already been found.

The rationale for identifying genes on the basis of heritability estimates from twin studies of substance abuse does not incorporate findings from other research designs, including family studies (*4*, *5*), prospective cohort studies (*6*, *7*), and adoption studies (*8*), that demonstrate the overwhelming importance of environmental factors in the development of substance use disorders {e.g., greater concordance for substance abuse among nonbiologic than biologic relatives [spouses, peers versus parents, siblings (*8*–*10*)]; greater similarity between twins reared together than those reared apart (*11*); and large cohort differences across very brief time periods (*12*)}. In fact, from an epidemiologic perspective, these studies suggest a pattern more consistent with a contagion or infectious disease model than genetic transmission (*13*).

We do not agree with the contention that gene discovery is critical for the identification of environmental influences on substance abuse. Although this may be true for other disorders, the environmental factors necessary for the development of substance abuse, namely exposure to cigarettes, alcohol, and/or drugs, and their social context, are already known. Even if the promise of genotype-targeted treatments were ultimately realized, only a very small proportion of those who suffer from substance dependence would be expected to receive benefit.

In summary, Volkow *et al.*'s position is inconsistent with the growing consensus of international health policy groups such as the World Health Organization who advocate a shift from the current focus on individual-based risk factor approaches to population-based interventions (*14*) to reduce smoking, binge-drinking, and other harmful health behaviors. The dramatic diminution of smoking behavior in the United States over the past decades is due largely to changes in social and public policy rather than to individual-level interventions (*13*, *15*). Likewise, the promise of "gene therapy" for such behaviors misleads the public about the promise and potential impact of genetic research in alleviating the burden of these epidemics. In fact, promoting the identification of susceptibility genes may even have a negative impact by diminishing the perception of the importance of individual choice in health behavior.

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*This letter represents the position of the authors and does not reflect the official position of the National Institute of Mental Health.

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Questions About Disclosure

IN THEIR POLICY FORUM "DISCLOSURE IN regulatory science" (19 Dec., p. 2073), D. Michaels and W. Wagner overstate the potential problems with privately funded research being used by regulators. Their proposed remedy is more moderate, however, and worthy of broader debate.

Most ominously, they advert to "accounts of… sponsor suppression or termination of research showing adverse effects" in light of the "limited prohibitions" against such behavior. In fact, federal law clearly mandates reporting to the EPA of information that "reasonably supports the conclusion that [a chemical] presents a substantial risk of injury to health or the environment" (*1*). A similar disclosure requirement applies specifically to pesticides (*2*). A manufacturer could also face staggering civil liability for covering up results that indicated adverse effects from its products.

The authors likewise contend that the quality of privately funded research is subject to little or no oversight. All research conducted at the direction of the EPA must be performed according to the Agency's Good Laboratory Practices (GLP) (*3*), and much privately initiated research for submittal to EPA also follows GLP. (By contrast, biomedical research funded by the EPA and NIH does not.) Any privately generated information that an agency relies on or otherwise adopts becomes subject to the Information Quality Act, which requires it to meet quality standards and mandates that it, and any supporting data, be made publicly available subject to confidentiality limits (*4*). And any federal agency has complete access to all information submitted to it, whether or not it is claimed to be confidential business information.

Finally, the authors imply that agencies and the public are unaware of potential conflicts of interest. EPA's Integrated Risk Information System (IRIS), which records most of the Agency's health effects assessments, clearly references the key studies it relies upon, and those entries typically disclose study sponsors. Studies published in the scientific literature virtually always cite funding sources. Much of EPA's data comes from mandated studies, and the source of such reports is clear to the agency.

Michaels and Wagner propose that, for research submitted to the federal govern-

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ment, the submitter disclose known conflicts of interest and indicate whether the researcher was free to publish the results without sponsor interference. In general, this proposal is sound. Indeed, the American Chemistry Council's Long-Range Research Initiative (LRI)—a multi-year, multimillion dollar program of research on basic questions underlying health and environmental risk assessment—has consistently followed such a policy. Research contracts require that investigators publish their results in the peer-reviewed literature regardless of the outcome, the LRI has no approval authority over publications, and investigators must abide by OMB Circular A-110 (*5*) (which requires data from federally funded research to be made public when used by the government). Disclosure of funding and of freedom to publish has the virtue of shifting debates from questions about sponsorship to more appropriate questions about underlying scientific merit.

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References and Notes

1. Section 8(e) of the Toxic Substances Control Act [U.S. Code (U.S.C.) 15, § 2607(e)], quoted above, addresses any chemical substance or mixture.
2. Section 6(a)(2) of the Federal Insecticide, Fungicide & Rodenticide Act [U.S.C. 6, § 136d(a)(2)] requires reporting to EPA of "factual information regarding unreasonable adverse effects on the environment of [a] pesticide."
3. Code Fed. Regul. 40, part 160.
4. U.S.C. 44, § 3516 note, *Fed. Regist.* **67**, 8452 (2002).
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Response

ALTHOUGH HENRY AGREES WITH OUR solution, she is concerned that we have overstated the problem of conflicts in research. The fact that the American Chemistry Council (ACC) has chosen to incorporate protections against sponsor influence into the LRI supports our contention that the problems we raise are real and deserve attention.

Unfortunately, the laws and regulations cited by Henry do not provide adequate protection against sponsor control of research and reporting (*1*). Although the EPA has adverse effects reporting requirements, most of the regulations leave sponsors with considerable discretion to determine, on their own, when new information "reasonably supports the conclusion that [a chemical] presents a substantial risk of injury to health or the environment." Even more problematic is the difficulty in enforcing these reporting requirements. EPA acknowledged the limitations of "self-reporting" and offered an amnesty in the mid-1990s for chemical manufacturers who previously failed to report adverse effects. EPA received

11,000 adverse effects reports—four times the number submitted since passage of the statute 15 years earlier (*2*).

Futhermore, other agencies charged with protecting the public's health—including the Occupational Safety and Health Administration, the Mine Safety and Health Administration, the Consumer Products Safety Commission, and the National Highway Traffic Safety Administration—have no such rules. These agencies do not even have a formal mechanism to inquire who paid for a study submitted for consideration in rule-making, to say nothing of issues related to data analysis and sponsor interference.

The Information Quality Act also provides little protection in this area, because the White House's Office of Management and Budget has exempted from coverage most research produced by regulated parties, while the Data Access Act explicitly applies only to federally funded research, exempting all privately produced research (the source of much data submitted by regulated parties) from its disclosure requirements.

We are grateful for Henry's support of our proposal, and we hope the ACC will join us in suggesting that the protections built into their LRI be extended to all research done by their member companies.

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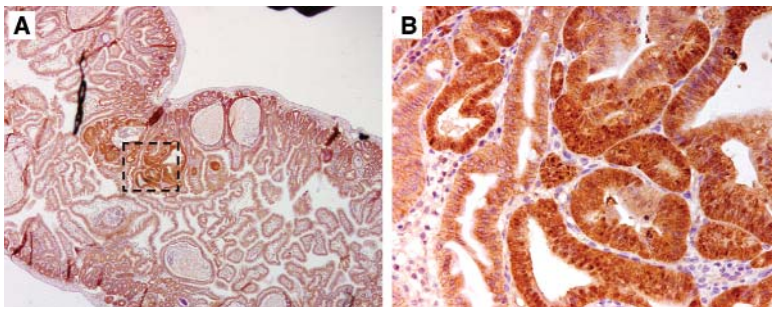
CORRECTIONS AND CLARIFICATIONS

Reports: "Vortex core–driven magnetization dynamics" by S.-B. Choe *et al.* (16 Apr., p. 420). In the first full paragraph of the first column on p. 422, a negative sign was omitted from the description of vortex susceptibility. The corrected text should read "We considered a square vortex of length l = 1 mm, for which the vortex susceptibility has been determined by simulations to be ~4×10^{-5} henries per meter in agreement with experiments (*14*)."

Reports: "De novo crypt formation and juvenile polyposis on BMP inhibition in mouse intestine" by A.-P. G. Haramis *et al.* (12 Mar., p. 1684). There was an error in Fig. 3. Fig. 3B should be an enlargement of the area boxed in Fig. 3A. The corrected figure is shown here.



Perspectives: "After the toll rush" by L. A. J. O'Neill (5 Mar., p. 1481). In the figure, Porin (influenza) is listed as a virus, but it is actually a bacterium. In the figure legend, the acronym RSV should be defined as respiratory syncytial virus, not Roux sarcoma virus.