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.submit2science.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.

Disclosure of Clinical Trials in Children

AFTER E. MARSHALL'S NEWS STORY ON THE drug industry's burying unfavorable clinical data ("Buried data can be hazardous to a company's health," E. Marshall, News of the Week, 11 June, p. 1576), there have been interesting outcomes. GlaxoSmithKline published full reports of clinical tests on paroxetine in children on its Web site and announced that, in the future, a clinical trial register will be created and made accessible to doctors and the public. In the meantime, another company (Foster Laboratories) was charged with "publication bias" by the *New York Times* for two antidepressant drug trials in children (*1*), suggesting the need for an urgent solution to this lack of transparency.

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Many attempts at creating publicly accessible, international clinical trial registries have been made to overcome issues related to the inaccessibility of trial information, such as the *meta*Register of Controlled Trials (http://controlled-trials.com/mrct). The pediatric population, like other subpopulations, is more strongly affected by limits to information, and this led to the creation of an international, pediatric clinical trial register in 2003. The project, the European register of clinical trials on medicines for children—Drug Evaluation in Children (DEC-net; www.dec-net.org)—is the first clinical trial register dealing with a specific population. The project is supported by the European Community as part of its Fifth Framework Programme. The DEC-net register's main objective is to help identify the few pediatric studies being carried out to help researchers and health care workers increase their knowledge on drug therapies derived from them. DEC-net also represents a resource for planning new studies, promoting collaboration between researchers, facilitating patient access to and recruitment into trials, preventing trial duplication and inappropriate funding, and identifying the therapeutic needs of children who remain neglected (*2*). The register will be freely accessible, and the information will be displayed in two interchangeable formats: a simple one for parents/lay public and a more advanced one for health professionals.

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References
1. B. Meier, "Drug maker acknowledges some negative test results," *N.Y. Times*, 26 June 2004, p. C2.
2. K. Dickersin, D. Rennie, *JAMA* **290**, 516 (2003).

Antidepressants' Use in Anorexic Girls

THE USE OF SELECTIVE SEROTONIN REUPTAKE inhibitor (SSRI) antidepressants in children is debated because of the potential risk of suicide ("Buried data can be hazardous to a company's health," E. Marshall, News of the Week, 11 June, p. 1576; "Volatile chemistry: children and antidepressants," J. Couzin, News Focus, 23 July, p. 468). In our work with adolescent girls suffering from anorexia nervosa, we have noticed that at least 50% are routinely prescribed SSRIs. Yet SSRIs have no effect on the psychiatric symptoms of anorexia, and there is no evidence that they affect outcome favorably (*1*). In addition, we have repeatedly [most recently in (*1*)] pointed out that serotonin, the neurotransmitter system that is stimulated by SSRIs, inhibits food intake, gonadotropin secretion, and sexual behavior; decreases body temperature; and makes learning difficult. These are highly undesirable effects not only in anorexic adolescents but in all developing women. Hence, there are many reasons other than the risk of suicide why SSRIs should not be used in young women.

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Reference
1. C. Bergh, J. Ejderhamn, P. Södersten, *Curr. Opin. Pediatr.* **15**, 344 (2003).

SSRIs in Children and Suicide

IN HER ARTICLE "VOLATILE CHEMISTRY: CHILDREN and antidepressants" (News Focus, 23 July, p. 468), J. Couzin writes about the complex situation regarding the use of selective serotonin reuptake inhibitors (SSRIs) in children, including the possible initiation of suicidal acts by SSRIs, concealment by industry of negative data, and the problematic state of diagnosis of childhood depression.

I am quoted as dismissing the SSRI fuss as "a tempest in a teapot." My point was that the available data showed that the ambiguous ratings considered putatively suicidal occurred before treatment in less than 1% of the children studied. After SSRI treatment, this approximately doubled, but it is still not clear if this "signal" is statistically significant or clinically meaningful. It is still a very minority "signal." No actual suicides occurred. The furor for immediate action is premature. It should also be noted that much public indignation comes from those who believe that any medical treatment of mental illness should be condemned. Severe depression is a serious illness and close therapeutic monitoring is necessary. This applies to all forms of treatment.

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Disparities in Cancer Funding

IN HIS EDITORIAL, "PERCEIVED THREATS AND real killers" (14 May, p. 927), R. I. Glass makes important distinctions between the health impact and scientific effort devoted to common and often controllable infectious agents such as influenza and rotaviruses and rare and unpredictable agents such as *Ebola* virus. Similar comparisons between perceived threats, real killers, and scientific emphasis could be made with human cancers. Although the threat of developing common cancers such as breast or prostate cancer is real and not perceived, the cancer that is most proficient at killing humans is lung cancer and the etiologic agent is tobacco. Tobacco is responsible for ~30% of all cancer deaths (*1*), and deaths from lung cancer in the United States exceed those of breast cancer, colorectal cancer, and prostate cancer combined (*2*). Yet the amount of dollars spent per cancer death by funding agencies has

historically favored breast and prostate cancers over lung cancer (sixfold less spent per lung cancer death than per prostate cancer death and ninefold less per lung cancer death than per breast cancer death for National Cancer Institute funding in 2001). The disparity between funding and mortality is consistent with a low level of commitment from the scientific community to study lung cancer: The number of investigators studying rare cancers such as those derived from bone marrow exceeds the number studying the biology of tobacco and lung carcinogenesis. State governments also appear not to perceive tobacco-related illnesses as a real threat because many have opted to use hundreds of millions of dollars in tobacco settlement money to balance skewed budgets and not to address tobacco addiction that fuels these illnesses. Important health issues such as diarrhea, influenza, and lung cancer may not be sexy, but they deserve the public's attention and commitment from policymakers and the scientific community.

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References

1. J. Mackay, M. Eriksen, *The Tobacco Atlas* (World Health Organization, Geneva, Switzerland, 2002).
2. A. Jemal *et al.*, *CA Cancer J. Clin.* **54**, 8 (2004).

The Case Against Stem Cell Research

IN HIS LETTER "HUMAN BEING REDUX" (16 April, p. 388), M. S. Gazzaniga constructs his defense of human embryonic stem cell research around his difficulty in thinking of a "miniscule ball of cells in a petri dish, so small that it could rest on the head of a pin" as a human being. This rhetoric may mislead the lay public, but scientists should recognize that the size or the developmental stage does not separate the embryo from the human being. The embryo and the adult are different stages in the development of the human being.

The embryo possesses more than just "the genetic material for a future human being." In ways that we do not yet fully understand, the embryo is organized so that it is capable of executing a developmental program and growing into what Gazzaniga will admit is a human being. This capability distinguishes the embryo from a differentiated cell in culture. Gazzaniga suggests that, because an embryo that is not implanted in the uterus of a woman will not be able to execute this program, the embryo has no moral status. I think he has it backwards. The scientist who destroys an embryo to harvest stem cells commits a wrong, for the scientist has denied that embryo the opportunity to grow into an adult.

My moral objections to human embryonic stem cell research are not assuaged by severing its connection to reproductive cloning. In my judgment, the developmental events leading from fertilized ovum, to blastula, to embryo, to fetus, to fully formed adult constitute a continuum. It is artificial, and even self-serving, to declare the embryo "not yet human" before some point, and to declare that we may do with that embryo as we will.

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Problems in FBI mtDNA Database

IN HIS EDITORIAL "FORENSIC SCIENCE: oxymoron?" (5 Dec. 2003, p. 1625), D. Kennedy wonders why the U.S. National Institute of Justice has regularly resisted comprehensive evaluations of the science underlying forensic techniques. A possible answer can be found in the poor quality of the forensic human mitochondrial DNA

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(mtDNA) database used by the Federal Bureau of Investigation (FBI), which is included in the Scientific Working Group on DNA Analysis Methods (SWGDAM) database (*1*).

A thorough inspection of the original "African-American" database, which has been contributed by the FBI laboratory, reveals a number of major deficiencies. Among 1148 entries, each comprising two separately sequenced segments from the mtDNA control region, we detected as many as five artificial combinations of totally unrelated mtDNA segments stemming from different samples, which suggest fatal sample mix-up in the lab or during data transcription (*2*). The most striking hybrid (USA.AFR.000942) we found combined segment I from an African haplogroup (referred to as L1b) (*3*) with segment II from a Native American haplogroup (called C1) (*4*).

Recently, the FBI attempted to correct this database by searching for clerical errors: only nine were spotted (*1*), three of which (in the "Hispanic" database) we actually communicated to Bruce Budowle (FBI laboratory) by way of example. Since only three of six clear recombinants (*2*) have been discovered by the FBI, one cannot exclude the possibility of mixups during sample-handling in the remaining instances, which could only be corrected through thorough resequencing of the original samples.

Several obvious clerical errors still remain in the revised database, such as the 100 base-pair shift that hit position 16126 in USA.CAU.000272. Moreover, biochemical problems are manifest, for example, in the "Greek Caucasian" series, where a large amount of undetermined nucleotides are recorded—up to six in one sequence (GRC.CAU.000056). These findings suggest that several parts of the SWGDAM database have not been subjected to the necessary scrutiny.

Since as early as 2001, the field of forensics has known (*5*–*7*) that many published mtDNA databases are of poor quality, obviously affected by contamination or sample mix-up, sequencing artifacts due to biochemical problems (yielding sporadic phantom mutations), misreading of automated sequencer outputs, and inadvertent documentation in print or in silico (*6*). These adverse

TECHNICAL COMMENT ABSTRACTS

COMMENT ON "Inhibition of Hepatitis B Virus Replication by APOBEC3G"

Christine Rösler, Josef Köck, Michael H. Malim, Hubert E. Blum, Fritz von Weizsäcker

Turelli *et al*. (Brevia, 19 March 2004, p. 1829) showed that APOBEC3G targets hepatitis B virus (HBV) pregenomic RNA packaging, yet significant nucleotide changes in newly synthesized HBV DNA were not detected. We found that this phenotype is cell line–dependent. APOBEC3G can edit a minority of HBV genomes and may contribute to the emergence of variants.

Full text at www.sciencemag.org/cgi/content/full/305/5689/1403a

RESPONSE TO COMMENT ON "Inhibition of Hepatitis B Virus Replication by APOBEC3G"

Priscilla Turelli, Stéphanie Jost, Bastien Mangeat, Didier Trono

The finding that APOBEC3G can occasionally mutate the HBV genome supports a role for editing in the genetic variability of this pathogen. We additionally show that HBV can be blocked by the related cytidine deaminase APOBEC3F. Both enzymes, and perhaps other APOBEC family members, may thus influence HBV-induced disease.

Full text at www.sciencemag.org/cgi/content/full/305/5689/1403b

effects could be directly observed in the most recent ring tests among European forensic laboratories (*8*).

A recent European initiative (European DNA Profiling Group, EDNAP) has fully addressed the notorious problems in forensic mtDNA analysis (*8*) by promoting the EDNAP mtDNA population database (EMPOP) project. EMPOP, currently based on cooperation between 33 forensic DNA laboratories worldwide, features fully automated error-free transcription processes and other technical improvements. Moreover, the DNA samples will be permanently linked to the corresponding raw data and database entries, so that present data are open to critical reexamination and future refinement.

In resisting comprehensive evaluations, the U.S. National Institute of Justice has certainly backed up the FBI in their advertising of the forensic utility of the SWGDAM database and thus inhibited the generation of a new reliable mtDNA database in the United States.

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References

1. See www.fbi.gov/hq/lab/fsc/backissu/april2002/miller1.htm.
2. H.-J. Bandelt, A. Salas, S. Lutz-Bonengel, *Int. J. Legal Med.*, in press.
3. A. Salas *et al.*, *Am. J. Hum. Genet.* **71**, 1082 (2002).
4. H.-J. Bandelt *et al.*, *Ann. Hum. Genet.* **67**, 512 (2003).
5. H.-J. Bandelt, P. Lahermo, M. Richards, V. Macaulay, *Int. J. Legal Med.* **115**, 64 (2001).
6. A. Röhl, B. Brinkmann, L. Forster, P. Forster, *Int. J. Legal Med.* **115**, 29 (2001).
7. C. Dennis, *Nature* **421**, 773 (2003).
8. W. Parson *et al.*, *Forensic Sci. Int.* **139**, 215 (2004).

CORRECTIONS AND CLARICATIONS

News Focus: "New dead zone off Oregon coast hints at sea change in currents" by R. F. Service (20 Aug., p. 1099). The location given for the Hatfield Marine Science Center was incorrect. The center is in Newport, Oregon, not Newport, Rhode Island.

NetWatch: "DNA surfing" (6 Aug., p. 759). Exons should have been identified as coding DNA and introns as noncoding DNA.

Policy Forum: "Genomic research and human subject privacy" by Z. Lin *et al.* (9 July, p. 183). In the figure, the word on the colored arrow should be "relationships."

Editors' Choice: "Tsunami and its shadow" (11 June, p. 1569). This item indicated that tsunamis travel slowly in the open ocean. This is incorrect; tsunamis travel fast in open water and slow down as they approach the shore.