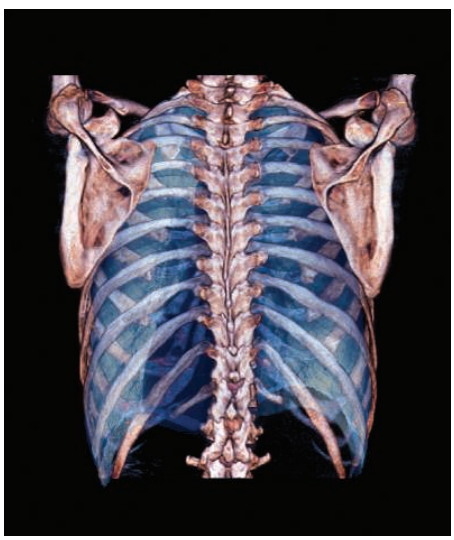
LETTERS

edited by Jennifer Sills

The Cost Benefits of Early Detection



IN HIS NEWS FOCUS STORY ("A BRUISING battle over lung scans," 2 May, p. 600), E. Marshall reports on the issue of screening smokers and patients at high risk for lung cancer with the use of computed tomography (CT)—an x-ray technique that visualizes internal structures in cross section. Opponents object to this procedure because it is "costly." Although conventional x-ray screening was dismissed in the article, it is an economical first step, and if suspicious indications are seen, it should be followed by a CT scan. It is possible, or even probable, that this would allow early detection and surgical removal of the cancer followed by a single course of chemotherapy. This management is not costly compared with extensive, and often futile, chemotherapy at later stages of the disease.

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Policy Forum Offered New Ideas

WE WISH THAT THE LETTER BY E. C. ELLIS ("Environmental revolution starts at home," 20 June, p. 1587), which we did not see prior to publication, had been based on a more careful reading of our Policy Forum ("Revolutionizing China's environmental protection," 4 January, p. 37). The main message of his Letter is that other countries have affected China's environment and that they should share responsibility for its environmental improvement. We certainly agree, as witnessed both by the Policy Forum that he criticizes and by our previous publication on these issues (*1*).

The Letter by Ellis also states that our suggestion to reform China's environmental governance is "nothing new." However, the reference used to support this claim (*2*) is 15 years old and does not address reforming the administrative system, as we did in our Policy Forum. Our article also provides new perspectives that reflect the current status of China's environment and governance. We understand that it was considered sufficiently new by the Chinese government that it immediately became the subject of a special report for high-level government leaders by China's official Xinhua News Agency. Following its publication, China's State Environmental Protection Administration was promoted to the Ministry of Environmental Protection (*3*), and environmental performance has been increasingly used as a criterion for evaluating government leaders [(e.g., (*4*)]. We also stressed the need to integrate multiple approaches at local to global levels, because no single approach at one location alone is sufficient to overcome complex environmental challenges.

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2. V. Smil, *China's Environmental Crisis: An Inquiry into the Limits of National Development* (M. E. Sharpe, Armonk, NY, 1993).
3. China's Ministry of Environmental Protection, www.sepa.gov.cn/xcjy/zwhb/200803/t20080327_119735.htm (2008) (in Chinese).
4. Xinhua News Agency, www.gov.cn/jrzg/2008-04/03/content_936002.htm (2008) (in Chinese).

Survey Says: Name a Role Model

"SCIENCE OFF THE AIR" (RANDOM SAMPLES, 28 March, p. 1741) analyzes a survey's results without paying attention to the actual question asked. The article discusses whether Americans "can" or "cannot" name living scientists. You would expect, then, that the survey question actually asked the respondents to name a living scientist. In fact, it asked "...who would you say are the science role models for the youth of today in America?" (*1*). The question did not ask for a specific person, it did not ask for a living person, and it did not ask for a scientist. It asked for "science role models." Why can't the life and career of a deceased scientist (such as Albert Einstein) serve as a model for today? Why can't an advocate of science (such as Al Gore) be a science role model for the youth of America, most of whom will not become scientists but will affect science through their votes? These were two common and entirely appropriate answers to the survey question, but are treated as disturbing by the article.

As a chemist, I would have no difficulty thinking of names of living scientists, but for a survey question asking about science role models of young Americans, I would probably pick "teachers." It would be interesting to see the results of a survey asking

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Americans to name a living scientist, and it might well be disappointing, but that question was not asked in the survey. The survey results were interesting enough without sloppy analysis.

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Reference

1. "The state of science in America," survey conducted by Harris Interactive for the Museum of Science and Industry, Chicago, IL (2008); www.stateofscience.org.

Gene Mutations and Cognitive Delay

WE CONGRATULATE T. WALSH *ET AL.* FOR A beautifully designed and executed study ("Rare structural variants disrupt multiple genes in neurodevelopmental pathways in schizophrenia," Reports, 25 April, p. 539). The demonstration that the frequency of gene deletions and duplications is elevated in schizophrenia as well as in autism and many forms of mental retardation must raise suspicions that such genomic variants are not really specific for a particular disease. Buried in the Supporting Online Material is the astonishing fact that 47% of the patients with poor cognitive function (IQ < 80) had these variants, compared with only 11% of the patients with normal IQ. Poor cognitive function is a common feature of these developmental disorders and is associated with similar anatomical anomalies across a range of disorders (*1*–*3*). Perhaps genomic deletions and duplications have a nonspecific effect—restricting the flexibility of coping responses during development, constraining neuroplasticity, and rendering cognitive function more dependent on intrinsic neurobiology.

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1. C. M. Leonard *et al.*, *Biol. Psych.* **46**, 374 (1999).
2. C. M. Leonard, M. Eckert, B. Givens, V. Berninger, G. Eden, *Brain* **129**, 3329 (2006).
3. C. M. Leonard *et al.*, *Neuropsychology* **22**, 147 (2008).

Response

WE AGREE WITH LEONARD AND KULDAU THAT the association between cognitive delays and rare structural mutations in our sample is striking, although the numbers are very small. Of the 15 patients with schizophrenia who were diagnosed with cognitive delays by full assessment, 6 carried chromosomal deletions or duplications. These mutations included some of the largest deletions and duplications that we observed. The co-occurrence of schizophrenia and intellectual deficits in these patients may reflect dosage effects of more than one gene in a large genomic region—i.e., a contiguous gene effect. If so, then the smaller genomic copy number variants that involve individual genes may have effects more specifically related to psychosis.

The neurodevelopmental impact of any one structural mutation can vary remarkably among individuals. For example, in the Scottish pedigree harboring the *DISC1* translocation, 29 translocation carriers presented variously with schizophrenia or bipolar disorder or major depressive disorder or no mental illness (*1*). Just as individuals with different neuropsychiatric illnesses may harbor mutations in the same gene, individuals with the same disorder may carry different mutations in the same gene or in different genes in convergent pathways. The elucidation of critical pathways disrupted in affected individuals will contribute substantially to our understanding of psychopathology and provide important targets for treatment development.

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TECHNICAL COMMENT ABSTRACTS

Comment on "Magnetic Resonance Spectroscopy Identifies Neural Progenitor Cells in the Live Human Brain"

Jeffrey C. Hoch, Mark W. Maciejewski, Michael R. Gryk

Manganas *et al*. (Reports, 9 November 2007, p. 980) used nuclear magnetic resonance spectroscopy to identify a biomarker of neural progenitor cells. However, their analysis relies on spectral processing methods that are known to be problematic. Absent detection using alternate methods of spectrum analysis or controls to quantify the false discovery rate, their conclusions may be premature.

Full text at www.sciencemag.org/cgi/content/full/321/5889/640b

Comment on "Magnetic Resonance Spectroscopy Identifies Neural Progenitor Cells in the Live Human Brain"

Seth D. Friedman

Manganas *et al*. (Reports, 9 November 2007, p. 980) used a metabolic biomarker identified in vitro to characterize the existence of neural progenitor cells in vivo. Although their detailed experiments and general approach are laudable, aspects of their magnetic resonance spectroscopy data and analyses raise questions about their results.

Full text at www.sciencemag.org/cgi/content/full/321/5889/640c

Comment on "Magnetic Resonance Spectroscopy Identifies Neural Progenitor Cells in the Live Human Brain"

Jacobus F. A. Jansen, John D. Gearhart, Jeff W. M. Bulte

Manganas *et al*. (Reports, 9 November 2007, p. 980) reported the discovery of a biomarker specific for neural progenitor cells detectable using magnetic resonance spectroscopy. A new algorithm was developed to extract the biomarker from noisy in vivo data. We question how this algorithm was validated, because the biomarker overlaps with peaks from nonspecific lipid signals.

Full text at www.sciencemag.org/cgi/content/full/321/5889/640d

Response to Comments on "Magnetic Resonance Spectroscopy Identifies Neural Progenitor Cells in the Live Human Brain"

Petar M. Djurić, Helene Benveniste, Mark E. Wagshul, Fritz Henn, Grigori Enikolopov, Mirjana Maletić-Savatić

We reported on a neural progenitor cell biomarker, a lipid-based metabolite enriched in these cells, which we detected using spectroscopy both in vitro and in vivo, and singular value decomposition–based signal processing. The study provided an outline of our computational methodology. Herein, we report more extensively on the method of spectrum analysis used, demonstrating the specificity of our findings.

Full text at www.sciencemag.org/cgi/content/full/321/5889/640e

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 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.

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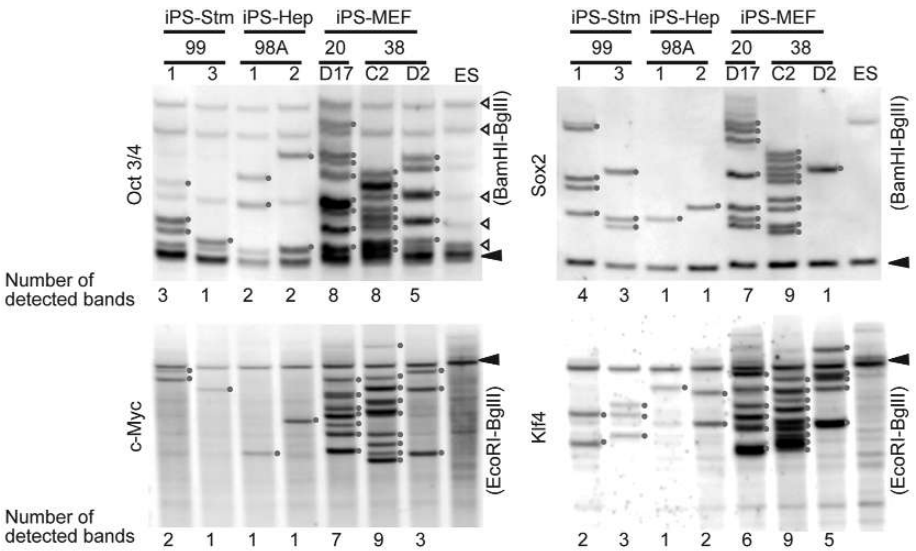
CORRECTIONS AND CLARIFICATIONS

Reports: "Generation of pluripotent stem cells from adult mouse liver and stomach cells" by T. Aoi *et al*. (1 August, p. 699). After publication of the *Science* Express version of our Report, it was brought to our attention that the number of integration sites shown at the bottom of the Southern blot of Fig. 3 differs from the number of visible bands. In addition, we found that genomic DNA of cell line iPS-Hep 98A2 was contaminated with DNA containing additional retroviral integrations. The incorrect version of Fig. 3 has been published in both the online *Science* Express version and the printed version of the paper. The correct Fig. 3, including Southern blots with lower background and with uncontaminated DNA of iPS-Hep 98A2, is shown here. In this corrected figure, corresponding adjustments have been made to the number of integration sites as indicated at the bottom of the blot. The numbers of insertion sites for iPS-Hep/Stm versus iPS-MEF range from 1 to 4 and 1 to 9, respectively (as opposed to 1 to 4 versus 1 to 12, as reported in the *Science* Express and printed versions of the manuscript).

Some errors present in the *Science* Express version of the paper are corrected in the print version and associated Supporting Online Material (SOM): the order of transgenic mouse crosses and greater explanation provided for mouse chimerism designated as "ND" (not determined) in table S2. (We thank Dr. Shi V. Liu, Eagle Institute of Molecular Medicine, for these clarifications.)

A revised version of the SOM is also available (www.sciencemag.org/cgi/content/full/1154884/DC2). Figures S5, S6, S8, and S9 reported data skewed by the contaminated DNA in the original inverse PCR experiments. We have repeated these experiments with uncontaminated DNA. The corrected versions of figs. S5, S6, S8, and S9, eliminating five integration sites that had been present due to iPS-Hep98A2 contamination, are shown in the revised SOM. In addition, the sequence of the primer Oct3/4R2 is 5′-AGGTGATCCTCTTCTGCTTCAG-3′, as opposed to 5′-TCCAATAAACCCTCTTGCAGTT-3′ described in the SOM.

The numbers of integration sites identified by Southern blots (Fig. 3) and inverse PCR (figs. S5 to S9) do not exactly correspond as a result of pseudogenes and overlapping bands or bands that are too big or too small for detection by Southern blot. Our Report stated that the generation of iPS-Hep and iPS-Stm cells does not require retroviral integration into specific sites. This conclusion is based on the data from four cell lines, so a more extensive analysis is needed to confirm this conclusion.



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Survey Says: Name a Role Model
Michael R. Webb (August 1, 2008)
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Editor's Summary

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