LETTERS

edited by Etta Kavanagh

In Support of Academic Freedom

WE, THE MEMBERS OF THE EXECUTIVE COMMITTEE OF THE INTERNATIONAL HUMAN RIGHTS Network of Academies and Scholarly Societies (Network), oppose renewed initiatives that support an academic boycott of Israeli academic institutions. We also oppose Israeli restrictions on Palestinian students that prevent them from studying at institutions of higher education in Israel, the West Bank, and abroad. We call on national academies affiliated with our Network to do the same.

We reiterate our belief in “the free exchange of ideas and opinions among scientists and scholars in all countries,” which thereby stimulates “the development of collaborative educational, research and human-rights endeavors within academies and the institutions with which they are affiliated.” Boycotts “deny our colleagues their rights to freedom of opinion and expression; interfere with their ability to exercise their bona fide academic freedoms; inhibit the free circulation of scientists and scientific ideas; impose unjust punishment,” and impede “the instrumental role played by scientists and scholars in the promotion of peace and human rights” (1).

We also oppose Israeli restrictions on Palestinian students such as the ban imposed in 2000 that prevents all Palestinian students in Gaza from traveling to the West Bank to study, and a statement earlier this month by the Israeli military that it will continue to prevent Gaza students from studying in Israel. Additionally, a recommendation by the Israeli Supreme Court that the Ministry of Defense submit criteria for allowing Palestinian students from the West Bank to study in Israel has repeatedly been delayed to the point that West Bank residents, still banned from studying in Israel, now risk missing Israeli university application deadlines for the coming academic year.

We reiterate the hope expressed in our 6 November 2006 statement to the Israeli authorities (2) that their “policy of academic exclusion will be promptly reversed.” In that same statement, we joined the Israel Academy of Sciences and Humanities in opposing “any measures, by any government, restricting or impairing the ability of scientists and students to carry out their scientific work and to discharge their scientific or academic responsibilities.” We also agree with four Israeli university presidents and a number of prominent intellectuals who recently wrote that “[b]locking access to higher education for Palestinian students from Gaza who choose to study in the West Bank casts a dark shadow over Israel’s image as a state which respects and supports the principle of academic freedom and the right to education” (3).

Lastly, we recall and continue to support the joint statement of cooperation, signed at our Network’s May 2005 meeting by Sari Nusseibeh and Menachem Magidor, presidents of Al-Quds University and Hebrew University, respectively, that said, “Our disaffection with, and condemnation of acts of academic boycotts and discrimination against scholars and institutions, is predicated on the principles of academic freedom, human rights, and equality between nations and among individuals. We therefore call upon academies here and worldwide to act in support of our mission, as one which might allow for ending our shared tragedy rather than prolonging it (4).

EXECUTIVE COMMITTEE OF THE INTERNATIONAL HUMAN RIGHTS NETWORK OF ACADEMIES AND SCHOLARLY SOCIETIES, ARJUNA ALUWIHARE (SRI LANKA), CLAUDE COHEN-TANNoudji (FRANCE), ABDALLAH S. DAAR (OMAN/CANADA), FRANÇOIS JACOB (FRANCE), BELITA KOILER (BRAZIL), IDA NICOLAISEN (DENMARK), JOHN POLANYI (CANADA), ALEKNA ŠELIH (SLOVENIA), PIETER VAN DIJK (THE NETHERLANDS), EDOARDO VESENTINI (ITALY), TORSTEN WIESEL (USA), CAROL CORILLON (EXECUTIVE DIRECTOR)

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References and Notes
3. The presidents of Ben-Gurion University (Rivka Carmi), the Hebrew University (Menachem Magidor), Haifa University (Aharon Ben-Zeev), the Technion (Yizhak Apel og), and a group of Israeli authors, including Amos Oz, A. B. Yehoshua, David Grossman, Nathan Zach, Ariel Hirschfeld, Agi Mishol, and Yitzhak Laor (see www.gisha.org/index.php?intLanguage=2&intItemID=426&intSiteSN=113).
4. The full text can be found in the Proceedings of the meeting: www.nap.edu/catalog/11740.html.

Problems with Genome-Wide Association Studies

IN THEIR NEWS FOCUS ARTICLE “CLOSING THE net on common disease genes” (11 May, p. 820), J. Couzin and J. Kaiser present an optimistic appraisal of genome-wide association (GWA) studies. Within the past year, Science has published results from seven GWA studies for obesity, cardiovascular disease, and type II diabetes (1–7). We would like to discuss three aspects of GWA studies.

First, of the seven GWA studies published in Science, four (1–4) reported as significantly associated with the phenotype under study either a single genetic variant or a single cluster of highly correlated genetic variants. The other studies claimed four (5), five (6), and three (7) new genetic associations. The phenotypes studied are all considered “complex”; thus, we would expect multiple genetic factors, environmental factors, and interactions among those factors to be associated with the phenotype. Furthermore, GWA studies are claimed to be “hypothesis-generating.” Given the substantial cost of GWA studies, is the generation of so few hypotheses a good return for the investment?

Second, readers of GWA studies need to be
careful to distinguish the total number of individuals studied from the number of individuals studied in the initial screen. For example, despite a total sample size of >23,000 individuals, the initial screen in McPherson et al. (4) included 322 cases and 312 controls, which is insufficient to powerfully interrogate small-to-modest effect sizes using 100K SNP arrays. The power to generate hypotheses derives from the sample size of the initial screen, not from any follow-up samples collected to test replication.

Third, an oft-cited problem with genetic association studies is the failure to replicate (8, 9). If common diseases are associated with common risks, then replication across populations would be expected. However, if common diseases are associated with population-specific risks, then failure to replicate across populations would be expected. Under the latter hypothesis, the failure to replicate does not necessarily imply that the original finding was a false positive; rather, it could indicate a population-specific risk. The implication is that we may have hastily discarded previous findings as false positives under the hypothesis of common risks instead of recognizing evidence supporting the hypothesis of population-specific risks. To achieve the clinical goal of personalized medicine, family data may be more informative than population data for identifying individual risks resulting from a complex combination of genetic and environmental factors and interactions (10).

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References

The recent News Focus article “Closing the net on common disease genes” (11 May, p. 820) on genome-wide association (GWA) studies presents a very optimistic picture of what lies ahead for discovering genes that predispose to complex diseases. Although GWA studies hold substantial promise, the reality is more complicated than the results presented in the article would make it appear.

First, unlike the examples described, not all GWA results replicate consistently. For example, Parkinson’s disease and obesity GWA stud-
ies have not been as successful as the GWA studies discussed. For the Parkinson’s disease GWA reported in 2005 (1), four studies failed to replicate the original findings (2–5), and a putative obesity gene reported in 2006 (6), using the Framingham study samples mentioned in the article, similarly failed to replicate (7–10). The fact that results replicate in some but not all studies is reminiscent of earlier candidate gene studies and conclusions should be similarly cautious (11, 12).

Second, it is unlikely that the majority of genetic risk in most complex diseases results solely from the effects of individual variations, as is usually implied in the GWA papers. Rather, an interplay of many modest genetic and environmental influences is much more likely for most common diseases (13). Under this scenario, failure to detect and replicate significant findings may be a consequence of epistatic interactions, because only a small part of the risk may be represented by any single variation (12).

Lastly, selecting predisposing SNPs solely on the basis of the most extreme P values (even after extensive data cleaning), as is usually done in GWA studies, may be extremely misleading because the most extreme P value alone is an inadequate predictor of true effects. Using only P values tells us the probability of finding such an event, not the biological importance of the event. For example, in the recent GWA studies for type 2 diabetes, PPAR-γ, one of the best replicated genetic effects for this phenotype, has a P value of 0.83, 0.019, 0.0013 in the individual studies and a value of 1.7×10^{-6} in the combined analysis of over 32,000 subjects (14–16). It is unlikely that this gene would be highlighted were it not for prior knowledge. Thus, although we may revel in the obvious successes, we must not be misled that GWA studies are a panacea.

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.
What Makes a Book a Work of Science?

At the end of Michael Shermer’s review of Richard Dawkins’s book The God Delusion (“Arguing for atheism,” Books et al., 26 Jan., p. 463), we find the following statement: “Dawkins’s latest book deserves multiple readings, not just as an important work of science, but as a great work of literature.”

The literary merits of this work are for others to judge. The assertion that the book is science is my concern. Science makes observations of the natural world and constructs testable models that explain these data. I would ask my colleagues: Where is the science in this text? What data make it a scientific work?

Perhaps it could then be considered a work of scholarship in philosophy. In that case, we would expect references to primary sources and reasoned criticism, taking into account the latest developments in the field. Consider chapter 3, where his refutation of Thomas Aquinas’s five ways reveals that Dawkins has read tertiary sources, if that, and makes common mistakes regarding what Aquinas was arguing (i.e., “design” as opposed to “governance”). He could have, for instance, used a recent discussion of the five ways [e.g., (J)] to correct his mistakes and bolster his critique, and that would have at least been scholarship.

So if the book contains no data and lacks scholarship, we must question the author’s and the reviewer’s credibility on this topic. For the reviewer to characterize such a book as science is disingenuous to the extreme. This is exactly the kind of statement, especially in an AAAS publication, that confuses the real issues in science and religion. How is it that these scientists and this respected journal have forgotten their own standards?

Martinez Hewlett
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Reference

Response
Martinez Hewlett holds a narrow view of what constitutes a work of science—primary research only, secondary sources cited only in discussion of the primary research. To that extent, only the type of articles that are published in the peer-reviewed sections of journals like Science would constitute real science, with everything else relegated to mere popularization. Were this the case, of course, it would obviate many of the greatest works in the history of science, from Charles Darwin’s The Origin of Species to Jared Diamond’s Guns, Germs, and Steel. If these are not works of science, then what are they?

They are higher-order works of science—synthesizing, integrating, and coalescing primary works of science into a unifying whole with the goal of testing a general theory or answering a grand question. This is what Richard Dawkins has done in The God Delusion, addressing what has to be the grandest question of all—God’s existence. Dawkins synthesizes, integrates, and coalesces hundreds of experiments, studies, hypotheses, models, and theories to provide a reasoned answer to the God question. One may disagree with Dawkins’s conclusions, but if that is the case, then one must specify which experiments, studies, hypotheses, models, and theories that he or she thinks do support the God hypothesis. The fact that Dawkins did not cite this or that theologian or philosopher favored...
by the reader or reviewer is not his problem. The God Delusion is not intended to be a comprehensive scholarly monograph listing every book and article ever written on the subject. For a science book written for a general audience, The God Delusion provides more than enough references to primary sources to provide most readers with the terms of the debate and the best arguments on both sides.

Yes, Dawkins has an agenda, a thesis, a point he wants to make. But that is another characteristic of great works of science, as Darwin himself noted in response to a critique he received that The Origin of Species was too theoretical and that he should have just let the facts speak for themselves: “About thirty years ago there was much talk that geologists ought only to observe and not theorize, and I well remember someone saying that at this rate a man might as well go into a gravel-pit and count the pebbles and describe the colours. How odd it is that anyone should not see that all observation must be for or against some view if it is to be of any service”—and Dawkins has followed it to the letter.

Finally, the fact that Dawkins writes so clearly and cleverly, with literary style, wit, and humor, elevates this work of science to a higher plane of literature. Those who bewail popular science writing typically have no idea how to do it, and if they tried, they would discover that it is actually much harder than technical science writing. To that end, to the usual horizontal divide of science writing into technical and popular (often artificial, in any case), I would add that there is a vertical divide of science writing: good and bad. Although no one fully understands why books land and stay on the New York Times bestseller list, I venture to say that one reason The God Delusion has been riding that wave to publishing success for over six months at the time of writing is that it is a good read.

MICHAEL SHERMER
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References

TECHNICAL COMMENT ABSTRACTS

COMMENT ON “The Spatial Extent of 20th-Century Warmth in the Context of the Past 1200 Years”
Gerd Bürger
Osborn and Briffa (Reports, 10 February 2006, p. 841) identified anomalous periods of warmth or cold in the Northern Hemisphere that were synchronous across 14 temperature-sensitive proxies. However, their finding that the spatial extent of 20th-century warming is exceptional ignores the effect of proxy screening on the corresponding significance levels. After appropriate correction, the significance of the 20th-century warming anomaly disappears.
Full text at www.sciencemag.org/cgi/content/full/316/5833/1844a

RESPONSE TO COMMENT ON “The Spatial Extent of 20th-Century Warmth in the Context of the Past 1200 Years”
Timothy J. Osborn and Keith R. Briffa
Reconsidering the basis for selecting proxy records according to their correlation with local temperature has no substantive influence on the statistical significance of 20th-century warming that we reported, provided that the degree of selectivity is correctly estimated. The conclusion that recent warming is unusually widespread compared with the past 1200 years therefore remains valid.
Full text at www.sciencemag.org/cgi/content/full/316/5833/1844b

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