Support for the Human Cancer Genome Project

IN "AN OPEN LETTER TO CANCER RESEARCHERS" (Letters, 21 Oct., p. 439), S. J. Elledge and G. J. Hannon questioned the wisdom of asking the NIH to undertake the Human Cancer Genome Project (HCGP) (*1*) recently proposed by a National Cancer Institute Working Group, of which we were members. Elledge and Hannon object to the HCGP on the grounds that the project is unlikely to achieve its goals, that the expenditures would decrease funding available for investigator-initiated projects, and that the funds could be better used to support other work, such as genetic screens for factors required for the growth and survival of cancer cells.

Although we welcome debate about the Working Group's proposal and do not dispute the value of genetic screens, the Letter misrepresents the HCGP. First, it undervalues the goal of the project, which is to provide as thorough an account as currently possible, now that the human genome has been sequenced, of the genetic damage responsible for many different types of human cancer. Second, it fails to describe the systematic and progressive aspects of the plan: to begin with pilot projects and to link clinical information about tumor samples to the underlying genetic changes in cancer cell DNA. The proposal limits resequencing to the coding exons of 1000 to 2000 genes, not entire genomes, and suggests that genes with altered copy number changes be given some priority (*1*). Third, Elledge and Hannon greatly underestimate the evidence that already supports the utility of such genotyping, including the many changes in proto-oncogenes and tumor suppressor genes that are already affecting the approaches to diagnosis, classification, and treatment of these diseases (*1*). Finally, the Letter fails to recognize a crucial implication of three recent studies that the authors cite in support of their opposition to the HCGP (*2*–*4*). In each of these three studies, it is apparent that a systematic study of larger numbers of well-defined tumor types and candidate genes, exactly the strategy embraced by the HCGP, will be required to identify the genetic damage that underlies these cancers. In fact, in two of the papers cited (*3*, *4*), because so few tumors from each of the specific histological types were examined, well-validated classes of mutations—*EGFR* mutations in lung adenocarcinomas and *KIT* mutations in seminomas—were not found.

Techniques for detection of some genetic changes are ready for systematic linking to clinical data. We recognize that resequencing is still difficult and expensive, that costs may decline in the future if we wait for methods to improve, and that tests for chromosomal translocations and epigenetic changes may not yet be ready for high-throughput use. Furthermore, budget projections for the NIH imply that the costs of the HCGP will require some reductions in other activities. Nevertheless, we contend that the cancer research community now needs a much better description of the genetic damage that drives human cancers; this will form the basis for all future studies of cancer in the laboratory and the clinic and will provide immediate benefit for molecular diagnosis of human cancers.

The National Cancer Institute and the National Human Genome Research Institute have recently endorsed the idea of conducting pilot projects to compare existing methods for characterizing cancer genomes, to evaluate the feasibility of resequencing genes on the scale proposed, and to examine the potential for discovery. We think that these are responsible first steps toward the goals of the HCGP.

HAROLD VARMUS[1] AND BRUCE STILLMAN[2]
[1]Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021, USA. [2]Cold Spring Harbor Laboratory, 1 Bungtown Road, Cold Spring Harbor, NY 11724, USA.

References
1. Recommendation for a Human Cancer Genome Project, Report of Working Group on Biomedical Technology, Feb. 2005 (available at www.genome.gov/Pages/About/NACHGR/May2005NACHGRAgenda/ReportoftheWorkingGrouponBiomedicalTechnology.pdf).
2. P. Stephens *et al.*, *Nat. Genet.* **37**, 590 (2005).
3. H. Davies *et al.*, *Cancer Res.* **65**, 7591 (2005).
4. G. Bignell *et al.*, *Genes Chrom. Cancer* **45**, 42 (2006).

> "[W]e contend that the cancer research community now needs a much better description of the genetic damage that drives human cancers; this will form the basis for all future studies of cancer in the laboratory and the clinic and will provide immediate benefit for molecular diagnosis of human cancers."
>
> –VARMUS AND STILLMAN

Attribution of Disaster Losses

IN HIS VIEWPOINT "INSURANCE IN A CLIMATE OF change" (12 Aug., p. 1040), E. Mills suggests that changes in climate have been responsible for some part of the trend in recent decades of increasing damage related to extreme weather. This claim is not supported by the peer-reviewed literature, including the most recent report of the Intergovernmental Panel on Climate Change (IPCC) (*1*).

Over recent decades, the IPCC found no long-term global trends in extratropical cyclones (i.e., hurricanes or winter storms), in "droughts or wet spells," or in "tornados, hail, and other severe weather" (*2*). Logically, in the absence of trends in these weather events, they cannot be responsible for any part of the growing economic toll. The IPCC did find "a widespread increase in heavy and extreme precipitation events in regions where total precipitation has increased, e.g., the mid- and high latitudes of the Northern Hemisphere" (*3*). But at the same time, the IPCC warned that "an increase (or decrease) in heavy precipitation events may not necessarily translate into annual peak (or low) river levels" (*3*). Indeed, although the IPCC found some changes in streamflow, it did not identify changes in streamflow extremes (i.e., floods) and concluded on a regional basis, "Even if a trend is identified, it may be difficult to attribute it to global warming because of other changes that are continuing in a catchment" (*4*). These findings are consistent with research seeking to document a climate signal in a long-term record of flood damage that has concluded that an increase in precipitation contributes to increasing flood damage, but the precise amount of this increase is small and difficult to identify in the context of the much larger effects of policy and the ever-growing societal vulnerability to flood damage (*5*, *6*). A recent study by the International Ad Hoc Detection and Attribution Group concluded that it was unable to detect an anthropogenic signal in global precipitation (*7*).

Presently, there is simply no scientific basis for claims that the escalating cost of disasters is the result of anything other than increasing societal vulnerability (*8*).

ROGER A. PIELKE JR.
Center for Science and Technology Policy Research, University of Colorado, UCB 488, Boulder, CO 80309–0488, USA. E-mail: pielke@colorado.edu

Published by AAAS

References
1. IPCC, *The Scientific Basis* (Cambridge Univ. Press, Cambridge, 2001).
2. See section 2.7.3.1 of (*1*) at www.grida.no/climate/ipcc_tar/wg1/091.htm#2731 and section 2.7.3.3 at www.grida.no/climate/ipcc_tar/wg1/092.htm.
3. See section 2.7.2.2 of (*1*) at www.grida.no/climate/ipcc_tar/wg1/090.htm.
4. See section 4.3.6.1 of (*1*) at www.grida.no/climate/ipcc_tar/wg2/167.htm#4361.
5. M. Downton, R. A. Pielke Jr., *Nat. Hazards Rev.* **2**, 157 (2001).
6. R. A. Pielke Jr., M. W. Downton, *J. Clim.* **13**, 3625 (2000).
7. International Ad Hoc Detection and Attribution Group, *J. Clim.* **18**, 1291 (2005).
8. R. Pielke *et al.*, *Bull. Am. Meteorol. Soc.*, in press.

Response

WHILE WORTHY OF DISCUSSION, THE HISTORically oriented questions raised by Pielke Jr. are tangential to the central focus of my Viewpoint, which explores the vulnerability of insurers, their customers, and governments to future climate change.

Climate change cannot be summarily dismissed as a driver of observed growth in global weather-related damages and economic losses. The disaster attribution literature upon which such assertions are based is fraught with data and measurement uncertainties and is decidedly incomplete, especially concerning events outside the United States (*1*). There is particularly scant treatment of important noncatastrophic processes such as small storms, lightning, soil subsidence, permafrost melt, the effects of mold and airborne aeroallergens on human health, coral reef decline, coastal erosion, or crop diseases. Such diffuse or small-scale phenomena today yield aggregate annual losses on a par with headline-catching catastrophes and will be amplified by climate change (*2*, *3*). Indirect effects, such as impacts on energy prices, are significant but rarely quantified.

Damage to oil storage tanks in Cameron, Louisiana, caused by Hurricane Rita.

A nonselective reading of IPCC's 2001 assessment does in fact support the linkage between rising damage costs and a combination of increased weather extremes and societal vulnerability. This is stated directly in the WG2 Technical Summary and elsewhere. IPCC's synthesis of the literature notes observed underlying changes in temperature and precipitation extremes, continental drying, and a range of associated impacts on physical and biological systems. Moreover, the body of literature demonstrating anthropogenic climate change has since bourgeoned, evidencing stronger and more pervasive trends (*1*, *4*) including changes in atmospheric and ocean circulation and elevated ocean heat content, as well as sea-level rise and associated coastal erosion, which, in turn, help drive many impacts of concern (*5*, *6*). The recent literature on the socially and economically devastating European heat wave of 2003 attributes a very high (90%) confidence that human activity doubled the probability of the event's occurrence (*7*).

It is clear that global economic losses from weather-related events are rising far faster than inflation, economic growth, or population. Thorough attribution analysis must address questions such as:

Why are losses from weather-related events rising faster than those from non-weather events?

What are the offsetting effects of human efforts to curb losses (building codes, early warning systems, fire protection, flood defenses, land-use planning, crop irrigation, etc.)? As noted by Pielke Jr. and co-authors with respect to flood risk [(*8*), p. 1081], "[o]ne can easily hypothesize that increasing population and urbanization in the United States has led to a commensurate increase in population at risk. Yet, one can also hypothesize that the various societal responses may have more than compensated for population growth and in fact fewer people are today at risk...." The Army Corps of Engineers estimates that flood control measures have prevented 80% of U.S. losses that would have otherwise materialized (*9*).

How do we explain rising economic losses (e.g., those to crops in the heartland or physical infrastructure built on melting permafrost) that are only weakly linked to oft-cited demographic factors such as populations clustering around coastlines?

Lastly, why would rising numbers of events (*10*) not translate into rising costs?

Assuming that only socioeconomic factors—rather than rising emissions—influence losses may yield ill-founded policy recommendations that focus exclusively on adapting to climate change while dismissing energy policy as a legitimate part of the toolkit for responding (*11*). As an indication of the potential value of emissions reductions, the Association of British Insurers, in collaboration with U.S. catastrophe modelers, estimated that U.S. hurricane or Japanese typhoon losses would vary by a factor of five for scenarios of 40% and 116% increase in pre-industrial atmospheric CO_2 concentrations (*12*). Others have projected a fourfold increase in mid-Atlantic U.S. flood loss costs under climate change (*13*).

In a narrow sense, it would be a relief to learn that the only cause of rising losses is that people are moving more into harm's way. That conclusion would, however, be premature and scientifically indefensible given the paucity of data, limitations of available analyses, and consistency between observed impacts and those expected under climate change. Nor should we make the opposite mistake of attributing the observed growth in losses solely to climate change. Rather than "proof" by vigorous assertion, the constructive approach is to better understand the compounding roles of increasing vulnerability and climate change, and take affordable precautionary steps to reduce greenhouse gas emissions and adapt to the changes rather than waiting for unaffordable consequences.

EVAN MILLS
Lawrence Berkeley National Laboratory, MS 90-4000, Berkeley, CA 94720, USA. E-mail: emills@lbl.gov

References and Notes
1. International Ad Hoc Detection and Attribution Group, *J. Clim.* **18**, 1291 (2005).
2. "Climate change futures: health, ecological and economic dimensions" (Harvard Medical School, Swiss Re, and the U.N. Development Programme, 2005) (http://climatechangefutures.org).
3. P. V. Vellinga *et al.*, *Climate Change 2001: Impacts, Adaptation and Vulnerability*, J. J. McCarthy *et al.*, Eds. (Cambridge Univ. Press, Cambridge, 2001).
4. K. Zhang, B. C. Douglas, S. P. Leatherman, *Clim. Change* **64**, 41 (2004).
5. A. Dlugolecki, "A changing climate for insurance" (Association of British Insurers, London, 2004).
6. C. Schar *et al.*, *Nature* **427**, 332 (2004).
7. P. A. Stott, D. A. Stone, M. R. Allen, *Nature* **432** ,610 (2004).
8. K. E. Kunkel, R. A. Pielke Jr., S. A. Changnon, *Bull. Am. Meteorol. Soc.* **80**, 1077 (1999).
9. United States Army Corps of Engineers, "Services to the public: flood damage reduction" (available at www.usace.army.mil/public.html#flood).
10. Per EM-DAT database, Center for Research on the Epidemiology of Disasters at the Université-Catholique de Louvain in Brussels.
11. R. A. Pielke Jr. *et al.*, *Energy Environ.* **11**, 255 (2000).
12. "Financial risks of climate change" (Association of British Insurers, London, 2005).
13. O. Choi, A. Fisher, *Clim. Change* **58**, 149 (2003).

Bilateral Action for Right Whales

IN THEIR POLICY FORUM "NORTH ATLANTIC right whales in crisis" (22 July, p. 561), S. D. Kraus *et al.* make clear the plight of the North Atlantic right whale, *Eubalaena glacialis*, and note that whale deaths from ship strikes and fishing gear entanglements have not been diminishing. Kraus *et al.* call for changes to U.S. National Oceanic and Atmospheric Administration (NOAA) management policy to put strong and immediate

CREDIT: TIM JOHNSON/REUTERS