

## 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

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

## 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

“ [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

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,

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<sup>1</sup> AND BRUCE STILLMAN<sup>2</sup>

<sup>1</sup>Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021, USA. <sup>2</sup>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](http://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).

## 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](http://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](http://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](http://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](http://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.

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 burgeoned, 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<sub>2</sub> 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](mailto: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://climatechange-futures.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](http://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).



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

## 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

emphasis on reducing human-induced mortality of right whales. The species, though, is not restricted to U.S. waters; it ranges from Florida to the Canadian Maritimes. It is listed as Endangered under both the U.S. Endangered Species Act and the Canadian Species at Risk Act.



coordinated, bilateral management; regular joint meetings; and cooperative actions are needed. The new U.S. recovery plan calls for bilateral cooperative efforts to maximize protection for right whales. Canadian recovery planning should follow suit and both jurisdictions should work together.

JESSE S. SAYLES AND  
DAVID M. GREEN

Redpath Museum, McGill University, 859 Sherbrooke Street West, Montreal, QC H3A 2K6, Canada.

#### References

1. National Marine Fisheries Service, Recovery Plan for the Northern Right Whale (*Eubalaena glacialis*) (National Marine Fisheries Service, Silver Spring, MD, 2005).
2. North Atlantic Right Whale Recovery Team, Canadian North Atlantic Right Whale Recovery Plan (Department of Fisheries and Oceans, Ottawa, 2000).

#### Response

**WE AGREE WITH SAYLES AND GREEN.** Migratory transboundary species like the right whale require bilateral efforts at many levels. For example, the U.S. National Marine Fisheries Services' Advanced Notice of Proposed Rulemaking (1) does require the U.S. government to work with Canada to

develop bilateral agreements related to shipping. Further, most co-authors on the Policy Forum have benefited from close working relationships with both researchers and managers within Fisheries and Oceans Canada (DFO).

Several breakthroughs in right whale conservation have already been made in Canada, including relocation of the internationally adopted shipping lanes in the Bay of Fundy to reduce ship kills, as well as the official recognition of two Conservation Areas where right whales aggregate. The Bay of Fundy shipping lane changes resulted from efforts by Irving Oil, Transport Canada, DFO, the International Maritime Organization, fishing organizations, whale watching groups, and right whale conservationists. Such multilateral partnerships are especially important in conserving transboundary species.

However, we are aware that DFO's ability to really make a difference to right whale conservation is dependent on funding for their initiatives, and support for recovery plan implementation has been limited. We encourage both the Canadian government and nongovernmental organizations to support increased funding for right whale conservation in Canada and welcome additional collaboration with our Canadian colleagues, particularly in the development

## LETTERS

of bilateral measures to ensure the protection of right whales throughout their range.

SCOTT D. KRAUS,<sup>1\*</sup> MOIRA W. BROWN,<sup>1</sup>  
CHRISTOPHER W. CLARK,<sup>2</sup> PHILIP K. HAMILTON,<sup>1</sup>  
ROBERT D. KENNEY,<sup>3</sup> AMY R. KNOWLTON,<sup>1</sup>  
SCOTT LANDRY,<sup>4</sup> CHARLES A. MAYO,<sup>5</sup>  
WILLIAM A. MCLELLAN,<sup>5</sup> MICHAEL J. MOORE,<sup>6</sup>  
DOUGLAS P. NOWACEK,<sup>7</sup> D. ANN PABST,<sup>6</sup>  
ANDREW J. READ,<sup>8</sup> ROSALIND M. ROLLAND<sup>1</sup>

<sup>1</sup>Egerton Research Laboratory, New England Aquarium, Boston, MA 02110–3399, USA. <sup>2</sup>Cornell Laboratory of Ornithology, Cornell University, Ithaca, NY 14850–1923, USA. <sup>3</sup>Graduate School of Oceanography, University of Rhode Island, Narragansett, RI 02882–1197, USA. <sup>4</sup>Provincetown Center for Coastal Studies, Provincetown, MA, 02657–1911, USA. <sup>5</sup>Department of Biological Sciences, University of North Carolina Wilmington, Wilmington, NC 28403–3201, USA. <sup>6</sup>Biology Department, Woods Hole Oceanographic Institution, Woods Hole, MA 02543–1049, USA. <sup>7</sup>Oceanography Department, Florida State University, Tallahassee, FL 32306–4320, USA. <sup>8</sup>Marine Laboratory, Duke University, Beaufort, NC 28516–8648, USA.

\*To whom correspondence should be addressed.

E-mail: skraus@neaq.org

### Reference

1. Department of Commerce, National Oceanic and Atmospheric Administration, 50 CFR Part 224

[040506143-4143-01; I.D. 052504C] RIN 0648-AS36  
Endangered Fish and Wildlife; Advance Notice of  
Proposed Rulemaking (ANPR) for Right Whale Ship Strike  
Reduction, *U.S. Fed. Reg.* 69 (No. 105), 30857 (2004).

## CORRECTIONS AND CLARIFICATIONS

**Reports:** "Air-stable all-inorganic nanocrystal solar cells processed from solution" by I. Gur *et al.* (21 Oct., p. 462). On page 464, in two places, it is mentioned that an aging experiment was carried out for 13,000 hours. These instances should read ~13,000 minutes. These errors occur in line 4 of the Fig. 4 caption and in column 2, fourth paragraph, line 8.

## TECHNICAL COMMENT ABSTRACTS

### COMMENT ON "How Science Survived: Medieval Manuscripts' 'Demography' and Classic Texts' Extinction"

Georges Declercq

Exciting though it may seem, the mathematical model developed by Cisne (Reports, 25 February 2005, p. 1305) to analyze the transmission of texts and manuscripts from Antiquity and the Middle Ages does not hold up to scrutiny. It seriously underestimates the losses, thus leading to conclusions that are unwarranted.

Full text at  
[www.sciencemag.org/cgi/content/full/310/5754/1618b](http://www.sciencemag.org/cgi/content/full/310/5754/1618b)

## RESPONSE TO COMMENT ON "How Science Survived: Medieval Manuscripts' 'Demography' and Classic Texts' Extinction"

John L. Cisne

Declercq's rejection of an otherwise well-supported model is based on demonstrably too narrow an interpretation of the use of Bede's *De Temporum Ratione* and on questionable appreciation of predictive modeling as a complementary alternative to traditional deductive methods. Additional evidence on library holdings further supports the original conclusions regarding the survival of manuscripts.

Full text at  
[www.sciencemag.org/cgi/content/full/310/5754/1618c](http://www.sciencemag.org/cgi/content/full/310/5754/1618c)

## 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](http://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.