detection of circulating tumor DNA over the enumeration of circulating tumor cells by means of the CellSearch System. Our findings provide the rationale for future studies to address the full clinical utility of analyses with circulating tumor DNA.

One apparent limitation of our work was that only two genes (*PIK3CA* and *TP53*) were analyzed for most patients. These are the two most commonly mutated genes in breast cancer, and as expected, they were informative in half the patients recruited. This does not represent a general limitation of circulating tumor DNA: as a proof of principle, we also found that we were able to monitor other somatic mutations and structural variants in a subset of patients who did not have mutations in *PIK3CA* or *TP53*. Our data indicate that any cancer-specific mutation can be monitored in circulating tumor DNA from patients with metastatic breast cancer.

The timing of blood and plasma collection is obviously an important variable. In our study, all samples were collected immediately before the administration of each treatment cycle. The possibility of measuring an increase in the release of circulating tumor DNA as an indicator of responsiveness is attractive and is supported by xenograft models.[1]

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Since publication of their article, the authors report no further potential conflict of interest.

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DOI: 10.1056/NEJMc1306040

Globalization, Climate Change, and Human Health

TO THE EDITOR: The scholarly review of globalization and climate change by McMichael (April 4 issue)[1] emphasizes the associated economic, social, demographic, and environmental threats to human health and suggests steps to mitigate these changes on a global scale. Although McMichael also mentions the effects of climate change and globalization on the geographic range of vectorborne infections, he does not alert readers to sobering examples of the emergence of tropical infections in the temperate zone (Table 1). Globalization and climate change promote the emergence of these infections synergistically. Globalization increases the number of infected travelers and the accidental importation of infected vectors. Climate change warms the environment to temperatures that permit reproduction of the vector and parasite. Increasing

Table 1. Effects of Globalization and Climate Change on the Spread of Tropical Infections to the Temperate Zone.*

Tropical Infection	Areas of Local Transmission	Comment	Reference
Dengue	Key West and elsewhere in Florida; Brownsville, Texas; France; and Croatia and other areas of southern Europe	A total of 5% of Key West residents have antibodies against dengue, and locally transmitted infections have been reported in other counties, including Miami–Dade; 39% of residents in Brownsville have antibodies against dengue	Jordan et al.,[2] Ramos et al.,[3] Butler[4]
Malaria	Greece	The CDC recommends precautions (level 1) for persons who travel to Greece, including consideration of drug prophylaxis for travel to some regions	CDC[5]
Chikungunya	Italy and France	Hundreds of persons have been infected in Italy	Butler[4]

* CDC denotes Centers for Disease Control and Prevention.

globalization and global warming make continued local transmission of these and other tropical infections highly likely.

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1305749

TO THE EDITOR: One of the effects of climate change on human health is the spread of vectorborne infections. Temperature changes may determine the redistribution of vectors, even if the presence of the vector within a region does not automatically translate to the disease.[1] Climatic factors (temperature, rainfall, and relative humidity), infection rates among reservoirs, social and economic conditions, and a lack of vector-control strategies may be associated with the emergence or reemergence of vectorborne diseases.

The increased incidence of West Nile fever throughout Europe and tickborne encephalitis in central and eastern Europe[2,3] has been described as a consequence of the climate warming in Europe and of changes in the distribution of the vectors of these viruses during the past decades.

In the highland regions of East Africa, the extent of the spread of malaria has been related to the increasing temperature; after 1999, there were cases in residents at altitudes up to 1650 m, where malaria was not previously present.[4] In Italy, an outbreak of chikungunya fever in 2007 was probably caused by globalization and climate change.[5]

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DOI: 10.1056/NEJMc1305749

TO THE EDITOR: McMichael's review implicated fossil fuel–derived emissions of carbon dioxide as the cause of catastrophic global warming. This conclusion was based on unproven assumptions. The first assumption is that fossil fuel is the major driver of carbon dioxide in the atmosphere. The second is that carbon dioxide is the driver of global warming. The third is that warming increases weather extremes. Computer models of warming that did not include solar activity or cloud formation have not predicted what has actually happened.[1-3] Indeed, global mean temperatures increased in the years from 1910 through 1940 at a rate quite similar to the rate during the period from 1970 through 2000, whereas there was a temperature decrease from 1940 through 1970, similar to what has been observed since 2000. Since the burning of fossil fuel did not start to increase until 1950 and has continued to increase until now, it is hard to implicate this burning as a substantial contributor to global warming.

The availability of affordable energy is crucial for economic development and thus health and welfare. Global health will be improved not by mitigation of global warming or fossil-fuel burning, but by conquering poverty. The focus on anthropogenic climate change diverts interest from the real threats to humanity.

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DOI: 10.1056/NEJMc1305749

THE AUTHOR REPLIES: Davis offers relevant additional information about the spread of tropical infections into countries in temperate zones with the combined influences of climate change, human mobility, and long-distance travel. Rossati and colleagues describe other examples of apparent influences of changes in climate on infectious diseases such as tickborne encephalitis in Europe, chikungunya fever in Italy, and malaria in the highland regions of East Africa. These factors and diseases all warrant systematic monitoring to clarify and confirm their relationships to ongoing climate change.

Juliusson contests three basic tenets of climate-change science. With regard to the first tenet: fossil-fuel combustion is now the major source of additional atmospheric carbon dioxide, with deforestation a distant second. For billions of years, the dominant sources of carbon dioxide have been vegetation decay and volcanoes. Humans are now releasing subterranean energy-rich fossil carbon that has been inert for millions of years. The fact that the recent increase in levels of atmospheric carbon dioxide derives predominantly from fossil fuels accords with the increasing carbon content of the marine and (not deforested) terrestrial environment. If either had contributed to the increase in carbon dioxide levels, their carbon content would have decreased.

With regard to the second tenet: carbon dioxide is the main driver of ongoing warming. Debate over closely related fluctuations in atmospheric carbon dioxide levels and temperature for the past 800,000 years has been simplistic. Neither "causes" the other. Each influences the other, with varying relative dominance during each glacial–interglacial cycle. The recent Berkeley Earth Surface Temperature study at the University of California, Berkeley, compiled detailed worldwide temperature trends from 1753 through 2011.[1] This model, when limited to solar and volcanic activity, could not explain the observed temperature trend over the past century. Various other research groups have reported similar findings.[2] However, when trend data on carbon dioxide were included, the modeled predictions and actual observations matched closely.

The third tenet is that both theory and observation indicate that warming amplifies weather extremes. A more energetic atmosphere generates greater variability.[3] The empirical evidence is now strengthening quite fast.[4,5]

Many such counterassertions persist, despite the increasingly convergent scientific research and empirical evidence. Interested readers will find a comprehensive discussion of such contested issues at www.realclimate.org/index.php/archives/2004/12/index/#Responses.[1] and in the Fourth Assessment Report of the Intergovernmental Panel on Climate Change.[2]

Juliusson's final point is both familiar and mistaken. The future does not necessarily compete with the present. Unabated, climate change would undermine much of the current progress in international development through floods, storms, infestations of crops, exacerbation of child diarrhea, facilitation of various vectorborne infections, water shortages, and regional tensions and perhaps conflict.

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Since publication of his article, the author reports no further potential conflict of interest.

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DOI: 10.1056/NEJMc1305749