

NEWS

Drug targeting: is race enough?

WASHINGTON DC

The expected approval in the United States of the first drug targeted to a specific racial group is sparking debate about the future of 'personalized' medicine.

Enthusiasts predict a future in which people are given genetic tests to help choose the drug to which they will respond best. But some experts worry about the precedent of accepting race as a crude marker for underlying biological differences — which could still leave many individuals being treated with drugs that don't work well for them.

Last week, an advisory committee to the Food and Drug Administration (FDA) recommended that BiDil, a drug for congestive heart failure, should be approved for sale with a label designating African Americans as the target population. The FDA usually follows the advice of its experts and is expected to make its decision by 23 June.

Francis Collins, director of the National Human Genome Research Institute in Bethesda, Maryland, says that the drug's effectiveness in blacks is "something to celebrate". Even so, he argues: "We should move without delay from blurry and potentially misleading surrogates for drug response, such as race, to the more specific causes."

BiDil is a combination of isosorbide dinitrate, used to treat angina, and hydralazine,

which lowers blood pressure. It is made by NitroMed of Lexington, Massachusetts. The drug was initially tested in a population that was about two-thirds white and one-third black by another company. The results weren't persuasive, and the FDA turned down a request for marketing approval in 1997.

But Jay Cohn, a cardiologist at the University of Minnesota, reanalysed the data and found that the black patients had responded much better to the drug.

Cohn and NitroMed were granted a precedent-setting patent on BiDil as a racially targeted drug, and the company launched a new trial in 1,050 black patients. BiDil reduced deaths by 43%, proving so successful that the trial was stopped early, in 2004.

The drug's anticipated approval has been greeted with enthusiasm by both cardiologists and the drugs industry. "This is the most important advance in the care of black people that we've seen in my lifetime," Charles Curry, president of the International Society on Hypertension in Blacks, told the FDA.

But Collins is wary of using the "biologically inaccurate and socially dangerous" surrogate of race, rather than pushing researchers and companies to investigate the genetic and environmental factors that determine individual

differences in drug response. Even if blacks respond better on average to BiDil than whites, he points out, the drug will still be ineffective for those who don't possess a particular cardiac physiology or combination of genes. There may also be a minority of whites who would benefit from taking BiDil.

Collins contrasts BiDil with Iressa (gefitinib), the AstraZeneca drug whose effectiveness at treating advanced lung cancer was so disappointing that the FDA last week restricted its use to current users and patients in clinical trials. Nevertheless, in about 10% of patients on Iressa, lung tumours shrink rapidly. Japanese patients are three times as likely as whites

to fall into this group. But the underlying difference is that patients who respond well have specific mutations in the receptor for epidermal growth factor.

This opens up the possibility of using Iressa to treat people whose tumours have these mutations. "Wouldn't it be unfortunate if at this point all we knew is that there is a better chance of responding if you are Japanese?" says Collins.

But will drug companies have sufficient incentive to go beyond using race or other crude surrogates, when to do so would entail

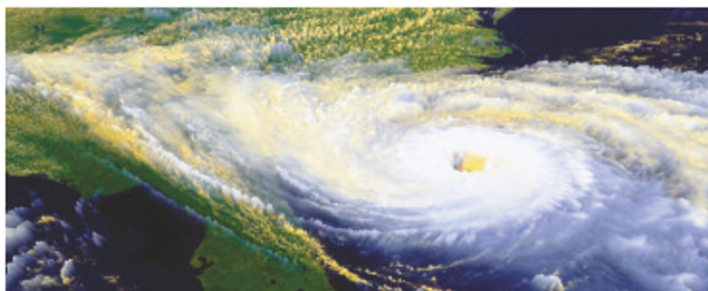
"We should move without delay from blurry surrogates for drug response to more specific causes."

Trouble brews over contested trend in hurricanes

The debate over whether global warming is making hurricanes worse has been nothing if not stormy.

The issue came to a head in January, when leading US meteorologist Chris Landsea resigned from the Intergovernmental Panel on Climate Change, complaining that a colleague on the panel, Kevin Trenberth, had supported a link between warming and storms in a press conference. Now, just in time for the 2005 hurricane season, Trenberth has clarified his views in print (*Science* 308, 1753–1754; 2005). He argues that the intensity, if not the frequency, of hurricanes and typhoons will increase as the oceans warm.

The hurricane seasons from 1995 to 2004 have been far above the long-term average in terms of the number of storms and accompanying rainfall. However, most scientists are still



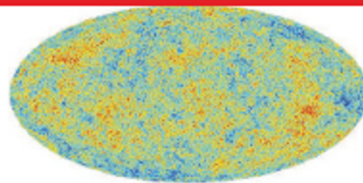
Open season: the latest hurricane analysis will wind up those who say that worsening storms are not related to global warming.

extremely cautious about connecting hurricane activity and global warming. Since satellite detection started 35 years ago, there has been no detectable trend in hurricane frequency, points out modeller Kerry Emanuel of the Massachusetts Institute of Technology in Cambridge, Massachusetts.

But Trenberth, head of the climate analysis

section of the National Center for Atmospheric Research in Boulder, Colorado, argues that because the number of hurricanes is relatively small, and fluctuates in cycles of various lengths, proving the existence of a trend from weather records is extremely difficult.

He has looked instead at how hurricanes form. "Trends in human-influenced environ-



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China's chicken farmers under fire for antiviral abuse

TOKYO

The much-feared H5N1 strain of bird flu has become resistant to one of the most effective antiviral drugs against it — and it seems that Chinese farmers' use of the compound in chickens is to blame.

This week the accusation was formally made — and formally denied. But at some point after 1997 the H5N1 strain became resistant to the amantadine family of antiviral drugs, and Chinese officials have now pledged to investigate the claim.

On 18 June, *The Washington Post* reported that Chinese farmers, encouraged by government officials, had been routinely using amantadine drugs in chickens. The United Nations Food and Agriculture Organization (FAO) and the World Health Organization (WHO) then questioned the Chinese government, which denied the reports, although officials did not comment on whether farmers were using the drugs.

The FAO's avian-flu surveillance network coordinator in China, Fusheng Guo, told *Nature* that the drugs have been widely used to combat the H9 family of viruses in chickens. Guo, who was a private consultant for Chinese farmers throughout the 1990s, says that he warned farmers not to use amantadine, because residues in the meat could make human viruses resistant. But, at the time, he did not worry about it in relation to H5N1. "Now I believe it's a serious problem," he says.

According to Guo, the agriculture ministry was probably not aware of the use. "The men selling it knew it was illegal," he adds.

China's health ministry told the WHO on 21 June that the problem is "worth following up in the closest way possible", according to Roy Wadiah, the WHO spokesman in Beijing. Surveillance and testing will now be required to find out how widespread the use has been and how common resistance to amantadine has become.

The first H5N1 strain that infected humans, in Hong Kong in 1997, was sensitive to the amantadines. But resistance to them, discovered in 2003, has left another — more expensive — family of antivirals, including oseltamivir (sold as Tamiflu) and zanamivir (Relenza), as the only line of defence against the virus. This leaves the poor countries of southeast Asia without a low-cost option. ■

David Cyranoski

Positive discrimination: BiDil, a drug to prevent heart failure, will be targeted at black patients.

costly research and might narrow their target markets? Experts agree that they might not. But some point out that further studies could in some cases expand the potential market, and pinpoint the markers predisposing some people to dangerous side-effects.

"If I were a drug company executive, in

addition to finding out about what works, I might be able to find out what causes problems, and save myself some liability," says Arthur Caplan, director of the Center for Bioethics at the University of Pennsylvania in Philadelphia. ■

Meredith Wadman

mental changes are expected to affect hurricane intensity and rainfall," he concludes.

One simulation that Trenberth reviewed suggests that warming tropical oceans will stretch the upper limit of cyclones' potential strength.

"Most storms may actually not reach the limit," says Tom Knutson, a co-author of the simulation based at the US National Oceanic and Atmospheric Administration in Princeton, New Jersey. "But in principle, Trenberth's conclusions are consistent with our studies."

Trenberth also argues that higher sea surface temperatures in the Atlantic Ocean and increased water vapour in the lower atmosphere — caused by global warming — are to blame for the past decade's intense storms.

His conclusions will not please some in the meteorology community. In an upcoming paper in the *Bulletin of the American Meteorological Society*, Landsea, Emanuel and colleagues argue that there is no proven link between greenhouse-gas emissions and hurri-

cane behaviour. They point out that even if there were a trend that had been missed in weather records, the change would have to be quite small relative to the year-to-year variability that already exists.

Trenberth counters that sceptics are ignoring the evidence. "I am trying to get people to think about things in a different fashion," he says. "The point is that all meteorological events around the world are influenced in some way by global warming."

In any case, everyone is hoping that there will be fewer severe storms this summer than last — when four strong hurricanes struck Florida, and Japan was hit by a record ten typhoons. They also hope that the storm that came ashore unexpectedly in Brazil on 28 March 2004 will not be a harbinger of things to come: Catarina, as it was christened, was the first ever recorded hurricane to develop in the southern Atlantic Ocean. ■

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