

Cancer-gene testing ramps up

Thousands to get personalized medicine in Britain's National Health Service.

BY EWEN CALLAWAY

In an approach that many doctors and scientists hope will form the medical care of the future, Massachusetts General Hospital in Boston has for the past year and a half been offering people with cancer a novel diagnostic test. Instead of assessing tumours for a single mutation that will indicate whether a drug is likely to work or not, the hospital tests patients for some 150 mutations in more than a dozen cancer-causing genes, with the results being used to guide novel treatments, clinical trials and basic research. This form of personalized medicine tailors treatments on the basis of the molecular and genetic characteristics of a patient's cancer cells, potentially improving the treatment's outcome.

Now Britain is set to test whether an entire health-care system is ready for the approach. Plans were unveiled this week to deploy broad genetic testing for selected cancer patients in Britain's government-run health-care provider,

the National Health Service (NHS). This form of 'stratified medicine' uses genetic information to group patients according to their likely response to a particular treatment.

"The United Kingdom is really the ideal place to do this," says James Peach, who heads the programme for Cancer Research UK, the charity that is leading the effort. As the NHS treats millions of people each year, unprecedented numbers of suitable patients could be enrolled in the genetic-profiling programme. "The idea is to scale this up to every patient in the NHS," says Peach. In its first phase, the programme will be rolled out to as many as 12,000 NHS cancer patients over two years, beginning in early 2011. By contrast, Massachusetts General has tested about 1,600 patients, and other hospitals' efforts each number in the hundreds.

The tests, which will look for several dozen mutations in about a dozen genes linked to cancer, will be carried out on people with lung, breast, colorectal, prostate or ovarian cancers,

or metastatic melanoma, who are being treated at six NHS hospitals. Therapies that target specific tumour-causing mutations have already been approved, or are on the verge of approval, for most of these conditions, says Peach.

Testing a clinical sample for so many mutations at once is a challenge in itself. Because most existing clinical tests probe individual genes, the NHS programme is working with the Technology Strategy Board, a government agency that supports technology development, and several companies to design a customized test that detects all of these mutations in one go. The partnership, which includes the pharmaceutical multinationals Pfizer and AstraZeneca, will also design software to make the results useful to researchers and clinicians. By genotyping patients for a broad array of cancer-causing mutations, the new tests will make it easier to assign subjects to clinical trials, Peach says.

That is already happening at Massachusetts General, where the test is helping to establish

clinical trials that wouldn't otherwise have happened, says Leif Ellisen, a geneticist who helps lead the hospital's cancer testing programme. For example, its broad genetic test detects a mutation in a gene called *BRAF* that is already known to be commonly mutated in metastatic melanoma. Finding such mutations in people with lung and colon cancer made it possible to put them in a trial of an experimental treatment targeting that gene, Ellisen explains.

Basic research should also benefit from the NHS programme, says Peach. Researchers will have access to consenting patients' genetic data

as well as to medical records of the outcomes of the treatment. These data could reveal how drugs targeting one molecular pathway are affected by mutations in another gene, says Andy Futreal, a cancer geneticist at the Wellcome Trust Sanger Institute in Hinxton, UK, and an adviser to the programme.

Peach hopes that the first phase of the cancer programme will pave the way for expanding genetic testing to more patients and other conditions, such as diabetes, AIDS and even psychiatric disorders. Cancer offers a good testing ground for personalized medicine,

because numerous targeted therapies already exist, but "there's no reason why this should be restricted to cancer", says Peach.

Fabrice André, who runs a similar cancer diagnostic programme that has so far been offered to about 100 patients at the Gustave Roussy Institute in Villejuif, France, says the NHS programme could point the way to implementing personalized medicine across an entire population. "It can really change the landscape of how molecular testing is being done for cancer," he says. "If they succeed, then it's going to be a major step forward." ■

MEDICINE

Global disease fund hit by cash crisis

Pledges fall short for fight against AIDS, TB and malaria.

BY DECLAN BUTLER

Going into a meeting of donors in New York City on 5 October, the Global Fund to Fight AIDS, Tuberculosis and Malaria was aiming high. Its representatives hoped to raise US\$20 billion, enough to scale up the campaign against these diseases. But countries pledged just \$11.7 billion for 2011–13, although the fund still hopes to raise the minimum \$13 billion needed to maintain its current programmes.

The fund accounts for a quarter of all international financing to fight AIDS, two-thirds of that for tuberculosis, and three-quarters of that for malaria. By its own estimates, it has saved 4.9 million lives since its creation in 2002.

"It's a classic good news, bad news story,"

says Andrew Hurst, a spokesman for the fund, which is based in Geneva, Switzerland. The pledge marks a 20% increase on the \$9.7 billion raised for the period 2008–10 at its last fundraising meeting in Berlin in 2007. Given today's economic climate, the outcome could have been far worse, he says.

The bad news is that the fund has not raised enough cash to reduce disease burdens among the poor by 2015, to levels to which countries have committed in the UN Millennium Development Goals. In the run-up to the meeting, the fund had estimated that it needed \$20 billion to start making serious progress on this task, whereas \$13 billion would buy only minimal burden reductions (see "The human cost").

The poor funding outcome starkly highlights a chronic structural weakness of the

Global Fund: its narrow base of donors. Just a couple of dozen countries donated, and a mere seven countries gave more than \$100 million — the United States, France, Germany, Japan, Canada, Norway and Australia. Three other countries traditionally supportive of the fund — the United Kingdom, the Netherlands and Sweden — were unable to officially pledge at the meeting because of the timing of national budgets, but are likely to commit sums that will allow the Global Fund to reach its \$13-billion lower target. Yet dozens of rich countries, including Italy, Spain and Saudi Arabia, gave nothing. The fund is seeking to persuade more nations to pledge, says Hurst, but admits that "we still have some way to go".

For the first time in its history, the fund will now be forced to reject otherwise-solid new proposals from recipient countries, and trim others. "Today marks a sad turning point in the fight against AIDS, TB and malaria, as world leaders have officially underfinanced the Global Fund," says Jennifer Cohn, HIV/AIDS policy adviser at Médecins Sans

Frontières in Geneva. "This decision will result in the deaths of millions of people from otherwise treatable diseases." ■

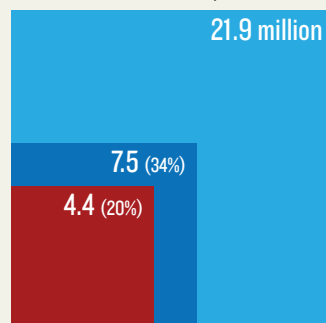
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THE HUMAN COST

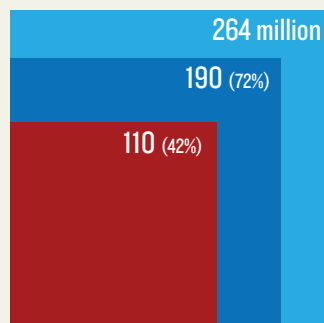
Estimating the effect of different funding scenarios for 2011–13 shows that although US\$20 billion would allow a significant scale-up of activities, \$13 billion yields far less progress towards internationally agreed targets for 2015.

■ Global target
■ \$20-billion fund
■ \$13-billion fund

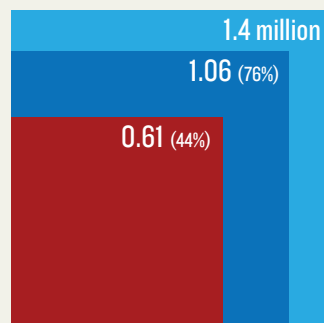
Number of people to get antiretrovirals for HIV/AIDS



Number of insecticidal bednets to tackle malaria



HIV-positive pregnant women on antiretrovirals



Number of AIDS orphans given support

