

# 'Rough draft' of human genome wins researchers' backing

[WASHINGTON] The major players in publicly funded efforts to sequence the human genome are proposing to create during the next three years a 'rough draft' of the genome that would be about 95 per cent complete.

Such an initiative would add a new element to a strategic plan that is being drawn up to guide the Human Genome Project (HGP) in the next five years. The sequencers say a 'rough draft' would allow other scientists to proceed more rapidly with projects that apply new-found sequence data, from discovering rare disease genes to pinning down the molecular details of disease genes that have been mapped but not yet identified.

It would also be different to the 'whole genome shotgun' sequencing approach recently announced by J. Craig Venter and the equipment manufacturer Perkin-Elmer, (see *Nature* 393, 101, 201 & 296; 1998).

"From the point of view of identifying genes, [the 'rough draft'] would be absolutely fantastic," said Leroy Hood of the University of Washington in Seattle during a two-day meeting in Virginia last week to refine details of the five-year plan.

The new strategy became a focal point of the meeting, with participants endorsing the idea that experiments should begin to see how feasible and accurate it would be. Francis Collins, the director of the National Human Genome Research Institute (NHGRI), said the strategy would speed up the process of getting "very useful" sequence "in the hands of the people who want it".

But Collins, whose institute is the main government funder of the genome project and also sponsored the meeting, emphasized that the rough draft "is not a substitute for finishing the whole thing".

Federally funded sequencers are using a two-part process to sequence the genome by analysing mapped clones covering the human chromosomes. The first step is 'shotgun' sequencing and assembly of random fragments from each clone; the second is the tedious and expensive process of 'finishing' by closing gaps and resolving uncertainties.

The new proposal involves dramatically accelerating the shotgun phase, which is the simplest and cheapest component (presently only 10 cents per base). Researchers estimate that this will require a two- to two-and-a-half-fold increase in the government's sequencing capacity, and could produce a high-quality rough draft by 2001. The complete version should still be finished by 2005.

The approach of Venter and Perkin-Elmer breaks the genome into random unmapped fragments for sequencing. But some scientists doubt whether the whole human genome, 70 per cent of which consists of highly repetitive sequences, can be reassembled.

The government's approach requires assembly of much smaller regions, each about one twenty-thousandth of the genome, decreasing the possibilities for error by a factor of 400 million.

The participants at the meeting said their project would mesh well with the private

venture by providing accurately assembled sequence across the genome, which the private venture's own sequence data could fill out. "It may be that the two together will be adequate to finish the job. If that's the case, everybody wins," said one sequencer.

But despite excitement at the prospect of producing a useful 'intermediate product' in three years, some sequencers thought the project could distract them from the primary goal of producing a complete, highly accurate, finished human sequence by 2005. The sequence-ready maps needed for shotgun sequencing of clones do not yet exist across the entire genome, and their construction could distract sequencing centres that are already stretched to meet the 2005 goal.

Nor is it clear whether Congress will allocate sufficient funds to double sequencing capacity quickly, even though government sequencers have said their labs could handle the extra capacity.

But nearly all participants agreed that the costs of raising sequencing capacity are modest compared with the long-term stakes and that more government sequencing capacity is needed urgently.

"More would be better, sooner rather than later," said Richard Lifton, a Howard Hughes Medical Institute investigator at the Yale University School of Medicine, who co-chaired the sequencing strategy session.

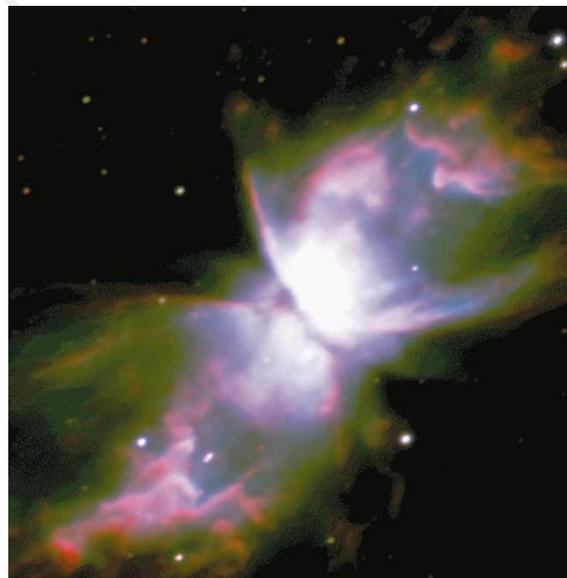
Collins says that the federal project is "massively undercapitalized" with regard to sequencing capacity. The consequences of not responding to that, he said, are not only that the finished human sequence would not be produced quickly enough, but that medical advances and the sequencing of other animals would be delayed.

He also says a push for faster sequencing makes sense on economic grounds alone: a "very rough" estimate of the current annual costs of US public and private cloning and sequencing efforts is \$500 million.

The draft five-year-plan circulated by NHGRI to participants — which will be modified by their input and released in final form in October — calls for the generation of 500 million base pairs of sequence per year by 2003, a tenfold increase on current levels.

Participants said their focus on the shotgun strategy, and boosting speed and capacity generally, was not influenced by the Perkin-Elmer/Venter venture. Rather than federal plans being "ignited" by the private effort, said Lifton, "the same opportunities that led to this new enterprise also led to realization within the Genome Project that there was a real opportunity to accelerate" sequencing.

## Very Large Telescope reveals first images



[LONDON] The European Southern Observatory last week unveiled the first images from its Very Large Telescope on Mount Paranal in Chile. The colour picture (left) shows the fine structure of the Butterfly nebula. It is a composite of three exposures through broad-band blue, green and red filters.

The optical/infrared telescope's image quality has surpassed expectations. The observatory's staff say the angular resolution is unequalled by any ground-based telescope. Its sensitivity in resolving point sources — such as stars — should be superior to anything achieved by a telescope on Earth.

As if to show that the public and private efforts are cooperating, Michael Hunkapiller, president of Perkin-Elmer's Applied Biosciences Division and its top official on the private venture, and Mark Adams, who works with Venter at The Institute for Genomic Research in Rockville, Maryland, were at the conference.

Also present were investigators from the federally funded sequencing laboratories, other university scientists, and officials from NIH and the Department of Energy, the other major government funder of the HGP, along with representatives of Britain's Wellcome Trust, which recently agreed to fund one third of the total sequencing effort of the human genome (see *Nature* 393, 201; 1998).

Hunkapiller fielded pointed questions about Perkin-Elmer's intellectual property intentions, and one federal sequencer predicted that the product of the new venture would be riddled with errors, but the overall tone of the gathering was collegial.

Harold Varmus, director of the National Institutes of Health (NIH), declared his pleasure at the private-sector participation, and urged federal scientists to make the public and private efforts "consensual, communal, collaborative and productive". He added: "There's every reason to believe that we can do that." Hunkapiller said that for the two efforts not to collaborate is "absurd".

The private group promised prompt and full public access to its raw sequence data, but publicly funded scientists and federal officials remain wary. Collins said that, although the venture's leadership was "reassuring" on the question of public access, he worries that "down the road somebody else who ends up as calling the shots may see this as too much of a give-away and retreat". **Meredith Wadman**

## UK seeks physicists for environmental research

[LONDON] Britain's Natural Environment Research Council (NERC) is to introduce a series of fellowships designed to encourage more physical scientists, computer scientists and molecular biologists to take up research on the environment.

"The environment presents the largest, the most serious and the most intractable challenges for the next 50 years," says John Krebs, NERC's chief executive. He says this requires a "new breed" of scientist, and new ways of problem solving that cut across traditional disciplines.

The main goal of the fellowships is to tackle an expected shortage in Britain of environmental scientists with mathematical, computational and statistical skills. A second aim is to involve more natural and social scientists in helping to solve questions in environmental research.

NERC hopes to get molecular biologists to work with ecologists in prospecting for genes from plants with medicinal potential, for example, and in using biotechnology to clean up pollution in soil and water.

The council also wants to see more social scientists working with Earth scientists in research that places values on environmental goods and services, and on the planning and management of towns and cities.

Up to 30 four-year grants could be on offer, paying around £50,000 (US\$82,000) a year. The sum includes the salaries of the main postdoctoral researcher and a research assistant, as well as research support.

"The big questions on the environment cannot be solved by one or two narrow disciplines on their own," says Krebs. "Many of the most innovative advances occur at the interfaces between disciplines."

Krebs says that NERC is not downgrading the importance of basic research, but plans to increase its investment in curiosity-driven research. It will soon launch five-year response-mode grants for basic research projects; its existing grants last three years.

"Anecdotal evidence tells us that there are not enough people with a physics or mathematics background going into the environmental sciences," says Krebs. "We need to bring such people to help tackle problems in meteorology, hydrology and in the oceans."

The grants and fellowships are expected to be announced after the government's Comprehensive Spending Review, due next month. Both schemes are part of NERC's latest science strategy, which was unveiled at the end of last month. A major aim of the strategy is to remove some of the uncertainty of research careers by tackling the issue of short-term contracts.

NERC's proposed four-year fellowships and five-year basic research grants are designed to provide more stability in research careers, and to encourage long-term interest in a field, says Krebs.

All contract staff employed for more than five years at NERC's research centres and surveys will either be offered permanent posts or released. **Ehsan Masood**

## Australian advisory body's first target is to reduce land salinity

[SYDNEY] At its first meeting since being restructured, the Australian Prime Minister's Science Engineering and Innovation Council has decided its most immediate task is to find solutions for the rising salinity which is adversely affecting the meagre soils supporting the nation's agriculture.

After more than a century of bush clearance, deforestation and irrigation, salinity has become a major threat to income from exports and the quality of the environment. John Stocker, the chief scientist, estimates that salinity now affects about 5 per cent of the land sown to crops or pastures, and contributes 12 per cent of the yield lost to land degradation.

The state of Western Australia is losing 200 hectares from its wheat belt every day and, with salinization increasing and proving difficult to treat or reverse, salt-affected land is expected to increase

sevenfold to 20 million hectares by 2050.

The move followed the acceptance of a scheme by Stocker for rationally determining preferences for the national support of research and development, which has been an unrealized goal of successive Australian governments. Stocker defines five criteria, which he calls "structural priorities", for assessing the public funding of science and technology.

Stocker argues that research programmes should be gauged by their effects on maintaining the national "science base", developing "applicable knowledge", promoting "interaction among providers and users" of research, stimulating "innovation in industry", and improving "awareness" of science and technology.

The council has expanded by absorbing the role of the Australian Science and Technology Council (see *Nature* 391, 624; 1998). Representatives of science

organizations have been augmented with leaders of business and grant-giving bodies, and should provide ministers with "high-level and independent advice", said prime minister John Howard in a statement.

The council told a working party, led by Stocker, to produce by August an action plan on salinity. "We'll have to demonstrate some agility to do it by then," Stocker says. His report may become caught in the last weeks of an (as yet undeclared) election campaign, in which Howard and Kim Beazley, the leader of the Labor opposition, are trading blows about tax reform.

Indications that science is unlikely to figure prominently in the election are reinforced by Howard's not capitalizing on the council's positive outcome to make a political point. But Beazley has called for urgent correction of the Coalition's declining taxation incentives for R&D in industry. **Peter Pockley**