US/UK statement on genome data prompts debate on 'free access'

The genomics company Celera is about to release the terms of access to its human genome data. Many will be reassured. But concerns remain.

Celera Genomics has promised to make the terms of access to its human genome sequence database publicly available within the next few days. The statement ends a week of fierce public and political debate over who should benefit from the use of genetic information.

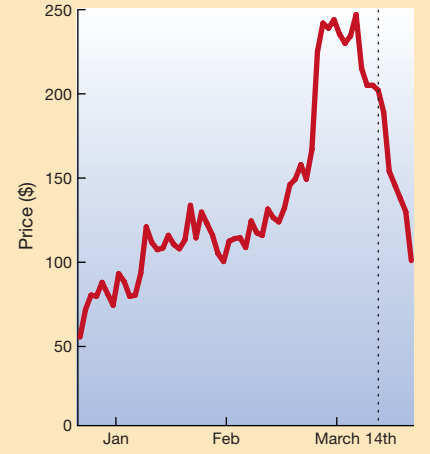
A Celera spokesman says it will not place any constraints on the way the data is used by academic researchers, apart from not allowing it to be redistributed. Also it will not be demanding any 'reach through' rights — a response to accusations that it aimed to exert excessive control over the work of other researchers based on its data.

This move comes hard on the heels of a joint statement by US President Bill Clinton and British Prime Minister Tony Blair, applauding "the decision by scientists working on the Human Genome Project to release raw fundamental information about the human DNA sequence and its variants rapidly into the public domain" and recommending other scientists around the world to adopt the same policy.

Their implicit target was Craig Venter's Celera Genomics. Paul Gilman, Celera's director of policy planning, says that typical licence agreements will be made available later this week. The release is likely to end months of speculation over terms of access.

"There are, unquestionably, a variety of significant issues in our contract negotiations," says a senior official at one large US university that has been negotiating a licence with Celera. "However, these issues are being discussed in detail with Celera, and they are clearly striving to identify terms that will allow academic investigators to have access to their sequence information, while also protecting their own interests. I think our differences could soon be ironed out."

Gilman says anyone will be able to access Celera's suite of data, software tools, annotation, and supercomputing power through annual subscriptions ranging from $5000 to $20,000, depending on whether they are in not-for-profit or commercial organizations.



Roller coaster: Celera's shares have fallen sharply since last week's statement by Clinton and Blair.

Non-subscribers will be able to access the basic consensus sequence at Celera's website or on a DVD disc "without restriction", he says. "They can publish data and file for intellectual property protection on their discoveries. We will not seek any 'reach through' shared royalties or fees on any discoveries they make." He adds that both subscribers and non-subscribers will be allowed to use the data to develop chips and claim intellectual property on it — "except for our competitors using it in competition with us".

At the same time, Gilman admits that Celera will only be able to achieve a full sequence of the human genome by this summer if it takes much of its data from the public human genome project, and that anyone could wait just a few months and have free use of an equivalent amount of data assembled single-handedly by the public project. People will go to Celera not for raw data but for sophisticated computing tools, he argues.

The moves have been welcomed as important concessions by concerned scientists. But several still contest the fact that scientists will not be able to redistribute the data. This is important for annotation, says one, when researchers annotate a sequence that is then made available to others.

Gilman says Celera "would not want the public project to take our data and place it in

Japan may place gene research on summit agenda

Tokyo

Japan is considering placing human genome research on the agenda for the upcoming Group of Eight (G8) summit to be held in Okinawa in July. Members of the ruling Liberal Democratic Party (LDP) last week expressed strong support for the joint statement released by Tony Blair and Bill Clinton calling for free access to raw sequence data (see above).

At a meeting on the life sciences last week hosted by LDP and attended by both scientists and politicians, Taro Nakayama, former foreign secretary and leader of LDP's science committee, called for the issues surrounding human genome research to be taken up at the G8 summit, and urged Japan to respond positively to the joint statement.

Keizo Obuchi, Japan's premier, is also said to be in support of this move to place the issues on the G8 agenda. He told the daily *Nikkei* newspaper that "it would be great if different countries decide to take a united approach [on the release of human genome data]".

But the science-related ministries are wary of becoming involved. "Politicians are all for the free access of raw human genome data, but bureaucrats are extremely reluctant [to make a commitment to this]," says one leading genome researcher present at the LDP meeting.

Japan was approached by the US and British governments last year to take part in the joint declaration. A tripartite agreement was never reached because the ministries — particularly the powerful Ministry of International Trade and Industry (MITI) — were concerned about references to "release of variants [of human DNA sequence]", in a draft of the declaration, according to a source close to the Japanese government.

Japan is currently carrying out its own initiative to identify single nucleotide polymorphisms (SNPs) in the Japanese population, as well as a full-length complementary DNA (cDNA) project aimed at sequencing 30,000 cDNA clones. Both SNPs and cDNA are considered as variants of human DNA sequence. **Asako Saegusa**

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GenBank for other commercial competitors to reuse it". But one leading genome scientist says, "People should be free to circulate complete copies of the database, with additions of their own, if they want to; that makes for healthy bioinformatics. If they are not allowed to do this, the data is not being released according to GenBank standards."

Gilman dismisses this. He claims that the public project rejected an offer by Celera to put the data in GenBank, provided that those accessing it accepted that any use of the data would be freely accessible and not used to compete with Celera. "They said the terms of their international agreements are such that they can put no such limitation on the data."

Venter: ending speculation.

The public project has been studying a similar 'click-wrap' contract, but this time intended to ensure that all those taking data — including Celera — agree to keep it open to all other potential users.

One burning question is whether leading scientific journals will agree to publish Celera's human genome, or whether they will prefer to publish that of the public project. Flood Bloom, for example, editor in chief of *Science*, is expected to publish a statement on this in tomorrow's issue of his journal.

At present, *Science's* policy is that "archival data sets (such as sequence and structural data) must be deposited with the appropriate data bank and the identifier code should be sent to *Science* for inclusion in the published manuscript," adding that the coordinates of this deposition "must be released at the time of publication".

Nature's policy is to require sequence data to be deposited in GenBank or a database of equivalent unrestricted accessibility, with an accession reference included in the publication. "Clearly we need to keep abreast of the changing landscape of databases, and the increasing involvement of private interests," says Philip Campbell, the editor of *Nature*. "It would be absurd to be fundamentally opposed to private database ownership, but the confidence of researchers and the public's stake in the content of the human genome are both of paramount concern." (See page 317.)

But some researchers are concerned that *Science's* policy does not explicitly require open access to data. Bloom told *Nature* that the magazine "will continue to advocate free access to nucleotide sequence data. Public databases are facing a challenge from the clash between the needs of two cultures — academia and industry. We at *Science* urge open, constructive dialogue between all parties so that unrestricted access to information can be assured, while still allowing enough protections that the biotechnology industry can flourish."

Declan Butler

'The human genome itself must be freely available to all humankind'

Bruce Alberts, president of the US National Academy of Sciences, and Sir Aaron Klug, president of the Royal Society of London.

"Through a public–private initiative of international proportions, science is about to provide the world with one of the most significant intellectual achievements of all time — the complete sequence of the human genome — which will provide a detailed map all of the genes in each cell that provide the blueprint for human life.

The implications are enormous. Last week, US President Clinton and UK Prime Minister Blair issued a joint statement applauding the effort. They emphasized the decision by scientists working on the Human Genome Project to release rapidly all of the information emerging from the project into the public domain, and urged scientists around the world to adopt the same approach.

We commend this powerful statement. But we also know that action by the world's scientists is not enough. More attention must be given to striking the appropriate balance between public and commercial interests.

Determining the sequence of the genome is similar to completing the list of the chemical elements: it tells us about the basic components, but not about how they behave in combination. In other words, it gets us to the starting line for a massive increase in understanding, but does nothing by itself to provide us with that understanding.

With the completed genome sequence, we will have all the instructions for making the 50,000 or more proteins present in the human body. But we will not know what each protein is for; still less about how the thousands of genes work together to produce and maintain the human body. And we will not know how the expression of a gene or genes can go wrong in the course of a disease.

In short, a huge amount of work will remain to be done. This will require effort in both the public and private sectors for generations to come. It is likely to lead to numerous breakthroughs in health care, benefiting all sectors of society. It is also likely to lead to numerous legitimate opportunities for creating wealth, underpinned by patent protection for the inventions and innovations of the individuals and companies involved.

What type of patent protection makes sense? Patent laws are based on the principle that public disclosure of a valuable new invention through the patenting process should be encouraged and rewarded, allowing others to use and build on the invention to create additional benefits to society. In return, the inventor is rewarded with monopoly rights over the use of the invention for a limited period of time.

It is critical that the benefits to the public be at least reasonably commensurate to this reward. Given the enormous potential of the human genome sequence, the granting of broad monopoly patent rights to any portion of it should be regarded as extraordinary — and occur only when new inventions are likely to confer benefits of comparable significance for humankind.

It is a trivial matter today — using a computer search of public databases — to use DNA sequences to identify new genes with particular types of biochemical functions. In our opinion, such a discovery should not be rewarded with a broad patent for future therapies or diagnostics using these genes when the actual applications are merely being guessed at.

The intention of some university and commercial interests to patent the DNA sequences themselves, thereby staking claim to large numbers of human genes without necessarily having a full understanding of their functioning, strikes us as contrary to the essence of patent law.

Those who would patent DNA sequences without real knowledge of their utility are staking claims not only to what little they know at present, but also to everything that might later be discovered about the genes and proteins associated with the sequence. They are, in effect, laying claim to a function that is not yet known or a use that does not yet exist. This may be in current shareholders' interests. But it does not serve society well.

Scientists are at the very early stages of this work: knowledge of the human genetic sequence is only the first step. The next will be to understand how the tens of thousands of genes that make up the genome work together to create the machinery that operates the human body.

This will be a huge scientific undertaking. For it to work effectively and bring widespread benefit as quickly as possible, it is vital that all researchers have access to the full genome without charge or other impediment. The human genome itself must be freely available to all humankind." ■

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