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A challenge to genetic transparency

Those engaged in the publicly funded effort to sequence the human genome should look on their new rival as healthy competition. But they will also need to protect the standards they have fought hard to establish.

Two weeks ago, when the laboratory equipment company Perkin-Elmer and genomics pioneer J. Craig Venter unexpectedly announced that they were joining forces to carry out a privately funded sequencing of the complete human genome, they sent tremors through the sequencing community. The language in which the announcement was made, speaking of a "breakthrough" in DNA analysis technologies that would allow an "ultra-high" throughput of samples, only reinforced concern. If it was really true that, as some press reports claimed, the new initiative would achieve its objective several years sooner, and ten times more cheaply, than publicly funded efforts, how much longer would it be before public agencies decided to pull the plug and divert funds elsewhere?

Criticisms

By the end of last week, much of the initial alarm had dissipated. Closer inspection of Perkin-Elmer's plans for its new sequencing machine revealed that, while a substantial improvement on current technology, it does not represent a quantum advance over that being offered by rival companies — while many of its claims to speed and effective automation remain to be demonstrated. Leaders of the government-funded efforts, such as Francis Collins, director of the US National Centre for Human Genome Research, made much of the alleged shortcomings in Venter's 'shotgun' approach to sequencing to argue the continued need for their own, more accurate, sequencing endeavours.

Such criticisms may be too defensive. But it is indeed important that there should be a reaffirmation of the publicly funded programme. In the Congress, staff on the committees responsible for the budget of the National Institutes of Health (NIH) have rightly made reassuring noises about the need to ensure that the $1.9 billion of public funds already invested in the Human Genome Project do not go to waste, or merely benefit the private sector (see page 201). Britain's Wellcome Trust last week gave public-sector sequencers a shot in the arm by its fortuitously coincidental decision to double its support for human genome sequencing, contributing a further £110 million ($175 million) over seven years — a move allowing it to shoulder responsibility for one-third of the total effort. The talk was of healthy competition rather than throwing in the towel.

Those attending last week's genomics meeting at Cold Spring Harbor, who had lived through an emotional week as details of the Venter/Perkin-Elmer initiative became known, greeted the Wellcome announcement, and the firm commitment to open access to sequencing data that accompanied it, with a visible sense of enthusiasm and relief. But it would be unwise for researchers to underestimate the magnitude of the technical and scientific challenge that the new project will present. Nor should they overestimate the depth of support in a Congress that frequently expresses its reluctance to pick up the bill for activities able to find financing from the private sector.

On the technical aspects, the public-sector sequencers have powerful benefits on their side. Public funding (including that from Wellcome) has ensured that a concern for accuracy and completeness has not been dominated by excessive demands for speed or high returns on investment. Collins has established high standards of quality that the half-dozen federally funded US sequencing laboratories are expected to achieve with their data, obtained by meticulously working through ordered fragments of DNA. Venter's strategy, although faster and probably cheaper, cannot yet claim to compete on the contiguity of the final product.

Challenges

The technical challenges arising from the initiative represent good and bad news. Positively, speeding up of sequencing will greatly increase the volume of material requiring integration into public databases and analysis. On the other hand, Venter's stated plans make it clear that the sequences will not be complete. Those interested commercially in sequencing primarily as a source of potential new diagnostic techniques and therapies can be depended on to pursue the level of accuracy required to understand the detailed functioning of individual genes. But they will have little interest in completeness for its own sake.

Prompt availability is an even more serious worry. Venter and Perkin-Elmer have promised to make their sequence data freely available to researchers, but they will be released only at three-monthly intervals — and then only in the form of 'consensus' sequences. Researchers will be denied access to the raw data from which these sequences are calculated, and thus unable to check their accuracy or to integrate the data into the continuing public sequencing programme. Perkin-Elmer has already made it clear that its interest in bankrolling the new sequencing initiative is not only to use it as a testbed for sequencing machines that will then be sold to others, but also to profit from the data — in particular information about genetic diversity, or 'polymorphisms', that are likely to emerge. Where fast access to raw data conflicts with pressure to skim it for potential commercial value, it is not difficult to see where the balance in a commercial venture is likely to be struck. That, in the absence of a firm commitment to public funding for sequencing, would be a significant threat to the science.

So far, those responsible for carrying out the Human Genome Project on both sides of the Atlantic have shown themselves impressively aware of the need for continual vigilance to ensure that commercial pressures are not allowed to encroach excessively. The Venter/Perkin-Elmer initiative must be welcomed as an important competitor in the genome sequencing stakes; even the most dedicated public enterprise benefits from healthy private competition. Arguments about ownership are inevitable. But for aggressive scientific entrepreneurs, collaboration with the publicly funded community is more profitable than hostility. That is a card the community has up its sleeve and should be prepared to play in maintaining essential values of complete scientific access to our genetic inheritance. □