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Getting it together

As *Nature Biotechnology* goes to press, the Human Genome Project and Celera Genomics are preparing to announce completion of a working draft of the sequence of the human genome. Unfortunately, this biotechnology milestone will have been achieved for the most part in an atmosphere of mutual hostility and suspicion rather than as a desirable collaborative effort between the public and private sectors. This is particularly disappointing, since the collaboration between J. Craig Venter of Celera Genomics and Gerald Rubin at the University of California at Berkeley proved that the two sectors can work fruitfully together (we couldn't resist), yielding the sequence of *Drosophila* in only a few months.

Celera's initial announcement describing plans to sequence the human genome by 2001—four years earlier than the target proposed for the Human Genome Project—was an anathema to the HGP, and one suspects that the decision to announce this plan at the 1998 Cold Spring Harbor conference, where many of the heads of the public sequencing centers were meeting, was timed for maximum effect. The suggestion that genome sequencers might want to give up sequencing the human genome, leave it to Celera, and instead concentrate on the mouse genome implies that Venter and his associates believed the human genome sequence was there for the taking and that the HGP was at a truly low ebb.

But the public project was in no mood to capitulate. Venter's challenge to the research community instead provoked a new sense of urgency and reality. In the UK, the Wellcome Trust responded by nearly doubling its funding of genome sequencing at the Sanger Center and, in the US, $81.6 million of new funding was allocated to a core group of five major centers in March 1999. In the subsequent months, sequencing was ramped up significantly to a turnover of 12,000 bases every minute. In November, the billionth base of the genome was deposited in GenBank; four months later, the two-billionth base was lodged. (It was a T, by the way.)

Today, Venter and the leaders of the HGP remain extremely wary of one another. Although attempts to find common ground for collaboration have been made—in December 1999 with the Department of Energy, and again in March of this year—these have foundered until now because of Celera's demands for control over access to the sequence data and intention to patent certain genes.

With the completion of the "first draft of the genome," it is now high time that private and public initiatives find a way to resolve their differences and collaborate together on the next stage of the project—producing the final draft. Some observers have suggested that the common pooling of resources could allow its completion by early next year. The conciliatory statements by HGP Director Francis Collins and Venter last month on joint publication suggest that relations are becoming more cordial. We hope so. There is too much at stake for petty rivalry, politics, or even money to distract us from addressing the real question of what all this sequence means.

What price e.commerce?

With what seems like clockwork regularity, the issue of price controls on medicines appears to surface every year for debate in national government. More often than not, events take a predictable turn: proposals are made, the pharmaceutical lobby savages them, they become bogged down in the committee process and quickly disappear into a legislative black hole.

This year, however, several US states—namely Arizona, California, Connecticut, Maine, New Jersey, New York, Pennsylvania, and Vermont—have taken matters into their own hands, setting in place measures that truly threaten to tackle the problem face on. In May, the first of these statutes was enacted; Maine Governor Angus King, Jr. signed into law a measure that will ultimately result in a price cap on biotechnology drugs sold in Maine.

Not surprisingly, the Maine price control bill has caused a considerable flap in industry circles. It authorizes the state to act as a pharmacy benefit manager and negotiate pharmacy discounts for Maine residents (estimated at 10%). The US Biotechnology Industry Organization has strongly criticized the Maine bill as "a shortsighted statute that will only hurt patients and damage the state's growing biotechnology industry." As usual, it argues that price controls discourage the private investment required to fund research and development into experimental drugs. Other industry observers also argue that the legislation is the first step down the slippery slope of a patchwork quilt of potentially conflicting state laws that could ultimately prove "chaotic" for drug companies.

They could have a point, considering that biotechnology drugs are among the most expensive medicines in the world, with the smallest target patient groups. And more biotechnology companies look like the will actually receive sales revenue, as increasing numbers of drugs make it through clinical development.

This may all be moot in the near future, however, if the introduction of e-pharmacies on the Internet, which will sell drugs directly to consumers, continues at its present pace. Patients using Internet-based services are likely to become increasingly aware of discrepancies in drug pricing over national boundaries, which have arisen as a result of historical differences in drug regulations and pricing controls across the globe.

Of course, companies that sell their products on the Internet will have to completely reexamine their sales margins. We just don't know yet how to exploit the web for direct selling to patients, how the supply chain will be redefined, how to reorganize the personnel and resources of the marketing and distribution teams, and indeed whether intermediaries such as wholesalers and pharmacists will actually be needed in the long term at all.

It would be very easy to leave all this to the pharmaceutical companies, which after all have the resources and know-how to market products. But whatever the virtual pharmacies of tomorrow finally look like, it is certain that the drugs of the future will be sold over the "information superhighways" as frequently as they are sold today in main street pharmacies. It is this change in health care delivery that will radically redefine the economics of drug pricing in the coming years. ///