Chinese institute makes bold sequencing play

China's BGI has become the largest next-generation genome sequencing center in the world after it purchased 128 new HiSeq 2000 genome sequencers from Illumina. The deal was announced in January by Jay Flatley, president and CEO of San Diego–based Illumina, at the 28th Annual J.P. Morgan Healthcare Conference in San Francisco (**Box 1**). The announcement comes amid a boom of scientific productivity in China centered around next-generation sequencing technology, which has resulted in the publication of three landmark papers by Chinese researchers in the past two months alone: the sequencing of the cucumber (*Nat. Genet.* **41**, 1275–1281, 2009) and giant panda (*Nature* **463**, 311–317, 2010) genomes and the human pan-genome (*Nat. Biotechnol.* **28**, 57–63, 2010).

BGI, which started life as the Beijing Genomics Institute but then moved to Shenzhen, China, will install most of the newly acquired Illumina sequencers at its new genome center at Hong Kong Science Park throughout 2010, says BGI executive director Jun Wang. "We will use these instruments to help build research and application platforms for sustainable development in agriculture, bioenergy, personalized health care and related fields in China."

The emergence of BGI as a sequencing powerhouse could have a significant upside for Hong Kong's biotech sector. "Having the largest DNA sequencing facility in the world in Hong Kong will hopefully contribute towards attracting talent in genomics and bioinformatics and stimulate collaboration with other local research groups, such as those in the two medical schools," says Dennis Lo, director of the Li Ka Shing Institute of Health Sciences (LiHS), a translational medicine research institute of The Chinese University of Hong Kong (CUHK).

Lo, who is also associate dean for research of the Faculty of Medicine at CUHK, adds that the facility's international visibility might also "trigger more investment from the Hong Kong government and the commercial sector to develop biotech in Hong Kong." LiHS recently installed 10 Illumina Genome Analyzers, eight of which are part of a joint CUHK-BGI genome research center that intends to conduct collaborative "projects in the fields of cancer, diabetes and plant genomics," he says.

BGI's vice president, Xiuqing Zhang, also points to a deliberate international agenda. "BGI's investment in Illumina's new HiSeq 2000 system is an important step in our effort to develop a premier sequencing facility that serves scientists globally," he says. The HiSeq 2000 platform is capable of generating two billion paired-end reads and 200 gigabases of quality-filtered data in a single run, allowing

China's BGI, now in Shenzhen, has become Illumina's largest customer overnight.

IN brief

Melanoma vaccine for dogs

A canine melanoma vaccine has received a full license from the US Department of Agriculture, the first therapeutic cancer vaccine approved for human or animal use. The San Diego–based Vical sees the approval of its DNA vaccine Oncept as an indicator of potential success for its human therapeutic vaccine currently in development for metastatic melanoma. Others are more cautious. "[It] is quite an achievement, but I don't believe that Oncept's approval has brought us any closer to a human therapeutic cancer vaccine, as researchers have seen cures in animal models of melanoma for quite some time," says Martin Bachmann, of Cytos, a company in Schlieren, Switzerland. Oncept contains a gene encoding human tyrosinase, an enzyme associated with skin pigmentation, which stimulates an immune response against canine tyrosinase in melanoma cells. "Canine melanoma is similar in disease course and spread to human melanoma, so the results could be relevant for predicting response in humans for a similar DNA vaccine. However, the study was not randomized, and it's hard to forecast how the human immune system will respond," says Christian Ottensmeier, a Cancer Research UK investigator at Southampton University. Oncept will be commercialized by Vical's licensee, Merial, the animal health subsidiary of Paris-based Sanofi-aventis. *Suzanne Elvidge*

Biotechs go virtual

Outsourcing the early stages of R&D is a growing trend among young biotech firms in the UK, a new report reveals. Researchers at Cass Business School in London tracked 68 university and public service laboratory spin-outs as part of a larger Engineering and Physical Sciences Research Council (EPSRC) project on high-tech business organization. The study reveals that up to one-third of these firms have embraced an innovative 'virtual biotech' business model to help reduce the time taken to reach clinical trials and build up a pipeline of early stage products. According to Dzidziso Samuel Kamuriwo, the report's author, this business model has flourished among fledgling biotechs thanks to a combination of local policies that favor the industrialization of public science, multiple sources of funding and high-quality science conducted in public labs. The advantages of going 'virtual' include flexibility and few or no capital costs, which help slow cash burn (*Nat. Biotechnol.* **27**, 886–888, 2009). Companies that adopt this virtual approach tend to outsource R&D to their founding institutions or to specialist service firms and are dependent on strong project management to succeed. The virtual model works best across several therapeutic areas, while the integrated model—keeping everything in house—thrives on fewer areas. In the long run, Kamuriwo points out, integrated companies are more likely to succeed, but after experiencing the short-term gains of the virtual approach, companies find it hard to change their organization model. *Susan Aldridge*

Box 1 A human genome in a week

The BGI deal represents Illumina's largest single order for sequencers so far and is estimated to be worth over $88 million, given that the retail list price of the HiSeq 2000 is $690,000, although BGI may have received a significant volume discount.

BGI signed an agreement last month with the China Development Bank under which BGI will receive $1.5 billion in 'collaborative funds' over the next ten years, which the institute plans to use for infrastructural development and to cover running costs.

However, BGI is not the only institute sequencing genes in China, so the country's overall annual equipment expenditure is likely to be in excess of $1 billion. "There are other scientists in China involved in gene sequencing," says Jun Wang. "There are another three genome centers and more labs with [sequencing] instruments."

Although the initial cost of the Illumina sequencers may be high, technical innovations "take the cost of sequencing a human genome below $10,000," says Illumina's Jay Flatley, noting that just three years ago, sequencing a human genome cost $1 million, whereas the new HiSeq 2000 sequencing system could "recreate the International Human Genome Project in a week."

According to the manufacturer, the HiSeq 2000 is capable of generating 200 gigabases of data per sequencing run and 25 gigabases of data per day. It uses two flow cells and an innovative dual-surface imaging method, enabling new levels of sequencing output as well as experimental flexibility. "With the rapid reduction in the costs associated with [gene] sequencing, this approach will soon be cost-effective enough to be used on a routine clinical basis," Lo predicts. *JF*

researchers to obtain 30-fold coverage of two human genomes in a single run. "Our goal is to build partnerships and collaborations around the world that contribute to our global society," says Zhang. "Creating solutions that enhance agriculture and food production, for example, are a key focus for us, [as are] more region-specific programs, such as the development of the personal genomics field in China."

"[BGI's investment] aligns well with some of (China's) strategies in a number of areas, like reducing medical costs and improving plant- and animal-based industry," says Charles Cantor, chief scientific officer of San Diego–based Sequenom. The company's technology is commonly used to follow up whole-genome studies to confirm newly discovered alleles and phenotypic associations, and Cantor expects China to be an important market. China has been "very successful" in efforts to develop genome analysis software, he adds.

BGI has also been establishing its own technical platforms based on large-scale genome sequencing, efficient bioinformatics analysis and innovative genetic healthcare initiatives, with these achievements having contributed considerably to the development of genomics in China and elsewhere.

BGI's Wang, who is also a professor in the Department of Biology at the University of Copenhagen, notes that genomic sequencing platforms would also open the door for further collaborative projects worldwide, including the 1,000 plant and animal reference project, to which BGI has pledged $100 million; the 10,000 microbial genomes project; and the Chinese Cancer Genome project.

BGI has already established itself as an important genome center on the world map. It successfully sequenced 1% of the human genome for the International Human Genome Project; contributed 10% of the International Human HapMap Project, with which CUHK was also involved; played a key role in the Sino-British Chicken Genome Project; completely sequenced the rice and silkworm genomes; and completed the first diploid human genome sequence of an Asian.

As reference genomes for certain organisms are now relatively common, "different strains are now being sequenced to discover the variations related to certain traits in those species," says Wang, noting that "large-scale studies in exomics, metagenomics, epigenomics and transcriptomics" have suddenly all become realistic propositions.

In terms of applications, Lo's group at CUHK has pioneered the use of next-generation DNA sequencing as a molecular diagnostics tool, using noninvasive prenatal diagnosis as an example. CUHK researchers have also been involved in viral and bacterial genomic sequencing. For example, "my group was one of the first two Asian groups to report the complete sequencing of the SARS [severe acute respiratory syndrome] coronavirus and to use genomic information to research the molecular epidemiology and evolution of this virus," says Lo.

In China, "the challenges are getting more resources, [especially] funding, samples, and collaborative agreements from various groups that study different subjects," says Wang. "We also need more young talent to work in this field, in particular to analyze the data." Finally, Wang stresses that although the Illumina deal may have made BGI the largest sequencing center in the world, "genomics cannot be done alone and must be performed on an international basis."

One of the best examples concerns the 1000 Genomes Project, an international research effort to establish the most detailed catalog of human genetic variation by sequencing the genomes of at least 1,000 individuals from different ethnic backgrounds, in which BGI is collaborating with genome centers in Germany, the UK and the USA.

The size of China's population could be a boon to international efforts at unraveling how genome variations contribute to disease. Indeed, China has also made a commitment to cancer research. "They are doing work to describe such patients, and one can only expect it's going to accelerate as they become more sophisticated and [Chinese people] get better and better healthcare," says Richard Cotton, who is head of the Genomics Disorders Research Centre at the University of Melbourne in Australia and convenor of the Human Variome Project, which focuses on collecting and curating human genetic variations that affect health.

Cotton's efforts have focused on single-gene disorders, and he is excited about the potential for new research to emerge from China's

New product approvals

Victoza (liraglutide [rDNA origin] injection)	Novo Nordisk (Copenhagen)	The US Food and Drug Administration approved the new drug application for Victoza, the first once-daily human glucagon-like peptide-1 (GLP-1) analog for type 2 diabetes. Victoza is indicated as an adjunct to diet and exercise to improve blood sugar control in adults with type-2 diabetes mellitus.
Xiaflex (collagenase clostridium histolyticum)	BioSpecifics Technologies (Lynbrook, New York) and Auxilium Pharmaceuticals (Malvern, Pennsylvania)	The US Food and Drug Administration approved Xiaflex for adults with Dupuytren's contracture with a palpable cord. Xiaflex consists of two microbial collagenases in a defined mass ratio, Collagenase AUX-1 and Collagenase AUX-II, which are isolated and purified from the fermentation of *Clostridium histolyticum* bacteria.

bulked-up resources. "I can see a renaissance in single gene disorder work because the sequencers can be put in there to find something useful for patients. There's no question in my mind that these sequencers will be put to work in the Chinese population," adds Cotton.

But that won't necessarily be enough, he says. Healthcare infrastructure will also be critical. "They've got to (obtain) the material to put in them. Single gene disease research is not high-throughput. A patient comes in the door of a doctor's office and then leaves, but that rate is not very high. If they get themselves organized in China, they could get a lot of samples coming in," adds Cotton.

Along with its continued strengthening of expertise in sequencing and analysis, "China is now producing more well-trained scientists than any other country," says Cantor. As long as this trend continues, China's impact on progress in research and technology is likely to continue to rise proportionally. "It is inevitable," he adds. And in terms of both investment (*Nature* **463**, 282, 2010) and scientific output, China's genome centers are already beginning to rival some genome centers in Europe and North America, although today the emphasis is more on collaborative research between many international centers than on competition.

China's efforts could well spur development elsewhere. "I think there is a tremendous opportunity for any country or funding agency to really empower that discovery by making some investment. I assume that China understands that. They have a good group at BGI, which has a pretty good track record of making this kind of thing work," says Richard Wilson, director of The Genome Center at the Washington University School of Medicine, St. Louis, Missouri. "If countries such as the US, or the UK, or anyone else sees that as a good reason to build up their own genetic sequencing infrastructure, I think that's a good thing. The more the better."

John Fox *Hong Kong and*
Jim Kling *Bellingham, Washington*

IN their words

"Women would not even know they had [a] *BRCA* gene if it weren't discovered under a system that incentivizes patents." Defense attorney Brian Poissant pitches the importance of gene patents in motivating commercialization of discoveries at a hearing in the lawsuit on Myriad's *BRCA1* and *BRCA2* claims opposed by the American Civil Liberties Union, a coalition of civil rights, research and women's health groups. (*GenomeWeb*, 2 February 2010)

"Over the last 30 years, we as a nation have spent $9 per American per year on cancer research. Enough to buy you a couple of lattes." Francis Collins recalibrates the US public's understanding of how much has been spent on the 'war on cancer' declared by President Nixon almost 40 years ago. (*CBS Evening News*, 28 Jan 2010)

"His members think he gave away the farm for nothing. So he was really tossed because of a falling out with the board over miscalculating how to negotiate." An unnamed industry source gives the inside view on Billy Tauzin's decision to resign as chairman of PhRMA, which spent $26,150,520 in 2009 on lobbying, according to the nonpartisan Center for Responsive Politics. (*ABC News*, 12 February 2010)

"I now believe it is time I move on and hand the mantle of leadership of this great organization to others as passionate as myself and to explore the many other interests I would like to pursue in this special second-chance life that I have been given." Billy Tauzin, cancer survivor and president of pharma industry trade group PhRMA resigns amid criticisms over the group's involvement in proposed US healthcare reform. (*ABC News*, 12 February 2010)

"There's no doubt there's risk in pharmaceuticals, and there should be! If you make 30% returns it should be a risky business. If you don't want risk, go be a grocery store and make 6%." Andrew Witty, GlaxoSmithKline's CEO, comments on pharmaceutical R&D in the light of controversy over anti-aging compounds developed by their 2008 acquisition Sirtris. (*Forbes*, 25 January 2010)

"There are physicians earning so much money [from drug makers] that they would give up their jobs…It's a shocking story. Normally, you'd give up the [company] honoraria." Steve Nissen, head of cardiovascular medicine at the Cleveland Clinic Foundation, comments on Lawrence DuBuske's decision to leave Harvard rather than forgo payments from industry (which had totaled $99,375 for 40 talks). (*The Boston Globe*, 23 January 2010)

"Arrays are a hundred times cheaper, a hundred times faster and materially more accurate than sequencing will be over the next couple of years." Illumina's Jay Flatley told delegates at the J.P. Morgan conference in San Francisco in January that arrays are likely to hold the upper hand for genome-wide association studies over next-generation sequencers. (*GenomeWeb*, 15 January 2009)

IN brief

RNAi delivery shop

Silence Therapeutics of London and Intradigm Corporation of Palo Alto, California, have merged, in a deal designed to boost their competitiveness as providers of RNA interference (RNAi) delivery solutions. The two firms have developed separate technologies to enhance RNAi delivery and stability, currently the biggest challenge in RNAi-based therapeutics. By merging, the new company hopes to offer a set of systems to overcome these problems. Silence will contribute the AtuPlex delivery platform designed to stabilize siRNA within a liposome, whereas Intradigm's system is a biodegradable, synthetic peptide–based polymer that allows any tissue in the body to be targeted by adding a ligand. The deal, which took place as a reverse merger and for which Silence issued close to 80 million shares to acquire Intradigm, has been valued at about £20 million ($32.6 million). According to Simos Simeonidis, an analyst at Rodman & Renshaw, the combined company (which retains the name Silence Therapeutics) may become a more attractive partner for big pharma than its predecessors were because it has more platforms to offer. But he doesn't think the merger makes Silence any more competitive compared with market leaders Alnylam and Sirna because pharma can always partner with multiple biotechs, each offering different technologies. Besides, said Simeonidis, "no one has all the answers, not even Silence with their multiple delivery technologies." *Nazlie Latefi*

Brazil boosts bioscience

Brazil's national economic and social development bank BNDES has signed an agreement to invest in a selection of innovative bioscience and infrastructure projects at the state-owned Oswaldo Cruz Foundation, part of the Brazilian Ministry of Health (*Nat. Biotechnol.* **27**, 1063–1064, 2009). The Rio de Janeiro–headquartered foundation, also known as Fiocruz, is planning a range of R&D projects that would require an estimated R$1 billion (US$536 million). BNDES will cover part of these costs, and Fiocruz hopes to get the rest through partnerships with the private sector. Fiocruz has already received the first R$40 million ($21.4 million) installment, which is being used to finish the facilities of a new Center for Technological Development in Health (CDTS) and to fund several projects at the Immunobiological Technology Institute in Rio de Janeiro (known as Bio-Manguinhos). Among the schemes selected for funding is the production of recombinant epoetin alpha, recombinant human alpha-interferon and PEG-interferon. The recently launched Integrated Center for Prototypes, Biodrugs and Diagnostic Reagents in Rio de Janeiro will partner to develop new bacterial and viral vaccines. This year, Fiocruz hopes to start producing 50 million doses of recombinant human insulin per year, thanks to a technological exchange with the Ukrainian Indar Institute. Brazil now imports around 170 million doses of insulin a year. *Ricardo Bonalume Neto*