issues that include a need for considerable oversampling to obtain haplotype information—significantly increasing the amount of sequencing required—as well as a dependence on PCR, which can exacerbate biases already associated with Illumina sequencing. For other users, the business model was problematic. "The cost was too high," says Vincent Magrini, who heads the Technology Development Lab at the Genome Institute at Washington University in St. Louis. "The data looked pretty good for smaller genomes, but it came to thousands of dollars to make a library." Without a strong user base, the technology seems ill-equipped to compete with newer systems that tackle fragments measuring 50–100 kb or longer.

Which is not to say that the road is entirely clear for 10X or Dovetail. 10X has only been tested with human DNA to date and may need fine tuning for tackling other genomes. With an instrument cost of $75,000 and at least $500 per library (if the instrument is run at capacity), the price may also be problematic, especially for groups that work primarily with exomes rather than genomes. "If you have something that basically doubles the cost of exome sequencing, that could be a significant deterrent," says Robison. Dovetail has not made any announcements about pricing, but because there is no requirement for an instrument Chicago could offer a lower-cost solution for *de novo* applications. But the 5-μg sample size makes the platform ill-suited for the limited amounts of DNA obtained from clinical research samples, and the Chicago/HiRise remain unproven as tools for tumor genome analysis. Illumina may also be pursuing its own in-house solutions, as demonstrated by a recent article describing a short-read assembly approach based on "contiguity-preserving transposition," which proved capable of reconstructing stretches of human haplotype with an N50 of up to 2.3 megabases (*Nat. Genet.* **46**, 1343–1349, 2014).

These synthetic long-read systems will also confront limitations inherent to Illumina technology, or any other short-read system with which they might be combined in the future. Long-reads have their own intrinsic problems arising from their low accuracy, which results in poor performance on segmental duplication. "There's always a bias associated with PCR-based strategies, and that's typically seen with these GC- or AT-rich sequences," says Magrini. "I think for many *de novo* applications, you will really need long reads." Robison cites a recent analysis of an extremely long, disease-related mucin gene, with extensive stretches of repetitive sequence, as an example of a target where true single-molecule sequencing proved advantageous (*Am. J. Respir. Cell Mol. Biol.* **50**, 223–232, 2014).

Other startups are now sniffing out the long-read space, such as Cambridge, UK–based Base4, which has developed a microdroplet-based single-molecule platform that they claim can sequence individual DNA molecules at up to 1 megabase per second, with the potential for scaling up to high-throughput analysis. Alternative approaches to long-range sequencing—mapping the physical location of individual sequences within large genomic segments—are also being pursued by Providence, Rhode Island–based Nabsys and San Diego–based BioNano Genomics.

Theoretically, one might expect steady improvements in the cost, throughput and quality of single-molecule sequencing to push out synthetic approaches altogether, but these may nevertheless continue to fill a valuable need. "A lot of people also thought that exomes would disappear once we got the $1,000 genome, and that hasn't happened," says Robison. Indeed, laboratories exploring a broadening spectrum of genomic questions may opt to maintain a diverse menagerie of solutions. "The long-range sequencing market continues to grow," says 10X vice-president of marketing Rob Tarbox. "It's not like the pie is the same size and everybody's just fighting over a bigger slice."

Michael Eisenstein *Philadelphia*

"Nobody wants a needle in their uterus when they can get a blood test, but that's just not the way it works in 2015." Joe Leigh Simpson of the March of Dimes, on an article in the *New England Journal of Medicine*, showing that noninvasive prenatal testing was better at detecting Down's syndrome than conventional methods. Ariosa's test called it correctly in 38 women carrying Down's babies, whereas standard screening methods detected it in only 30 of those women. (*Philly.com* 2 April 2015)

"23andMe's gene tests are banned in the United States because the evidence for the health claims they make has not been confirmed. Superdrug is acting irresponsibly by selling unregulated gene tests with no medical involvement." Helen Wallace, director of GeneWatch UK, reacts to the announcement that 23andMe has partnered with the Superdrug pharmacy in the UK, which will be 23andMe's first foray into a commercial venture. (*The Guardian* 31 March 2015)

FDA approves 23andMe gene carrier test

23andMe, based in Mountain View, California, has received word from the US Food and Drug Administration (FDA) that their Bloom syndrome carrier screening test was approved as a class II device. The approval came in February, 15 months after the personal genomics company received a cease and desist letter from the regulator for its genetic tests because the company was dispensing health-related information to consumers without having obtained marketing clearance. The FDA website lists class II devices as moderate risk, requiring some regulatory controls, putting carrier screening tests in the same category as condoms. This turnaround follows the company's submission of extensive documentation for its Bloom syndrome carrier screen, including validation, replication and educational materials. The Bloom test detects the BLM(Ash) variant in *BLM*—a 6-bp deletion and 7-bp insertion at nucleotide position 2281 in the *BLM* cDNA. Bloom is a rare, cancer-predisposing disease, more common in Ashkenazi Jews. Somewhat surprisingly, in its approval letter, the FDA said it would exempt carrier screening tests for Bloom Syndrome from premarket review, leaving the door open for 23andMe and others to develop direct-to-consumer tests for such genetic traits. Given that the approval for Bloom's came after extensive studies, what this statement means for future tests is unclear. The FDA plans to issue a guidance for genetic screening tests, which might clarify this situation.

Court sides with Sandoz over Neupogen biosimilar

On March 19, less than two weeks after Zarxio (filgrastim-sndz) became the first biosimilar product to be approved in the US, a California court sided with its maker, the Sandoz unit of Novartis, based in Basel, to clear away one obstacle to its market launch. The US District Court for the Northern District of California denied Amgen's request for an injunction to delay sales of Zarxio—a biosimilar of Amgen's blockbuster drug Neupogen (filgrastim) used to treat neutropenia. Sandoz, the court ruled, did not violate the Biologics Price Competition and Innovation Act by its refusal to fully disclose proprietary information to Amgen regarding its application and manufacturing processes, as the law provided for an alternative scenario in case of noncompliance. The court order, however, did not address still-pending claims of infringement made by the Thousand Oaks, California–based Amgen, meaning that if Zarxio entered the market and was later found to infringe, Sandoz would be liable to Amgen for any reimbursements or penalties. Amgen said it would appeal the decision. The two companies previously agreed to seek an expedited review of any appeal at the US Court of Appeals for the Federal Circuit. The outcome of this case will likely influence other similar disputes, such as the Janssen unit of Johnson & Johnson's suit against Celltrion and Hospira that could delay or block the US launch of Remsima, a biosimilar of Johnson & Johnson's drug Remicade (infliximab) used to treat autoimmune diseases.