Falling prices and unfair competition in consumer genomics

To the Editor:

In the November issue, Malorye Allison's News Feature (*Nat. Biotechnol.* **30**, 1027–1029, 2012) described the changing face of the direct-to-consumer (DTC) genomics industry. As founder and CEO of a DTC genomics company myself and an avid proponent of DTC, I was disturbed by 23andMe's (Mountain View, CA, USA) announcement last year to cut the price of its genetic testing down to $99—a move I regard as stifling competition in what remains a small and nascent sector. Indeed, I contend that Illumina (San Diego) and 23andMe have colluded to kill the remaining competition in DTC testing. This pricing war spans the globe and involves major genetic superpowers in the United States, Iceland and China.

23andMe's timing could not have been more right—on the same day of its announcement, Amgen (Thousand Oaks, CA, USA) also announced the acquisition of the Icelandic DTC flagship deCODE (Reykjavik, Iceland) for $415 million. Amgen's takeover of deCODE, which now ceases to be a DTC player and will transition into clinical diagnostics, follows a bitter tug of war between BGI (Shenzhen, China) and Illumina over the acquisition of Complete Genomics (Mountain View, CA, USA). However, the first 'shot' in the hostilities was fired by Life Technologies when it acquired another DTC genomics player, Navigenics (San Francisco), earlier last year.

Who is behind this price war? The main players are Illumina, LifeTech, BGI and 23andMe. LifeTech took out Navigenics, Illumina's second biggest customer in the United States, possibly because 23andMe was too expensive. Next, BGI opted for full vertical integration and began capturing strategic players across the globe with acquisitions, ranging from a Czech fertility center as a "customer store front" to Complete Genomics as technology differentiator.

Seeing these losses to its major private customer base (the rest of its market consisting of genomic centers funded by cash-strapped governments), one explanation is that Illumina embraced 23andMe as its only remaining customer. The recent deal is therefore an expansion of 23andMe's strategy to provide testing at cost and rely on the future licensing revenue from its patents. The 23andMe model depends on acquiring health data from its consumers and then using its internal database of genetic markers for disease association analyses and discovery; indeed, the company has already successfully used this approach to identify novel markers for Parkinson's disease. In my view, this strategy was a fair game until recently, but not anymore.

The DTC market is becoming increasingly anticompetitive because of changes on several fronts. First, after repeated assaults from regulators and the US Food and Drug Administration, the DTC industry is in its death throes, with 23andMe emerging as the sole survivor, thanks to deep-pocketed investors attracted by the halo of Google.

Second, by setting the price point at $99, 23andMe has ceased to play fair with its remaining competition because $99 is clearly set below cost. I believe that setting its service at this level is not intended as a move to drive consumer recruitment to help galvanize genetic association analyses discovery, but rather a cynical move to choke the remaining DTC competition. The move has been funded by 23andMe's most recent round of financing, which raised $50 million—an amount unheard of for other DTC companies.

And third, 23andMe's price-dumping move required close partnership with Illumina. Presumably, Illumina played along mainly to outcompete BGI and perhaps increase the barrier to market entry for upcoming third-generation sequencing companies as well.

Is this price war good for American consumers? What about the US position as an innovation leader? After all, Illumina and 23andMe are US technology pioneers trying to defend themselves from hostile foreign competition (e.g., BGI in China or Oxford Nanopore in the United Kingdom). Perhaps nationalistic concerns are one reason why we still have not heard a word from the US Federal Trade Commission (FTC; New York) about market distortions? If this is the case, it is regrettable as history teaches that short-term, parochial and protectionist business practices have a price: when Rockefeller lowered oil prices, he not only killed the competition, but also laid the foundation for the United States' energy-wasting economy. Rockefeller's monopolistic move echoes to this day with clean-tech innovation still struggling to get off the ground and compete with unfair oil prices. The 'Mac versus PC' story is another example of an overdominant US player (Microsoft; Seattle) unbalancing the US market for decades and using its monopolistic powers not only against the competition but also against consumers; as a consequence, most of corporate IT systems still run on Windows XP.

What do these changes to the DTC market augur for the future of healthcare and genetics? In my view, if 23andMe wins this game, consumers will suffer not because the company will hike the prices one day—unlikely, as consumers will revolt—but rather because 23andMe will have a stranglehold on the market. Microarray technology providers have already been relegated to niche players. Therefore, with a drive toward bargain basement pricing from

one or a few dominant DTC players, the danger is consumers will be saddled with a cheaper, but technologically inferior service. What's more, genome sequencing could be relegated to the sidelines for decades due to the dominance of less effective, technologically obsolete, single-nucleotide polymorphism genotyping technology in the dominant commercial DTC providers.

In a worst-case scenario, this could mean our children will end up relying primarily on patented disease associations provided and owned by 23andMe, with independent disease diagnostic development impeded across the globe—a situation not so fanciful, given how Myriad Genetics' (Salt Lake City, UT, USA) *BRCA1/2* patents have been used to monopolize the breast cancer diagnostics market. 23andMe's target of one million customers can also not be justified as a goal to improve the power of its genetic association studies—one needs only ~200,000 patients (not a million patients) to power a genome-wide association study. In addition, I fear that excessively low-cost genetic testing could promote spurious applications of the technology in the future—perhaps even the type of testing without the consent of potential partners as was imagined in the science fiction movie *Gattaca*.

What can be done to remedy this situation? I doubt that regulatory bodies, such as FTC and the World Trade Organization (Geneva) will move swiftly enough to save the day. Ironically, the only solution lies in the hands of consumers. My advice to them would be as follows: feel free to buy 23andMe's test. But whatever you do, do not provide them with your health data. In doing so, you risk giving away your data into the hands of a monopolistic corporation.

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The ethics of participant-led biomedical research

To the Editor:

In 2011, *Nature Biotechnology* published an article on the effects of lithium on patients suffering from amyotrophic lateral sclerosis[1]. The study was unusual in being initiated and conducted by patients belonging to the online community PatientsLikeMe (http://www.patientslikeme.com/). It was completed with the assistance of PatientsLikeMe researchers who developed an algorithm for matching controls and wrote up the research for publication. The finding that lithium had no positive effect was subsequently confirmed by larger standard clinical trials.

The PatientsLikeMe lithium study is the first of what is likely to be an increasing number of such trials. It is emblematic of two major, interconnected and increasingly powerful trends in the evolving terrain of biomedical research. The first is the increased use of social media, including for the self-reporting of data[2]. The second is the emergence of novel research models that rely heavily on participatory approaches, such as crowdsourcing, citizen science and the like[3]. This emerging model is often termed participant-led research (PLR), in contrast to conventional investigator-led research (ILR), although the lines between the two are often blurred because of the very heterogeneous character of PLR. Indicative of the diversity of PLR is the butter-mind study, in which a group engaged in self-experimentation to determine whether the intake of fats improves performance in arithmetical tests (http://genomera.com/studies).

Although ILR remains the standard research model, it can have drawbacks with regard to its scientific quality, speed of execution and ethical soundness[4,5]. Against this background, PLR offers a promising complementary approach. By drawing on the participation of larger communities of individuals, PLR can gather data that standard research systematically overlooks (e.g., drug side-effects or off-label uses). By means of crowdsourcing, data can be collected more rapidly, thereby accelerating the process of discovery. Participants may self-track and report online or by means of mobile devices, giving PLR projects access to real-time data. Moreover, engaging larger cohorts enhances sensitivity to diversity—a weakness of the existing drug development process. PLR is enabled by online media that cross national borders, allowing it to achieve international and global participation. PLR may be driven by individuals motivated by noncommercial goals, with the result that it can more easily focus on diseases that have been neglected by commercially oriented researchers. Finally, PLR provides ordinary people with valuable opportunities to contribute to the advancement of medical knowledge and thereby achieve personal empowerment and fulfillment.

For all its potential benefits, however, PLR clearly faces scientific and ethical challenges. Issues of bias and scientific validity related to PLR research have been discussed elsewhere[6] and we do not intend to discuss them here. Instead, we would like to draw readers' attention to ethical questions, in particular, the fact that PLR is on the horns of a dilemma. On the one hand, given the risks potentially involved in research with human subjects, PLR's future sustainability depends upon instituting effective mechanisms of ethical oversight that are capable of securing the trust of participants and other stakeholders. On the other hand, the wholesale imposition of the standard ethics review[2] that is legally required in the case of ILR—a procedure involving scrutiny by an institutional review board (IRB) and other forms of ethical oversight—threatens to stifle PLR, subjecting it to a regulatory straitjacket that may act as a disincentive to adoption and innovation.

A vivid illustration of the complexity of this dilemma is the recent controversy about the appropriate ethical oversight of the uBiome project, a citizen science, crowdfunded initiative aimed at mapping the microbiome. The project has been heavily criticized for not undergoing IRB review from the beginning, notwithstanding initial protests from those running the project that such review was neither mandatory nor available[7,8]. Such problem cases are likely to become increasingly common in the future, making it urgent to formulate a principled way of responding to them.

Elsewhere, we have advocated a scheme that seeks to meet this challenge by tailoring ethical oversight to the distinctive and pluralistic character of PLR[9]. If the entity conducting PLR is substantially equivalent to an ILR body, then standard ethical review should be mandatory. Such an equivalence exists when research is carried out by an institutional agent that is either recognized by the state or is profit making in character. Institutions have the power to coerce, exploit or exert pressure on research