Just the facts, please

To the Editor:

As co-founder and CEO of 23andMe, I was disturbed to read a Correspondence from Geneyouin founder and CEO Ruslan Dorfman in the September issue[1] that includes assertions and innuendo regarding my company that are false and misleading. I would like to correct these errors and set the record straight for *Nature Biotechnology*'s readership.

In stark contrast to Dorfman's depiction, 23andMe offers the public an accessible avenue to explore their genetic data, empowering them with a wealth of information that may help them manage their own health and wellness. It's the kind of information that can help usher in a new era of cutting-edge research and discovery while at the same time enhancing an individual's understanding of his or her genetic information. 23andMe adheres to rigorous scientific standards. We are open and transparent about our research, working cooperatively with other groups and university scientists in the study of diseases. Indeed, in the past three years, we have published more than a dozen peer-reviewed papers[2–17] revealing novel genetic findings on as diverse a range of topics as myopia[5], Parkinson's disease[14,16] and allergies[3]. We offer a valuable service to our >475,000 customers and are committed to protecting their personal data.

You would not know any of this from reading Dorfman's letter[1]. Although he is free to express his opinion, he does not have the license to put forth what amounts to arrant mis-statements of fact under the guise of opinion.

I cannot attempt to address all of Dorfman's false statements in the original Correspondence[1], but would like to correct for your readers a few of his most egregious.

First and foremost, 23andMe has never "colluded" with any other company. This offensive and baseless assertion, which forms the thesis of Dorfman's letter[1], is simply false. Let us be clear: 23andMe has never engaged in any such activity. Furthermore, we are surprised that *Nature Biotechnology* allowed Dorfman to publicly accuse our company of serious criminal activity—without any proof or facts—under the guise of opinion. We are an innovative leader in the field and we always seek to operate fairly, honestly and in adherence to all applicable laws.

Second, 23andMe did not coordinate the timing of its price change with Amgen's (Thousand Oaks, CA, USA) decision to buy deCODE Genetics (Reykjavik). This allegation is not just false but absurd. 23andMe could not, and did not, have any prior knowledge of Amgen's acquisition plans regarding deCODE Genetics, or when the two companies would make the acquisition public.

Third, neither did 23andMe set its price "below cost" nor was our $50 million in new financing used toward that end. 23andMe does not price its service below cost. Our decision to lower the price of our DNA kit from $299 to $99 was fundamental to giving more people access to our services and achieving a strategic goal of reaching one million customers, which we clearly stated in the press release we issued on December 11, 2012. Also clearly stated in the press release (and reiterated in many subsequent public statements) is that the company would use the funding to "...expand the necessary infrastructure to support growth in its research and operational capabilities, including product development, genetic research, software development, recruitment and marketing."

Fourth, Dorfman states, again without presenting any factual support, that "... one only needs 200,000 patients (not a million patients) to power a genome-wide association study"[1]. One need only find a few examples to prove this wrong. For instance, the genome-wide association study (GWAS) being conducted by the Genetic Investigation of Anthropometric Traits consortium is already pushing far beyond 200,000 subjects. Given the low prevalence of most diseases, and that GWAS must be performed in ethnically homogeneous populations, a sample of 200,000 people would not even begin to compete with existing cohorts. But, ultimately, why would one ever seek a smaller population sample for study when it is possible to obtain a more statistically reliable sample?

And fifth, Dorfman makes a false comparison between genotyping—what 23andMe does—and genome sequencing—what his company does. Genotyping and genome sequencing are different technologies meant for different purposes. Genotyping via our platform is meant for assaying known single-nucleotide polymorphisms, as well as the thousands of rare variations and mutations covered by our custom platform. This form of chip-based genotyping provides a very high-level of accuracy and is the most efficient way to collect large amounts of genetic data, as one can see from the fact that all other genetic cohorts with >10,000 individuals are based on genotyping or something similar. Dorfman knows that or, at least, he should. Our technology is the state of the art for genotyping.

To summarize, Dorfman's portrayal of 23andMe's motives are exactly the opposite of our long-stated mission, falsely suggesting that 23andMe would close off access to genetic information and "impede" independent disease diagnostic development. Our core value statement, which can be found on our website, is as follows: "23andMe was founded to empower individuals and develop new ways of accelerating research." We invite Dorfman and your readers to visit our website, where they can read further about our mission, vision and commitment to providing people with greater understanding of, and direct access to, their genetic information. We are transparent in how we operate. We work cooperatively with private and academic research institutions to advance scientific discovery. We have worked—and continue to work—on behalf of consumers for better protections against genetics-based discrimination. We follow institutional review board protocol and adhere to detailed rules governing informed consent

for research participants. For Dorfman to ignore our stated mission, vision and goals, as well as our actions, while alleging that 23andMe would usher in an era of testing "without the consent of potential partners," reflects a deliberate disregard for facts easily accessible by any member of the public—including him.

In science and business alike, we are strong supporters of fact-based inquiry and analysis. Reckless and unfounded opinion, motivated by self-interest, however, should have no place in a publication such as *Nature Biotechnology*. Like many scientists, those at 23andMe rely on the quality of work that appears in the journals published by the Nature Publishing Group. It was a disappointment to see a piece that so clearly falls outside of those standards. 23andMe abides by those same standards in respecting robust and honest scientific inquiry. We have taken a risk as a business, making a bet that those kinds of standards paired with our innovative business model and research platform will lead to critical discoveries that will benefit us all.

COMPETING FINANCIAL INTERESTS
The author declares competing financial interests: details are available in the online version of the paper (doi:10.1038/nbt.2771).

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Ruslan Dorfman replies:

The intent of my letter of correspondence was to stir debate about the direct-to-consumer (DTC) genetic testing market. The DTC industry is being embraced by consumers, but is struggling to gain acceptance from a more skeptical community of medical professionals.

As an enthusiastic proponent of genetic testing for health improvement, I applaud the pioneering efforts of DTC companies like 23andMe (Mountain View, CA, USA) in educating consumers in the field of genetics. At the same time, I worry about the push to expand commercial genetic testing to swaths of the general population who may not have a clear understanding of the benefits and limitations of such testing. Nonselective marketing can net customers who might have been better served by opting for clinical genetic diagnostic tests for a specific disease. Disillusioned customers can become deeply suspicious of all DTC providers, and their negative feedback reflects on all companies[1]. As I mentioned in my original letter[2], regulatory agencies have responded to the expansion of the DTC market by making "repeated assaults" to protect consumers; indeed, objections were voiced by the US Food and Drug Administration when Pathway Genomics (San Diego) tried to market genetic testing in partnership with Walgreens (Deerfield, IL, USA) in 2010 (ref. 3); elsewhere, German regulators have practically banned DTC testing altogether[4].

Expanded marketing efforts have repositioned DTC genetic testing from being "fun genomics" done to identify things like ancestry, to being more medically oriented. Many consumers take these tests in hopes of finding a solution to medical issues running in their families. Last week, I met a woman whose family was frustrated with their genetic testing results as their reports failed to mention the genetic predisposition to colon cancer that devastated her family. Such cases demonstrate the limitations of genotyping technology that are not always evident to the general public.

The validity of disease risk prediction estimates from genome-wide associated study (GWAS) data is still controversial[5]. The concern is that consumers with a poor understanding of genetic statistics may take DTC reports calculating risks for conditions at face value, without understanding family history might be more important[6]. Does every customer clearly understand the limitations of a test's sensitivity and the significance of false-negative discovery rates?

The information asymmetry—that is, the gap in understanding of the underlying technology—makes consumers vulnerable to exploitation; thus, from an ethical perspective, this puts exceptional onus on the service providers to ensure that customers fully understand what they are paying for. At Geneyouin (Maple, Ontario, Canada), we do not accept customers if we feel that our testing options will not be able to address a customer's needs. I hope that other providers will do the same.

As for the argument that a larger number of customers is absolutely essential for advancing research, according to statistical power calculations for GWAS studies, the power of discovery for genes with reasonable size effects saturates toward 100,000 samples[7], even with low-density arrays[8]. The UK's 100k Genomes Project[9] is an example of an adequately powered study for analysis of multiple diseases by sequencing. Imputation of rare alleles further reduces the need for mass scale genotyping[10], so the argument that millions of samples are needed for research discovery is weak. There is also a concern related to all DTC companies concerning the need to preserve the privacy of genetic data, especially when millions of genomes are under one roof. Even aggregate and deidentified data pose significant concern over possible subject re-identification[11,12].

I did not mean to accuse 23andMe or any other company of using insider information with regards to M&A activity in the DTC industry[13]. However, in the past two years, the number of players in the DTC industry has decreased sharply. And it would be of interest to readers to learn whether 23andMe receives substantial volume discounts from suppliers like Illumina (San Diego); certainly, friends and colleagues in academia are still paying almost double the price (~$200, http://www.dnadtc.com/#jumpNav4) for just the Illumina array genotyping without taking into account the additional costs of DNA extraction, data processing and marketing.

The DTC industry is suffering from growing pains and when one of the players is growing too fast, like a cuckoo other players in the nest are adversely affected. The rapid pace of takeovers in the industry are shaking the tree, and a couple of blows inflicted by a big player or regulatory agencies will destroy the nest altogether.

Disclosure

Opinions expressed here are of those of the author and not of Geneyouin Inc.

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The author declares competing financial interests: details are available in the online version of the paper (doi:10.1038/nbt.2772).