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Testimony Before The
Committee on Small Business
U.S. House of Representatives

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Chairwoman Velázquez, Ranking Member Luetkemeyer, and other members of the Committee:

Thank you very much for the opportunity to share our experience with the Small Business Innovation Research (SBIR) program with you as you consider the reauthorization of the program. 23andMe benefited greatly from this investment in research, and we are pleased to express our support for the continuation of this important program.

Background on 23andMe

23andMe is a leading consumer genetics and research company. Founded in 2006, based exclusively in the United States with offices in California and testing performed in a laboratory in North Carolina, the company's mission is to help people access, understand, and benefit from the human genome. 23andMe has pioneered direct access to genetic information as the only company with multiple FDA clearances for over-the-counter testing ("OTC") for carrier testing and genetic health reports, and has created the world's largest crowdsourced platform for genetic research, with 80 percent of its customers electing to participate. This research platform has generated more than 180 publications on the genetic underpinnings of a wide range of diseases, conditions, and traits. The platform also powers the 23andMe Therapeutics group, currently pursuing drug discovery programs rooted in human genetics across a spectrum of disease areas, including oncology, respiratory, and cardiovascular diseases, in addition to other therapeutic areas.

History of 23andMe's Participation in the SBIR Program

Over approximately eight years (2010-2017), 23andMe applied for ten SBIR grants and received eight (Table 1). When we first began applying for SBIR grants, 23andMe was a small company: in 2010, the year of our first grant application, we had fewer than 50 employees and minimal revenue from our

direct-to-consumer genetics product. In addition to selling a consumer product, the business also had a goal to accelerate scientific discovery by developing a highly scalable consumer-centric research platform. A significant amount of investment was required in order to develop the infrastructure, breadth, and size needed to make this platform scientifically valuable asset. Because we were a small business and because our mission to help people benefit from the human genome aligned with the mission of the National Institutes of Health's (NIH) mission to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability, we felt the SBIR program could be an appropriate mechanism to fund some of the development of the consumer-centric research platform.

Table 1. SBIR applications submitted by 23andMe

Year Applied	Grant Title	PI	Awarded (Y/N)	Amount	Year Closed
2010	Web-based Phenotyping for Genome Wide Association Studies of Drug Response	JOANNA L MOUNTAIN	Y	$189,844	2012
2011	Web-based studies of the genetics of Parkinson's disease	NICHOLAS ERIKSSON	N	N/A	N/A
2012	Development of DNA Sequence Data-Quality Metrics for Personal Genomics	BRIAN T NAUGHTON	Y	$197,398	2013
2012	Development of a web-based database and research engine for genetic discovery	NICHOLAS ERIKSSON	Y	$232,602	2014
2012	Genetics of Allergic Disease in a Participatory Research Cohort	DAVID A HINDS	Y	$143,253	2014
2013	Development of a web-based database and research engine for genetic discovery (Phase 2)	NICHOLAS ERIKSSON --> JOANNA MOUNTAIN	Y	$1,367,504	2015
2014	A new reference panel to boost African American genotype imputation	ADAM AUTON	Y	$1,758,557	2018
2015	Estimating disease risk using genetic data	NICHOLAS A FURLOTTE	Y	$241,905	2019
2016	Admixture-driven discovery of disease-associated genetic variants not found in Europeans	KATARZYNA BRYC	Y	$260,360	2018
2017	Fast track SBIR for Latino Sequencing project	ROBERT GENTLEMAN	N	N/A	N/A

Benefits

Reflecting back on our participation in the SBIR program, we believe we saw four main benefits to being a grant recipient:

1. Establishment of scientific credibility
2. Development of a commercially viable research platform
3. Contribution to the scientific community
4. Development of the next generation of scientific leaders

More details on each of these benefits are provided below.

Establishment of scientific credibility

One of the major challenges that our research program faced initially was significant skepticism from the scientific community about our ability to produce high quality research. Thus, an initial focus of our SBIR-funded work was to publish in peer-reviewed scientific journals and present at scientific conferences, which are the primary currency of credibility amongst scientists. In total, the work funded by our SBIR grants produced at least 32 scientific presentations and publications, many of which were in collaboration with academic researchers (Table 2). We believe this body of work substantially improved our scientific reputation. For example, in 2012, a group of academic researchers rejected our participation in a collaboration on asthma; in contrast, today we receive approximately one hundred requests for collaboration from academic researchers each year and have collaborated with many of the major pharmaceutical companies as well.

Development of a commercially viable research platform

As mentioned above, the work we were able to conduct with SBIR funding helped us establish a strong scientific reputation. This was critical to developing a research platform that could contribute meaningfully to the business. By 2014, paid research collaborations with industry made an important contribution to the company's revenue. The growth and development of the research platform also enabled the establishment in 2015 of a 23andMe Therapeutics group whose drug discovery program is rooted in human genetics insights from the 23andMe research program.

Contribution to the scientific community

As mentioned above, one of the reasons we sought funding by the SBIR mechanism was because our mission to help people benefit from the human genome was well aligned with the mission of the NIH. As shown in Table 2, the work funded by our SBIR grants directly contributed to at least 32 scientific papers and presentations, and shared genetic insights on conditions ranging from stretch marks, to asthma and allergy, to Parkinson's disease. More than half of those publications were written in collaboration

with academic researchers, at no cost to them, and the underlying statistics have been shared with a broader set of researchers upon request.

We have also used SBIR funding to chip away at the large gap in diversity in genetics research. The vast majority of genetic research has been performed with participants of European descent which limits the benefits of that research (Figure 1). As part of our grant, “A new reference panel to boost African American genotype imputation”, we generated whole genome sequence data from more than 2,300 of our African American research participants and, with their consent, deposited those data into a protected NIH data repository for use by other researchers. This expands the diversity of the toolkit that is available to researchers. We believe that we have an important obligation to be a contributing member of the scientific community and moreover, our research participants, who are also our customers, want us to make a contribution to society. The SBIR program has helped us make good on that obligation.

Table 2. Scientific publications and presentations stemming from 23andMe research funded by SBIR grants.

Mountain et al., “Web-based phenotyping yields replication of genetic associations with sensitivity to warfarin” (Abstract #626). Presented at the Annual Meeting of The American Society of Human Genetics, 2012 Nov, San Francisco, California.
Barnholt et al., “Web-based phenotyping for pharmacogenomics research” (Abstract #1391). Presented at the Annual Meeting of The American Society of Human Genetics, 2011 Oct, Montreal, Canada.
Durand et al., “Reducing pervasive false positive identical-by-descent segments detected by large-scale pedigree analysis”. Mol Biol Evol. 2014 Apr 30.
Kiefer et al., “Genome-wide analysis points to roles for extracellular matrix remodeling, the visual cycle, and neuronal development in myopia”. PLoS Genet. 2013;9(2):e1003299.
Tung et al., “Genome-Wide Association Analysis Implicates Elastic Microfibrils in the Development of Nonsyndromic Striae Distensae”. Journal of Investigative Dermatology (2013) 133, 2628–2631.
Shmygelska et al., “Genome-wide association analysis identifies novel associations in uterine fibroids”. Presented at the Annual Meeting of The American Society of Human Genetics, 2013 Oct, Boston, Massachusetts.
Tian et al., “GWAS Identifies Classical HLA Alleles Associated with Susceptibility to Infectious Diseases”. Presented at the Annual Meeting of The American Society of Human Genetics, 2013 Oct, Boston, Massachusetts.
Hinds et al., “A Large Scale Genome Wide Association Study of Asthma in the 23andMe Cohort:. Presented at the Annual Meeting of The American Society of Human Genetics, 2013 Oct, Boston, Massachusetts.
Tung et al. “Genome-wide association analysis of diverse immune-related phenotypes highlights complex overlapping pathways of immune response”. Presented at the Annual Meeting of The American Society of Human Genetics, 2013 Oct, Boston, Massachusetts.
Eriksson et al., “Using correlated phenotypes to functionally classify GWAS loci”. Presented at the Annual Meeting of The American Society of Human Genetics, 2013 Oct, Boston, Massachusetts.
Hinds et al. "A genome-wide association meta-analysis of self-reported allergy identifies shared and allergy-specific susceptibility loci". Nature Genetics volume 45, pages 907–911(2013).

Revez et al., "A new regulatory variant in the interleukin-6 receptor gene associates with asthma risk." Genes and Immunity, 15 Aug 2013, 14(7):441-446.
Ferreira et al. "Genome-wide association analysis identifies 11 risk variants associated with the asthma with hay fever phenotype". The Journal of Allergy and Clinical Immunology" 2014 Jan.
Campbell et al., "Escape from crossover interference increases with maternal age". Nat Commun. 2015 Feb 19.
Chang et al., "Assessment of the Genetic Basis of Rosacea by Genome-Wide Association Study". J Invest Dermatol. 2015 March 12.
Day et al., "Shared genetic aetiology of puberty timing between sexes and with health-related outcomes". Nat Commun. 2015 Nov 9.
Day et al., "Causal mechanisms and balancing selection inferred from genetic associations with polycystic ovary syndrome". Nat Commun. 2015 Sep 29.
Dorsey et al., "Virtual research visits and direct-to-consumer genetic testing in Parkinson's disease". Digital Health. 2015 Jun 29.
Ferreira et al., "Genome-wide association analysis identifies 11 risk variants associated with the asthma with hay fever phenotype". J Allergy Clin Immunol. 2013 Dec 30.
Fuchsberger et al., "Minimac2: Faster genotype imputation". Bioinformatics. 2014 Oct 22.
Gharahkhani et al., "Chronic gastroesophageal reflux disease shares genetic background with esophageal adenocarcinoma and Barrett's esophagus". Hum Mol Genet. 2016 Feb 15.
Hromatka et al., "Genetic variants associated with motion sickness point to roles for inner ear development, neurological processes and glucose homeostasis". Hum Mol Genet. 2015 Jan 26.
Hu et al., "GWAS of 89,283 individuals identifies genetic variants associated with self-reporting of being a morning person". Nat Commun. 2016 Feb 2.
Jorgenson et al. "A genome-wide association study identifies four novel susceptibility loci underlying inguinal hernia." Nat Commun. 2015 Dec 21.
Lubke et al., "Gradient Boosting as a SNP Filter: an Evaluation Using Simulated and Hair Morphology Data". J Data Mining Genomics Proteomics. 2013 Oct 20;4.
Lunetta et al., "Rare coding variants and X-linked loci associated with age at menarche". Nat Commun. 2015 Aug 4.
Minikel et al., "Quantifying prion disease penetrance using large population control cohorts". Sci Transl Med. 2016 Jan 20.
Nalls et al., "Diagnosis of Parkinson's disease on the basis of clinical and genetic classification: a population based modelling study". Lancet Neurol. Epub 2015 Aug 10.
Nalls et al., "Large-scale meta-analysis of genome-wide association data identifies six new risk loci for Parkinson's disease". Nat Genet. 2014 Jul 27.
Paternoster et al., "Multi-ancestry genome-wide association study of 21,000 cases and 95,000 controls identifies new risk loci for atopic dermatitis". Nat Genet. Epub 2015 Oct 19.
Rietveld et al., "Replicability and Robustness of Genome-Wide Association Studies for Behavioral Traits". Psychol Sci. 2014 Oct 6.
Zheng et al., "Whole-genome sequencing identifies EN1 as a determinant of bone density and fracture". Nature. Epub 2015 Sept 14.

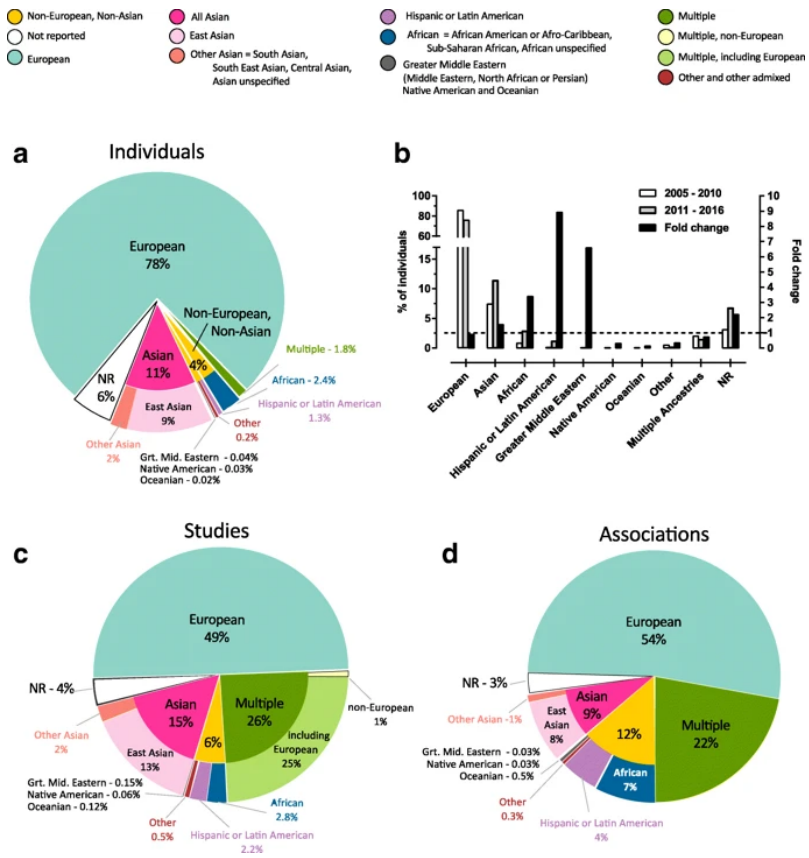

Figure 1. Ancestry category distribution in the GWAS Catalog (this is Figure 2 from [Morales, J., Welter, D., Bowler, E.H. et al. A standardized framework for representation of ancestry data in genomics studies, with application to the NHGRI-EBI GWAS Catalog. Genome Biol 19, 21 (2018). https://doi.org/10.1186/s13059-018-1396-2](https://doi.org/10.1186/s13059-018-1396-2)).

Development of the next generation of scientific leaders

A final benefit that might be less obvious - the value of SBIR grants in the development of scientists themselves - should not be overlooked. Many of the principal investigators on our grants were first time recipients of NIH grants. The exercise of applying for and executing a grant builds very useful skills for the investigator, which benefits not only the individual herself (a grant is a very positive line item on a CV), but also the company by developing a highly trained workforce. While most NIH-administered grants focus on funding academic research, an increasing amount of research is conducted in industry, and investing in those scientists will pay off in greater innovation and discovery. As Vannevar Bush said in his report to President Franklin D. Roosevelt, Science - The Endless Frontier, “The responsibility for the creation of new scientific knowledge — and for most of its application — rests on that small body of men and women who understand the fundamental laws of nature and are skilled in the techniques of scientific research. We

shall have rapid or slow advance on any scientific frontier depending on the number of highly qualified and trained scientists exploring it."

Challenges

We were very fortunate in having a high success rate with our SBIR applications (80% success rate; the overall success rate for SBIR applications in 2020 was 15.9%). Despite our success, the main challenge we encountered was the administrative overhead of running the grant. Specifically, one of the most challenging aspects of executing on the grant was adequately meeting the accounting requirements. Unlike academic research institutions, most small businesses do not have a formal grants office to help manage all the paperwork and navigate the funding guidelines. Moreover, the accounting system requirements, which include time-tracking on an hourly basis, audit preparation, and setting up an accounting infrastructure, can be extremely intimidating to scientists who have little to no training in this kind of work. There are eight tutorials alone for the accounting system on the SBIR website (https://www.sbir.gov/tutorials/accounting-finance/). The first tutorial itself states, "Many SBIR/STTR applicants underestimate the importance or difficulty of the cost proposal portion of their Phase I or II submission. Errors made here usually result in financial losses to the applicant, and reductions in the SBIR/STTR award amount, both of which are detrimental."

We were lucky enough to have a colleague in our Finance department with audit experience who was able to wade through all the requirements and help us set up a system for time-tracking that was audit-ready. Even so, the team spent multiple hours every week recording time, moving time-tracking reports back and forth for signature, following up on people who hadn't submitted reports, etc. Our impression is that NIH grants for academic investigators do not have this degree of administrative overhead.

Another challenge was the size limit to the awards. Some of the large-scale types of projects we considered involved generating genetic information on large cohorts and would not fit into the dollar limit. In particular, given the costs of setting up an accounting program for time-tracking and audits, we eventually realized that smaller grants (in the low hundreds of thousands) would only be worth applying for if we already had a grant management system actively running.

Recommendations

Based on our experience with the SBIR program, we have three recommendations:

1. Reduce administrative overhead (e.g., time-tracking)
2. Consider increasing the maximum award
3. Maintain participation from venture-backed companies

Reduce administrative overhead
Time-tracking and setting up and maintaining an accounting system was by far the most difficult and costly part of accepting an SBIR award. This certainly impacted our grant strategy and motivation to apply for grants. While we understand the desire to ensure that taxpayer money is being used responsibly, we suspect many small businesses with good ideas look at these requirements and give up before they even get started. In addition, the time our scientists spent on paperwork and accounting was time they were not spending on science. We believe there is likely a better balance between accounting for how grant dollars are spent and having scientists focus on the science.

Consider increasing the maximum award
As described above, the size limit to the awards did influence the ambitiousness of the projects we tried to pursue through the SBIR program. Given the costs of setting themselves up to administer an SBIR award, some small businesses might be more motivated to apply for the program if the potential reward were greater.

Maintain participation from venture-backed companies
As described above, the development of our consumer-centric research cohort and platform, which is unique in its scale and breadth, was supported in part by the SBIR grants we received. This cohort and platform now plays a central part in our business (see slide 15 of the 23andMe investor presentation). In the early days, however, there was skepticism about our ability to build a high quality research program in this way, and most investors were interested in the development of the consumer product rather than the research platform. Without SBIR support, it would have been more difficult for us to build our program at the pace that we did. In addition, the venture-backed development of the consumer business provided some resources that allowed us to execute on the grants successfully (e.g., finance and accounting, product and engineering). Two of the goals of the SBIR program are to stimulate technological innovation and to increase private-sector commercialization of innovations derived from federal research and development funding. For this, we see venture funding and SBIR funding as complementary resources to drive higher risk, higher reward technological innovation and commercialization.

Closing

SBIR grants supported our scientific innovation at a time when we lacked the track record and credibility to get significant funding from other sources for our research. This additional source of funding helped us bridge to a stage in which we were able to demonstrate our capabilities and potential, and thus acquire paid research partnerships, develop a therapeutics business, support the broader scientific community through published research, and even contribute a small part to closing the diversity gap in genetics research. We believe supporting research in industry, particularly in small startups, will play an increasingly important role in innovation and that the SBIR program can play a critical role in nurturing that innovation. Though we are now too large to be eligible for the SBIR program, we are happy to add our vote of support to its reauthorization.