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# Consuming Genomes: The Coproduction of a New Scientific and Technological Order for Genetic Testing

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# Abstract

At the intersection of consumer culture, venture capital, biotechnology, and increased patient autonomy, a new biomedical service industry has emerged. Since 2006 companies in the US have been altering the landscape of health care by offering Direct-to-Consumer (DTC) genetic testing for a variety of diseases and traits. Recently, the activities of 23andMe and Navigenics, the two leading providers of DTC genetic services, have come under the scrutiny of various regulators and institutions, including the Food and Drug Administration (FDA) and the House of Representatives' Committee on Energy and Commerce. In this dissertation, I situate direct-to-consumer genetic testing within the historical trajectory of genetic testing technology and the increasing profitability of information technology and biomedicine. I then analyze the recent encounters between DTC providers and regulators to identify the key scientific and discursive resources that are being employed to position the genetic testing technology with respect to regulatory initiatives. My empirical analysis of a rich set of primary sources (including websites, policy documents, and interviews) shows that the emergence of DTC genetic testing is a conspicuous instance of coproduction: a new social and technological order for genetic testing has led to the emergence of a new figure, the genetic consumer.

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| ANT | Actor-network theory |
| ASHG | American Society for Human Genetics |
| BRCA1 | breast cancer susceptibility gene 1 |
| BRCA2 | breast cancer susceptibility gene 2 |
| CDC | Centers for Disease Control and Prevention |
| CDPH | California Department of Public Health |
| CLIA | Clinical Laboratory Improvement Amendments |
| DOE | Department of Energy |
| DTC | direct-to-consumer |
| FDA | Food and Drug Administration |
| FTC | Federal Trade Commission |
| GAO | Government Accountability Office |
| GINA | Genetic Information Nondiscrimination Act |
| HGP | Human Genome Project |
| HHS | Department of Health and Human Services |
| IVD | in vitro diagnostic |
| KPCB | Kleiner Perkins Caufield & Byers |
| LDT | laboratory developed test |
| MDV | Mohr Davidow Ventures |
| NEA | New Enterprise Associates |
| NGO | non-governmental organization |
| NIH | National Institutes of Health |
| PKU | phenylketonuria |
| SACGHS | Secretary's Advisory Committee on Genetics, Health, and Society |
| SCOT | Social Construction of Technology |
| SNP | single nucleotide polymorphism |
| TGFT | Task Force on Genetic Testing |

# INTRODUCTION

"We've discovered the secret of life."

*Francis Crick, 28 February 1953*

In February 2001, *Nature* and *Science* published the first complete draft of the human genome sequence (J. C. Venter 2001; Anon. 2001). The publication in *Nature* was the product of the Human Genome Project (HGP), a major initiative of the United States Department of Energy and the National Institutes of Health. The HGP had been working for over a decade to identify the approximate 20,000 to 25,000 genes in human DNA, and to determine the sequence of the three billion chemical base pairs in the human genome (Francis S. Collins 2009). In parallel to the efforts of the publicly funded HGP, Craig Venter headed a privately-funded project to sequence the human genome by his company Celera Genomics, which led to the *Science* article. In response to the *Nature* and *Science* publications, Bill Clinton, then President of the United States, compared the HGP to the cartography of Lewis and Clark: "Today the world is joining us here in the East Room to behold a map of even greater significance. We are here to celebrate the completion of the first survey of the entire human genome. Without a doubt, this is the most important, most wondrous map ever produced by humankind" (Francis S. Collins 2009, 304).

Ten years after its historic publication of the first draft sequence, *Science* asked a cross-section of individuals, representing different communities, to reflect on its significance. Along with other respondents, Eric Lander, President of the Broad Institute, a genomic medicine research center affiliated with Harvard and MIT, recalled the beginnings of the

project: “When the Human Genome Project (HGP) was proposed some 25 years ago, the notion was so foreign to biology that commentators had to resort to metaphors from physics. The HGP was biology’s Manhattan Project, biology’s Moon Shot, biology’s Superconducting Supercollider particle accelerator” (E. S. Lander 2011). With the proposition that this was biology’s equivalent breakout moment, he said, “In the end, though, the HGP might indeed best be viewed as a ‘high-energy accelerator’—not of particles, but of scientific work and scientific imagination” (E. S. Lander 2011).

While the completion of the HGP has been an accelerator of scientific imagination, changing approaches to understanding human disease and variation, it has also been an accelerator of social imagination. As knowledge builds on the work of the HGP, we are developing new understandings of ourselves in relation to our genomes. What does it mean to be human now that we have “the language of life”? How has an increased knowledge of human genomics changed social arrangements and understandings?

In that same special issue of *Science*, Emmanouil Dermitzakis, professor of Genetic Medicine and Development at the University of Geneva Medical School observed that, “Each person’s genome tells slightly different stories, and fascination comes with discovery of the differences in those stories” (Dermitzakis 2011). Offering a different perspective, Charmaine Royal, associate research professor at the Institute for Genome Sciences & Policy and the Department of African and African American Studies at Duke University, argued, “Humans are so much more than a genome!” (Royal 2011). Sheila Jasanoff, Pforzheimer Professor of Science and Technology Studies at the John F. Kennedy School of Government, said that it is

too soon to judge whether the predicted benefits were oversold: "What matters is that we found a powerful new way to represent human identity, and the moral implications of that re-representation are just beginning to unfold" (Jasanoff 2011). Jasanoff compares the human genome to the sparse Constitution of the United States to argue that as with the Constitution the meanings of the human genome will evolve over time, "as scientists, lawmakers, and publics make sense of the fixed elements of the sequence in relation to the variables and unknowns in the surrounding environment" (Jasanoff 2011). In this way, the human genome is a malleable document, a "biological living constitution," from which different human understandings can emerge.

The private sector has been one domain in which new human understandings and relationships have co-emerged with advances stemming from the HGP. In this dissertation, I explore this co-emergence through an in-depth analysis of two companies, 23andMe, Inc. and Navigenics, Inc., which have been offering genetic testing services directly to consumers since 2007. Their genetic tests provide probabilistic risk profiles for genetic conditions. These analyses are based on genome-wide association studies (GWAS), which are an examination of all or most of the genes of different individuals to see how much the genes vary from individual to individual. Through statistical analysis, these variations are then associated with different traits, such as diseases. 23andMe and Navigenics have harnessed the publicly available GWAS to develop a panel of genetic tests that communicate, for example, one's risk of developing asthma, prostate cancer, lactose intolerance, and male pattern baldness. Consumers can purchase and access the genetic testing services of 23andMe and Navigenics

through the companies' websites.[1] With a mail-order kit, the consumer provides a saliva sample that is then processed and analyzed by the companies' laboratories. The personalized test results are accessible through the companies' secure online portals. This novel approach to genetic testing attracted attention from academics, policy makers, members of the scientific and medical communities, and journalists. In 2008 *Time* magazine even name the DNA retail test one of the best inventions of the year (Hamilton).

My dissertation takes 23andMe and Navigenics, the two leading competitors in direct-to-consumer (DTC) genetic testing, as a case study that raises broader questions about how genomic information is both shaping and being shaped by new social arrangements. I explore the resources being used by the companies to claim a new domain of market expansion for genetic testing. In addition to advances in science and technology, like the HGP, the companies have relied on social innovation to re-represent genetic information as a form of personal information and to re-configure the contexts within which genetic information can be interpreted. I examine the extent to which the companies are able to carve out a space for genetic testing outside the jurisdiction of the established medical and scientific communities while still drawing on them for credibility. In the process, the companies are coming up against institutions of power, namely, the Food and Drug Administration (FDA) and the U.S. House of Representatives Committee on Energy and Commerce. These confrontations provide fertile ground for understanding how public, private, and state interests influence the shaping of an uncertain technology.

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[1]23andMe's website is available at: https://www.23andme.com/
Navigenics' website is available at: http://www.navigenics.com/

In the process of expanding the realm of genetic knowledge well beyond the walls of medical institutions, a new and direct link is being created between the providers and users of this knowledge. In establishing this link the direct-to-consumer genetic testing firms are remaking genetic testing as a commodity. The direct link between provider and user is also shaping a new figure, the genome-consuming citizen, whose differences from the patient of the traditional clinical setting are manifold, but appear especially prominent through the lens of individual rights and entitlements. I argue that the viability of this direct link between providers and users of genetic knowledge rests precisely on the severing – and reshuffling – of technical, scientific, medical, and social standards. 23andMe and Navigenics are constructing a new sociotechnical architecture for genetic testing.

In her recent work, science and technology studies (STS) scholar Shobita Parthasarathy, developed the concept of sociotechnical architecture. In her comparative work on the development of genetic testing for breast cancer in the United States and the United Kingdom, sociotechnical architecture refers to the human and technological components of innovations and the ways developers fit them together to perform specific functions (Parthasarathy 2010; Parthasarathy 2007). Parthasarathy's work aims to open the "black-box" of genetic testing technology to better understand how context shapes science and technology. She builds on the work of STS scholars who have shown that technologies are shaped by social action. For example, the Social Construction of Technology (SCOT) approach argues that social groups have an impact on the contingent development of technologies (Bijker 1997; Bijker, Hughes, and Pinch 1987). Actor-network theory (ANT) also points to how

technologies have multiple potentialities by arguing that technologies come into being through a network of both human actors (for example physicians and patients) and non-human actants (for example the laboratory reagents used to process DNA samples) (Latour 1987). The concept of sociotechnical architecture, however, allows one to investigate how social, political, and cultural contexts figure in their construction, and to focus on the consequence of each element of a technology's architecture (Parthasarathy 2007). In the case of direct-to-consumer genetic testing, sociotechnical architectures illuminate how the choice of each component and their assembly into a functioning whole (genetic testing delivery system) influences a technology's social consequences.

I argue that the viability of the direct link between providers and users of genetic knowledge rests precisely on the severing – and reshuffling – of technical, scientific and moral standards. I propose that this scientific and social innovation is best understood as a particularly revealing example of co-production (Jasanoff 2004). In Science and Technology Studies (STS) co-production refers to a theoretical framework that investigates the mutual constitution of scientific and social orders. Its theoretical premise lies in the thoroughly symmetrical scrutiny of the natural and the social, the scientific and the normative. These dichotomies, all too often assumed as neutral categories in the analysis of technoscientific developments, are instead treated as points of arrival rather than departure, as resources and results rather than as causes of new settlements. Thus, in the analysis of how techno-scientific ingenuity encounters social legitimation, co-production does not assign a *a priori* causality in the generation of new settlements. Rather, it probes how these encounters shape new scientific and social orders, and investigates the technological, institutional, and discursive resources

used to develop them. The strength of this approach lies in its emphasis on the mutual constitution of arrangements and closures that are epistemic as much as normative. In turn, this symmetry moves analysis beyond the relatively shallow acknowledgment that any techno-scientific development is inevitably the result of scientific and social factors. It provides the analytical tools to grasp how science and society do not simply allow the circulation of objects that bear the stamps of their respective authorities. They co-produce instead each other's settlements to the effect that that circulation is as much a statement about epistemic criteria or technical solutions as it is an assertion - and at times a moment of revelation – of the norms and institutional arrangements that enabled it.

Researchers have successfully tested this heuristic approach through several case studies. Two examples that involve human genetics are highly relevant for our analysis. The first concerns the development of genetic tests for BRCA1 and BRCA2, the two genes associated with hereditary breast and ovarian cancer. Comparative analysis of testing systems in the United States and the United Kingdom shows that distinct business and public health models aligned with different technical infrastructures and epistemic goals to produce radically divergent arrangements (Parthasarathy, 2005). In each country, the type of knowledge and the technological solutions that relevant actors pursued (for example Myriad Inc.'s decision to sequence its customers' entire BRCA1 and BRCA2 genes as opposed to the British National Health Service choice to probe only the more prevalent mutations) upheld distinct normative understandings of the social meaning of genetic tests. For Myriad Inc. genetic tests are part of a profitable business model, whereas for British authorities they are just one part of an integrated health care system. Similarly, in her analysis of the Human

Genome Diversity Project (HGDP), Reardon exposed how the co-production of scientific and ethical criteria were needed for the stabilization of the project. HGDP devised the notion of group informed consent in an attempt to win support from indigenous populations and avert criticisms of biopiracy or neo-colonialism. Informed consent was an available bioethical tool from Western medicine, which focuses on individuals as autonomous agents and research subjects. In this case the HGDP tailored this practice to an entire population that held culturally diverse notions of personhood. This grouping at the level of populations, however, ended up framing the level of genetic diversity that was deemed relevant for sampling, leading to scientific controversies that eventually reshaped much of the original project design (Reardon, 2001). Reardon argues that the HGDP took upon itself the work of co-production, attempting the alignment of a new scientific and social order. She proposes co-production not only as an interpretive framework for the analyst, but also as a template for socially robust science policy.

Building upon this theoretical framework, we trace the emergence of genetic knowledge providers in the free market and their confrontation with existing institutions and practices, as a co-produced technological and social innovation. In the process, knowledge and norms are re-ordered to demarcate facts from values, technical from moral standards, and personal genes from personal choices.

**The Space for "Non-Medical" Genetic Testing**

23andMe makes the following disclaimer in an open letter to the medical community: "What we do not and will not do is provide medical advice to our customers. Though our

service delivers personalized data, the information it provides is tailored to genotypes, not to individuals" (23andMe 2010). In a similar vein, Navigenics states inconspicuously at the bottom of every page of its website: "Navigenics does not provide medical advice, diagnosis or treatment. You should consult your doctor if you have questions regarding any medical condition, before starting any new treatment, and before stopping any treatment that has been prescribed for you" (Navigenics 2010). These quotations capture the attempt to draw a distinction that appears integral to the development of genetic testing as a free-flowing commodity in the market economy. It is a separation between gene testing as a medical act performed in the context of a physician-patient relationship and gene testing as a market act performed in the context of a company-consumer transaction.

These company claims are striking because genetic testing has traditionally been thought of as medical. Genetic testing originally developed as part of medical care in the United States. Over the second half of the twentieth century the medical clinic became the site for interventions such as prenatal and newborn screening, predictive testing and risk assessment for adult-onset disorders, and genetic cancer diagnostics. A physician or health care provider traditionally has been the mediator of genetic information, helping to counsel, or interpret the meaning and significance of genetic tests for patients. In the health care setting, genetic counseling became an important feature of genetic testing in the 1990s and 2000s. It has been seen as necessary to enabling patients to make informed decisions about whether to undergo testing and how to move forward with test results. Given that there is often no cure for many testable genetic diseases, health care providers have been trained to be non-directive when counseling patients and to focus on "achieving supportive patient education, enabling an

informed decision, providing accurate risk assessment and risk perception, facilitating decisions, attending to psychological needs for the patient and the family, empowering the patient, and facilitating future care" (Sharpe and John 2006, 2). Some have argued that the successful introduction of such technologies into medical practice requires an expert context of care" (Gastmans 2002, 9).

The physician-patient relationship, however, has been fraught with tension. Beginning in the 1960s and continuing through the 1970s and 1980s, activists and patients critiqued the medical establishment and the authority of physicians. The "expert" position of the physician seemed to these critics to create a dynamic in which there was the potential for the abuse of power, especially in situations where people were presenting their most vulnerable selves. While the physician-patient relationship was still viewed by many as central to the success of health care delivery, there was concern that "expert power" could be used against patients if the physician were to exercise complete control with the justification that he or she is, after all, the "expert." It has been argued that this type of care diminishes the patient's sense of self-esteem and potential for recovery (Rinehart 1991, 5).

In light of these concerns, talk turned to patient autonomy, patient empowerment, patient rights, and informed consent. Activists in support of patient rights asked whether patients were informed enough and whether physicians were making decisions for patients without including them enough in the process. Historically, patients had a passive role in their treatment. Often they were told little about their diagnosis or various treatment options (Shannon 1996, 174). The concept of "patient rights" emerged in the 1970s to communicate

the idea that a person who is sick does not give up his personal autonomy just because he is sick (Charman 1992, 14-15). They included the right to information, to refuse treatment, to privacy, and to access hospital records (Shannon 1996, 176). The idea was that the more the patient knew, the more he could exert control over his fate (Charman 1992, 26). In fact, the emphasis today on physicians providing non-directive counseling so that patients can make informed decisions comes out of the raised awareness this activism engendered.

As part of the critique of the medical establishment scholars examined what was considered medical. In the 1970s the term "medicalization" appeared in the academic literature and was taken up by social scientists, jurists, politicians, social critics, medical scientists, and physicians to argue that society had become "medicalized" (Fox 1977). The term, which sociologist have used to refer to the process of turning human conditions and problems into medical conditions or diseases, has been used to challenge the expansion of medical authority into domains of everyday existence (Conrad 1992). Sociologists of medicine have noted that an increasing number of social phenomena have been medicalized from sexuality (Tiefer 1994; Carpiano 2001), to reproduction (Crawford 1980), to women's bodies more broadly (Riska 2003). Psychopharmacology has raised questions about the pharmaceutical industry, which has been criticized for forcing everyday problems into a biomedical domain (Conrad 2005). As a consequence of this expanding domain of what was considered medical, a greater number of social aspects of life were seen to come under the authority of doctors and health professionals. Those interested in promoting patient autonomy

saw this as a form of control that further heightened the power of the medical profession in relation to the patient.[2]

The model of 23andMe and Navigenics, given this brief history, can be understood as a rejection of the "bad" aspects of the medical establishment: for example, the encroachment of physician authority on everyday problems and the potential for physicians to leverage their power in ways that cause harm to patients. Against this backdrop, 23andMe and Navigenics have taken genetic testing out of the clinic and have made genetic information, explicitly advertised as non-medical, available to consumers. In the process they have imagined a genetic consumer who is empowered by accessing his personal genetic information. The companies' claims echo the rhetoric of the new media, which allege to empower users by focusing on their feedback and the free flow of information. The media's overblown attribution of the recent North African revolutions to social networking technologies like Twitter and Facebook further demonstrate that access to information has been equated with empowerment.[3]

The companies have also carried over the rights language of the 1970s and 1980s. 23andMe argues in its online "policy forum" that people should have access to their personal genetic information:

> 23andMe believes people have the right to access their personal genetic information. Genetic information is a fundamental element of a person's body, identity and

[2] Others had already noted that the area of public heath was a domain of public control (Foucault and Collège de France. 2008; Szasz 1997).
[3] Journalist and social commentator, Evgeny Morozov, provides compelling evidence to challenge the idea that the Internet is a democratizing technology (Morozov 2011).

> individuality. As such, the rights that people enjoy with regard to financial, medical and other forms of personal information should apply to genetic information as well (23andMe 2011).

Similarly, in an interview in 2008, Mari Baker, then chief executive of Navigenics, said in reference to cheaper consumer-driven gene-testing technologies, "We believe this is a fundamental right, for people to have access to their own DNA" (Duncan 2008). In these statements, the two leading providers of personalized genetic testing tap into neo-liberal discourse, focusing attention on the rights of the individual. The companies imagine the genetic consumer as a rational individual capable of self-governance. The companies advertise their services as empowering individuals with genetic information. For example, Navigenics states as part of its mission: "We believe that we can fundamentally improve health outcomes across the population by empowering people to act based on an understanding of their genetic predisposition for certain medical conditions" (Navigenics 2009).

Anthropologist Jenny Reardon has argued that the companies' recruitment of "empowered" and "liberated" consumers was a necessary step toward being able to access human beings and their genomes in support of making genomics a human science (Reardon 2011). As will be discussed in chapter two, these companies have developed platforms for conducting "consumer-based" research. Reardon references the criticisms that previous efforts to study human genetic diversity (for example the Human Genome Diversity Project) led to treating people as mere objects of study rather than as human beings with rights, to argue that the ideal research participant for the companies is a rational individual imbued with rights, centrally, the right to consume. By accentuating rights and empowerment, the companies can

recruit subjects (consumers) to study human genetic variability while avoiding the perceptions of research subject exploitation. The research dimensions of the companies are discussed in chapter two.

23andMe and Navigenics' claims to empower consumers, however, have been criticized by bioethicists on the grounds that the ability to understand and interpret genetic information is a condition of empowerment (Rabino 2003). If the consumer cannot understand his genetic information, he cannot be empowered. The companies argue that the "lay public" can understand genetics, an argument that sounds like one STS scholars might make as they critique the deficit model of science-society relations, which blames the public for inadequately understanding science (Bodmer 2010; Wynne 1992; Irwin and Wynne 1996). 23andMe has stated on its website: "We believe our customers are capable of understanding the context of the information we provide them. We also think the benefits our customers accrue in accessing their genetic information outweigh potential risks. We believe providing genetic educational material is part of our responsibility. We actively look to work with other groups to create new educational tools" (23andMe 2011).

Promoting an early adopter model for DTC genetic testing, a board member of 23andMe analogized the future of personal genomics to that of the personalized computer. While he acknowledged that there currently might be gaps in the genetic knowledge consumers bring to the testing platform, he argued that education follows interest. If people are curious about their genetics and they are given the means to probe this information they will become adept at using the available tools. The parallel to personalized computers, he

argued, was that knowledge of RAM and ROM were initially a condition on computer use, but one no longer needs to have the same depth of understanding to use the terms in a functional sense. He predicted that knowledge of genomics would achieve similar status (personal communication 2010).

The companies' model for consumer-driven genetic testing is an explicit rejection of the "problematic" aspects of the paternalistic medical model that undermined patient rights. The companies attempt to create an autonomous consumer, who is a further extension of the autonomous patient, claiming that this move is liberalizing. The story 23andMe and Navigenics promote looks liberationist – the genetic consumer is liberated from the control of the physician, and is granted his right to personal information that is intimately tied to his identity. I want to tell a cautionary tale. This is not about whether individuals can handle this sort of information or whether they need the expertise of a physician to make sense of it, but rather a cautionary tale about who has the power and authority to read and interpret individual genomes. What are the consequences of having the control of the medical establishment replaced by that of the market and venture capital interests? Are these companies positioning themselves to gain access to genomes for market expansion purposes? Has geneticization[4] replaced medicalization as a new channel to control bodies? In their run-ins with FDA and Congress, which are discussed in chapters three and four, these questions tacitly play out in the discussions of how to regulate the new industry.

[4] For work that explores the implications of geneticization see: (Hedgecoe 1999; Hedgecoe 2001; Hoedemaekers 1998).

I want to challenge the idea that the consumer is liberated in the act of consumption. I argue that there is no premade consumer, that the consumer gets made in the process of corporate market-making. This argument builds on an extant body of work on the co-development of the user and a technology. STS scholars have shown how assumptions about users are built into the design of technologies in ways that afford particular kinds of agency (Woolgar; Oudshoorn and Pinch 2005). The user, or the consumer in the case of DTC genetic testing, is configured in his interaction with the technology (Grint and Stève Woolgar 1997). Other studies have shown how new medical technologies engender certain types of patients (Webster 2002; Mort, Finch, and May 2009; Corbett 2009). In my analysis of 23andMe and Navigenics, I understand the design of their genetic testing technologies as both shaping and being shaped by the genetic consumer. This point is addressed in chapter two where I provide an overview of the companies' practices and discuss how their unique features construct distinct consumers.

**Legal Constraints**

In the process of creating a new market for genetic testing, 23andMe and Navigenics have come up against state and federal institutions. This has affected the ability of the companies to provide their services, the first example was the companies' encounter with the California and New York Departments of Health. In 2008 California and New York ordered 23andMe and Navigenics to stop selling their services until their laboratories met state regulations for quality assurance. In 2010 they met their first wave of regulatory attention from the Food and Drug Administration (FDA) and were investigated by the United States House Committee on Energy and Commerce. These confrontations illustrate the ways in

which these companies are in the process of finding space in a domain that already has legal constraints. In this section I want to briefly outline how issues of privacy, liability, and regulation have been addressed with respect to genetic testing.

Federal and state law applies to genetic testing. State common law, or case law, develops through court decisions that then serve as precedent for future cases. In this legal area, genetic testing has led to issues of tort liability. Torts are breaches of civil duty that involve wronging another person. In cases of negligence, for example, those who have been wronged can bring about a lawsuit to seek "damages." At the state level torts have led to the following types of lawsuits: breach of duties for incomplete disclosure of risk, wrongful life cases related to known heritable diseases, and general negligence. There have also been cases of medical malpractice, where physicians have put research interests before their duty to the patient. The companies' distancing of their services from medical care can be seen as a strategy to avoid issues of liability.

States have been developing their own standards concerning the duty to share the results of genetic tests with relatives and a duty to report incidental findings, for example information about paternity. State law also addresses issues related to genetic testing. All fifty states prohibit the unauthorized practice of medicine. States have also developed their own privacy statutes for medical information, but privacy protection has been articulated with respect to whether genetic testing is for clinical or criminal/forensic purposes. Roughly half of the states have laws that apply to direct-to-consumer genetic testing (Genetics and Public

Policy Center 2007). Some address the quality and reliability of laboratory processing, while others require that physicians order all genetic tests.

At the federal level, genetic tests have been treated like all other laboratory tests and are subject to federal control through the Clinical Laboratory Improvement Amendments of 1988 (CLIA). CLIA established quality standards for all laboratory testing to ensure the accuracy and reliability of patient test results. The Act is administered by the Center for Medicare and Medicaid Services (CMS). Laboratories are exempt from CLIA if the state in which they are located has requirements equal to or more stringent than CLIA. New York, for example, was granted exemption in 1995. The companies' compliance with CLIA regulation is discussed in chapter three.

Another important federal law, the Genetic Information Nondiscrimination Act (GINA) was signed by President Bush in 2008 (P.L. 110-233, 122 Stat. 881). GINA prohibited health insurers and employers from asking or requiring a person to take a genetic test and from using genetic information in setting insurance rates or making employment decisions. As the states provided varying degrees of genetic privacy and protection against genetic discrimination, GINA was enacted to provide a baseline of protection for all Americans (Health and Human Services 2009). GINA substantially enhanced the protections against the misuse of genetic information in the workplace. The Health Insurance Portability and Accountability Act (HIPAA) of 1996 (P.L. 104-191) imposed some restrictions on the use of health-related information by group health insurers in determining eligibility for benefits and setting premiums. GINA went further to specifically list genetic information as protected

health information and state explicitly that a genetic risk factor for a disease could not be considered a preexisting condition. The passage of GINA in 2008 helped the direct-to-consumer genetic testing industry. 23andMe and Navigenics' websites have provided extensive information about GINA, in what looks like an attempt to minimize any associated social risks to producing personal genetic information.

**Structure of the Dissertation**

Chapter one provides a historical overview of what has made the emergence of 23andMe and Navigenics possible, including a discussion of genetic testing technology, information technology, the multiple uses of genetic information, and the changing bio-economy. Chapter two lays out the corporate biographies of the two leading competitors in direct-to-consumer genetic testing in order to explore how 23andMe and Navigenics have emerged as a force in this field. I provide descriptions of their services, while highlighting points of contrast between their business models. I show that although 23andMe and Navigenics present their services as two distinct flavors of the same genetic testing phenomenon, they are responding to deeper norms that traditionally have structured genetic testing. In creating a new market for genetic testing, they have come up against institutional forces. Chapters three and four examine the industry's confrontations with FDA and Congress. I discuss how FDA is able to bring genetic testing technology under its jurisdiction while shaping the very status of an uncertain technology. I show how FDA, Congress, and industry representatives concurred that some form of regulation and clear scientific standards were needed. I discuss the implications of this proposed regulatory approach in both chapters three

and four. I conclude by revisiting the companies' liberationist claims to draw some lessons from the case study.

# CHAPTER 1: FERTILE GROUND FOR A NEW BIOMEDICAL SERVICE INDUSTRY

To fully understand the emergence of 23andMe and Navigenics it is important to look at the dynamics that have made them possible. Why did 23andMe and Navigenics appear in 2008 as purveyors of direct-to-consumer genetic testing services? What conditions made the new biomedical service industry possible? How did genetic testing slip the boundaries of medical care? How were private companies able to claim that people have a right to access their genetic information? What made direct-to-consumer genetic testing a feasible business model that could draw interest from venture capital? This chapter explores this set of questions. I first provide an overview of how genetic testing technology was established in the United States to show how laboratory services were increasingly distanced from the site of clinical care in the late 1980s and 1990s. Second, I explore how information technology has been combined with experimental biology to create a new approach to understanding human biology and in particular, genetics. Third, I consider the different uses and meanings of genetic information to show how the context matters for who can read and interpret such information. Lastly, I examine how shifts in the biotechnology industry and health care practices over the last three decades created a changing bio-economy.

**Genetic Testing Technology**

Genetic testing is often thought of as simply the analysis of DNA. There are many reasons, however, to be wary of such a reduction. These tests involve relationships (physician-patient, consumer-vendor), objects (sequencing machines, for example), and contexts (the clinic) to bring genetic information to light. In one early attempt to define the concept, the

National Institutes of Health and Department of Energy (NIH/DOE) Task Force on Genetic Testing (TFGT) stated that a genetic test is more than just the laboratory test (NIH 1997). TFGT defined a genetic test as part of a broader testing service that encompasses patient identification, education and referral, and the ultimate delivery of the test results and their interpretation to those tested (NIH 1997). This definition moves beyond the narrower idea that genetic testing is simply the analysis of DNA to incorporate the context in which testing occurs. NIH constructed a definition broad enough so that it could not only say something about the technical aspects of genetic testing, but also the boundaries within which it should occur. Although not stated explicitly, the terms "identification," "education," "referral," and "delivery" imply that human interactions, in addition to the laboratory test, are part of the genetic testing technology. This idea resonates with the arguments made by scholars of science and technology studies, that "technology" can only be understood, or have meaning, in the interactions between artifacts (the material things such as reagents, machines, and donor samples) and humans (patients and physicians, for example) (Bijker, Hughes, and Pinch 1987, 17-50; MacKenzie, Wajcman eds. 1999). As I trace the history and development of genetic testing technology in the United States, I understand it as existing through both technical artifacts and human interactions. This allows me to analyze how the context of genetic testing matters for its development.

Before Watson and Crick discovered the structure of DNA in 1953, and subsequent molecular understandings of the "basic units of heredity" (genes), knowledge of Mendelian genetics informed patient care. In the first half of the twentieth century physicians were able to diagnose some hereditary genetic disorders. If a patient presented a condition that seemed to

have a hereditary component, physicians would take a family history and use that information in support of a diagnosis. This form of genetic consultation first occurred in clinics affiliated with universities, so medical genetics was able to serve both medical and research purposes. Researchers and physicians could collaborate to characterize the genetic basis of diseases. Simultaneously, advances in the analysis and manipulation of DNA rapidly permitted an increasingly accurate understanding of the effects of genetic sequence variations on human conditions. For example, the discovery of the correct number of human chromosomes in 1956 (Hsu and Moorhead 1956) allowed for genetic testing techniques to detect chromosomal abnormalities.

In the 1960s and 1970s the first genetic tests were biochemical assays and chromosomal analyses performed in hospital or research laboratories (Lindee 2000). Still widely applied, these tests are exemplified by the screening of newborn babies for the genetic metabolic condition, phenylketonuria (PKU), by measuring phenylketone levels in blood samples. Karyotyping, a method to detect abnormal or extra chromosomes, was also established to diagnose other genetic conditions such as Down's syndrome. These first genetic tests were provided as laboratory services to aid diagnoses. Medical geneticists still served as the primary mediator of patient care, synthesizing genetic test results with patients' family and medical histories.

In the 1970s and 1980s, DNA-based testing became available as researchers identified single-gene disorders like sickle cell disease and cystic fibrosis. While these genetic tests were initially performed in hospital and research laboratories, the increase in volume of genetic

tests coupled with test developers advertising such tests directly to consumers increased demand. Physicians began to outsource testing to specialty laboratories, a trend that also included other clinical assays such as those to detect glucose and hemoglobin levels. In general, research laboratories at academic medical centers were not equipped to accommodate large scale genetic testing. Private companies like Genzyme Genetics, Genomic Health, GeneDx, and DNA Diagnostics emerged throughout the 1980s and 1990s to meet the increasing demand for clinical testing services. Such services were useful to academic medical centers that did not want to build up infrastructures within their diagnostics laboratories to conduct particular tests for which there might be a low demand. These companies marked a shift from academic to commercialized laboratory services. Laboratory analyses and clinical care were no longer coordinated within the same institution, and any physician, not just medical geneticists, could access genetic testing services for patient care. This shift began to open a space for biomedical service industries. Private companies began to develop business models based on the ability to provide large-scale laboratory services. These changes were important for the viability of companies like 23andMe and Navigenics.

### *Evaluative Criteria for Clinical Genetic Testing*

With the accumulation of genetic knowledge and the increasing availability of genetic tests, health care professionals and patients who lacked formal genetic training needed help to interpret this new technology. Given that there was little guidance or regulation for the provision of genetic testing, and that it was increasingly becoming routine in clinical care, policy makers thought that the integration of genetic tests into clinical activity demanded new guidelines. Key developments included policy documents from the Hastings Center in 1972

(Lappé, Gustafson, and Roblin 1972), the National Academy of Sciences in 1975 (Committee on Inborn Errors of Metabolism), the President's Commission on Ethical Issues in Medicine Biomedical and Behavioral Research in 1983, the Institute of Medicine (Andrews 1994), the National Institutes of Health Task Force in Genetic Testing in 1997 (Hotzman and Watson), and most recently, the National Office of Public Health Genomics, branch of the Centers for Disease Control, in 2004.

Although these reports did not result in any formal regulations, together, they highlighted a number of requirements that tests should fulfill, including precision of information (in order to minimize misrepresentation), acceptable accuracy, validity, sensitivity, and specificity (Wilfond, Thomson 2000). Eventually, these concerns were taken up by the National Office of Public Health Genomics and crystallized into the terms analytic validity, clinical validity, and clinical utility. The result was the ACCE Model Project, whose initials stand for those criteria, along with the technology's ethical implications: *A*nalytic validity (test accuracy), *C*linical validity (strength of gene-condition correlation), *C*linical utility (usefulness for patient care), and *E*thical, legal and social implications. The ACCE Model Project became a standard framework in both the United States and worldwide, because it was the first major effort to evaluate genetic tests (Centers for Disease Control and Prevention 2010).

The evaluative framework laid down in the ACCE Model Project has been endorsed in the information resources that directly target the final users of gene testing technologies. While the criteria initially were developed to aid health care providers in providing clinical

care, the framework soon became a resource to inform and empower consumers. The most important example is Genetics Home Reference. As a service of the U.S. National Library of Medicine, and part of the National Institutes of Health, Genetics Home Reference (2009) is an online educational forum that provides "consumer-friendly information about the effects of genetic variations on human health." The document titled, "How can consumers be sure a genetic test is valid and useful?" defines the three evaluative criteria—analytic validity, clinical validity, and clinical utility:

> Before undergoing genetic testing, it is important to be sure that the test is valid and useful. A genetic test is valid if it provides an accurate result. Two main measures of accuracy apply to genetic tests: analytical validity and clinical validity. Another measure of the quality of a genetic test is its usefulness, or clinical utility (Genetics Home Reference 2009).

This online forum was designed to arm consumers with knowledge that was initially intended for health care providers.

With a growing gap between laboratory services and clinical care, genetic tests became more available to patients/consumers as test developers advertised their services directly to consumers. The fact that testing could be provided through any physician, coupled with the beginning of direct-to-consumer advertising of genetic tests in the 1990s, facilitated consumer demand. The policy recommendations, which sought to establish criteria for the evaluation of genetic tests, can be understood as a response to genetic testing first slipping beyond medical geneticists' realm of expertise and control. The advent of companies like 23andMe and Navigenics represented yet another step in genetic testing moving beyond the boundaries of

warranted medical expertise. The direct-to-consumer genetic testing services resembled the model of other biomedical service companies, but made testing available to consumers without any physician mediation. The distancing of laboratory services from patient care is one dynamic that allowed for the emergence of direct-to-consumer genetic testing. Companies like Genomic Health, Genzyme, and DNA Direct opened the space for a genetic testing service industry. 23andMe and Navigenics, which more dramatically bypass the clinic, can be understood as the next step along a trajectory where the clinic and the genetic tester occupy spheres that overlap less and less.

**Information Technology**

"Information has always been the lifeblood of business and industry. Those who control or influence the flow of information tend to thrive. This is no less true in the health professions and businesses" (Goodman 1998)

Direct-to-consumer genetic testing has been enabled by information technology. The business models of 23andMe and Navigenics rely on the circulation of genetic information that is the product of a new bioinformatics-based approach to biological and biomedical research. Bioinformatics derives knowledge from computer analysis of biological data. Genomics, transcriptomics, proteomics, metabolomics, and lipidomics are just some of the many research platforms that are based on the use of bioinformatics tools for the storage, manipulation, and analysis of data. Throughout the second half of the twentieth century, researchers produced extensive knowledge characterizing DNA, transcripts, genes, and proteins. Less was known, however, about how these biological components interacted with

each other and environmental variables. To understand these dynamic paths and processes, researchers argued for a methodological shift from the "local" to the "global" perspective. Instead of studying single genes or proteins, attention was focused on how they interact (Duyk 2002; E S Lander 1999). In this shift from the "local" to the "global" bioinformatics has provided tools to handle and analyze biological data.

The Human Genome Project, which began in 1990, was a global demonstration of the power of information technology. The United States Department of Health coordinated the sequencing of the human genome at universities and research centers in the United States, United Kingdom, Japan, France, Germany, and China. As mentioned in the introduction, the main goals of the project were to identify the approximate 20,000 to 25,000 genes in human DNA, and to determine the sequence of the three billion chemical base pairs in the human genome.[5] The significance of sequencing the human genome extended beyond the production of a complete human "map." The public and privately funded projects established the power and potential value of producing knowledge that could be stored in databases and retrieved for analysis (MacMullen and Denn 2005).

Bioinformatics has also provided tools for data analysis. This point was shown in the privately funded human genome project. The shotgun sequencing technique used by Venter's company was based on slicing the human genome into small, randomly organized DNA fragments, which were then assembled into a running sequence by computer algorithms

[5] See Francis Collins' *The Language of Life* for a history of the sequencing of the human genome (Francis S. Collins 2009, 299-305).

(Glasner, Atkinson, and Greenslade 2007). In 1999, Celera Genomics read up to forty million bases per day. The assemblage of this data was made possible through bioinformatics analytical tools.

Landmark achievements like the HGP coupled with the increasing sophistication of bioinformatics tools opened the field of genomics, which combines information science and experimental biology. This approach has focused on the ability to create large amounts of data rapidly and retrieve it for analysis. As a result, the private and public sectors have incentivized the development of tools to sequence DNA rapidly at reduced costs. The publicly funded HGP sequenced a single genome at the expense of $4 billion, while Venter's Celera Genomics was able to do so for $100 million. Technological transformations throughout the 2000s decreased the cost of sequencing each base pair at a rate that has been compared to Moore's Law (Anon. 2009). The newer sequencing machines, which borrow ideas from silicon-chip manufacturing, have brought down prices by a factor of ten every year since their introduction in 2005 (Anon. 2009). Many have argued that affordable whole genome sequencing is in the near future, an enterprise that has been further incentivized by the X Prize Foundation. The charity is offering $10 million to the first group to sequence 100 human genomes in ten days at a cost of $10,000 or less per genome.

The value in being able to generate large amounts of sequenced DNA, however, has been articulated in the analysis of the data. Researchers have used this approach to find genomic variability between individuals and populations and the potential correlation of that variability to differences in physical traits. Studies that seek to understand this sort of

variability have been made possible through the analysis of small DNA changes, called single nucleotide polymorphisms (SNPs). These single base variations have aided the discovery of genes that are linked to traits. Databases of human SNPs have made possible association studies, which compare the frequency of genetic markers among people who have a certain trait and those who do not. Association studies can provide insights about the genetic basis of traits, including disease traits, predispositions to diseases, and effects to certain drugs. 23andMe and Navigenics' genetic test panels are based on association studies.

Genomics has been shaped not only by technological innovation and epistemic advances, but also ideas for potentially successful business models. The X Prize competition also points to this mutual shaping. The truly lucrative prize would not be $10 million, but rather an edge in the speculated multi-billion-dollar commercial market for affordable, accurate sequencing of whole genomes. Genomics has enabled the circulation of genetic information as a form of currency. In the words of anthropologist Kaushik Sunder Rajan, genomics allows "a particular type of materialization of information, and its decoupling from its material biological source (such as tissue or cell line)" (Sunder Rajan 2006, 17). This decoupling is a condition for 23andMe and Navigenics' operations. Their businesses rest on the ability to process and handle large amounts of information cheaply, as well as the commodification and circulation of such information.

**Genetic Information: Multiple Uses**

Genetic information has multiple uses from structuring familial relations to making reproductive choices to providing evidence in criminal trials. In these various contexts, genetic

information acquires different meanings. 23andMe and Navigenics have claimed, respectively, new "recreational" and "health-related" uses for genetic information. In this section I explore different uses of genetic information to show how the context structures the sort of expertise, or non-expertise, that is typically deemed appropriate to "read" and interpret genetic information.

DNA fingerprinting, a scientific technique that identifies individuals based on unique patterns in their genetic material, was first introduced into the American legal system in 1987. It was thought to be a foolproof form of scientific identification that could link individuals to crime scenes. (Aronson 2007). Genetic information has also been used to link biological parents to children. In legal cases where child support is in question, state law tends to permit the use of genetic testing to establish paternity claims, but not to challenge existing ones (Rothstein 2005). Implicit in this structuring of the law is the idea that paternity is not established solely through genetics. Where a stable family structure exists, it would be too disruptive to allow for paternity challenges. Courts have traditionally outsourced forensic and paternity testing to laboratory diagnostic companies, such as DNA Diagnostic Center[6] and Identigene.[7]

At another familial level, the availability of genetic tests had an impact on reproductive choices. The availability of pre-implantation genetic diagnosis and the genetic screening of fetuses have armed reproducing individuals with information that has altered the families they

[6] The company's website is available at: http://www.forensicdnacenter.com/accreditations.html [last accessed 15 April 2011]
[7] The company's website is available at: http://www.dnatesting.com/ [last accessed 15 April 2011]

make (Lindee 2005). Monica Konrad has argued that the availability of these genetic tests has altered notions of parental responsibility and has led to the emergence of the "new genetic family" (Konrad 2005, 124-143).

Genetic information is also configuring new dynamics around disease understandings and health care practices (Muin J. Khoury M.D, Wylie Burke M.D, and Elizabeth J. Thomson M.D 2000, 3-23). From firm diagnoses to disease risk probabilities, genetic testing has influenced clinical practice. The information provided by clinical genetic tests, however, has produced a spectrum of epistemic certainty:

> "Some of the newer genetic tests being offered move beyond testing for traditional Mendelian disorders—where the presence of certain gene variants is highly correlated with the development of the condition—and into the arena of more common complex diseases, where the relationship between specific genetic variants and disease is less clear" (Hogarth, Javitt, and Melzer 2008).

Physicians have traditionally been the relevant experts, but policy makers and bioethicists have raised questions about whether health care providers have the proper education to navigate the multiple meanings of genetic information.

From the courtroom to the family to the clinic, genetic information holds multiple meanings. Common across these domains is the fact that we cannot know our genomes directly. The production of genetic information requires, in addition to technical artifacts, a human reading and interpretation. Who in these various contexts and with what authority should be able to read and interpret our genomes, and who should control these translational

acts? Scholars of science and technology studies have shown that genetic information in the courtroom does not speak for itself (Daemmrich 1998; Jasanoff 1998b; Michael Lynch and Jasanoff 1998). The act of bringing genetic evidence into the courtroom presented the problem of interpretive flexibility, raising questions about whose vision, expert or lay, counts when interpreting the meaning of DNA fingerprinting (Jasanoff 1998b). In the court setting, trained molecular geneticists have been called as expert witnesses to interpret genetic evidence. In the clinical setting health care providers have traditionally have interpreted genetic test results, but there has been a debate about whether physicians outside the specialty of medical genetics have sufficient expert vision to read and interpret genomes for medical purposes (Batra et al. 2002; Doukas and Berg 2001; Gollust, Wilfond, and Hull 2003; Hunter et al. 1998).

23andMe and Navigenics have claimed a new personal use for genetic information, and in doing so have attempted to create a new context in which genetic information is brought closer to lay person, or consumer vision. Yet to do so, the companies have become the readers and packagers of genetic information. This represents a new form of scientific expertise that is shaped by private interests. The commodification of genetic information as a form of personal information has most notably brushed up against the norms that structure the use of genetic information in medical care. In the clinical context, genetic information is ensured both by medical expertise and the ethical standards dating back to the Hippocratic Oath that structure the doctor-patient relationship. In the consumer context, the genetic information is ensured by the companies' own scientific expertise within a vendor-consumer transaction. To carve out a new space for genetic information, 23andMe and Navigenics are

trying to re-order expertise, claiming to bring lay or "consumer" vision closer to genetic information, albeit through the companies' own "certified expert mediation."

## Changing Bio-Economy

Existent biotechnology and biomedical markets made the emergence of 23andMe and Navigenics possible. In this final section I explore the economic dynamics that have made the intersection of information technology and the biosciences a profitable domain. To do so I look at the history of the biotechnology industry and the making of the medical consumer throughout the latter half of the twentieth century.

### *A Venture Capital Backed Biotechnology Industry*

In 1973 Herbert Boyer and Stanley Cohen developed a technique to splice, or cut and join together, DNA molecules. In their first published experiment, Boyer and Cohen cut a section of DNA from an *E. Coli* bacterium and transferred it into the DNA of another bacterium (Cohen et al. 1973). Through recombinant DNA technology (RDT) bacteria and viruses could adopt external genes and produce proteins of another organism. RDT, however, produced concerns within the scientific community and broader public about the safety and potential risks of the genetic engineering technique. In response to these concerns, Paul Berg, a biochemist at Stanford University, organized a meeting at Asilomar State Beach, California in February 1975 to address the potential biohazards and regulation of biotechnology. Berg brought together a group of 140 professionals, mostly biologists, with some representative physicians and lawyers. The aim of the meeting was to establish voluntary guidelines to ensure the safe use of RDT. The Asilomar meeting succeeded in convincing state authorities

that scientists were capable of regulating themselves. As a result, venture capitalists saw this as an increasingly attractive space because they believed it was free of burdensome regulations that they felt hampered other industries (Birch 2007, 101).

Members of the venture capital community became interested in the therapeutic potential of proteins produced by RDT. In 1976 venture capitalist Robert Swanson and biochemist Herbert Boyer founded Genentech, Inc. (Russo 2003). In 1978 Genentech harnessed RDT to produce synthetic human insulin and licensed the production to Eli Lilly and Company. This opened the door for the production of other therapeutically valuable human proteins like human growth hormone for the treatment of hypopituitary dwarfism and chronic renal failure, and interferon for viral diseases.

In conjunction with these scientific and technical breakthroughs, a United States Supreme Court ruling further bolstered the biotechnology industry. On June 16, 1980 in the case of *Diamond v. Chakrabarty*, the Court ruled that genetically modified bacteria were patentable, apart from the process in which they are used. This ruling opened the door for the patenting of cell lines, DNA, genes, animals, and any other living organism that has been sufficiently modified by humans to qualify as "products of manufacture," or not occurring in nature. With this ruling, the U.S. Patent and Trademark Office extended intellectual property rights to segments of DNA whose role in the organism was not understood. This decision meant that scientists who sequenced genes had intellectual property that could be licensed for proprietary value.

The same year that the patenting of genetically engineered microorganisms was allowed, Congress passed the Bayh-Dole Act (35 *USC* 200-212), which facilitated the transfer of technology between academic institutions and industry. More broadly, the Act gave universities, small businesses, and nonprofit institutions title to inventions made with federal research funds (Krimsky 2004, 27-55). Publicly funded research now offered the potential of being profitable.

The biotechnology industry was made possible through both scientific and social innovation. RDT technology demonstrated how biology could be engineered to produce valuable therapeutics and the *Diamond v. Chakrabarty* ruling and the Bayh-Dole Act protected this area of innovation. In conjunction these events made the biosciences a domain of increasing profitability. Throughout the 1980s and 1990s venture capital firms grew as they increasingly invested in the biosciences. Genentech served as the model for start-up biotechnology companies that could turn a profit either by selling their technologies to larger pharmaceutical companies or by trading their stock publicly.

***The Making of the Medical Consumer***

Throughout the second half of the twentieth century, medical and business practices merged. As discussed in the introduction, this was facilitated through the re-making of the physician-patient relationship. In the 1970s and 1980s there was a movement to challenge the "doctor knows best" in support of increased patient autonomy (Speedling and Rose 1985; Haug and Lavin 1979). This was a reaction to the influence and authority that the medical profession gained in the first three quarters of the twentieth century (Starr 1982). Physicians

had authority over anything seen to be health or illness related. As a result, patients' rights were truncated, including limitations on access to their own medical information and records. In 1997 President Bill Clinton in his State of the Union address called on Congress to enact a national bill of rights in health care. The President said, "You have the right to know all your medical options, not just the cheapest. You have the right to choose the doctor you want for the care you need. You have the right to emergency room care, wherever and whenever you need it. You have the right to keep your medical records confidential" (Clinton 1997). These recommendations supported a new model of care that placed greater emphasis on patient autonomy. Advocates of patient rights supported the idea that patients should play an active rather than passive role in the management of their care.

At the same time, major changes were occurring in the delivery of health care in the United States. These shifts included: "the transformation of the professional practice of medicine in the United States from a service orientation to a market orientation; the emergence of powerful pharmaceutical and healthcare corporations with global reach; the development of new, innovative, and expensive biomedical technologies by for-profit enterprises; and steadily increasing healthcare costs in industrialized nations" (Arnold 2009, 1). In important ways these changes encouraged patients to become consumers of their health care and physicians entrepreneurs who could benefit from strong ties to the pharmaceutical industry (Adair and Holmgren 2005).

In the context of these changes patients began actively to access genetic testing technologies (Sharpe and John 2006, 1). Before the advent of direct-to-consumer genetic

testing, health care consumers were already benefiting from genetic technologies, although with physician mediation. In many ways the former patient turned consumer was the antecedent to the genetic consumer. The companies have taken the argument for patient autonomy and empowerment further. 23andMe and Navigenics have built on the grassroots activism of the 1970s, which was co-opted by a free market, neo-liberal discourse that linked ideas of free choice and consumer freedom to the medical field. The direct-to-consumer genetic testing industry is an outgrowth of this movement, but also a more recent "personalized" marketing discourse, largely enabled by the Internet, that emphasizes the "me" or "I".

**Conclusion**

The direct-to-consumer genetic testing industry emerged at the intersection of several powerful social and technological vectors. Genetic testing technology developed in the United States as part of clinical care. Companies like Genomic Health and DNA Direct can be seen as the antecedents of 23andMe and Navigenics. The genetic tests provided by 23andMe and Navigenics move beyond the first biochemistry and DNA-based analyses, and are based on large association studies that rely on information technology to identify and link human genetic variation to traits. In doing so they have created a space in which consumer vision and interpretation is brought closer to genetic information through the companies' own scientific expertise.

The emergence of the biotechnology industry in the early 1980s and changes in health care delivery throughout the 1980s and 1990s created a market in which health related

services and products became increasingly available to patients as consumers. 23andMe and Navigenics entered this market in 2007 with a new model to further bypass the clinic. To do so, however, they have had to do quite a bit of work to change the socio-technical architecture of genetic testing, namely claiming a new status for genetic information: it is being marketed as personal information, not as medical information. The company strategies for doing so will be discussed in my overview of their business models. Their framing of genetic information as just another form of personal information, however, has met alternative framings – those of FDA and Congress. In the following chapters I will both point to moments of friction and agreement in the broader struggle over who should control or regulate DTC genetic testing and with what understanding of the technology.

# CHAPTER 2: A RIGHT TO CONSUME: A NEW BUSINESS FOR GENETIC TESTING

*"Best Inventions of 2008: 1. The Retail DNA Test" (Time Magazine)*

"I'd rather spend my money on my genome than a Bentley or an airplane," said Mr. Stoicescu, 56, a biotechnology entrepreneur who retired two years ago after selling his company. He says he will check discoveries about genetic disease risk against his own genome sequence daily, "like a stock portfolio." (Harmon, *NYTimes*). At the time this statement was printed in March 2008, Mr. Stoicescu was the first person to have his entire genome sequenced by the Cambridge, Massachusetts private company, Knome. With a price tag of $350,000, in the same ballpark as that of a Bentley or an airplane, entire genome sequencing was first offered by Knome in November 2007. In comparison to the Human Genome Project, which cost $3 billion, this was a relative bargain—if not exactly cheap. Today, the company, co-founded by Harvard's pioneering human geneticist, George Church, who helped to initiate the Human Genome project, offers its entire genome sequencing service for $50,000.

Mr. Stoicescu's comparison of his genomic profile to a stock portfolio immediately captures how sequencing was sold. It was and continues to be advertised as a long-term investment. As we gain more knowledge about how genes correspond to and influence disease, one's personal genomic information will become more valuable, or meaningful. Whereas in the case of the stock portfolio, risk assessment is used as a tool for managing economic investments, the value of the genomic profile is knowledge of one's risk for certain genetic conditions.

On the heels of Knome's launch in 2007, 23andMe and Navigenics, began offering a more affordable, less comprehensive form of genetic analysis. While Knome offered to sequence every single base pair in an individual's genome, these two companies began offering people information about selected portions of their genomes, called single-nucleotide polymorphisms. While humans are genetically 99.6% the same (Francis S. Collins 2009, 12), SNPs are examples of the small genetic differences between humans and can be useful for understanding how genetics relate to phenotypes, or observable characteristics. If SNPs are studied in a large enough population, statistical correlations can be drawn between specific genetic differences and phenotypes. These genome-wide association studies have been primarily directed towards understanding diseases.

At the end of 2007 and beginning of 2008, respectively, 23andMe and Navigenics made a splash when they began selling genetic tests based on the publicly available genome-wide association studies. Both companies combed the scientific literature to identify SNPs that would potentially be of interest to individuals who want to know something about their genomes. Instead of using complete sequencing technology like Knome, the companies used a smaller-scale approach to probe specific portions of the human genome where variations had been identified and linked to phenotypes such as "Alcohol Dependence," "Celiac Disease," and "Freckling." This form of correlative genetic information was made available by both companies over the Internet and advertised directly to the consumer. Markedly less expensive than Knome's $350,000 complete genome, the genetically curious person who still had considerable pocket change could purchase Navigenics' service for $2,499 and 23andMe's for

only $999. As in the case of the complete genome, however, these services were advertised as an investment. In fact, customers could pay an additional annual fee to have their genetic information updated as the companies expanded their test portfolios. In comparison to Knome's approach, which was like putting money on every ticker in the New York Stock Exchange, these companies provided a more select genetic portfolio, similar to making investments in a few companies with known performance potential across a few business sectors.

Even at the more affordable price of $2,499 or $999, questions were raised about who stood to benefit from such services and whether it was appropriate to offer genetic testing outside the traditional clinical setting. Headlines such as, "Gene Map Becomes a Luxury Item" followed, along with mounting concerns that 23andMe and Navigenics would create a genetic elite. As Amy Harmon put it in the *New York Times*,

> Biologists have mixed feelings about the emergence of the genome as a luxury item. Some worry that what they have dubbed 'genomic elitism' could sour the public on genetic research that has long promised better, individualized healthcare for all. But others see the boutique genome as something like a $20 million tourist voyage to space – a necessary rite of passage for technology that may soon be within the grasp of the rest of us (Harmon, NYTimes).

The Human Genome Project may have taught us that we are more alike than different, but genetic consumerism would teach us that only some are privileged enough to know their genetic characteristics. As 23andMe and Navigenics attempted to carve out a new domain for

genetic testing, what the service was and who it was for began to emerge around decisions about the cost, panel of tests offered, advisory boards, and partnerships.

This chapter lays out the corporate biographies of the two leading competitors in direct-to-consumer genetic testing in order to explore how 23andMe and Navigenics have emerged as a force in this field. I begin with discussing the origins of the term "direct-to-consumer," asking what the word "direct" captures about the relationship between the companies, consumers, and individual genomes. I then provide an overview of each company with attention to how the companies have evolved over the past four years. Lastly, I explain how the companies have distinguished themselves in a competitive market niche.

**What is Direct-to-Consumer?**

To understand what direct-to-consumer means in the case of genetic testing, it is helpful to look to the marketing of pharmaceuticals for comparison. In the 1980s it was hotly debated whether pharmaceutical companies should be able to market drugs directly to patients as well as doctors. Pharmaceutical companies wanted to reach potential patients through print, TV, and radio advertisements. After a couple of controversial attempts in the early 1980s, FDA legalized direct-to-consumer advertising of pharmaceuticals with a caveat. Advertisements needed to include extensive information about the risks of the drugs. If consumers were informed of the risks, FDA would not need to be overly paternalistic. As in many other debates over medical and scientific technologies, FDA managed concerns by identifying the main "risks" and articulating standards to minimize them. From the side of the medical profession, there were worries that consumers should not have unmediated access to

information about prescription drugs, because they did not have the knowledge and expertise to understand when specific drugs were needed, and thus make potentially harmful decisions through misinformed choices. From the side of consumers, there was the opposing idea that individuals should be in control of their own health (Applbaum 2006). Having access to information about pharmaceuticals was a logical consequence of that belief. From the industry side, there were clear advantages in increasing sales by motivating consumers to talk to their doctors and encourage them to prescribe drugs they had seen advertised.

In the case of personal genomics, direct-to-consumer refers at one level to a marketing strategy. And as in the pharmaceutical case, the direct-to-consumer marketing of genetic tests has also stirred a debate. Myriad Genetics, Inc. launched one of the earliest and most notable direct-to-consumer marketing campaigns in 2002. The company used print and television advertisements to push its commercial test for the BRCA1 and BRCA2 genes, which are linked to breast and ovarian cancer. Myriad was criticized for using a marketing strategy that prompted fear, leading women to demand the test from their physicians, in what were often deemed inappropriate circumstances. Based on examples like this, bioethicists Gollust, Hull, and Wilfond (2002) concluded that advertisements for clinical genetic tests overstated the value of genetic testing for clinical care, provided misinformation about genetics, exaggerated the risks, and endorsed a deterministic relationship between genes and diseases. As in the case of pharmaceutical advertising, the direct-to-consumer approach to marketing clinical genetic tests threatened the place of medical expertise and authority.

At another level, "direct-to-consumer" refers to the advertising approach of the companies. The service is marketed to consumers, not healthcare providers for clinical practice. But at an important level, direct-to-consumer personal genomics diverges from the parallel pharmaceutical case. 23andMe and Navigenics provide a service that does not require a physician's prescription, or at least it did not when the services were first offered. Initially consumers could log on to the companies' websites and purchase the genetic tests, no physician needed. When consumers purchased testing services over the Internet, the companies would send a saliva sample collection kit through the mail. The consumer would then send back the sample to a laboratory where DNA would be extracted from it and analyzed for genetic variation. Encrypted laboratory results would then be sent to the companies, which made the results available to the consumer through a secure online portal. "Direct-to-consumer" thereby took on an added level of significance, since the consumers were left to interpret the results for themselves.

California and New York law, however, required that the genetic tests, while purchased by consumers, be ordered by a physician. Both 23andMe and Navigenics maneuvered around this requirement by having an in-house physician order all tests. As a sort of formality, the physician became an intermediary, buffering state concerns about the genetic testing platform with the image of medical expertise.

Interestingly, just prior to the FDA public meeting and Congressional hearing in June 2010, Navigenics changed its genetic testing platform, taking away some of the "direct" in its direct-to-consumer genetic testing service. A vice president at Navigenics, explained that

when the company entered the market, they understood that they were navigating a new space and that the company's business model would evolve. Concerns about being responsible prompted the company to change its platform in 2010 (personal communication 2010). In contrast, a board member to 23andMe, explained that the company chose not to pursue a business model of marketing its service directly to physicians because too much red tape would be involved (personal communication 2010).

The direct-to-consumer dimension of genetic testing services mirrors at one level the direct-to-consumer advertising of pharmaceuticals, and at another, it marks (in some cases) the consumer's ability to purchase genetic testing without having to interface with a physician. State regulation, however, brought the physician back in to formally "order" the genetic tests. And while 23andMe continues to operate with an in-house physician, Navigenics consumers can no longer directly purchase its service over the Internet. Instead, they must sign up for Navigenics' services through their physician or corporate wellness program. As with the instance of direct-to-consumer advertising of pharmaceuticals, direct-to-consumer genetic testing has reordered and recalibrated the doctor-patient relationship. Consumers are now in the position to decide whether certain types of genetic tests are relevant to their health care.

**23andMe**

"The business is moving ahead in a positive trajectory," Ms. Wojcicki said in 2010. "We've hit some bumps in the road but we are learning and continuing to evolve. We did not start this company thinking it was going to be easy to create an entirely new market" (Pollack 2010). In April 2006, Anne Wojcicki and Linda Avey co-founded 23andMe, Inc., launching

its genetic testing service at the end of 2007. The women shared a vision that people should be connected to their genetic information and that if people were so connected, they could find ways to accelerate research that would further personalized health care. 23andMe defines itself as: "a leading personal genetics company dedicated to helping individuals understand their own genetic information through DNA analysis technologies and web-based interactive tools" (23andMe, Inc. Fact Sheet).

Wojcicki and Avey's experience and leadership shaped the company. Avey had spent 20 years in the biopharmaceutical industry working at companies that developed bioinformatics tools and gene sequencing technologies. Of note, she helped establish translational research programs at Affymetrix, a company that manufactures DNA microarrays, which can be used to measure changes in DNA expression levels and to detect SNPs. This type of sequencing would become the technological bedrock of 23andMe's service. She also worked for Applied Biosystems, which pioneered automated genetic engineering in the 1980s and 1990s, developing the principal brand DNA sequencing machine used by the Human Genome Project consortium centers. From this industry-side perspective, Avey was intimately familiar with cutting edge gene sequencing technologies and the value in being able to demonstrate genetic variations between individuals. While Avey continues to support the mission of 23andMe openly, she left the company in September 2009 to start a foundation related to Alzheimer's disease (23andMe Press Release 2009). Her work, however, continues to focus on participant-driven research, but she has chosen to do so in a nonprofit setting (Field notes, meeting at the Broad Institute spring 2010).

Anne Wojcicki, who currently serves as Chief Executive of 23andMe, brought 10 years of experience in healthcare investing, with special emphasis on biotechnology companies. She realized that genomic studies were becoming increasingly important for clinical trials, as companion genetic diagnostics were being developed alongside therapeutics. She also concluded from her years in healthcare investing that expensive clinical trials were often ineffective. Convinced that there must be a more efficient way to generate genetic information for the development of new drugs and diagnostics, she and Avey partnered their enthusiasm to accelerate personalized healthcare. With an eye towards larger research projects, the company began by promoting itself as being in the business of providing consumers access to their genomes.

The initial novelty of the service was that one could gather cool genetic facts about oneself, for traits like "Hair Color," "Earwax Type," and "Muscle Performance" mixed with other "Disease" traits like, "Heart Attack," "Male Infertility," and "Type 1 Diabetes." The idea was that genetic information was another form of personal information to which people had a right. These genetic tidbits could be "fun facts" distinguishing one person from another, conversation starters at parties, or topics of conversation among family members in 23andMe's online forum. Accordingly, 23andMe has often been characterized as providing recreational genomics. This image was furthered by other marketing strategies, like the throwing of "spit parties" during New York's Fashion Week in 2008. 23andMe rented out a space in SoHo and gathered dressed up clientele to spit into tubes, providing a DNA sample while sipping cocktails (Salkin 2008). Celebrities such as director Harvey Weinstein, actor

Chevy Chase, socialite Ivanka Trump, fashion designer Diane Von Furstenberg, and media magnate Rupert Murdoch were among the spitting party-goers.

23andMe gained added attention because Anne Wojcicki through her marriage to Sergey Brin, has become part of a Silicon Valley power couple. Sergey Brin is the co-founder of Google, Inc., the world's largest Internet company and search engine. This connection has led Forbes.com to dub 23andMe "Google's genetic start up." Google and Brin have formally invested in 23andMe. In May 2007, Sergey Brin and Google gave $3.9 million in Series A funding, which refers to the company's first significant round of venture capital funding in the Silicon Valley startup model. In 2010 Google invested another $2.6 million in the company, helping 23andMe to achieve other funding benchmarks in the startup model. Wojcicki also contributed an undisclosed amount of her own funds, as a personal loan to the company.

The Google connection raised a lot of eyebrows. Many wondered whether 23andMe would become another information goldmine from which Google could prosper. Would Google's mission "to organize the world's information and make it universally accessible and useful" to incorporate genomes? Would the Google approach to mining information be applied to 23andMe? Who had the power and capital to drive such an agenda? Later, Sergey Brin would turn out to have a heavy hand in the research direction of the company.

In addition to support from Google, 23andMe has been successful at drawing capital from some of the most elite venture capital and successful biotechnology companies. Series A financing was completed in May 22, 2007 with the backing of Mohr Davidow Ventures

(MDV), New Enterprise Associates (NEA), and Genentech, Inc. In a 23andMe press release, Linda Avey reflected: "Achieving this significant funding milestone enables us to move forward with our core mission of connecting people with their genetic information…We are thrilled and honored to have attracted the backing of such a diverse, proven and innovative group of investors" (23andMe Press Release 2007).

MDV, which invests in higher risk, early stage startups, contributed $9 million (CrunchBase). The venture capital firm focuses on the following areas of innovation: Information Technology, Life Sciences, and Cleantech. Partners at MDV have been involved with notable companies, Adobe, Affymetrix, Cisco, Hewlett Packard, Microsoft, and Yahoo!. The venture capital firm also has companies in its portfolio with missions that overlap with 23andMe's approach. For example, Pacific Biosciences is working on a new paradigm for DNA sequencing, which "could ultimately make it possible to sequence individual genomes as part of routine medical care."[8] Another company, VitaPath Genetics, is developing molecular diagnostics for disease-linked genetic mutations, which they claim can be safely and easily corrected.

NEA, the world's largest venture capital firm, with $11 billion in committed capital, gave 23andMe $9 million towards Series A funding (CrunchBase). NEA invests in Information Technology, Healthcare, and Energy Technology. Like 23andMe, other companies in its portfolio use social networking principles in their business models. Other crossover companies include GoodGuide, a company, which claims to be "Delivering

[8] Available at: http://www.mdv.com/ [Last accessed 15 November 2010]

environmental, social and health information to consumers through the web and cell phones."[9] 23andMe gained additional credibility with support from Genentech. As mentioned in chapter one, Genentech was the first company to use recombinant DNA technologies, and the founding of the company has been referred to as the beginning of the biotechnology industry.

Even in difficult financial times and with a cutback of nearly half the company's work force in 2009, 23andMe has continued to raise capital. In 2009 the company raised $27.8 million in Series B funding, that is, capital provided to companies that have begun production but do not yet have positive cash flow to take care of their growing needs. A portion came from an earlier $10 million loan from Google's Brin, which was converted into 23andMe stock. And in November 2010 the company closed on $22 million in Series C financing – third stage capital that is provided for market expansion after a company has established commercial production. In addition to Google, the third round of funding included new investor Johnson & Johnson Development Corp. And in January 2011 venture capital firm, MPM Capital, which invests globally in healthcare innovation, rounded Series C funding out to $31 million. With this support, MPM Capital Managing Director, Ashley Ledbetter Dombkowski, a Ph.D. in mathematics, joined 23andMe's board of directors (23andMe Press Release 2011). Following Dombkowski's addition, Anne Wojcicki offered an upbeat assessment: "With MPM Capital joining Johnson & Johnson Development Corporation, Roche Venture Fund, Google Ventures and New Enterprise Associates as investors, 23andMe has aligned a powerful constellation of expertise in strategic healthcare, healthcare venture funding, consumer markets, information technology, and business strategy that will enable us

[9] Available at: http://www.nea.com/ [Last accessed 15 November 2010]

to bring the vision of personalized medicine to consumers faster" (23andMe Press Release 2011). 23andMe has world-class investors backing it as well as an important and strong personal tie to Internet mogul, Google. In the words of Board Member, Esther Dyson, "We've become a business from being a scientific adventure company, basically" (Pollack 2008).

23andMe has also drawn on another crucially important form of capital – the scientific research community. For its editorial advisors and scientific advisory board, 23andMe has picked from elite academic institutions, predominately Stanford, but also the University of California, Berkeley and Los Angeles, University of Chicago, and Harvard University. Advisors include professors of genetics, bioengineering, computer science, and human genetics. The best-known scientific advisor, George Church, Professor of Genetics at Harvard Medical School, has committed himself to the intersection of personal genomics and industry through his involvement with Knome and Complete Genomics, a company that is developing complete genome sequencing technologies. 23andMe's ties to the scientific community provides a way to establish credibility, to demonstrate that the company's service is certified by a community of credible and impartial academics.

***What does the 23andMe Customer Consume?***

"580,000 data points about you" (*Wired* Science)

On its website, 23andMe advertises: "Get to know your DNA. All it takes is a little bit of spit." The ability to extract DNA from a saliva sample has been integral to the business model of 23andMe. Unlike for a blood sample, one does not need the aid of a healthcare provider to spit into a tube. The less invasive saliva collection enables the consumer to

purchase 23andMe's Personal Genome Service™. The consumer also does not need to interact with any other persons when providing a DNA sample. The computer screen becomes the only necessary interface between company and consumer. And in contrast to the clinical setting, consent is not given in person, but rather over the Internet.

Once the consumer has purchased the service over the Internet and sent in a sample by mail, 23andMe's laboratory processes it. DNA is extracted from the saliva and specific regions are analyzed through hybridization microarray analysis,[10] using the Illumina® Infinium HumanHap550-Quad+ HD Bead Research Use Only Chip. Illumina CEO, Jay Flatley, says the company makes "what are known as DNA chips, devices that can sample the genome in hundreds of places." He further claims that, "These chips have been leading to a revolution in genetics, with dozens of DNA variations being potentially linked to diseases this year [2007]" (Herper 2007). For 23andMe's purposes, Illumina uses a chip that analyzes more than 500,000 SNPs in addition to 25,000 SNPs that have been hand picked by 23andMe scientists. After nearly 600,000 specific points in the genome have been read, electronic data is created, encrypted, and sent to 23andMe. The laboratory processing and analyzing the samples does not receive any personal identifying information. Soon after, the consumer receives an email that his or her profile is ready to be accessed through 23andMe's website with "access to navigational tools that enable you to explore your genome and discover a

[10] The SNP genotyping assays provided by Illumina utilize the technology of oligonucleotide microchip arrays. Briefly, segments of single stranded DNA that range in length from 20 to 60 bases are called oligonucleotides. These can be chemically synthesized and imprinted on a glass slide or "chip." A sample of genomic DNA is then fragmented and washed over the chip. A fragment will hybridize or adhere to the oligonucleotide if the two have an identical sequence. These companies can determine a subject's SNP profile by imprinting all of the known human SNPs on a chip and determining to which SNPs the subject's DNA hybridizes (Hartwell et al. 2006).

whole new world of you" (corporate fact sheet). In this statement, 23andMe claims not just to provide information, but a means to know oneself better. The consumer, however, must still enter into an agreement with the company and consume a layer of scientific interpretation to attain the state of greater self-knowledge.

From the beginning, 23andMe's service has included both ancestry and health-related testing. According to a company press release, the aim is to let consumers:

> Search and explore their personal characteristics, such as lactose intolerance, athletic ability, and food preferences; Learn how the latest research studies relate to their genomes; Compare their profiles to family and friends who are also 23andMe participants and trace the inheritance of genes associated with specific traits; Discover their genetic roots and learn about where and how their ancestors might have lived and the prehistoric events they experienced, and; Actively participate in a new research approach and contribute to the advancement of the field of genetics (23andMe Press Release 2008).

The packaging and size of the genetic testing service has undergone many changes since 23andMe first launched the service in 2007. At that time 18 genetic tests were available. By April 2008 the test panel had grown to 58 different conditions, and by May 2009 to 114. Currently 23andMe offers analysis for 193 genetic conditions. Over the years, the company has adopted different strategies to organize its tests, or different forms of test classification. Originally tests were subdivided into two categories, "Research Reports" and "Clinical Reports." This two-tier system was intended to indicate the degree of scientific soundness

behind the tests. The categories have been changed to "Established Research Reports" and "Preliminary Research Reports," with the former presented as more reliable than the latter. In the company's words, "Established Research reports give you information about conditions and traits for which there are genetic associations supported by multiple, large, peer-reviewed studies" (website). In contrast, "Preliminary Research reports are based on peer-reviewed, published research where the findings still need to be confirmed by the scientific community. They also include topics where there may be contradictory evidence."[11] If new discoveries are made, Preliminary Research reports can be bumped up to Established Research reports.

While the organization of genetic tests into these two categories may seem trivial, it indicates that 23andMe is not just a passive filter through which scientific knowledge flows to the consumer. The company makes judgment calls about what science to include and further labels it with categories that do not exist in the scientific literature. Classification also gives the image of credibility, because it demonstrates in seemingly objective terms that 23andMe has a reliable vetting process for the inclusion of tests. But the process also highlights 23andMe's own subjectivity. In its corporate fact sheet, 23andMe refers to its selection method as a "rigorous scientific review process," explained as follows, "Many genetic associations reported by the mass media are exciting because they are brand new and/or challenge scientific consensus. 23andMe employs a systematic vetting process to determine which scientific findings to include in our Health Edition" (corporate fact sheet).

[11] Available at: https://www.23andme.com/health/all/ [Last accessed 15 April 2011]

Currently 23andMe's 193 tests are divided into four categories: "Carrier Status" (24), "Disease Risk" (100), "Drug Response" (19), and "Traits" (50).[12] Genetic tests that indicate how one might process drugs were added to the panel at the beginning of 2010. This form of categorization can be seen to help the consumer navigate the ever-expanding panel of tests. Whereas the earlier "Clinical Reports" – "Research Reports" dichotomy lumped together tests for breast cancer with a test for caffeine metabolism, the four categories communicate that there are different types of information available from genetic tests. The distinction between "Established" and "Preliminary" reports is now just indicated with a small asterisk. At present, only 38.5% of 23andMe's tests qualify as "Established."

Carrier Status tests include, for example, those for cystic fibrosis, malaria resistance, and Tay-Sachs Disease. Drug Response tests include those for antidepressant response, beta-blocker response, and caffeine metabolism. Genetic tests for Traits include, HIV progression, height, and alcohol flush reaction. And examples of Disease Risk tests are those for colorectal cancer, preeclampsia, and schizophrenia[13]. These groupings again illustrate how 23andMe is actively involved in packaging genetic information. The company constructs its genetic tests through the categorization. The 23andMe consumer does not get direct access to his or her genome, but rather to 23andMe's interpretation through scientific judgment calls.

In addition to different approaches to selecting genetic tests, 23andMe has experimented with how to carve up the different aspects of its service. Originally the company

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[12] Available at https://www.23andme.com/health/all/ [last accessed 15 April 2011]
[13] For a complete list of all offered tests, please refer to supplemental material.

provided the following features: "Health and Traits," "Ancestry," "Sharing and Community," and "Research." When 23andMe stopped allowing consumers to purchase either ancestry or health testing, meaning you had to purchase the whole package, its features collapsed into the headings "Your Health" and "Your Ancestry" (company website – accessed different times). One reason may be that the company is striving to collect as much information on its research participants as possible. An Editorial Advisor to 23andMe, said that ancestry information could be used to check the facticity of the answers consumers provide in the research surveys. The research component is no longer set up as a separate area on its website, but is rather promoted as a bonus: "You'll also get exclusive access to participate in groundbreaking genetic research."[14] Marketed as a privilege, research participation is advertised as a novel form of social capital.

***Building Momentum for Research Participation***

Central to 23andMe's business model is its social networking feature. As a bridge to its research community, the company has put a good deal of attention into providing ways for consumers to connect with each other online over their genetic profiles. Chia Hwu, community manager at 23andMe, explains some of the key social networking platforms: "The social aspect is that you can share your genome with others. We have a tool called 'Family Inheritance,' where you can see if you have similarity between you and someone else. So if you do the test and you're sharing with a cousin, you'll see like a certain amount of similarity in your genome. If you do it with a sibling, you'll have regions where you're completely identical" (Interview 2008). When asked about other community-building features on the site

[14] Available at: https://www.23andme.com/ [Last accessed 10 February 2011]

Chia Hwu explained: "We have a forum where you can talk to others about your results. We have a lot of people who want to talk about, for example, 'Oh, we're both haplogroup R1b1a. Can we talk about where your family is from, and do we all come from the same area of Europe?' There is also a health part. Someone will say, 'I have this weird toe, and I want to know if there is something that is genetic about it. Can we compare our genetic data and see if we can find something?'" (Interview 2008). In this way, 23andMe presents itself as a social entrepreneur. It is not just about connecting people to their genomes, but also about finding ways to get people to form communities around their genetic information.

When asked to describe 23andMe in a promotional interview just as the service was being launched, Linda Avey told Wired Science, "So, 23andMe is a way to empower individuals to really access their genetic information for the first time and really start to dive into what does this mean and how do I understand this in the context of what is going on in the research world" (*Wired* Science 2007). From the beginning, the goal of empowering individuals by providing them with access to their genomes was linked to furthering personalized medicine and accelerating research that would improve therapeutics and diagnostics. While the company has predominantly pitched its service to the empowered genetic consumer, the goal of allowing individuals to express their right to access their genomes has always been intimately tied to the goal of conducting research studies. In the same interview with *Wired* magazine, Anne Wojcicki also explained how research was one of the company's fundamental goals: "we want to be able to give you all of your information, we want you to be able to play with it and use it, but the idea is that if we can bring everyone together you can create a database of a half a million or a million people, suddenly you have

the ability to do something we call consumer oriented research" (*Wired* Science 2007). A board member for the company confirmed that from the beginning the company intended to develop a platform for research (personal communication 2010).

On May 29, 2008 the "me" in 23andMe was officially expanded to "we." 23andWe, the research arm of the company, was launched with the mission to dramatically accelerate the pace of genetics research. In a press release 23andMe explained how the new venture would work:

> 23andMe will evaluate and approve research proposals for inclusion in the 23andWe program. Once a proposal is approved, 23andMe researchers will develop on-line surveys for collecting phenotypic information from 23andMe customers. Customers can then participate in the study by completing the on-line surveys. When the data are compiled, 23andMe researchers will analyze it with the goal of determining the genetic basis for certain traits or diseases. 23andMe will provide 23andWe participants with regular updates about 23andWe projects and information as to how they can become more involved in genetics research (23andMe Press Release 2008).

In light of this development, the consent procedure was reworked to include a section on research. By purchasing 23andMe's service, customers now agreed to allow 23andMe to use their "genetic and other voluntarily contributed personal information" as part of the company's research "with the purpose of advancing the field of genetics and human health."[15] The customer is reassured, however, that account information will never be associated with

[15] Available at https://www.23andme.com/about/consent/ [Last Accessed 20 April 2011]

the research, and 23andMe claims that genetic information would only be shared with third parties in aggregate form.

This proposed model for "consumer-driven" research represented a moment in which the pendulum swung again, from the sequencing of the human genome telling us that we are more alike than different to companies selling "personal" genetic information that is particular to individuals to bringing the collective back in, that the goal over time is to define genetic difference better. In such moments, human genetics is used to bring us together and set us apart.

The first 23andWe research study aimed to better understand the genetic underpinnings of Parkinson's, a progressive degenerative neurological disorder. Not coincidentally, Parkinson's is common in Sergey Brin's family. His mother has been diagnosed with it, and Brin has a mutation in a gene called LRRK2, which has been associated with higher rates of the disease. A mutation in LRRK2 increases the chance that the disease will emerge sometime during the carrier's life to between 30 and 75 percent (Zimprich et al. 2004). With this awareness, he has invested $50 million in Parkinson's research, albeit a tiny fraction of his net worth, which is estimated at $16 billion (Goetz 2010). Part of this investment was directed towards 23andMe's first "consumer-driven" research study. While the exact amount was not disclosed, Brin heavily funded the study, so that the complete 23andMe service could be offered to study participants for a nominal fee of $25 (Pollack 2009).

With this modest pricing structure, 23andMe hoped to sign up 10,000 people with Parkinson's disease for the study. While the company fell short of this goal, the low cost significantly augmented the company's database of genomic profiles: "Two and half years after beginning its service, 23andMe has only 35,000 customers. And at least a quarter of them got the service free or for only $25, instead of the hundreds of dollars on which the business model is based" (Pollack 2010). These pricing strategies begged the question of profitability? Board member, Esther Dyson offered some hype about the company's long-term thinking: "We're going to be businesslike… We're going to make money off research. We're going to market more effectively. And over time the product is going to be better, because over time, the data is going to be more meaningful" (Pollack 2010).

Apparently, then, 23andMe has adjusted its pricing structure with the primary goal of expanding its database for research purposes. Other examples point the same way. The Personal Genome Service™ was originally priced at $999 in 2007. In September 2008 23andMe dramatically reduced the price of the "health and traits" feature of its service to $399. In a press release titled, "23andMe Democratizes Personal Genetics," Anne Wojcicki explained how changes in the technology enabled the price reduction:

> By taking advantage of continuing innovation we are able to introduce a new chip that will give people more relevant data at a lower price…We are excited that we are opening doors for more people to learn about their health and ancestry and for more people to be able to participate in advancing research. It is important to demonstrate personal genetics and make it more accessible (23andMe Press Release 2008).

In November 2010, the company again altered the price structure of its service. Instead of providing the option of either purchasing the "Ancestry Edition" or "Health Edition," 23andMe started offering just the "Complete Edition" for $499 (*Genome Web Daily News* 2010). And beginning in 2011, the company further reduced the cost to $199, advertising the change as, "Our New Low Price For All!"

In addition to having reduced the cost of its service over the past four years, 23andMe has also used promotional periods to recruit consumers. In an effort to get families to receive testing together, 23andMe announced a holiday season multi-pack discount in 2008 (Press Release, December 8, 2008). In July 2009 23andMe promoted a $99 "Research Edition." For that price customers could have 90% of 23andMe's reports if they agreed to participate in research studies (email advertisement). Upgrades for the full service could be purchased for an additional $299. In October 2010 the company used social media outlets to promote a discounted $99 day. On that day, 23andMe recruited 20,000 consumers, at the time representing one third of the company's entire database.[16] Due to the unexpected high demand, the company closed the offering early. Most recently, 23andMe had a holiday sale during December 2010. Again, customers could purchase the genetic testing service for only $99.

These promotional periods allowed 23andMe to understand how cost affects the recruitment of genetic testing consumers, but they also underscore the company's primary mission to expand its research potential. The most recent price reductions do not come on the

[16] From an off the record source.

heels of any technological improvements. Rather, they show how 23andMe is using pricing incentives to grow its core business – by expanding its database and customer pool to be able to produce research studies. Price, however, becomes interestingly linked to notions of democracy. How does reduced cost translate into the democratization of research? Linda Avey offered some insight into 23andMe's stance: "When we first started the company, the first clients were people who already had some knowledge of genetics but now the demographics are changing…That was always our mission, to take genetics into the public arena and make it less white coat and more street clothes." (Bonetta 2009). Is the company's notion of democratizing simply the expansion of its consumer demographic? If so, it is a particular and narrow notion of democracy, refracted through the lens of the market and counted only in the number of bodies recruited into the database.

To what extent, though, does 23andMe provide for a more participatory notion of democracy? To explore this question, we can ask how the genomic consumer/citizen is being made through 23andMe's notion of democracy. How much say in or control do consumers have? A staff scientist at 23andMe said that the company receives hundreds of emails from consumers concerning the company's research, but they have not yet figured out a way to incorporate the range of comments and feedback into the decisions the company makes about its research programs (personal communication, Personalized Medicine World Conference 2011). In this way it seems that the company controls the research agenda and consumer "participation" is limited to filling out questionnaires.

**Navigenics**

Navigenics was co-founded in November 2007 by David Agus and Dietrich Stephan. In contrast to Avey and Wojcicki, who brought industry and investment experience to the vision of 23andMe, Agus and Stephan came from the medical and scientific communities. Agus, an M.D. trained at the Memorial Sloan-Kettering Cancer Center in New York, held the position of professor of medicine at the Cornell University Medical Center. Currently, he is professor of medicine at the University of Southern California, director of the Center for Applied Molecular Medicine, and director of the University's Prostate Cancer Center. Still a practicing a physician, he provides treatment in the areas of prostate cancer, oncology, clinical trials, and drug development. In addition to clinical practice, "his research focuses on the application of proteomics and genomics for the study of cancer and the development of new therapeutics for cancer research."[17] In addition to co-founding Navigenics, he founded Oncology.com, the largest online cancer community.

Dietrich Stephan, who holds a Ph.D. in human genetics, is currently the Chief Scientific Officer at Navigenics. Previously, he was deputy director of discovery research at the Translational Genomics Research Institute in Phoenix, Arizona. The nonprofit institute, founded in 2002, uses genetic discoveries to improve disease outcomes by developing diagnostics and targeted therapeutics. He has also served as the academic chairman of the National Institutes of Health Neuroscience Microarray Consortium. Stephan has built his scientific career on research that links genes to disorders, including autism and infant death syndrome.

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[17] Available at http://www.doctorsofusc.com/doctor/bio/view/110799 [Last accessed 10 February 2011]

With this combined experience in the medical and scientific communities, Agus and Stephan shared a vision for Navigenics that would focus on the health implications and relevance of the genetic tests provided by the company. From the beginning, the company made clear that it was in the business of improving health outcomes. How this would flow from the genetic information the company provides, however, could take on different forms. For example in an interview for the *Wall Street Journal* Agus explains how his test results have changed his health behavior:

> Agus "says he took the test and found he had a 68% risk of having a heart attack in his lifetime, compared with about 40% in the general population. His kids, he says, now help him stay away from French fries. 'I'm a believer in empowerment,' he says" (Winslow 2007).

One could question whether he needed genetic information to know that he should reduce his intake of French fries. The company claims, however, that even if one knows that eating fatty foods increases one's risk of heart disease, knowing one's genetic risk has additional motivating power to change behavior. The stated mission of the company is to "provide clinically guided genetic analysis with the goal of empowering individuals to act based on an understanding of their genetic predispositions."[18]

Mari Baker furthered this vision as the first Chief Executive Officer of Navigenics. Previously, she served as the CEO of BabyCenter, an online site for mothers, and also worked for Intuit, helping to develop and market to consumers personal finance software. Baker was appointed CEO of Navigenics to help incubate the company and launch the genetic testing

[18] Available at http://www.navigenics.com/visitor/about_us/mission/ [Last accessed 10 February 2011]

service while she was an executive-in-residence at the venture capital firm, Kleiner Perkins Caufield & Byers.

Like co-founders Agus and Stephan, Baker embraced the vision that genetic information has (special) motivating power to change human behavior in a healthy direction. While promoting Navigenics' genetic testing service she said: "When you're reading your genetic risk and you realize that you might get this disease, that's when it's real and relevant" (Winslow 2007) With this sort of genetic reality check, the idea behind the company's service was that preventive measures would follow as a result of the consumer's own greater awareness of risk:

> With that information in hand, patients have a powerful tool for homing in on potential medical problems before they show up, said Mari Baker, president and chief executive of Redwood Shores-based Navigenics. "Our goal as a company is to improve health outcomes," said Baker. "This isn't about genetic curiosity" (Wohlsen 2007).

Whether these preventive measures would translate into dietary changes, such as the exclusion of French fries, or changes in medications, left the health value of the testing open to debate.

Navigenics and 23andMe patterned as foils even early in their trajectories, Navigenics took additional steps to create the image of being the more responsible, sober, medically relevant direct-to-consumer genetic testing provider. Whereas 23andMe sold genetics as entertainment to enroll more subject for research. As already noted, in 2010 Navigenics stopped selling its tests directly to consumers, and a physician or employee wellness program was brought into the loop. But an important shift also occurred when the Board of Directors appointed Dr. Vance Vanier to serve as President and CEO in January 2010. Vanier had joined

Navigenics as Chief Medical Officer in April 2008. In this role, he helped to expand the company's clinical offerings and formed institutional research programs through corporate partnerships. Earlier, as a partner in the life science branch of Mohr Davidow Ventures, Dr. Vanier had spent ten years working in the area of preventive and personalized medicine with companies that develop molecular and electrical diagnostics. While Dr. Vanier has turned his attention to the intersection of industry and medical technologies, he is still on faculty at Stanford Medical Center.

Through Vanier's leadership, Navigenics underwent some dramatic changes in self-definition. Vanier's biography on Navigenics' website provides a good summary of the company's transformation:

> Dr. Vanier created a vision for Navigenics built around a powerful idea - that the most effective and responsible way to introduce preventive genomic testing to the public was with the support and partnership of corporate medical directors, medical centers, and physician offices, in addition to Navigenics' own team of Genetic Counselors. Within two years, he built a series of clinical collaborations and distribution relationships that have made Navigenics the #1 physician endorsed company in the preventive genomics space. These achievements include orchestrating the Scripps Genomic Health Initiative, one of the largest behavioral genomics initiative in the U.S., partnering with premier national physician groups such as MDVIP with its

100,000 patients, and building a network of large self-insured marquee employers who are incorporating Navigenics into their wellness and benefit programs.[19]

Navigenics has gone to great lengths to project the image of being a responsible company that provides information with clinical relevance. Also by bringing the medical community back in, through direct endorsements and research collaborations, the company has made an effort to define its distinct value. Its service is not for recreational genetic curiosity, but to provide clinically actionable information, even if that just means cutting French fries from one's diet.

Like 23andMe, Navigenics has drawn both capital and financial credibility from world-class venture capital firms. By November 2007, Navigenics completed Series A and Series B financing, totaling $25 million in investments from Kleiner Perkins Caufield & Byers (KPCB), Sequoia Capital, and Mohr Davidow Ventures (MDV) (Navigenics Press Release 2007). KPCB is interested in startup companies in the areas of Greentech, Information Technologies, and Life Sciences, specifically diagnostics. KPCB has invested in such notable companies as Amazon, Sun Microsystems, Electronic Arts, Genentech, Intuit, AOL, Genomic Health, and Google. Sequoia Capital seeks to invest in all sectors with a focus on services, including financial, healthcare, Internet, outsourcing, retail, and wireless. MDV, which also invested in 23andMe, may be hedging its bets as the two companies provide different flavors of direct-to-consumer genetic testing. This is an indication that the companies have distinct business models that could potentially tap into different consumer pools. In February 2010 Navigenics rounded out Series C funding at $18 million, a benchmark that the company is

[19] Available at http://www.navigenics.com/visitor/about_us/team/executives/vance_vanier/ [Last accessed 10 February 2011]

progressing towards profitability, with an investment from the Proctor and Gamble Company (Navigenics Press Release 2010).

Furthering its image of responsibility, Navigenics has an executive team that touches on all key aspects of the genetic testing service. The company has a Vice President of Policy and Business Affairs that also serves on the Policy and Ethics Task Force. Navigenics also has a physician with over twenty-five years of experience in the commercialization of healthcare technologies serving as its laboratory director. In addition the company has a Vice President who focuses solely on Clinical Lab Operations. And a feature that was unique to Navigenics until 2010, the company provides genetic counseling as part of its service, run by the Vice President of Genomics Services.

Navigenics has Clinical and Scientific Advisory Boards as well as a Policy and Ethics Task Force. This is striking given the fact that 23andMe has fewer structures of responsibility. The co-founder, Dr. Agus, as well as physicians from Stanford University Medical Center and Harvard Medical School serve on the Clinical Advisory Board. The Scientific Advisory Board consists of Ph.D.s in the areas of genomics and computer science who are currently professors at Princeton and Harvard Medical School. Greg Simon, a trained lawyer and president of FasterCures (The Center for Accelerating Medical Solutions), chairs the Policy and Ethics Task Force. Paul Slovic, founder and president of Decision Research, a company known for its pathbreaking work on public risk perception and decision analysis, aids the company with policy decisions. Interestingly, his company studies human judgment, decision-making, and risk analysis. Decision Research has developed methods to describe risk perception and

measure the impacts of risk descriptions on individuals, industry, and society.[20] This sort of expertise might prove useful for Navigenics' future partnerships with medical institutions to conduct studies on how individuals understand predictive genetic information.

***What Does the Navigenics Customer Consume?***

Like 23andMe, Navigenics began offering its Health Compass™ directly to consumers, in the sense that consumers could purchase the service online and submit a DNA sample to the company for analysis without an intervening physician. As described above, this feature was removed in 2010. Navigenics now requires that consumers sign up for its services through a physician or corporate wellness program. The company, however, provides the consumer with a list of physicians who are already participating in the services it provides. The company also encourages potential consumers to help their doctors learn more about working with Navigenics by informing them of the resources the company provides to physicians. While the physician is seemingly brought back in to mediate the initial genomic transaction, the consumer is still fairly free to access his or her own genetic information after the test has been ordered. As before, the company sends the consumer a saliva collection kit by mail. The sample is then sent to the company's lab where the DNA is analyzed with an Affymetrix microarray chip. In about three weeks, the consumer receives an email that his or her analysis is available through a secure online account. As an asterisk to accessing information online,

[20] Available at http://www.decisionresearch.org/ [Last accessed 10 February 2011]

Navigenics states, "If you sign up through your physician, your results may be delivered directly to your physician, who will contact you to review them."[21]

What sort of genetic test results does the Navigenics consumer or physician receive? From the beginning, Navigenics claimed only to provide genetic tests that had clinical significance. In order to be included in Navigenics' test panel, three criteria had to be met: the condition has to be medically relevant; the condition must be one that you and your doctor can act on; and research findings from multiple well-designed studies have to show consistent, reliable, and significant association between a genetic marker and a health condition.[22] On the criterion of medical relevance, Navigenics explained on its website at one point why it would not include tests for traits such as height and eye color, explaining that it would not provide tests for things that could be known from one's phenotype (Navigenics 2008). Genetic tests for height and eye color were at the time, and still continue to be, provided by 23andMe.

With its stricter focus on "medically relevant" tests, Navigenics had 18 genetic tests for disease conditions when it launched its service at the beginning of 2008. By May 2009 the panel had only grown to only 28, and currently the company offers genetic tests for 40 "Conditions" and "Medications." At the beginning of 2010, Navigenics added 12 tests that indicate how individuals may process certain drugs, beta blockers for example. This group of drugs is often used to protect the heart after a heart attack, as well as to treat high blood pressure, irregular heartbeat, glaucoma, migraine headaches, and other conditions. Navigenics

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[21] Available at http://www.navigenics.com/visitor/what_we_offer/how_it_works/ [Last accessed 10 February 2011]

[22] Available at http://www.navigenics.com/visitor/what_we_offer/conditions_we_cover/ [Last accessed 10 February 2011]

also offers a genetic test to estimate one's risk of side effects to the cholesterol-lowering drug Simvastatin. The benefit, the company claims, is that "knowing your genetic risk of side effects allows you and your doctor to choose the right drugs or dose for you, and opt for alternatives if needed."[23] Examples of genetic tests for "conditions" include, Alzheimer's disease, breast cancer, glaucoma, and prostate Cancer.[24]

Navigenics, like 23andMe, has its own vetting processing for the inclusion of genetic tests into its panel. Certain strict scientific criteria must be met. According to a promotional statement on the company's website: "We only report on genetic markers that have been consistently associated with health conditions and validated by multiple well-designed studies." The company also claims that its "genetic test results are based on science of the highest possible caliber. We only report on genetic markers that have met stringent criteria developed by our team of Ph.D. geneticists."

The sorts of tests offered by Navigenics and its claimed rigorous scientific review process have been integral to how the company defines its service. From the beginning Navigenics has sought to strike a more serious tone in comparison to its main competitor, 23andMe. In April 2008, just after the company began offering its service, then Medical Director, Michael Nierenberg, was interviewed by Elaine Warbuton of the blog Genetics and Health. Michael Nierenberg took the opportunity to do some serious boundary-work as to what the company was and was not: "Navigenics is in no way a 'recreational' genomics

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[23]Available at http://www.navigenics.com/visitor/what_we_offer/conditions_we_cover/ [Last accessed 10 February 2010]

[24] For a complete list of all offered tests please refer to the supplemental material.

company and does not wish to contemplate entering any 'recreational' field. It is a company focusing on wellness and prevention aspects of health. Our service focuses on actionable entities and things of substance such as cardiac disease, not eye color or such like. We welcome regulation and make heavy use of genetic counseling" (Warbuton 2008).

The consumer pays $999 for the smaller, more "scientific" and "medically relevant" Navigenics test panel. The cost dropped in July 2009 from $2,499. And although the cost of Navigenics' Health Compass™ has never dropped as low as 23andMe's Personal Genome Service™, Navigenics has also used promotional periods to entice customers. Never featuring the dramatic price cuts offered by their competitor—for example, 23andMe's $99 day—in March 2009 Navigenics promoted its "premiere" Health Compass test for $1,499 instead of the retail value of $2,499. And in August 2009 the company offered its testing service for $499, half the regular price. While it is estimated that Navigenics has significantly fewer customers than 23andMe, roughly 20,000 in 2010, a quarter of those customers had received discounts to be in a study (Pollack 2010).

***Partnerships***

The list of Navigenics' partnerships and planned studies is long. The company under the direction of Vanier has developed relationships with leading medical institutions, including Cleveland Clinic, Georgetown University, Mayo Clinic, Scripps Health, and Partners HealthCare, an integrated health system founded by Brigham and Women's Hospital and Massachusetts General Hospital, and a principal teaching affiliate of Harvard Medical School. According to Navigenics, these institutions have the expertise in genomic medicine to

support customers in follow-up care and diagnosis. The company has also signed agreements with Mayo Clinic to provide health information on the Navigenics website and with Medscape to develop continuing medical education materials for physicians. Board Member, John Doerr summarizes the importance of these activities: "And the company is attracting world-class partners and institutions to ensure state-of-the-art medical advice and services" (Navigenics Press Release 2009). Setting aside the benefits of state-of-the-art medical advice and services, the key sentiment is that Navigenics has partnered with credible, world-class *medical* institutions.

The first of these partnerships to bear fruit was the Scripps Genomic Health Initiative. In October 2008 Navigenics, Scripps Translational Science Institute, Microsoft Corp., and Affymetrix teamed to conduct a research study that would assess how people respond to personal genetic testing. The 20-year study involves 10,000 participants and seeks to analyze whether these participants will make positive lifestyle changes that benefit their health after receiving personal genetic test results. Early findings from this longitudinal study have already been published in January 2011 the *New England Journal of Medicine.* The article, titled, "Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk," concluded: "In a selected sample of subjects who completed follow-up after undergoing consumer genomewide testing, such testing did not result in any measurable short-term changes in psychological health, diet or exercise behavior, or use of screening tests. Potential effects of this type of genetic testing on the population at large are not known" (Bloss, Schork, and Topol 2011). Such publications mark a huge step forward for Navigenics' business. The article could not have come out at a better moment, as all of the heavy hitters (investors) in the

area of personalized medicine gathered in late January at the Personalized Medicine World Conference. Speaker after speaker featured, or at least footnoted, the published work that had been done through the Scripps Genomic Health Initiative (Field notes January 2011). The direct-to-consumer genetic testing industry is eager to conduct such studies to appease concerns about the technology and go ahead with its agenda for personalized medicine. Such studies are important demonstrations that companies like Navigenics are not causing harm. While the study has yet to demonstrate the benefits of personalized genetic testing, a company like Navigenics would likely argue that the "good" will come as the genetic information becomes more valuable.

**Conclusion: Common Building Blocks, Distinct Products**

23andMe and Navigenics have taken substantially different approaches to framing their genetic testing services, from the choice of leadership to choices about which types of tests to include, and how to relate to the scientific and medical communities. Nonetheless, the companies have used common building blocks in carving out a new domain for genetic testing. At the foundation of their services are the shared and publicly available Genome-Wide Association Studies. The two companies also use the same microarray sequencing technology, albeit from different providers, Illumina and Affymetrix, respectively. The companies have also drawn from the same pool of Silicon Valley venture capital to get their services off the ground. And both companies have used the Internet as the essential medium through which to interface with its consumers. With these tools, 23andMe and Navigenics have created a new sociotechnical architecture for genetic testing. In taking something that was traditionally

offered in a clinical setting, and moving it into the consumer market, these companies have put into motion a redefinition of "clinical" and "medical" in relation to genetic information.

The Internet has played a crucial role in the commodification of genetic information, not just as the medium through which consumers access their genetic information. The malleability of the Internet has allowed 23andMe and Navigenics to rapidly adapt and evolve their genetic testing platforms. Both companies dramatically changed their tests panels when they incorporated genetic tests relating to how individuals process drugs. This bold move further blurred the line of whether or not their services are part of medical practice. And in the summer of 2010, 23andMe began offering referrals for genetic counseling. Suffice to say, the nature of these changes, the number, and speed with which they happen could not occur in a clinical context. The implementation of new initiatives in a clinical setting requires that they be consistent with certain standards of care.

The companies are clearly in dialogue with each other but also with a broader discourse about the merits and potential threats posed by direct-to-consumer genetic testing. The two approaches reflect two understandings of what the genetic information is, how it should be used. For 23andMe the genetic information is for recreational purposes, whereas for Navigenics it can be used to improve health choices. In their marketing and other communications the companies have an imagined consumer that drives how they frame their services. This has implications for the ways in which regulation would follow their particular vendor-consumer relationships.

While there is some debate as to whether, given the distinct flavor of each company, they can or should be grouped under the broad heading of direct-to-consumer genetic testing. This is a fair question given all the differences I have drawn out in this chapter. Their differences, however, point to the fact that the companies are responding to norms that already guide the practice of genetic testing. And the differences I have highlighted in a very important way recede when both FDA and Congress decide to investigate the practices of direct-to-consumer firms.

# CHAPTER 3: INSTITUTIONALIZING DIRECT-TO-CONSUMER GENETIC TESTING: FDA

The human genome is a zone of ambiguity. As we have gained more knowledge about our genes, and continue to build on the monumental sequence of the human genome, we keep coming back to the question: who are we in relation to our genomes? 23andMe and Navigenics provide an important window. The direct-to-consumer genetic testing industry is attempting to carve out a new space for the commercialization of genetic information. In the process they are claiming a new status for genetic information: it is being marketed as personal information. As early initiators of boutique genetic consumerism, the companies provide different modes of genetic interpretation. 23andMe offers, as we have seen, recreational genetics for the curiosity-driven buyer who would like to share cool facts at cocktail parties or in online forums. Navigenics, in contrast, has adopted a more serious medical tone while still claiming not to provide medical advice. The flexibility of these approaches and the companies' own changing representations of their services, though, point to the fact that both companies are navigating a space in which society already has some established norms as to how we can and should relate to our genomes. In attempting to create a new business model centered on the commodification of genetic information, the companies are coming up against other forces.

This chapter explores how the emerging genetic testing industry is interacting with the state, particularly the Food and Drug Administration, through regulation. I begin by situating FDA's current interest in regulating genetic testing in its broader historical context. This is a story about genetic information being safely bounded within one regime, that of the physician-

patient relationship, and then slipping out of those boundaries. As a result, FDA has called for a new regulatory regime around genetic testing. In this chapter I analyze the tools available to FDA to bring genetic testing back under its jurisdiction. FDA's challenge, I argue, is to bring the law to bear on an uncertain object – genetic information – by determining the status of that very object. By representing genetic information as medically significant, FDA is able to control how companies like 23andMe and Navigenics dispense genetic information. In turn, however, FDA is moving towards a system of regulation that would distance genetic information from medical expertise and bring it closer to scientific expertise. In the process FDA has to recruit the authority of science to stabilize the status of genetic information.

**The History of DTC Genetic Test Regulation**

In 2006 the Food and Drug Administration, the Federal Trade Commission (FTC), and the Centers for Disease Control and Prevention (CDC) first took note of direct-to-consumer genetic testing. A small cluster of companies had begun to offer nutritional genetic testing, which is based on nutrigenomics, the science of how food and ingested nutrients affect gene expression. The aim of nutrigenomics, a term which emerged in the late 1990s, has been to optimize nutrition with reference to individual genotypes. In the early 2000s, private companies began to market this new area of science through the direct-to-consumer marketing of nutritional genetic tests.

One of the first companies to enter this space was Sciona Inc., a nutritional genetic testing company, founded in 2000 and based in Boulder, Colorado. The company claims to provide "health and nutrition information to consumers based on an individual's diet, lifestyle

and unique genetic profile." Genelex Inc., founded in 1987 as a paternity and forensic DNA testing laboratory, claims to provide nutritional genetic testing for a presents itself as "the first company in the world to offer direct-to-consumer DNA Drug Sensitivity Testing.™"[25] While the testing is marketed directly to consumers, Genelex requires a physician prescription for such genetic testing. Suracell Inc., "provides Personal Genetic Health programs formulated to measure, assess, monitor and work with the body's individual genetic needs. The testing and analysis programs are designed to look at an individual's DNA and provide personalized recommended protocols of specially formulated nutraceuticals and positive lifestyle choices."[26] These self-descriptions show a move away from the traditional model of medicine, which then raised flags in the regulatory community.

By 2006, in response to these company claims and offerings, FDA, FTC, and CDC jointly published a consumer fact sheet titled, "At-Home Genetic Tests: A Healthy Dose of Skepticism May Be the Best Prescription." The document warned against the claims made by DTC genetic testing companies and encouraged consumers to involve a physician or genetic counselor to understand the value of genetic testing (FTC 2006). At the same time, the Government Accountability Office (GAO) issued a report titled, "Nutrigenetic Testing: Tests Purchased from Four Web Sites Misled Consumers" (GAO 2006). Gregory Kutz, Managing director of Forensic Audits and Special Investigations at GAO, conducted the investigation. Four companies were examined, including the three mentioned above, by sending fourteen fictitious consumer samples from two donors to them. Gregory Kutz cautioned, "I want to

[25] Available at http://www.healthanddna.com/dna-learning/book-resources.html [last accessed 15 April 2011]
[26] Available at http://www.suracell.com/ [last accessed 15 April 2011]

send a message to consumers across the country: Buyer beware" (GAO 2006). The GAO report concluded that providers of direct-to-consumer nutrigenetic testing "mislead the consumer by making health-related predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers" (GAO 2006).

Although academics (e.g. Castle 2008; DeBush 2010) criticized the report for its methodology, even calling GAO's description of the testing services "irresponsible,"[27] the investigations raised concerns as to whether there was sufficient oversight of DTC genetic tests. Further, the report addressed the question of whether there were any circumstances under which direct-to-consumer genetic testing could be appropriate. Kathy Hudson, then Director of the Genetics and Public Policy Center, testified before Congress in 2006: "If sufficient regulations were in place to ensure the analytic validity of tests and the clinical validity of tests, I think we could really have a conversation about whether or not it's appropriate for consumers to access some tests directly – All genetic tests are not created equal so we need to have a nuanced approach to whether a healthcare provider's intervention is required always, sometimes, or never" (Genetics & Public Policy Center 2006).

While no formal oversight emerged from this first confrontation between regulatory agencies and the direct-to-consumer genetic testing industry, it was an important demonstration that FDA and other state agencies have the power to decide what is health-related and medically relevant. As the FDA, FTC, and CDC collectively decided that nutritional genetic information was not actionable in any medically relevant sense, the

associated risks were low. Direct oversight was not necessary. The nutritional genetic testing industry, however, suffered from the warnings. Expected sales dropped off following the report.

On the heels of this considerable blow to direct-to-consumer nutrigenetic testing, 23andMe and Navigenics embraced Kathy Hudson's observation that all genetic tests are not created equal. Distancing their companies from the perceived fraud of nutrigenetic testing, these companies entered the market in 2007 claiming to offer non-medical, health-related genetic information. Both companies provided correlative information between genotypes and disease or trait phenotypes. Both companies have claimed that is just another form of personal information. Kari Stefansson, C.E.O. of the Icelandic company deCODE and its subsidiary, deCODEme Genetic Scan, echoed this theme. Stefansson said of predictive, pre-symptomatic, genetic testing: "It doesn't increase your risk. It doesn't decrease your risk. It measures your risk. It's a description of who you are" (Wadman 2008). By casting genetic test results as just another form of personal information, both Stefansson and the two U.S.-based companies in effect have made a case for new standards of evaluation.[28] As a result of this attempt to link genetic information to private personal information like bank statements, much of the focus of the companies' attention was on ensuring privacy and the protection of the data.

These attempts by direct-to-consumer genetic testing companies to situate themselves as providers of personal, as opposed to medical, information demonstrates how the technology

[28] German regulation of genetic testing provides a good contrast to this position. In April 2009 the German Bundestag passed the Human Genetic Examination Act. The regulations, which are heavily paternalistic, including a ban on DTC genetic testing, was constructed on the belief that genetic information is qualitatively different from other forms of personal or medical information (GenDG 2009).

became more malleable as the institutional framework within which it sat became more rigid. As the regulatory borders around the technology became more clearly defined, the companies choose to redefine the technology to pass through those borders.

While private companies were developing new frames through which to deliver genetic testing directly to consumers, the Department of Health and Human Services (HHS) was actively engaged in finding methods to assess the quality and reliability of all types of genetic tests. In 2007, then secretary of HHS, Michael Leavitt, commissioned his Advisory Committee on Genetics, Health, and Society, or SACGHS, to investigate the adequacy and transparency of the current oversight system for genetic testing. The committee published its review a year later, titled, "U.S. System of Oversight of Genetic Testing" (SACGHS 2008). The long report identified major gaps in the regulation of genetic testing, including insufficient oversight of laboratory quality, clinical validity, and knowledge of the intended uses and outcomes of genetic testing. On the heels of this report, the first regulation of direct-to-consumer genetic testing focused on analytic validity, specifically whether the laboratories processing consumer samples were properly certified under the federal provisions of the Clinical Laboratory Improvement Amendments of 1988 (CLIA). The amendments, which apply to all laboratories that provide genetic tests, aim to ensure a homogenous standard in the accuracy of laboratory tests across the country. Providers of clinical laboratory tests not only have to demonstrate analytic validity of their tests, but also to satisfy the requirements of the Centers for Medicare and Medicaid Services relating to quality control, personnel qualifications and records maintenance.

When 23andMe and Navigenics began selling genetic testing over the Internet, twenty-five U.S. states and the District of Columbia permitted direct-to-consumer laboratory testing without restriction, thirteen states prohibited such testing, and twelve states permitted it only for specified classes of tests (Genetics & Public Policy Center 2007). Some states have denied direct-to-consumer laboratory testing on the grounds that a licensed physician or healthcare practitioner must order the tests. The most significant commonality underlying this patchwork of policies was a ubiquitous reliance by states on CLIA.

It was not until California and New York halted the sale of their genetic tests in 2008 that 23andMe and Navigenics sought to demonstrate CLIA compliance. After investigating twenty-five genetic testing firms, the California Department of Public Health sent a "cease and desist" letter to 23andMe and Navigenics in June 2008 requesting that they stop the sale of tests to Californian residents. The letter focused on two points under the state Business and Professions Code Sections 1241 and 1288: the companies needed a clinical laboratory license or registration, and they could not offer a clinical laboratory test directly to the consumer without a physician order, unless specifically exempt (CDPH 2008). Similarly, New York Department of Health regulations stipulate that direct-to-consumer genetic testing laboratories must obtain a permit and that a New York State licensed physician must order the tests (Powell 2009).

With these initiatives the California and New York Departments of Health framed direct-to-consumer genetic testing as a medical service that had to be accommodated within the existing regulatory framework for laboratory tests. Beyond the technicalities, however, this

confrontation around the need for obtaining CLIA certification appears significant precisely because it is the first opposition by public institutions to the two companies' construction of genetic tests as commodities distinct from medical services. Through the requirement of CLIA certification, the states reinserted a layer of technical assurance. It was a reassertion not only of the power of the state, but also of the primacy of certain types of test evaluation. And yet by complying with CLIA regulatory requirements, the companies were able to further transform genetic testing into a product by focusing attention on test accuracy.

An emphasis on test accuracy was also apparent in the reaction of 23andMe to its alleged mishandling of 96 customer samples. In June 2010 the company was told by a consumer that her genetic information was not correct. 23andMe investigated the matter and discovered that, due to "human error," a plate holding 96 consumer samples had mistakenly been inverted, leading to the incorrect processing of these samples. The company rectified the problem within days. Emphasizing that analytic validity is a concern for all laboratories, proponents of the new industry were quick to point out that 23andMe's laboratory blunder did not result from the "consumer" aspects of its services, for example, the collection method. In other words, there was nothing new in direct-to-consumer genetic testing that could make this technological infrastructure more prone to failures in analytic validity. This was simply business as usual, including the possibility of error, and the company's framing of the mishap focused attention on its concern with data accuracy. On the June 8, the company posted the following on its blog: "We want to clarify what happened with the sample errors, how it happened and what we're doing to prevent it from happening again. Providing each and every

one of our customers with *accurate data* is 23andMe's number one priority, and we fully realize the gravity of this incident" (23andMe 2010).

This overview of direct-to-consumer genetic testing regulation shows how the status of genetic information has been contested. From the example of nutrigenetic testing, the genetic information was deemed misleading, but not medically relevant. And with the more recent emergence of companies like 23andMe and Navigenics it has also been unclear when balancing company claims and state interventions what the genetic information is. The companies have claimed that is not medical, but the California and New York Departments of Public Health brought the service back into a medical register by requiring CLIA certification. From these confrontations with state authorities we see that the state has the ability to intervene on the framing of genetic information. Both the companies and the government are trying to assert their authority to shape the still-fluctuating sociotechnical architecture of DTC genetic testing. As private companies try to create a new space for genetic information this regulatory overview shows how they are brushing up against well-established norms or ways of thinking about the provision of genetic testing. In contrast to companies like Sciona and Suracell, 23andMe and Navigenics were viewed by state authorities as infringing on the norms of clinical genetic testing. The following section explores how beginning in 2010, FDA took a renewed interest in genetic testing through the regulatory framework of laboratory-developed tests. In this broader debate I examine the resources used by FDA to bring direct-to-consumer genetic testing back into a medical register and therefore subject to regulation.

**FDA**

In the summer of 2010, FDA became interested in DTC genetic testing companies. The agency asserted its authority over the industry by classifying the genetic testing services as a medical device. This development followed on the heels of a controversial marketing move made in May 2010 by a younger genetic testing firm, Pathway Genomics. The San Diego based company, which offers a similar panel of genetic tests to 23andMe and Navigenics, had partnered with major retail chains, Walgreens and CVS. Pathway Genomics had planned to sell its genetic testing kits directly to consumers on the shelves of these stores (Pollack 2010). In light of bad press and an impending FDA inquisition, however, the partnership fell through.

On June 10, 2010 FDA sent letters to 23andMe, Navigenics, and Pathway Genomics informing the firms that their services were medical devices under the Federal Food, Drug, and Cosmetic Act of 1938. According to the Act, a medical device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar article that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease" (PL 95-295, 90 Stat 539). The definition leaves room for interpretation, but to provide some guidance, FDA states that a medical device can be anything from a thermometer to an artificial heart to an at-home pregnancy test. In letters sent to the companies, FDA clarified why medical devices are subject to premarket review:

> [It] enables FDA to protect the public from medical products that may pose an unreasonable risk of harm. It is important that they be analytically and clinically accurate so that individuals are not misled by incorrect test results or unsupported clinical interpretations. Premarket review allows for an independent and unbiased

> assessment of a diagnostic test's ability to generate test results that can reliably be used to support good healthcare decisions (Department of Health and Human Services 2010).

From the reasoning of FDA, harm and unreasonable risk could result from both incorrect and unsound data, which could lead to bad or harmful healthcare decisions. This is a clear attempt by FDA to reassert its framing of genetic testing as medical, and therefore subject to its regulatory control.

In July 2010 FDA hosted a public meeting to address the oversight of a broader set of tests, laboratory developed tests (LDTs). The two-day public meeting convened with the purpose of "seeking to gain input from stakeholders on different issues related to oversight of LDTs" (FDA 2010). The stakeholders involved included representatives from the medical and scientific communities, non-governmental organizations (NGOs), healthcare consulting firms, and the academic community. The meeting was divided into four sessions: patient and clinical considerations, clinical laboratory challenges, direct-to-consumer testing, and education and outreach. Alberto Gutierrez, Director of the Office of In Vitro Diagnostic and Device Evaluation, and Dr. Joshua Sharfstein, Principal Deputy Commissioner of the Food and Drug Administration hosted the event. Also representing the FDA were several top members of the Center for Device and Radiological Health.[29]

[29] Members of the Center for Device and Radiological Health, including the Director, Dr. Jeffrey Shuren; Sally Hojvat, Director of the Division of Microbiology Devices; Elizabeth Mansfield, Director for Personalized Medicine; Dr. Ginette Michaud, Deputy Director for Science and Medicine; and Katherine Serrano of the Office of In Vitro Diagnostic Device Evaluation.

In his opening remarks, Sharfstein framed the importance of LDT oversight within the broader context of personalized medicine. Citing an article published in the *New England Journal of Medicine* by FDA Commissioner Margaret Hamburg, and NIH Director, Dr. Francis Collins (Hamburg and Francis S. Collins 2010), Sharfstein made the case that LDTs are intimately tied to the future of personalized medicine. He cautioned, however, "that from our perspective the area of personalized medicine is an area with tremendous public health value, and also in that area some public health risk" (FDA 2010). With this in mind he said: "The goal of regulation is to find the right approach to maximize the public health value and minimize the risk. I think one of the factors to consider there is how, in a regulatory structure, it incentivizes the kind of research that gives good data that helps people to really make good decisions" (FDA 2010). With these remarks, the Deputy Director effectively put forth two overarching themes that continued to emerge throughout the public meeting: concerns about the risks of LDTs and the perceived need to balance regulation with innovation.

Underlying the idea that regulation must be balanced with innovation, or "good research," was the idea that science produces future goods for the public, while law inhibits or slows progress. The framing of the meeting within the broader context of personalized medicine further strengthened the idea that science is a generative force, and if channeled to personalized medicine, will lead to better individual healthcare at a reduced cost. The positioning of LDTs within the broader discourse of personalized medicine also reaffirmed the tests as medical objects. The force of this vision served as a political tool to set up a narrative in which regulation was closely tied to defined risks. On this view, if FDA defines technical

and science-derived risks in a tractable manner, then the science and technology behind LDTs can move forward to further personalized medicine.

***FDA's jurisdiction over LDTs***

FDA has classified genetic tests as a type of in vitro diagnostic, a subset of medical devices. To understand the power of these classifications, I use the concept of blackboxing. Black-boxing refers to the process of making facts extent that the internal contingencies that have been settled in the stabilization of that very fact become taken for granted (Latour 1999; Latour 1987). For FDA, the entire chain of development and delivery of genetic tests has been translated into the language of laboratory-developed test – language so vague and inclusive that the entire system is rendered opaque. For the most part, the opaqueness of the black box of laboratory-developed tests has been unproblematic, because such tests have traditionally been delivered in a context in which the mechanics of the test are well oiled with certifiable medical and scientific expertise. The example of Pathway Genomics, however, serves as an example of how such black boxes can be forced open. A new mode of delivery, of one subset of LDTs—genetic tests—can challenge an entire system that had stabilized around, for example, the norms of the physician-patient relationship. In the case of LDTs, FDA has been forced, with much reluctance, to open up and examine the larger system of laboratory developed tests. What is most interesting about FDA, though, is how it has attempted to stabilize this subset of medical devices through the articulation of risks. If FDA can clearly define and regulate the risks of LDTs, the whole system of development and delivery—the black box—can be closed again.

***A risk-based approach to regulation***

Under the Act of 1938, the FDA developed a system for classifying medical devices into three classes, corresponding to the degree of risk to the patient of an undetected incorrect result. Based on this classification system, FDA policy accords greater scrutiny to higher risk tests. The classes are as follows:

> **Class I**, subject only to general controls applicable to all devices, is the lowest risk category for a device. Class I IVDs include certain reagents and instruments, as well as a number of highly adjunctive IVD tests, where one test is dependent on the results of another; consequently an incorrect result would generally be detected easily. Most Class I devices are exempt from premarket review. An example of a Class I test is a luteinizing hormone test that, if it gives a false result, may lead to delayed conception but is unlikely to directly harm the patient.
>
> **Class II**, generally subject to general controls and special controls, is the most moderate-risk category for a device, and includes many standard laboratory tests, such as chemistry and immunology tests. Most Class II tests are subject to FDA review through premarket notification under section 510(k) of the Act. For example, a false sodium result (a Class II test) may be life-threatening if the error is unrecognized and treatment decisions to correct the sodium level are made on the false result.
>
> **Class III**, subject to premarket approval requirements, is the highest risk category for a device and includes devices and tests that present a potentially unreasonable risk of illness or injury. For example, a false negative result for a hepatitis C virus test (a Class II test) may result in a failure to provide appropriate treatment, leading to risk of

liver failure due to delayed treatment. In addition, without the knowledge that he or she is infected, the patient may put others at risk by spreading the disease (FDA 2010).

During the FDA public hearing in July 2010, Dr. Harper, director of the Division of Chemistry and Toxicology, clarified how this structure came about in practical terms. As medical devices include a range of objects, from a knee implant to a toothbrush to a tongue depressor, the classification system was employed to ensure that devices would receive appropriate FDA scrutiny and regulation based on the risks associated with their intended use. In the process of classification Dr. Harper acknowledged that FDA has employed experts from relevant fields to better understand the risks involved in the particular use of a device (FDA 2010). These appeals to external expertise, as described by Jasanoff, blur the conventional boundaries between science and policy: "The agency freely permits its expert advisers to receive evidence from nonscientists as well as scientists and to deliberate on such topics as the appropriate cost of producing more information or the acceptable risk level for hypersusceptible consumers" (Jasanoff 1998a, 177-178). Although as Jasanoff points out, these appeals to expert advice often leave the FDA's decision-making authority undefined, "this approach to seeking advice works well at reducing conflicts over the interpretation of regulatory science" (178). Through the blurring of science and policy in its recruitment of non-adversarial expertise, FDA is able use the authority of science to support its own policy agenda. The agency gathers what it thinks it needs and then slaps a label such as good science over what it wants to shield from conflict, because those claims now carry the authority of expert knowledge.

What FDA means by a risk-based approach was repeated by Katherine Seranno of the Office of In Vitro Diagnostic Device Evaluation and Safety, "When we talk about risk of an in vitro diagnostic, we really do so in the context of intended use" (FDA 2010). In the case of genetic tests, there are two relevant risk profiles. FDA attempts to judge the risks of the intended uses of the tests, and the tests aim to say something about future risks to the person who has had his or her DNA analyzed. FDA's ability to attach a number to these risk profiles allows the agency to better defend its decisions and standards. Such a process, with the recruitment of external expertise, allows FDA to further deploy the resources of science in this construction of DTC genetic testing's sociotechnical architecture.

***In vitro diagnostic tests: bifurcated regulatory pathway***

In the system of regulatory classification laid down by FDA, genetic tests are in vitro diagnostic tests, a subset of medical devices. FDA has developed a bifurcated pathway for such tests to reach the market or, as originally intended, clinical practice. One is the commercially distributed pathway, which generally requires premarket review by FDA. It was described by Harper as follows: "These are tests that are manufactured in the factory, and they are assembled there, and the manufacturer collects data on their performance and their safety effectiveness; and where devices may be a moderate or high risk, they come into the FDA for premarket review, and the FDA will grant clearance or approval" (FDA 2010). Following approval or clearance, the tests can be distributed to other labs for patient and commercial use. Laboratory developed tests, in contrast, are defined as "tests that are designed, manufactured, and used within a single laboratory" (FDA 2010). FDA has assumed that the laboratory sources all its own reagents, designs the methodology, and validates the test following all

applicable regulations, such as CLIA. Historically, LDTs have not required FDA approval prior to going to market. This is because these tests were supposedly developed in the laboratory as part of patient care in coordination with physicians and pathologists. FDA defined its lack of direct regulation over this class of tests as an act of enforcement discretion. FDA, in other words, has the authority to decide when direct oversight is necessary and when it is not. In the case of LDTs, the agency held that the existing doctor-patient relationship provided sufficient protection and added government review was not needed.

***Enforcement Discretion***

FDA's use of enforcement discretion, according to Dr. Harper, applies to all medical devices. And according to the agency, even if direct regulation is not in place, the law applies still applies to all products that are medical devices (FDA 2010). Enforcement discretion, based on her testimony, should be understood as a matter of changing the practical application of those laws and regulations. The risk-based approach provides reasoning for such a risk-based approach. Harper explains: "Sometimes it arises because of lack of resources or timing issues, but as FDA chooses to continue to practice enforcement discretion, it will generally always be based on risk, and that the risks in doing so don't outweigh the benefits of doing so. However, sometimes those risk profiles may change and when they change, FDA may choose to change the practice of enforcement discretion where it makes sense" (FDA 2010).

FDA's recent interest in DTC genetic testing, and LDTs broadly, begs the question: what has changed to the extent that the agency felt obliged to organize a public meeting to discuss future regulation? While the public meeting was the result of changes that go beyond

the articulation of risk profiles, FDA narrowed the rationale for its intervention to two main issues that have increased risks for patients. One set of concerns deals with changes in the science and technology behind the LDTs, and the other set to changes in the context and incentives behind new modes of delivery. In its assessment, FDA pointed out that the bifurcated pathway to market originated when LDTs were low in volume, noncommercial, and performed in hospital laboratories. In this context, the tests were developed within a close clinician-patient-pathologist relationship to improve diagnosis and treatment. Expertise came from pathologists as they worked with physicians to develop tests that would improve patient care.

In the 1990s, however, there was both an increase in genetic information and the development of multiplex tests, which combine tests for several different medical conditions. FDA said that it intentionally took a stance not to hamper innovation while relying on some measures to ensure the quality of laboratory processing and reagents. In 2007, for example, FDA developed stricter guidelines for the reagents used in LDTs but with an exemption for reagents that were used for research. Test developers, however, were easily able to skirt this restriction by labeling their reagents "For Research Use Only." FDA had the policy of not regulating reagents that were for research purposes. In addition to concerns about the consistency and quality of laboratory reagents, FDA also acknowledged that the establishment of clinical validity—how consistently and accurately the tests detects the outcome of interest—was not a straightforward matter. There was an increase in the number of tests lacking proper clinical validation, as it became more difficult to establish these outcomes. FDA stated, for example, that "high density testing with multiple signals were being

statistically correlated into non-transparent results" (FDA 2010). Furthermore, tests of this non-transparent fashion were being offered for "high risk intended uses," such as cancer and Alzheimer disease, without an independent review of data claims. FDA also argued that the use of tests developed through complex software instead of expert interpretation increased risks to patients in some cases, as human intervention was removed from the equation.

Given the new era of bioinformatics, FDA expressed concern about assuring the clinical validity of statistical models. Although currently clinical validation for LDTs is not required, Harper pointed to increased risks to patients due to the fact that "there is no independent review of data claims before those tests go on the market" (FDA 2010). On this point, Dr. Mansfield, Director of Personalized Medicine, acknowledged that the lack of oversight of LDTs in the current bifurcated system was actually enabling business interests: "So we see LDT being more and more used as a loophole in many cases, as a way to go to market quickly without independent premarket oversight" (FDA 2010). 23andMe and Navigenics entered the equation against this changing backdrop in the development and implementation of LDTs. These personal genomics companies were cited as contributing to the increase in LDT risks by providing genetic tests with "high risk clinical claims." A whole session of the hearing was devoted to the topic of DTC genetic testing (FDA 2010).

**The politics of assigning an ontology**

FDA's decision to classify direct-to-consumer genetic testing services as a medical device was an important move. In deciding the status of the companies by defining their services as a medical device, FDA assigned a medical ontology to the uncertain technology.

FDA could have decided, as in the case of nutritional genetic testing, to take a more hands-off approach. With nutritional genetic tests, FDA, CDC, and FTC concluded that the genetic information provided had no medical value. As such, defining nutritional genetic testing services as a medical device would have been incoherent, because they had no medical value. In the case of companies like 23andMe and Navigenics, however, FDA has constructed a tie between the provided genetic risk profiles and their (contested) medical value. In this act, FDA also became the relevant institution to intervene on the technology. FDA claimed authority over the very object that it defined.

Returning to the definition of a medical device, one needs to look at the chain of events that allow the consumer to purchase and receive personalized genetic information over the Internet to appreciate the full sense in which the entire service can be understood as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar article." The services supplied by 23andMe and Navigenics have relied on a sample collection method that involves a sort of chain of custody for one's DNA sample. The consumer collects his or her own sample, a postal service then ensures that the DNA arrives at the correct laboratory, the sample is then placed in the hands of laboratory personnel who extract DNA from the saliva sample, use machinery to amplify the DNA, and sequence the DNA with the aid of microarray analysis made possible by the separate manufacturing of a microarray chip that holds the collection of relevant SNPs.

Yet the service relies on the publicly available scientific knowledge that is used to the DNA samples. All of the genome-wide association studies referenced by the companies in the

selection of SNPs-of-interest can be seen as part of this testing service. Additionally, each company has its own group of qualified scientists who decide which studies are sound enough to include in the test panel. When considering all of these components that make the genetic testing service possible, it becomes difficult to clearly define the parameters of the service. Where does the medical device begin and end? By classifying direct-to-consumer genetic testing services under the broad definition of a medical device, FDA was able to black box the inherent complexity, messiness and intractability of the network that supports such a service.

When FDA asserted its authority to manage the "unreasonable risk of harm" that could result from the medical product, the agency argued that the testing services have implications for the "diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease." While FDA took responsibility to mitigate these risks, in the same move FDA also focused the scope of relevant risks to those of analytical and clinical accuracy, the hallmarks of pre-market review. As analytical and clinical accuracy are used to evaluate the technical aspects of a medical device, other dimensions of the testing platform, such as its utility, have been lost in this representation. In the case of genetic testing, medical expertise has usually played an important role in determining the utility of a test.

**Enforcement discretion: reinforcing law's lag?**

With FDA's power to decide the status of a limited class of objects in the world comes an additional point of leverage. Wherever a medical device exists (is brought into being), FDA has the power to decide whether or not to directly regulate that device depending on its risk profile. FDA justifies this use of enforcement on the ground that the risk profiles of medical

devices can change. What does this really mean when it is translated into practice? As explained by Harper, sometimes the use of enforcement discretion is due to timing or resource issues, but the justification is always given in terms of balancing risks: "that the risks in doing so don't outweigh the benefits of doing so." In other words, FDA is willing to set aside or maybe overlook the review of certain medical devices if others are more pressing, and the risks of the overlooked devices are not too high. But Harper also indicated that risk profiles can change. In these cases, again, it is a discretion whether FDA "changes the practice of enforcement discretion." FDA, however, did not clarify in the meeting how these assessments are made and how often devices are revisited.

FDA originally chose not to regulate LDTs because it viewed the system such tests operated in as not providing undue risk. With reference to changes in the science, technology, and modes of delivery, however, FDA decided to assert its latent power on the grounds that there were new associated risks arising from scientific and technological advancements.

Enforcement discretion reinforces the conventional narrative of societal response lagging behind science. According to this account, science and technology move along at such a rapid pace, and with such unforeseen consequences that society, law, and regulation consistently lag behind. In December 2010, Michael Specter of *The New Yorker*, talked with FDA Commissioner, Margaret Hamburg, about the job of regulating one-third of the economy, truth in labeling and packaging, and the potential benefits and dangers of genomics. With respect to these regulatory issues, Hamburg characterized scientific innovation as running ahead of the agency. She explained:

> An important issue that is always on the plate of the FDA, which is the fact that in the modern era science is evolving more rapidly than our abilities as a society to cope with some of the innovation and our ability as an agency and as a scientific community always to assess some of the safety concerns, and for me what this speaks to is the need to really strengthen our system to address those concerns, and is why for me, the FDA plays this very important and unique role, because we need to whether it's genetically modified foods or nanotechnology or synthetic biology, you know we need to be really at the forefront of asking and answering these important questions about safety, and many of them are not easy, many of them are straightforward, but explaining them is more complex (Hamburg 2010).

This is inconsistent with FDA's actual actions, which shape the context for science with considerable authority.

FDA does not see itself as constituting the law or medical devices, because it sees itself as implementing the law. FDA officials refer to the use of enforcement discretion simply as a matter of policy:

> The law is in effect. We have simply, as a matter of policy, determined not to exercise or not to enforce that authority as of right now. So when we engage in enforcement discretion, either put it in place or take it back, that is a guidance process. It is a matter of policy. It is not imposing new enforcement. The requirements are already there (FDA 2010).

What does this seemingly conflicting narrative about the relationship between science and the law achieve for FDA? On one level it serves as an example of the agency's commitment to a

particular vision of the future, in which science can only produce public goods if innovation is balanced with appropriate regulation. Enforcement discretion is a demonstration of this sort of balance. FDA only interjects with "policy" where the risk profiles of new drugs or devices demand agency intervention. Innovative science can only serve the public good without burdensome FDA oversight, an example being the development of LDTs within a physician-pathologist-patient relationship. At another level, FDA maintains supreme authority to intervene at any moment with the justification that the law was always present. This translates into "discretion," or power, to sustain particular visions of the future.

This power is evidenced in the case of Pathway Genomics and direct-to-consumer genetic testing, broadly. Why did the pathway of delivery matter so much for FDA? Was it simply due to an assessment that a new mode of delivery for genetic testing, on the shelves of Walgreens, posed new risks? I argue that it is much more than this simple change in risk profile that woke FDA from its enforcement discretion slumber. Pathway Genomics was the tipping point that disrupted FDA's ability to contain the associated risks of laboratory testing within the stable network of physician-patient relationships. More importantly though, when Pathway Genomics attempted to partner with Walgreens, the question of who has the power and authority to imagine individual futures through genetic testing came to a head.

FDA was able to rein back the technology back in by invoking the power of the law. With legal backing, FDA positioned itself to control individual access to genetic information, shaping what we can know in relation to our bodies. Similarly, and at the same time, the California Department of Health intervened on the University of California Berkeley's plan to

bring its incoming freshmen closer to their genes. In May 2010, the University announced that in lieu of the traditional, "On the Same Page" freshman community building exercise of reading a book over the summer, consenting freshmen could submit a DNA sample for genetic testing. The "Bring Your Genes to Cal" experiment was conceived with the idea that freshman DNA samples would be analyzed with respect to three genetic markers: the ability to process lactose and metabolize alcohol; and the genetic marker for folic acid metabolization.[30]

The program raised concerns among campus bioethicists and policy analysts. Jesse Reynolds, of the Berkeley-based Center for Genetics and Society, objected to the program design, implications, and content. Given the university context and the age of the participants, he argued that the program had a coercive nature that goes against consent standards. Some of the entering freshmen might not even be of a legal consenting age. Additionally, the "experiment" seemed to legitimate the controversial DTC genetic testing industry, and the suggested genetic tests were not innocuous, namely, the genetic test indicating how individuals metabolize alcohol (Reynolds 2010). The drinking behavior of students could be affected by the genetic information. Berkeley faculty members were also shocked that the administration did not involve them in discussions about the program design (Field notes Tarrytown Meeting 2010).

By August 2010 the California Department of Public Health (CDPH) stepped in and ordered changes to the experiment that prevented students from receiving their individual genetic test results. CDPH insisted that since students would be given access to their own test

[30] Available at http://onthesamepage.berkeley.edu/ [Last accessed 25 January 2011]

results, the academic exercise was not exempt from laws designed to assure the accuracy and quality of diagnostic tests used in providing medical care to patients. The federal CLIA and the California Business and Professions Code applied to the laboratories processing the student samples. The examples of DTC genetic testing and "Bring Your Genes to Cal" raised questions about were to draw appropriate boundaries and according to whom. Who should have the power and authority to control bodies? CDPH like FDA brought genetic information back into a medical register and in doing so had the ability to control who provides genetic testing. In these examples the state has played an important role in controlling this relationship by defining genetic information as a medically relevant category.

**Access to genetic data**

While FDA has plans to regulate the channels of delivery for genetic information, the agency has taken the stance that it wants to allow individuals access to their genetic data. On this topic, Dr. Alberto Gutierrez, head of FDA's Office of In Vitro Diagnostics, does not want the agency to be viewed as paternalistic: "We really don't have any issues with denying people information," he said, "We just want to make sure that the information they are given is correct" (Pollack 2010). This position is also echoed in 23andMe's "Core Values." While the company used to take the stronger normative stance that "individuals have a right to their DNA," this statement has been removed and replaced with the slightly weaker derivative, "We believe that having the means to access one's genetic information is good" (23andMe 2010). In a moment when FDA is heavily scrutinizing the practices of genetic testing firms like 23andMe, what does it mean for FDA to converge with an industry-supporting stance, that individuals should have access to their genetic data?

At one level it reaffirms a story about who we are in relation to our DNA. Materially, DNA is found in every cell of our bodies and is therefore part of our physical composition. But as evidenced in the discourse surrounding the Human Genome Project, the sequence of our "collective" DNA has been constructed as a biological force that has the power to unite us in our shared "humanness." Following the complete sequencing of the human genome in 2001 we were told that we are more alike than different – a "global family." Francis Collins, then Director of the National Center for Human Genome Research, referred to the human genome as the "instruction book for human biology" (F. S. Collins 2001). Increasingly in the 1990s and through the completion of the Human Genome Project, an understanding of our shared genetic composition changed how we thought about ourselves. In 2001, Svante Pääbo, the director of the Department of Genetics at the Max Planck Institute for Evolutionary Anthropology, reflected:

> The successes of medical genetics and genomics during the last decade have resulted in a sharp shift toward an almost completely genetic view of ourselves. I find it striking that 10 years ago, a geneticist had to defend the idea that not only the environment but also genes shape human development. Today, one feels compelled to stress that there is a large environmental component to common diseases, behavior, and personality traits! There is an insidious tendency to look to our genes for most aspects of our "humanness," and to forget that the genome is but an internal scaffold for our existence (Pääbo 2001).

While some pointed to environmental factors as a way to counteract ideas of genetic determinism, the notions that our genes and our DNA are central to who we are increasingly

became part of everyday vernacular. And while the complete sequencing of the human genome initially led to talk that we were more alike than different, plans to conduct comparative studies were quickly launched to reveal just how dissimilar humans are to each other and other species. The sequenced human genome had the potential to be the primary reference from which we could also know our differences. The identification of SNPs through genome-wide association studies became an extension of this vision. People understood that their own genetic sequence could tell them something specific about their genetic predispositions for traits and diseases. The position of FDA and companies like 23andMe that people have a right to their genetic information becomes compelling if genetic information provides unique information about who we are. Individuals should have access to something that has been constructed as fundamentally "mine."

The separation of raw genetic data from the significance of those sequences, however, is problematic. In equating what is fundamental to one and what is fundamentally one's, FDA is drawing a line between DNA sequences and their meaning. The tacit understanding is that DNA is fundamental to each individual, and data representing sequenced DNA fundamentally belongs to the individual. Wrapped into this idea that one should have access to one's sequenced DNA is an important regulatory move. If there is agreement about access to this sort of data, then concerns about the provision of genetic information narrows to the quality and accuracy of the data. Following this logic, FDA decided to pursue a regulatory approach that focused on the technical dimensions of data provision.

FDA's position favoring access to genetic data also marks an important departure from the clinic. Individuals can consume their raw genetic data and then shop around for the sort of genomic interpretation that suits their needs or desires. With an emphasis on individuals having a right to their genetic data, FDA's responsibility to contain risks is more straightforwardly constructed as those risks relating to the reliability and quality of the information. Accurate laboratory processing and sequencing should be ensured, and the different flavors of DTC genetic testing should be subject to standards of clinical validity, a measure of how consistently and accurately the genetic test detects or predicts the outcome of interest. Not surprisingly, most talk about regulation has centered on plans to ensure analytical and clinical validity. With the recent formation of a voluntary NIH genetic test registry, the foundation is being laid to standardize genetic testing practices across technical dimensions with an emphasis on clinical validity.

***Standardizing futures***

One of the main outcomes from FDA's public meeting to address the regulation of LDTs was growing consensus that all genetic tests should be subject to standards for clinical validity. In June 2010, 23andMe sent a letter to Margaret Hamburg, Commissioner of the Food and Drug Administration, and Francis Collins, Director of the National Institutes of Health, asking their respective agencies to help develop broadly applicable standards and guidelines for the provision of genetic test results and risk estimates.[31] Echoing a similar sentiment to this request for standards, Amy DuRoss, Navigenics' Vice President of Policy

[31] Available at http://spittoon.23andme.com/2010/07/06/23andme-letter-to-heads-of-fda-and-nih/ [Last accessed 15 December 2010]

and Business Affairs, agreed that measures to standardize the provision of genetic tests would serve the industry well (personal communication 2010). From the epistemic point of view, however, this approach has raised concerns related to the evolving nature of the genetic knowledge. If genetic knowledge continues to be a moving target, it may not be amenable to a rigid framework that does not accommodate improved genetic understandings. Duke geneticist Arthur Beaudet expressed this concern and argued that such a move would be detrimental to all genetic testing:

> If regulatory agencies block testing until the clinical sensitivity, specificity [clinical validity] and utility of all the genetic markers involved in any one diagnosis have been assessed and approved, the use of genetic diagnostics will come to a standstill. In such a situation, almost all complex forms of genetic testing would become outmoded before they could be approved (Beaudet 2010).

From his perspective, standardization would represent the wrong balance of regulation and innovation.

Standardizing clinical validity reflects an attempt to make the epistemic uncontested. 23andMe's request and Navigenics' recommendation rest on the argument that although the genetic knowledge in question is in its formative stages, it should still be standardized. This seeminlgy approach, which avoids social questions about the intended uses of the tests, is favorable for both 23andMe and Navigenics in framing their companies as producers and dispensers of genetic knowledge as just one kind of personal information and hence as a commodity. By focusing attention on the epistemic aspects of genetic testing, embodied in the

criterion of clinical validity, the companies attempt to put genetic testing in a technical and scientific register. In doing so, they bolster their market credibility with claims to objectivity.

This focus on standardizing clinical validity is also favorable for FDA, but for different reasons. Through the classification of direct-to-consumer genetic testing services as a medical device, the agency has already channeled the controversial technology into a well-established pre-market review process. The criteria of analytical validity and clinical validity are central to market approval. With an emphasis on these evaluations of genetic testing, FDA positions science as the stabilizer of the perceived risks. In the words of Dr. Hamburg, "as the science gets better we will be able to define the risks better" (Hamburg 2010). Risks are controlled through the recruitment of technical and scientific expertise. Scientific standardization serves as a method of containment for a broader spectrum of risks. This is consistent with work that has shown that national context matters in the ways scientific uncertainty is resolved for policy-making purposes. Jasanoff has argued that U.S. regulators, for example, appeal to formal analytic and quantitative methods to deal with scientific uncertainty (Jasanoff 2007).

**Conclusion**

In a moment when direct-to-consumer genetic testing has raised questions about the status of genetic information and who has the power and authority to decide that status, FDA has taken center stage. What appears to be FDA proceeding with business as usual, with the mandate of promoting public health goods while minimizing harm, is an important instance of how the agency is able to take an uncertain and changing technology and assert control over it.

In the case of direct-to-consumer genetic testing, has FDA simply enforced its discretion to regulate a technology based on changing risk profiles? I argue that FDA's classification of 23andMe's and Navigenics' testing services as a medical device is an ontological move. This is a characteristic of all regulatory power moves, and where social order and knowledge are coproduced (Jasanoff 2004). In the same moment that the agency decided the status of these testing services, FDA reconfigured the sociotechnical architecture of genetic testing. The recruitment of scientific expertise in the proposed plan for standardization is one approach to stabilizing an uncertain technology with uncertain uses. It does, however, change which experts are recruited in the regulation of genetic testing. Whereas physicians have traditionally evaluated the clinical utility of genetic testing, pre-market review would rely on the expertise of scientists.

With the proposed pre-market review structure, FDA exerts its authority to define a regulatory regime in which technical and scientific dimensions of genetic information come to the forefront. Margaret Hamburg's story about how law and regulation lag behind science and innovation masks the full extent of a regulatory agency's power. FDA does not just catch up to changing technologies, such as direct-to-consumer genetic testing, but rather in the process of regulating makes important decisions about the very status of that technology. In doing so, FDA is not just acting as the guardian of public health; it is an institution with the ability to shape the public's relationship to science and technology. For FDA, governance is about channeling science toward desirable futures, and in the case of direct-to-consumer genetic testing, the future of personalized medicine. Its power to construct these desirable futures is

surely a political process. FDA's risk-based regulatory approach founded on science-based medicine, however, serves to shield this very process from the traditional political forums.

In the direct-to-consumer genetic testing industry's confrontation with FDA, where does the genetic consumer stand? When FDA brought direct-to-consumer genetic testing under its jurisdiction, the genetic consumer was distanced from medical expertise in the act of genomic consumption. FDA's plans to standardize the technical and scientific dimensions of genetic testing afford a form of consumer protection. The agency does not want to deny people access to their genetic data, but it does want to control its quality. With this application of the law, the genetic consumer is emerging with the ability to purchase FDA-certified genetic data, but is not guaranteed its significance or utility.

# CHAPTER 4: INVESTIGATION BY COMMITTEE ON ENERGY AND COMMERCE

*"If it's not really a controversy until Congress starts investigating, direct-to-consumer personal genetic testing has officially arrived!" (Hobson 2010).*

During the 2010 Congressional hearing, "Direct-To-Consumer Genetic Testing and the Consequences to the Public Health," scientific and medical expert Dr. James Evans testified:

> DTC genetic testing appeals both implicitly and explicitly to the purported medical value of the genetic tests in question. We hear claims that scanning your genome for genetic variants provides a "roadmap to better health", allows one to "take control of your health future" or that "knowledge is power" with regard to disease. Indeed, these are the central advertising logos of the three most prominent players in genomic DTC arena. Yet on each page of every report provided to patients by these companies, some variant of the following disclaimer is made: "Information provided is not intended as, nor does it provide, medical advice, treatment, diagnosis, or treatment guidelines." The explicit health claims and the accompanying disclaimer (in tiny font) cannot both be true (Evans 2010).

Dr. Evans, Bryson Professor of Genetics and Medicine at the University of North Carolina at Chapel Hill and Editor-in-Chief of *Genetics in Medicine*, said that the information provided by the companies was only of entertainment and not medical value. Throughout the hearing, company representatives, FDA officials, and Congressional representatives debated the status of the genetic information provided by the companies. Their questions centered on whether the information was medically significant and scientifically sound.

The consequence of this debate was captured in the *Nature* headline, "Consumer gene testing in the hotseat: A week of hearings sows uncertainty for the fledgling consumer genomics industry" (Katsnelson 2010). The headline captured uncertainty not only about whether the industry would survive anticipated regulation, but also uncertainty about the status of the genetic information. Amongst the stakeholders brought together to discuss concerns about the personal genetic testing services, consensus grew that some form of regulation was needed, but that it should not inhibit personalized medicine. The stakeholders differed, however, on their understandings of the nature of the tests, their significance, the role of the consumer, and what forms of expertise were appropriate.

This chapter begins with Congress' first open confrontation with the companies. In May 2010, the Congressional Committee on Energy and Commerce sent letters to the companies requesting materials on the nature of their genetic testing services. The common letter immediately stripped away the differences between the companies, grouping them together for evaluation. The content of the letters revealed which aspects of the business were vulnerable to regulation. I contextualize these requests within the broader debate over direct-to-consumer genetic testing which dates back to 2007 when the American Society for Human Genetics (ASHG) produced a report on the industry. The companies' responses to concerns raised by ASHG, policy analysts, and academics provide a background for how the companies would position their services before Congress.

On July 22, 2010 Congress held a hearing titled, "Direct-To-Consumer Genetic Testing and The Consequences for the Public Health." In this chapter I analyze the content of

this hearing from opening remarks made by members of Congress, to an investigative report produced by the Government Accountability Office to the testimony of an FDA official and company representatives. My analysis of this forum shows how understandings of science and medicine get shaped in the debate over how or whether to regulate direct-to-consumer genetic testing. In the face of criticism, the companies collectively justified their practices as further personalized medicine.

**Letters from the House Committee on Energy and Commerce**

On May 19, 2010, the Chairman of the House Committee on Energy and Commerce, Henry A. Waxman, Ranking Member Joe Barton, Subcommittee Chairman Bart Stupak, and Subcommittee Ranking Member Michael C. Burgess sent investigative letters to 23andMe, Inc., Navigenics, and Pathway Genomics Corporation (U.S House 2010b, 2010b, 2010d). Under the Committee on Energy and Commerce, the Subcommittee on Oversight and Investigations requested information from the companies as part of an examination of personal genetic tests sold to consumers over the Internet. Like FDA, the Subcommittee referred to Pathway Genomics' plan to sell their tests in retail stores as the impetus for the letters. Congress responded because this attempt to provide genetic tests in retail stores clearly transgressed the established boundaries of medical practice.

The Subcommittee requested that the personal genetic testing companies provide information dating from January 1, 2007 to the present. The beginning of 2007 roughly marked the launch of 23andMe's and Navigenics' genetic testing services. Within these parameters, the companies had to prepare the following materials: a list of the specific

diseases and drugs for which the services provide genomic risk data; policy documents and material on genetic counseling or physician consultation; data showing the accuracy of the risk predictions delivered by the services; policies regarding handling of DNA samples; and documents pertaining to whether the companies were acting in compliance with FDA regulation (U.S. House 2010b, 2010b, 2010d).[32] These requests reflected concerns about laboratory processing, the accuracy of test claims, and the handling of genetic test results.

Anne Wojcicki, CEO of 23andMe, received an additional letter from the Subcommittee on June 14, 2010 in response to the sample mishandling mentioned above. The Subcommittee sought to learn more about the incident by gathering data about collection and processing procedures, as well as by probing into two new areas of inquiry: "All internal company policies, directives, and written guidance materials relating to the company's handling of errors in the collection, processing and analysis of DNA samples; and all documents relating to previous instances in which 23andMe customers received DNA results belonging to other persons" (U.S. House 2010e).

In these letters the Subcommittee focused the majority of its attention on the technical dimensions of the service. The Subcommittee's interest, however, in "policy documents and material on genetic counseling or physician consultation" pointed to a broader debate between health care providers, academics, and policy makers about the role of professional guidance and medical expertise in the provision of genetic tests.

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[32] From an off the record source, Navigenics reportedly spent $1,000,000 preparing for the FDA and Congressional hearings.

The first formal articulation of concerns about providing genetic testing directly to consumers was in September 2007. The American Society for Human Genetics prepared a statement on "Direct-to-Consumer Genetic Testing in the United States" that was published in the *American Journal of Human Genetics*. Combining academic and policy experience, Kathy Hudson, Gail Javitt, Wylie Burke, and Peter Buyers prepared the statement with the ASHG Social Issue Committee. The authors articulated concerns about providing genetic testing over the Internet:

> This context has led to the concern that consumers will not receive adequate counseling—either in advance, to ensure that the test is appropriate, or on receipt of test results, to ensure that consumers comprehend the complex information and understand the consequences of testing for themselves and their family members (Hudson et al. 2007, 635).

ASHG did not insist that genetic counseling be incorporated into direct-to-consumer services, but did recommend that the companies disclose all risks associated with testing, including psychological risk and risks to family members. Others have taken a harder line, insisting on the importance of genetic counseling. Academics Heidi Howard and Pascal Borry, who have written about the ethical, legal, and social aspects of genetic tests, considered the potential risks and benefits of the direct-to-consumer platform. They drew the conclusion that genetic counseling was essential to consumer education:

> Concerns should be raised regarding pre- and post-test counseling offered within the DTC services. This is a far-reaching concern, since without the obligation to meet with a physician, pre- and post-test counseling is the only way to increase consumer

> knowledge and understanding of the testing process, the meaning of the test results, and the possible consequences for the consumer and his/her relatives (Howard and Borry 2008, 318).

The recommendations of Howard and Borry follow from their immersion in the clinical context where genetic counseling has traditionally been provided before and after testing.

The topic of how consumers handle genetic information also figured prominently in an event co-hosted by 23andMe and California State Senator Alex Padilla in July 2010. Held just one week prior to the FDA's public meeting, the event can be seen as the company's attempt to create a responsible image, willing to engage a broader community about the implications of its services while gaining credibility from a representative for California. The daylong policy forum titled, "Genomics and the Consumer: The Present and Future of Personalized Medicine," brought together lawyers, scientists, ethicists, business representatives, elected officials, and consumers. The event was structured around three panel discussions that addressed, in order: regulation, integration of genomic research into clinical practice, and the risks and benefits of direct-to-consumer access to genetic information. After the meeting 23andMe stated that the final panel on direct-to-consumer access touched "on some of the most nuanced and sensitive issues in the growing field of genomics and personalized healthcare" (23andMe 2010a). The company concluded that the panel members agreed: "It's all about the data" (23andMe 2010a). 23andMe reformulated the panel's findings as having communicated: more studies must be done to understand how consumers handle genetic information. Their argument was that without this sort of data, conclusions could not be drawn as to whether consumers need professional guidance when undergoing genetic testing.

23andMe's emphasis on such data is not surprising given the company's position that people have a right to access their genetic information. Requiring professional mediation could be cast as a restriction on this sort of right. Therefore the company makes the case that we should understand the consequences of providing genetic information directly to consumers before placing restrictions on access. In essence, more "scientific" justification would be needed to justify regulation that assumes the consumer cannot handle his genetic information.

23andMe's summary of the panel, however, overlooked the contribution of Amy L. McGuire, JD, PhD, Associate Professor of Medicine and Medical Ethics and Associate Director of Research with the Center for Medical Ethics and Health Policy at Baylor College of Medicine. McGuire was outspoken in her critique of providing genetic information outside a clinical setting. Her comments centered on the important role health care providers play to integrate such information into a holistic approach to care (Field notes 14 July 2010). McGuire has also expressed her concerns about direct-to-consumer genetic testing in the *Journal of Law, Medicine & Ethics*. She and co-author Cynthia Marietta, a fellow lawyer, argued that the status of genetic information has legal implications: "The pertinent legal issue relates to whether the services offered by DTC genetic testing companies fall within the scope of medical practice, and if so, to what extent must a physician or other health care provider be involved?" (Marietta and McGuire 2009, 369). McGuire and Marietta reasoned that while competent adults generally have a right to purchase available information about themselves, "if that information is related to an individual's health or susceptibility to disease and would warrant additional follow-up from a licensed health care provider, then there is an obligation to ensure that the information is accurate and that the consumer is well-informed about the

potential clinical implications of the information and the risks and benefits of receiving it" (Marietta and McGuire 2009, 370).

In contrast to 23andMe's position that consumers have a right to their genetic information, McGuire and Marietta argue that some forms of personal information require professional mediation. If the genetic information provided by companies like 23andMe is medically significant, preexisting legal structures shape its provision. Genetic counseling in the medical context is meant to play an important role in promoting patient autonomy and decision-making. Genetic counseling has also been understood as a significant departure from other forms of medical care in not giving overt advice concerning decision making by a patient (Sharpe and Carter 2006, 5). This non-directive stance is meant to take into account the complexity of genetic information. Considerations include whether effective treatments are available, the impact on family members, the patient's objectives, concerns, values, and beliefs (Khoury, Burke, and Thomson 2000, 362-363). The importance of addressing this set of issues has been seen as both promoting good patient care and reducing the risk of patient misunderstanding, dissatisfaction, and allegations of malpractice (Sharpe and Carter 2006).

The debate over the place of genetic counseling in direct-to-consumer genetic testing shows how the companies' services are coming up against other well-regulated domains in which genetic testing has traditionally been provided. The genetic consumer stands in contrast to the patient, whose autonomy is bolstered by genetic counseling. 23andMe imagines a consumer whose autonomy is captured in the very act of consumption. The consumer has a right to his or her personal information and therefore the act of consuming one's genome is an

act of empowerment, free from the constraints of the clinic. The making of this new figure, however, is coming up against the norms of medical care. Congress' request for "policy documents and material on genetic counseling or physician consultation" implicitly raised questions about the status of the genetic information and the person who receives testing. If the genetic tests provide medical information then the person undergoing genetic testing is more like a patient and less like a consumer. In the medical context there are norms in place for how patients can access this information. In what seems to be a straightforward request for information about genetic counseling we can see the state's contestation of and intervention in the emergence of a new biomedical service industry.

***Building a Case***

In the wake of these letters and prior to the Congressional hearing, 23andMe and Navigenics took to their blogs to publicly voice their commitment to working with Congress. On May 19, 2010, 23andMe posted on The Spittoon: "We look forward to providing information to the Committee and Subcommittee and engaging with them on the topic of personal genetic testing, explaining how our services connect people to information about their own bodies, and highlighting the meaningful research we facilitate through our services" (Cline 2010). With the concluding sentiment that the company believes genetics has an important role to play in the coming age of personalized medicine, 23andMe laid out themes that would later be rehearsed before Congress. The company began to make the case that its services and activities are vital to the pursuit of personalized medicine through its generation of novel genetic research.

Striking a similar chord, Navigenics expressed its continued commitment to working closely with regulators. The company cited examples of state and federal compliance such as CLIA and HIPPA. Navigenics also highlighted the fact that it was the first personalized genomic service to be licensed as a clinical laboratory by the State of New York, receiving a permit in January 2010. Neither 23andMe nor Pathway Genomics are licensed in New York. Like 23andMe, Navigenics concluded the blog post reasserting its commitment to working with regulators, such as FDA, as part of its belief that continuing such dialogues is important to ensuring transparency and "the optimal use of genetic information as it applies to personalized medicine" (Navigenics 2010).

Both companies tap into the powerful allure of personalized medicine. This emerging medical domain has been promoted as having the potential to transform clinical practice through genetic information at a reduced cost (Hamburg and Francis S. Collins 2010). 23andMe and Navigenics' services have circumvented the clinic, but they are attempting to find ways to establish credibility through the medical establishment. The direct-to-consumer genetic testing industry has seen that promoting itself as vital to the pursuit of personalized medicine may be a way to buffer itself from burdensome regulation.

While 23andme and Navigenics make the case that their companies will help achieve the promises of personalized medicine, they diverge in their approaches. Navigenics has aligned its genetic testing platform with the medical community:

> Our mission is to improve health outcomes across the population by providing clinically actionable genetic insights, and we believe that a healthcare professional

> should be an integral part of the process. We remain committed to providing support for individuals and their physicians at every step in the personal genetic analysis process – at no additional cost. We are the only company with a staff team of board-certified genetic counselors with years of experience specializing in personal genomics, and we have made physician education and clinical integration a fundamental focus of our service" (Navigenics 2010).

Navigenics views its service as integral to the clinic and has reinforced this point by advertising its tests as clinically actionable. Genetic tests such as those for eye color and earwax type are not offered by Navigenics, as they are by 23andMe. Navigenics has tried to define its service as an ally to the clinic.

23andMe has more directly sidestepped the clinic. Its genetic testing service has not been developed for or advertised to physicians, and the 23andMe consumer has access to information about ancestry and traits that are not clinically actionable. 23andMe has developed another approach to establish credibility through the medical community by calling attention to its research branch, 23andWe. The company has demonstrated how its database of genetic profiles can be mined to produce research with claimed clinical significance. In June 2010 researchers at 23andMe published the article, "Web-Based, Participant-Driven Studies Yield Novel Genetic Associations for Common Traits," in *PLoS Genetics*. The study, which was a sort of proof of principle, demonstrated that they could in parallel study a wide assortment of traits within a single cohort. This was achieved by taking advantage of the interactivity of the Internet to gather data and present genetic information to research participants (Eriksson et al. 2010). The 23andMe researchers were able to use their web-based

approach to replicate associations for hair color, eye color, and freckling (Eriksson et al. 2010). Currently the company has consumers enrolled in studies to find genetic associations to Parkinson's disease, a neural degenerative disorder, and sarcoma, a type of cancer that arises in connective tissue cells.

23andMe and Navigenics, while taking different approaches to how they frame their services, both rely on a business model that takes genetic testing out of the traditional clinical context. In doing so, their services are found by many to be at the fringes of what is acceptable from either a medical, ethical, or consumer point of view. In an attempt to establish credibility, 23andMe and Navigenics have developed channels to the medical community – 23andMe through its web-based research and Navigenics through its partnerships with physicians.

**"Direct-To-Consumer Genetic Testing and the Consequences to the Public Health"**

On July 22, 2010 the Subcommittee on Oversight and Investigations of the House of Representatives Committee on Energy and Commerce convened to discuss direct-to-consumer genetic testing. Henry A. Waxman, a Democratic representative from California, who served on the Energy and Commerce Committee's Subcommittee on Health and Environment since 1979, chaired the Subcommittee. Other Congressional members included Michael C. Burgess, a Republican representative from Texas; Parker Griffith, a former Democrat, now Republican, who used to represent Alabama; Diana DeGette, a Democrat representative from Colorado; Robert Latta, a Republican representative from Ohio; Donna Christensen, a Democrat serving as a non-voting Delegate from the United States Virgin Islands; John Philip Gingrey, a Republican representative from Georgia; and Bart Stupak, a Democrat representative from

Michigan. Notably, half of the Subcommittee members, representatives Burgess, Griffith, Christensen and Gingrey, earned a medical degree.

Stupak provided opening remarks, stating that the investigation was a matter of public health as he referenced examples of how direct-to-consumer genetic information could impact health and medical decisions. He boiled his concerns down to the following: "But how accurate are the companies' analyses of direct-to-consumer genetic tests? Sending the customer the results of genetic tests without counseling or medical advice may cause more harm than good for some consumers. How accurate is the health information? How do companies explain differences in their analyses? Is there sufficient government oversight of the practices of direct-to-consumer genetic testing manufacturers?" (Stupak 2010). Stupak argued that these considerations become even more important when considering that currently some of the available direct-to-consumer genetic tests provide information about a person's predicted response to medications.

For these reasons, Stupak explained that the hearing was the continuation of previous inquiries made by the Subcommittee on Oversight and Investigations on genetic testing issues. Chairmen Stupak and Waxman, as well as ranking members Barton and Walden, requested in March 2009 that the GAO follow up on the observation that "the genetic testing market appears to have expanded rapidly and consumer fraud in this area is on the rise" (U.S. House 2010a). The letter requested that GAO direct its Forensic Audit and Special Investigations Unit to "perform proactive testing of the advertising methods used to sell these products to consumers" (U.S. House 2010a). The report, which became central to the hearing and the

basis for questions to company representatives, had not been provided to the companies in advance and was made public on the day of the hearing.

Representative Waxman echoed similar unease about the advertising claims of the companies linking these worries to the questionable status of the knowledge: "The science informs us that there is no widely accepted consensus linking genetic markers to specific illnesses" (Waxman 2010). He worried that the companies were overselling their services in light of the fact that the science was questionable. The status of the information, in his opinion, was critical as he went on to argue that it had implications for health decisions. Given this assessment, he pointed to FDA as the relevant institution to regulate what he identified as diagnostic tests (Waxman 2010).

The Subcommittee members unanimously agreed that steps should be taken to ensure that the American public was presented with accurate, safe, and effective information. The members diverged, however, as to how to achieve these ends. Burgess and Waxman agreed that the industry should not be overregulated at the expense of advances in personalized medicine. Griffith and Gingrey drew from their medical training to express concerns about how consumers might handle unreliable genetic information with medical implications. DeGette highlighted privacy concerns, questioning the sufficiency of GINA, and Christensen questioned whether ethnic and racial minorities were guaranteed correct information. With these tone-setting remarks, the Subcommittee turned to what would be the main focus of the rest of the hearing – the report produced by GAO.

***"Direct-to-Consumer Genetic Tests: Misleading Test Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices"***

The Budget and Accounting Act of 1921 established the Government Accounting Office (GAO) (Pub.L 67-13, 42 Stat. 20). Under this Act, GAO took over the auditing, accounting, and claims functions of the Treasury Department in attempt to better manage federal spending after WWI. While the primary purpose of the Office was to track the spending of public funds, in the 1960s and 1970s the duties of GAO expanded to provide Congress with information on government programs, energy policy, consumer protection and the environment (Krusten 2001). GAO's increased responsibility paralleled the expansion of the federal regulatory apparatus in the late 1960s and early 1970s (Krusten 2001). To accommodate Congressional requests, the Office started to recruit scientists, actuaries, and experts in fields such as health care, public policy, and computers.

In 2004, the name of the Office was changed to the Government Accountability Office to better reflect its aims.[33] At the request of the Subcommittee, GAO produced a report that focused on the scientific claims and marketing strategies of direct-to-consumer genetic testing companies. Congress' investigative arm reported that the companies misled consumers and used deceptive marketing with the disclaimer, "GAO did not conduct a scientific study but instead documented observations that could be made by any consumer." The report documented inconsistent test results between and within companies, raised questions as to

[33] The GAO defines its mission: "The Government Accountability Office, the audit, evaluation, and investigative arm of Congress, exists to support Congress in meeting its constitutional responsibilities and to help improve the performance and accountability of the federal government for the American people. GAO examines the use of public funds; evaluates federal programs and policies; and provides analyses, recommendations, and other assistance to help Congress make informed oversight, policy, and funding decisions. GAO's commitment to good government is reflected in its core values of accountability, integrity, and reliability (GAO 2010).

whether tests results were accurate for ethnic and racial minorities, and cited misleading company interpretations of genetic information in post-testing interviews. While GAO presented the report as a simple fact-finding mission, it was not simply a description of the world. Rather, GAO was actively advancing ideas about what constitutes good science and what is medically relevant in a new and uncertain industry.

Congress called Gregory Kutz, Managing Director of the Forensic Audits and Special Investigations at GAO, to present the findings of the report. Kutz had also been the lead investigator of the 2006 GAO report on nutrigenetic testing. The 2010 report examined the practices of four companies in depth and expanded to evaluate test reliability, privacy policies, and supplement sales in eleven additional companies (GAO 2010).

*Inconsistent Test Results*

To assess test reliability and accuracy, GAO purchased tests from four companies, which were later identified as 23andMe (Company 1), deCODEme (Company 2), Pathway Genomics (Company 3), and Navigenics (Company 4). The companies were found using online search terms and were selected because "they were frequently cited as being credible by the media and in scientific publications and because they all provided consumers with risk predictions, accessible through secure Web sites, for a range of diseases and conditions" (GAO 2010, 2). GAO purchased ten tests from each company to compare five donor samples with respect to the genetic risk prediction of fifteen diseases. Two profiles were created for each donor, one using factual information about the donor, and one using fictitious information, including: "age, race or ethnicity, and medical history" (GAO 2010, 3). For

fifteen disease traits the companies reported different risk profiles for the same DNA sample. For example, Company 1 communicated an above average risk for leukemia to a female donor, while Company 2 reported below average risk and Company 3 average risk (GAO 2010, 5). GAO observed this sort of inconsistency 58% of the time.

These contradictions have been attributed to the fact that companies look at different SNPs, or genetic markers, which have different predictive abilities. Craig Venter, who was instrumental in the privately funded sequencing of the human genome, and his colleagues demonstrated this point in a 2009 *Nature* article (Ng et al. 2009). With reference to this article, GAO reiterated that the companies access the same publicly available genome-wide association studies to decide which risk markers to include in their analyses. They do not, however, use the exact same markers in their tests. As a result different risk profiles can follow from markers that are correlated to the same trait.

From post-testing interviews the report stated, "representatives from all four companies acknowledged that, in general, DTC genetic test companies test for different risk markers and that this could result in companies having different results for identical DNA" (GAO 2010). When company representatives were asked about the accuracy of their tests as compared to those of competitors, the following statements were made:

> Company 1 said that it offers consumers more information than other companies because its results are based on both preliminary research reports as well as clinical data. Company 2 claimed that other companies do not test for as many markers as it does and that while none of the companies are "wrong," using more markers is

> "probably more accurate." Company 2 also stated that disparate test results from different companies are "caused, in part, due to a lack of guidance from the federal government, CDC in particular" (GAO 2010).

The companies framed inconsistencies in disease-risk reporting as a problem resulting from the absence of standards set by a third party authority. Concerning this recommendation, Kutz agreed that standards should be put in place, suggesting a form of regulation that would focus on a technical dimension of the genetic testing services.

*Contested Genetic Claims*

GAO reported that risk predictions did not match donor family medical histories or factual illnesses. Three instances were cited of donors receiving reports indicating their risk was average or below average for having a heart attack although they had a family history of heart disease. This section of the report received a good deal of attention throughout the Congressional hearing, as Subcommittee members repeatedly cited an example of a donor who had a pacemaker implanted thirteen years ago to treat an irregular heartbeat and received a test result stating that he was at decreased risk for developing a heart condition (GAO 2010, 9; Stupak 2010).

These examples on the surface seem illustrative of misleading company claims, but are more indicative of how notions of predictive and diagnostic genetic testing have been conflated. Predictive genetic tests estimate one's chances of developing diseases. For example, mutations in the breast cancer susceptibility genes 1 and 2 (BRCA1) and (BRCA2) have been linked to hereditary breast cancer. A woman with a mutation in either of these genes is about

five times more likely to develop breast cancer than a woman who does not have a mutation (Ford et al. 1998). Women can present mutations in these genes and not develop breast cancer, and conversely women can develop breast cancer without mutated BRCA1 and BRCA2 genes. Diagnostic genetic testing, in contrast, are usually for single-gene disorders such as adult-onset Huntington's disease. If a person has an abnormal number of repeated base pairs in the Huntington's gene on chromosome four, the person will develop the disease (Perutz and Windle 2001). Diagnostic testing can confirm a diagnosis in both pre-symptomatic and symptomatic individuals. Given this distinction between predictive and diagnostic testing it could make sense that a predictive test could communicate average risk for a heart attack in a person who already has heart disease.

Genetic tests, like those provided by the DTC companies, are based on genome-wide association studies. The associations between genetic mutations and disease phenotypes are probabilistic and therefore have traditionally been thought of as predictive. A scientific advisor to 23andMe, however, argued that a clear distinction between predictive and diagnostic tests is shaky with tests developed from genome-wide association studies (Personal communication 2010). She said that as more studies are conducted risk probabilities can increase and pre-symptomatic genetic testing can become more diagnostic. Companies like 23andMe, however, have relied on a clear distinction between predictive and diagnostic testing to make the case that they do not provide a medical service. They argue that the predictive genetic tests they provide are not medical, because they do not confirm a diagnosis.

If the companies had been able to respond to the GAO's interpretation of the examples, they most likely would have asserted that they do not offer diagnostic testing, a point argued at length on their websites. For example, under 23andMe's frequently asked question—"Why can't 23andMe diagnose me?"—the company explains: "in order to make a diagnosis, your doctor considers not only your genetic information, but also your particular personal and family history and your physical condition, as well as any symptoms you are experiencing. Other confirmatory tests are usually required, since your genotype is only part of the equation."[34] In this answer, 23andMe carves up expertise along a distinction between predictive and diagnostic testing. While the company is able to provide predictive testing with its own team of scientific experts, diagnostic testing would require medical expertise.

*The Persons Behind Personal Genetic Testing*

Another finding from the report was that the companies did not accommodate differences in risk profiles for ethnic and racial minorities, a point illustrated through the fictitious donor profiles. The primary concern amounted to the following:

> Many of the studies the companies use to make risk predictions apply only to those of European ancestry. Consequently, our fictitious Asian and African American donors did not always receive risk prediction that were applicable to their race or ethnicity, although the companies either did not disclose these limitations prior to purchase or placed them in lengthy consent forms (GAO 2010, 10).

[34] 23andMe website. "Frequently Asked Questions." Available at: https://www.23andme.com/howitworks/ [cited 15 April 2011]

While company representatives acknowledged in post-test interviews that race and ethnicity affect disease risk predictions, GAO's attention to this issue points to more than risk profile discrepancies based on race and ethnicity. Taking for granted that the categories of "race" and "ethnicity" exist separate from the production of genetic knowledge,[35] GAO problematizes the notion of "personal" in personal genetic testing. GAO's interest in this dimension of their services raises the question: for whom is personal genetic testing personal?

23andMe's blog response to this aspect of the GAO report revealed how the company views its service within the genetic information production chain:

> Unfortunately, because of where and how biomedical research is funded, there are comparatively few studies looking for genetic associations in populations that form a minority in the countries where much of the latest research takes place. In other words, most of the associations have only been confirmed in populations of European ancestry. A FAQ on our website explains this situation and lays out how it can result in fewer results for people with African American or Asian ethnicity. In addition, our Terms of Service explain the limitations of genetic research, especially with regard to ethnic minorities, and note that a free demo version of our service is available for people to examine exactly what they will be getting if they choose to purchase.[36]

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[35] In her study of the Human Genome Diversity Project, Jenny Reardon has shown how scientific ideas and practices co-emerge with social and political decisions about who can define race and for what purposes (Jenny Reardon 2004). Troy Duster has also argued that genetic screening policies have tended to reinforce already existing power structures and racial difference (Duster 2003; Duster 2006). In both accounts the notion of "race" is constructed in relation to particular uses and understandings of genetics.

[36] 23andMe website. "Frequently Asked Questions." Available at: https://www.23andme.com/howitworks/ [cited 15 April 2011]

In this answer, the company passively positions itself as simply mirroring or channeling existing knowledge. The logic follows that the critique made by GAO does not originate in the companies, as it was already present in the shortcomings of the research studies. While acknowledging that its service is tied to the "problem," 23andMe fails to acknowledge how the dynamic, or "racial" inequality gets reinscribed in its service.[37] 23andMe makes a "Google" argument, simply characterizing itself as a filter and dispenser of knowledge. In doing so, the company fails to take responsibility for/acknowledge its role in reaffirming a particular order that includes and excludes certain types of persons through the repackaging and commodification of genetic knowledge.

The GAO's attention to race and ethnicity, although presented simply as companies misleading consumers, forces an examination of how the commodity—genetic information—gets produced. Who gets excluded and included in the genome-wide association studies backing the predictive tests? For companies like 23andMe and Navigenics to provide genetic information as a commodity, personal dimensions such as "race," "ethnicity," and family medical histories are either made opaque or erased in the personal genetic testing service.[38]

*"Observations anyone could have made"*

The second part of the investigation consisted of findings from undercover phone contact with the companies. Posing as a genetic consumer, GAO asked company

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[37] Keith Grint and Steve Woolgar have shown with the example of computers that social dynamics can get tacitly embedded in the design of technological systems (Grint and Stève Woolgar 1997, 65-94).

[38] Steven Epstein's work has looked at how beginning in the 1980s new laws, regulation, and bureaucratic offices transformed the funding of medical research to include (and make visible) racial and ethnic minorities (Epstein 2007). This came about as a reaction to the fact that medical studies historically only included white males, overlooking potential biological differences and needs of underrepresented groups.

representatives questions about the significance of test results and privacy policies. To summarize the main findings, GAO found that some genetic tests were fraudulently being used to encourage customers to buy ineffective supplements. Concerns about consent procedures were raised when a company representative encouraged a fake customer to submit the sample of her fiancé for genetic testing. This is illegal in more than twenty states (Genetics and Public Policy Center 2009). And excerpts were provided from post-test counseling sessions to demonstrate that company representatives were making incorrect and misleading interpretations of test results. For example, in response to a fictitious customer's question about whether results indicated she was at above average risk for breast cancer, a representative from Company 4 was cited as saying: "You'd be in the high risk of pretty much getting it" (GAO 2010, 16).[39] On this point the report stated, "Experts also called this statement 'disconcerting' and 'horrifying' because it erroneously implies that the test can diagnose breast cancer and could needlessly alarm consumers" (GAO 2010, 16).

While this section of the report was heavily publicized through a YouTube montage of disturbing company claims (Anon. 2010), the sensationalistic nature of this approach led to criticisms of GAO's methodology. 23andMe challenged GAO for wrongly grouping too many companies together without separating the more credible from the less credible:

> One of the most unfortunate parts of the GAO report is that it unfairly lumps together reputable and well known companies such as 23andMe with un-named companies making verifiably untrue endorsement claims, spurious scientific claims, and also

[39] From an off the record source, Navigenics could not figure out the source of this statement.

> selling potentially fraudulent supplements in addition to genetic testing services (23andMe 2010).

In this critique the company attempts to boost its credibility in an arena that is not fully established. A simple division of the field into "good guys" and "bad guys" would give the appearance of removing uncertainty about 23andMe's genetic testing service.

The statement made by GAO that it "did not conduct a scientific study but instead documented observations that could be made by any consumer," was used to fuel questions about the merits of the report. The companies' blogs became a forum for these attacks. 23andMe had this to say:

> …now that the report is public and we [23andMe] have had a chance to review it, we are troubled and find the report is deeply flawed. We note that while such an exercise as conducted by GAO has the potential to raise questions, it does not provide the answers that a more rigorous scientific study would provide. This report raises questions, but leads to few conclusions because of its unscientific nature. The GAO itself recognizes this, writing, "It is important to emphasize that we did not conduct a rigorous scientific study"… (23andMe 2010).

While Navigenics commented:

> The ultimate aim of the GAO report was to inform and protect consumers. At its best, the report sheds further light on an important and well known issue in the personal genomics field – how the current lack of regulatory standards can lead to very different approaches between personal genetics companies. But as the writers of the report acknowledged, they "did not conduct a rigorous scientific study." As a result, many of

the report's findings are anecdotal, partially informed, or incomplete (Navigenics 2010).

Navigenics argued that discrepancies between companies were due to the absence of standards for the genetic markers used to construct their tests. From the industry's standpoint, if the report had been more rigorously scientific, this technical solution would have been obvious.

GAO and the genetic testing companies both appeal to the authority of science to establish credibility in their own practices. The authority of science, as understood within STS, refers to the ability of scientific claims to the truth to trump other assertions.[40] GAO invokes the absence of scientific authority in an attempt to present its findings as readily apparent and accessible to a broad audience. As STS scholars have demonstrated, scientific "facts" often require expert mediation and instruments that make them less accessible to lay vision (Latour and Steve Woolgar 1986; Pinch 1985). GAO's statement that it did not conduct a scientific study was an attempt to bring its collected evidence closer to every person, or "any consumer." Following Jasanoff's analysis of DNA fingerprinting in the courtroom, scientific evidence does not speak for itself. This observation raises questions about whose vision is warranted to interpret the meaning of such "facts." When expert vision is brought to bear on its significance, Jasanoff has shown that expert witnesses can overcome skeptical challenges by: "seeking to establish a common 'economy of credibility' with lay fact-finders – whether by blinding them with science…or by making science appear so transparent that no discrepancy remains between lay and expert vision" (Jasanoff 1998b, 731-732).

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[40] See Steven Shapin's *Cordelia's Love: Credibility and the Social Studies of Science* (Shapin 1995).

Like scientific evidence in the courtroom, the findings in the report produced by GAO did not speak for themselves. GAO framed the report as non-scientific to create a common "economy of credibility" to align its vision with that of any consumer. One does not need to conduct a "scientific" study to demonstrate that the companies make misleading claims. Even without resorting to the methods of science, we can see that the testing is questionable, pointing to the shakiness of the operations. The non-scientific language that GAO used in the report such as, "misleading" and "fraudulent," were concepts that could be understood by any consumer.

While GAO did not claim to conduct a scientific study, it did question the scientific soundness of the tests: "given the scientific evidence currently available, many experts remain concerned that the medical predictions contained in the results mislead consumers" (GAO 2010, 2). At one level GAO referenced the authority of science to demonstrate that the services in question were fraudulent and misleading. Yet, at another level GAO framed its findings as non-scientific to make the report more accessible and readable to a broader audience.

23andMe and Navigenics took the statement, "we did not conduct a scientific study but instead documented observations that could be made by any consumer," to question the credibility of GAO. From the industry's perspective, the findings of the report were "anecdotal" and "incomplete" because the report was unscientific. The companies directly appeal to the authority of science to argue that what GAO represented as "fraudulent" and "misleading" was simply a shortcoming due to the lack of scientific standards. A scientific

review of the companies would have revealed this solution. Again drawing from the example of DNA evidence in the courtroom, such DNA fingerprinting was excluded initially in a number of trials because the methods were shown to be non-standard and therefore unscientific in the eyes of experts and laypersons (Jasanoff 1998b, 728). Jasanoff argues, "Standardization offered to testing laboratories and law-enforcement institutions an attractive way out of such quandaries. Standards serve to black-box messy technical practices: behavior conforming to explicit standards tends to be more resistant to sceptical questioning" (Jasanoff 1998b, 728). Like the production of DNA evidence, direct-to-consumer genetic testing would benefit from standards that make the services appear more scientific and therefore less susceptible to critique.

The production and presentation of the report on direct-to-consumer genetic testing demonstrated how GAO is able to appeal to notions of science and medicine to shape an uncertain technology. At the core of GAO's critique was the idea that the science behind the genetic tests was too unreliable, and therefore misleading and not medically actionable. Countering these critiques, the industry has proposed a scientific solution to stabilize and lend credibility to its services.

***Testimony***

Following the presentation of the GAO's findings, Dr. Jeffrey Shuren, FDA's Director of the Center for Devices and Radiological Health, testified before Congress. Again the converging vision of FDA Commissioner, Margaret Hamburg, and Director of the NIH, Francis Collins, to pursue the future of benefits of personalized medicine while balancing

potential risks, was referenced to frame FDA's regulatory approach. Shuren explained FDA's system of oversight for medical devices, specifically how direct-to-consumer genetic testing posed increased risks that forced the agency to intervene recently. He concluded: "FDA is working towards a reasonable and fair approach to regulation that can give patients and doctors confidence in these [direct-to-consumer] tests and facilitate progress in personalized medicine" (Shuren 2010).

The three company representatives began their testimonies arguing that regulation, while needed, should not curtail innovation. Vanier, C.E.O. of Navigenics, first referred to the $3 billion cost and 13 year timeline of the Human Genome Project to communicate the profundity of fulfilling the promises of personalized medicine: "We stand at a critical juncture in our country's ability to realize the true potential of personalized medicine and of the landmark Human Genome Project" (Vanier 2010). Ashley Gould, General Counsel for 23andMe, spoke to how direct-to-consumer genetic testing leverages the findings from the Human Genome Project (Gould 2010). David Becker, C.E.O. of Pathway Genomics, also emphasized the importance of the Human Genome Project in relation to the future of personalized medicine: "Since the completion of the Human Genome Project in 2003, scientists, physicians, policy makers and consumers have eagerly anticipated the era of 'Personalized Medicine,' which means providing targeted preventive care and therapeutic treatment based on an individual's genetic makeup" (Becker 2010). Becker presented Pathway Genomics as empowering consumers with this information.

While company representatives created a collective sense that the industry is essential to the future of personalized medicine and the anticipated benefits of the Human Genome Project, they also took the opportunity to accentuate the unique features of their companies. Vanier pointed out that Navigenics only provides its service through two professional channels, medical centers and physicians, or employer wellness programs at Fortune 100 companies (Vanier 2010). The new model allowed Vanier to represent Navigenics as committed to working with healthcare professionals to create tools for the integration of its service into the clinic.

Gould defined 23andMe as a "personal genetics company dedicated to research and helping individuals understand their own genetic information through DNA analysis technologies and web-based interactive tools" (Gould 2010). The company's commitment to research was later used as a segue to explain how 23andMe has accelerated medical research: "One of the unique features of 23andMe's DTC genotyping service is the company's focus on 23andWe, a community-centered research effort in which consumers are encouraged to contribute to medical science by answering surveys" (Gould 2010). In contrast to government funded genome wide association studies, Gould argued that 23andMe's research is driven by consumer interest and provides the ability to pursue research in over 600 conditions simultaneously. The power of this research model was linked to the company's ability to determine the clinical significance of genetic markers: "Because we have such a large research database and engaged customers, we are able to assess the clinical significance of genome associations. We are in a unique position to tell our customers, and the community, how clinically significant this information is" (Gould 2010).

In contrast to the other companies' platforms, Becker explained how Pathway Genomics (although temporarily not offering its service) took an approach to contextualizing the significance of genetic test results in relation to other health data. While providing its service, the company incorporated a health survey in which relevant data on lifestyle, environment, and family history were collected and used to better communicate the significance of test results.

*Building on the Human Genome Project*

The direct-to-consumer genetic testing industry has positioned itself collectively as part of the realization of the expensive, government-funded exploration of the human genome. On the heels of the 10th anniversary of the publication of the sequenced human genome, there is continued discussion about the anticipated benefits. To commemorate the publishing of the first draft, *Science* asked a cross-section of individuals to discuss what it has meant to have access to human genome sequences. Francis Collins referenced examples to demonstrate that "the once-hypothetical medical benefits of individual genome sequencing are beginning to be realized in the clinic" (Francis S Collins 2011). Craig Venter, in contrast, looked ahead to argue that amongst the many improvements needed to realize the benefits of human genome research, "the most important is the collection of human phenotypes (according to agree-upon parameters and standards), in conjunction with tens of thousands of accurate human genome sequences" (J Craig Venter 2011). Venter concluded that such data sets would be the foundation for accurately predicting clinical outcomes from DNA sequence information (J

Craig Venter 2011). Visionaries like Craig Venter have linked this sort of research to the future of personalizing medical care through increased knowledge of the human genome.

The vision of personalized medicine revolutionizing health care is creating new channels to access former patients, now consumers. The new market is being built on a discourse of tailored care to individuals at a reduced cost. This vision was nowhere more apparent than at 23andMe's policy forum, "Genomics and the Consumer: The Present and Future of Personalized Medicine." Dr. Leroy Hood of the Institute for Systems Biology in Washington gave the keynote lecture, which was also repeated at the 2011 Personalized Medicine World Conference. Hood's talk aimed to "catalyze a revolution from reactive to proactive medicine." He argued for a new model, "4P medicine," that would be predictive, personalized, preventive and participatory. With this approach he said we would no longer talk about disease and treatment, but rather wellness and prevention. In the same breath he explained how this approach would reduce healthcare costs while opening a new market (Field notes 14 July 2010). The subtext of personalized medicine can be read as code for a new market, new "preventive" and "personalized" goods and new channels to pre-patient bodies.

In this context, companies like 23andMe, Navigenics, and Pathway Genomics want to work with regulators to create guardrails that would lend credibility to the new personalized genetic testing industry. If the companies can influence the form of regulation it could help to black-box their services, making their operations less susceptible to critique. Standards, for example, would give their services the appearance of being more scientific and therefore

reliable. Some form of workable regulation would also provide stability for the companies to grow their businesses.

*Balance Innovation and Regulation*

Company representatives carried over the theme of balancing innovation with regulation from the FDA's public meeting. Becker testified, "While it is critical to ensure public safety, it is also important that new regulations do not stifle innovation or restrict an individual's access to information that impacts their health" (Becker 2010). Vanier told a history of Congress' successful collaborations with regulatory agencies and industry:

> We welcome the Subcommittee's interest in personalized genetic testing, which is rooted in a long history of congressional promotion of innovation and balanced, science-based regulation. From the 1975 Asilomar Conference on the regulation of recombinant DNA (rDNA) research through this Committee's biotechnology hearings led by Chairman *emeritus* Dingell and then-Subcommittee Chairman Waxman in the 1980s, to the recent, extraordinary success of the historic Human Genome Project, Congress has worked collaboratively with regulatory agencies, academe and industry to create the conditions that allow American researchers and companies to lead the world in creating new life-saving and life-improving health solutions (Vanier 2010).

The reference to Asilomar had a particular political caché, as it has been revisited as the exemplar of striking the right balance between taking into account risks while allowing future goods to flow from innovation. The Asilomar meeting, however, was organized to agree on terms of self-regulation within the scientific community to try to avoid heavy-handed regulation from the government (Hanna and Making 1991, 258-307). Asilomar has been retold

to draw the conclusion that we would not have the profitable biotechnology industry had Congress set overburdensome regulation. Vanier provoked the Subcommittee to draw a parallel to the case of direct-to-consumer genetic testing. He made the case that the new biomedical service industry stands to benefit the American economy and that over-regulation would threaten to drive the industry abroad (Vanier 2010).

*Regulation as Standardization*

Behind the idea that innovation must be met with unburdensome regulation is the idea that science produces future goods (in this case goods for the public health), while law and regulation slow progress.[41] This framing of science and technology lends itself to a regulatory approach that seeks definable, and hence, tractable risks. Direct-to-consumer genetic testing has been framed as part of personalized medicine and FDA and Congress do not want inhibit innovation in this domain. The industry has found a way to articulate its value in relation to medicine, but in doing so through non-traditional channels it has produced uncertainty about the associated risks. If those risks can be narrowed to the technical and scientific dimensions of the services, though, regulation could be put in place that does not inhibit innovation.

In this context the push for standardization makes sense from both the FDA and industry's perspectives. The argument would follow that it is risky to provide consumers with genetic information that is inconsistent and unreliable. Standards to ensure consistency between the genetic testing providers would make the services reliable for consumption. Standardization would stabilize the industry by restricting the companies to use certain SNPs,

[41] For a comprehensive work that challenges the notion of law-lag see *Science at the Bar* (Jasanoff 1997).

or genetic markers. This would black-box, or prevent an ongoing debate about the scientific studies used for personalized genetic testing. Such stabilization would allow the companies to grow their businesses. As Vanier pointed out in his testimony, it has been difficult to grow their business in an uncertain regulatory climate (Vanier 2010).

*Expert Testimony: "Interests of the public and companies are fully aligned"*

In support of innovation, scientific and medical expert, Dr. James Evans, expressed how technological breakthroughs will revolutionize medicine, ushering in a new era of genomic medicine: "These advances will lead to great progress in our basic understanding of disease, improved diagnostic abilities, new therapies and personalized prescription of drugs" (Evans 2010). Striking a chord with Hood's participatory theme, Evans testified that individuals should be the primary directors of their own healthcare. As an extension of this, he argued that people should have access to the information contained in their own genome. Concerning the reliability of the direct-to-consumer genetic testing industry, he took issue with the fact that the companies both implicitly and explicitly appeal to the medical value of their genetic tests, concluding that the genetic information lacks medical significance.

Evans suggested a regulatory solution that would allow direct access with the condition that the companies not oversell their genetic tests as medically relevant. On the topic of how consumers would handle this information he argued that the vast majority of tests "are simply of entertainment, not medical value." He concluded, "I see little potential harm and see no problem with the public having full access to such information – so long as it is not oversold in the way I've just been describing" (Evans 2010). If the genetic tests have medical

value, however, he felt they should be ensured by FDA: "The public deserves access to information contained in their own genomes – but deserve honest accounting and assurance that it is derived in a manner that ensures quality, reliability and confidentiality" (Evans 2010).

**Conclusion**

23andMe, Navigenics, and Pathway Genomics have taken genetic testing out of the traditional medical context. In doing so, they claim to empower consumers by bringing them closer to their genomes. They argue people have a right to access their genetic information. This new delivery system, however, has raised concerns for Congress as articulated in the investigative letters, the hearing, and the GAO report. In these forums, state officials raised questions as to whether the science behind the tests was sound, samples were handled and processed properly, and test results provided medical information. Members of Congress have raised concerns about whether the consumer could be harmed by unsound, inaccurate, and medically significant information.

The Congressional examination of the companies put certain aspects of the genetic testing industry under the microscope. The report produced by GAO, although drawing the conclusions that the companies misled consumers and engaged in fraudulent practices, more importantly revealed how the companies have been able to construct a new biomedical service industry. The reported inconsistent test results showed how the companies have used their own methods to determine which scientific studies to reference for the construction of their test panels. The contested genetic claims that seemed to not match family histories or factual illnesses showed how the companies have relied on a distinction between predictive and

diagnostic testing to claim that their services were not medical. GAO's attention to discrepancies in risk reporting for "racial" and "ethnic" minorities raised a question about which groups are actually served. The companies were able to redraw the boundaries of genetic testing by obscuring certain aspects of their services, from scientific judgment calls, to a predictive-diagnostic dichotomy, to consumer personal information.

Yet, in redrawing the boundaries of genetic testing to include company-consumer transactions, the companies have met resistance. Congress asked whether direct-to-consumer genetic testing strayed too far from the norms of medical practice. Pathway Genomics' attempt to partner with retail stores was the tipping point that led government institutions to evaluate the status of genetic information and appropriate regulation. In response to an uncertain regulatory climate the companies have found channels back to medical care. Company representatives, Congressional representatives, FDA officials, and expert witnesses have furthered the idea that these companies fall under the umbrella of personalized medicine. More specifically, 23andMe emphasized its ability to produce clinically relevant research and Navigenics framed its service as an ally to the clinic by partnering directly with physicians.

In these reshufflings, though, is the consumer brought closer to his or her genome as the companies claim? Is the consumer empowered? In the relationship between the companies and the consumer, genetic information has been understood as something absolutely fundamental to the consumer and who she is. Yet, the consumer has needed the company to translate it into something meaningful. It is unknowable without an added layer of knowledge and expertise, which has to date come from the companies. This point is problematic,

however, in light of the fact that the companies disavow medical expertise and make claims that the consumer is back in control of his or her most fundamental information. As consensus grows that standardization is the regulatory way forward, a new relationship is forming between the companies, the consumer, and the state.

What is most noteworthy in these confrontations between DTC providers and institutions of power like Congress is that there has been no proposal to regulate clinical utility, which has traditionally required medical expertise. Can the consumer now stand in as her own "expert" to interpret and contextualize the meaning of probabilistic genetic tests? Is it enough for the state to just guarantee the safety and accuracy of genetic testing or should the state also guarantee a context that provides interpretation and meaning? How ought we to think about individual empowerment in relation to forms of state protection or paternalism?

# CONCLUSION

In this dissertation I have traced the emergence of direct-to-consumer genetic testing as a prominent innovation in the acquisition and distribution of genetic information, focusing on the two leading providers (23andMe and Navigenics) and the main public institutions (FDA and the House of Representatives Committee on Energy and Commerce) that have been shaping its development. My empirical analysis of primary sources, including web-sites, policy documents and interviews, highlights the contours of a transition that, while still in the making, appears already highly significant in its challenge to long-standing settlements in the scientific and social order around human genetics. It is a transition from patient to consumer and runs parallel to the transformation of genetic knowledge from a highly specialized aspect of medical care to a commodity of potentially widespread use.

In chapter one I show how 23andMe and Navigenics have been framing their services explicitly as non-medical and both have been constructing genetic knowledge as another kind of personal information, though they are also quick to emphasize its potential medical benefits. In turn, this framing appears integral to the broader claim that individuals are entitled to acquire this information, and that access to it does not necessarily need the mediation of traditionally certified professionals such as physicians or clinical geneticists. The companies' claims that they are not providing a medical service is significant given the destablization of the medical establishment in the 1970s and 1980s, when patient's rights groups challenged the authority of the physician in conjunction with a movement to increase patient autonomy. The patient became an active consumer of and participant in her health care. Patients and activists

viewed better access to medical records and information as one important step in achieving increased patient autonomy. This overlapped with development of the biotechnology industry, which has demonstrated that business models can be built on advances in the biosciences. Genomics is another domain that has been shaped by industry forces. Against this backdrop, 23andMe and Navigenics have developed business models that rely on the circulation of genetic information as capital. To attract consumers, the companies have also tapped into the neoliberal discourse of the 1970s and 1980s, claiming to empower consumers with access to personalized genetic information.

23andMe and Navigenics draw on many of the same resources to carve out a new domain for genetic testing. Both companies access the same publicly available GWAS, use similar microarray technologies, interface with consumers through the Internet, and draw from the same pool of Silicon Valley venture capital. With these tools, 23andMe and Navigenics have created a new sociotechnical architecture for genetic testing. The companies have taken something that was traditionally offered in a clinical setting and moved it into the consumer market. This has put into motion a redefintion of "clinical" and "medical" in relation to genetic information.

Yet, the companies have distinguished their services in the shared goal of creating a new genetic testing industry, which I have discussed in chapter two through comparing the companies' business models. 23andMe advertises its service for the genetically curious consumer, while Navigenics markets its services to the consumer who is interested in making better health decisions. This difference in self-characterization comes out in the companies'

decisions about the cost, panel of tests offered, advisory boards, and partnerships. While these features point to their differences, my analysis has shown that company choices about genetic counseling, or whether to only include clinically actionable tests, shows that the companies are responding to deeper currents that traditionally have structured the provision of genetic testing.

In the process of creating a new market for genetic testing, 23andMe and Navigenics have come up against institutions of power, including the medical profession, FDA, and Congress. My analysis of these confrontations in chapters three and four has shown how defining the boundaries of genetic testing technology was as much if not more about the regulatory, economic, and moral concerns of the companies and state institutions, as it was about any technical characteristic. What is at stake in the debates about the status of genetic information has been its intended uses and appropriate forms of regulation. The industry-state interactions bring to a head the question of who has the power and authority to read and interpret personal genomes and with what understanding of the emerging technology.

From this perspective, the advent of direct-to-consumer genetic testing is an instance of co-production in which a new social and technical order is emerging around genetic testing. As a theoretical framework for understanding the interaction between scientific and social order, coproduction prompts the analyst to subject to a symmetrical scrutiny both the epistemic and the normative and probe just how much they shape each other's assumptions and commitments in each given settlement (Jasanoff 2004). Applied to the empirical evidence I have presented, the co-productive lens brings into relief accuracy and standardization as the

key features of regulatory initiatives. From the letters by the Departments of Health on CLIA compliance to 23andMe's reaction to the mishandling of samples, and from the exchange with the scientific community on the pages of *Nature* over the need for standards in clinical validity to the FDA's framing of direct-to-consumer genetic tests as medical devices, genetic knowledge emerges as a product whose viability rests on technical precision and epistemic accuracy. Genetic information must be reliable and true: these are the defining features arrived at through the encounters between the main direct-to-consumer providers and the various institutions that have intervened on their operations. To be sure, all actors involved seem keenly aware that, of these two concerns, technical reliability is far more readily available than truth, due to the inherent difficulty of tracing traits to genotypes in the highly variable human population. Yet this limitation becomes in turn the rationale to expand the DTC project further, and turn customers into research participants who will contribute their genomes towards the goal of making genetic knowledge more accurate.

Yet, if accuracy and standardization are being constructed as key features of DTC genetic knowledge, the coproductive lens uncovers them also as critical components in the symmetrical configuration of a new market and the further commodification of genetic information. This new market implies a new figure, the genetic consumer. I have argued that the genetic consumer and genetic testing technology co-emerge and come into further relief through their confrontations with institutions of power. When FDA decided that direct-to-consumer genetic testing services are medical devices, the genetic consumer was entitled to protection from the state. In broad strokes, FDA imagines a world in which consumers get accurate and correct genetic information, but consumers are not guaranteed the utility of such

information. It looks as though individuals will be able to consume their raw genetic data and then shop around for the sort of genomic interpretation that suits their needs or desires. With an emphasis on individuals having a right to their genetic data, FDA's responsibility to contain risks is more straightforwardly constructed as those risks relating to the reliability and quality of the information.

Regulating clinical validity would satisfy both the companies and FDA. In June 2010, 23andMe sent a letter to Margaret Hamburg, Commissioner of the Food and Drug Administration, and Francis Collins, Director of the National Institutes of Health, asking their respective agencies to help develop broadly applicable standards and guidelines for the provision of genetic test results and risk estimates. Echoing a similar sentiment to this request for standards, Amy DuRoss, Navigenics' Vice President of Policy and Business Affairs, agreed that measures to standardize the provision of genetic tests would serve the industry well.

This approach, which avoids social questions about the intended uses of the tests, is favorable for both 23andMe and Navigenics in framing their companies as producers and dispensers of genetic knowledge as just one kind of personal information and hence as a commodity. By focusing attention on the technical and epistemic dimensions of genetic testing, embodied in the criteria of analytical validity and clinical validity, the companies attempt to put genetic testing in a technical and scientific register. In doing so, they bolster their market credibility with claims to objectivity.

This focus on standardizing clinical validity is also favorable for FDA, but for different reasons. Through the classification of direct-to-consumer genetic testing services as a medical device, the agency has already channeled the controversial technology into a well-established pre-market review process. The criteria of analytical validity and clinical validity are central to market approval. With an emphasis on these evaluations of genetic testing, FDA positions science as the stabilizer of the perceived risks. In the words of the Commissioner of the FDA, Margaret Hamburg, "as the science gets better we will be able to define the risks better." Scientific standardization serves as a method of containment for a broader spectrum of risks. This is consistent with work that has shown that national context matters for the ways scientific uncertainty is resolved for policy-making purposes. In the United States, for example, regulators have traditionally appealed to formal analytic and quantitative methods to deal with scientific uncertainty.

I would now like to provide few remarks about the implications of these proposed structures of responsibility and the companies' claims to be empowering consumers. In the midst of a proposed regulatory approach that emphasizes the technical aspects of genetic testing, which in turn would allow for the expansion of this new market, where does the genetic consumer stand? Is genetic consumerism yet another step in patient autonomy? While the companies have positioned their services as empowering consumers, against the limitation of patient's rights, I would like to conclude by pointing to the fact that the consumer is being constrained by a new set of actors. While the patient was subject to the authority of the physician, the consumer is now subject to the interests of private industry. And whereas

genetic testing in the clinical context was subject to the expertise of medical professionals, scientists stand to replace those experts in the proposed plans to regulate clinical validity.

In the case of direct-to-consumer genetic testing, a broader set of issues come out that deal with our understandings of science in relation to medicine, patients in relation to consumers, and structures of responsibility imposed by the state in relation to those of the market. It is important to pay attention to the understandings that are coming out of the case of direct-to-consumer genetic testing, as they will undoubtedly be reflected in and have an impact on other emerging technologies.

# METHODOLOGICAL APPENDIX

This dissertation is based on a variety of empirical resources gathered from 2007 to 2011, including published articles in newspapers, magazines, and academic journals, documents generated by those involved with direct-to-consumer genetic testing, the companies' websites, and ethnographic observation.

**Published Sources**

I began to research the direct-to-consumer genetic testing industry in the fall of 2007 by searching the Internet, the general media, and academic journals for relevant information. This often included a broader survey of genetic testing technology, information technology, and new media resources. This allowed me to track the sequence of events from 23andMe and Navigenics being founded in 2006 and 2007, respectively, to their confrontations with FDA and Congress in 2010. I was also able to gather a sense of the debates surrounding the new technology and identify the major stakeholders.

**Document Analysis**

This work relied heavily on documents produced by stakeholders who described how direct-to-consumer genetic testing should be or was already being regulated, provided, and used. The following types of documents were analyzed in my dissertation:

- Transcripts of public hearings and meetings
- Letters sent by state and federal institutions
- Reports by government and other advisory committees who issued recommendations relevant to direct-to-consumer genetic testing

- Policy statements from scientific and medical organizations
- Corporate fact sheets
- Press releases issued by the companies and the venture capital firms that invested in them
- Promotional information provided by the companies

**Company Websites**

From 2007 to 2011 I performed systematic weekly reviews of the companies' websites. As the websites were the primary medium through which the companies engaged consumers it was important to track the changes in their genetic testing platforms. Given the flexible nature of the websites, the companies were able to adapt and change features of their services quickly, often on a weekly or monthly basis.

**Ethnographic Observation**

For my work I also wanted to understand the broader communities within which the direct-to-consumer genetic testing companies interacted. To do so, I attended conferences, including the Network Biology 2.0 at the Broad Institute (Cambridge, MA 2010), the Tarrytown Meeting (Tarrytown, NY 2010), and the Personalized Medicine World Conference (Mountain View, CA 2011). I also attended 23andMe's public forum on "Genomics and the Consumer: The Present and Future of Personalized Medicine" (Burlingame, CA 2010), and most recently an event hosted by Harvard University to discuss the 10$^{th}$ year anniversary of the draft publication of the human genome (Cambridge, MA 2011).

All of these sources were augmented with a small set of interviews with key members associated with the direct-to-consumer genetic testing companies. While these interviews often solidified my understanding of some of the key issues, they also provided insights that were otherwise unavailable. Some of these individuals I identified through the companies' websites, while others I met during conferences. In sum, I interviewed the following types of individuals:

- Board members
- Vice presidents
- Scientific advisors to the companies
- Staff scientists at the companies
- Sales representatives
- Legal counsel to the companies

All interviewees gave verbal consent to be interviewed with the condition that their statements would be anonymized unless I received permission to quote them directly.

# SUPPLEMENTARY MATERIAL

**23andMe's Test Panel:**

(Available at: https://www.23andme.com/health/all/ [last accessed 15 April 2011])

* Indicates "Established Research Reports," which are defined by the company as reports that provide "information about conditions and traits for which there are genetic associations supported by multiple, large, peer-reviewed studies." The other tests are classified as, "Preliminary Research Reports." 23andMe defines these reports as "based on peer-reviewed, published research where the findings still need to be confirmed by the scientific community."

***Carrier Status (24)***

Alpha-1 Antitrypsin Deficiency *
BRCA Cancer Mutations (Selected) *
Bloom's Syndrome *
Canavan Disease *
Connexin 26 Related Sensorineural Hearing Loss *
Cystic Fibrosis *
Factor XI Deficiency *
Familial Dysautonomia *
Familial Hypercholesterolemia Type B *
Familial Mediterranean Fever *
Fanconi Anemia (FANCC-related) *
G6PD Deficiency *
Gaucher Disease *
Glycogen Storage Disease Type 1a *
Hemochromatosis *
Limb-girdle Muscular Dystrophy *
Maple Syrup Urine Disease Type 1B *
Mucolipidosis IV *
Niemann-Pick Disease Type A *
Phenylketonuria *
Rhizomelic Chondrodysplasia Punctata Type 1 (RCDP1) *
Sickle Cell Anemia & Malaria Resistance *
Tay-Sachs Disease *
Torsion Dystonia *

***Drug Response (19)***

Abacavir Hypersensitivity *
Alcohol Consumption, Smoking and Risk of Esophageal Cancer *
Antidepressant Response
Beta-Blocker Response
Caffeine Metabolism
Clopidogrel (Plavix®) Efficacy *
Floxacillin Toxicity
Fluorouracil Toxicity *
Heroin Addiction
Lumiracoxib (Prexige®) Side Effects
Metformin Response
Naltrexone Treatment Response
Oral Contraceptives, Hormone Replacement Therapy and Risk of Venous Thromboembolism *
Postoperative Nausea and Vomiting (PONV)
Pseudocholinesterase Deficiency *
Response to Hepatitis C Treatment *
Response to Interferon Beta Therapy
Statin Response
Warfarin (Coumadin®) Sensitivity *

***Traits (50)***

Adiponectin Levels
Alcohol Flush Reaction *

Asparagus Metabolite Detection
Avoidance of Errors
Birth Weight
Bitter Taste Perception *
Blood Glucose
Breastfeeding and IQ
C-reactive Protein Level
Caffeine Consumption
Chronic Hepatitis B
Earwax Type *
Eye Color *
Eye Color: Preliminary Research
Food Preference
Freckling
HDL Cholesterol Level
HIV Progression
Hair Color
Hair Curl *
Hair Curl: Preliminary Research
Hair Thickness
Height
Hypospadias
Lactose Intolerance *
Leprosy Susceptibility
Longevity
Malaria Complications
Malaria Resistance (Duffy Antigen) *
Male Pattern Baldness *
Measures of Intelligence
Measures of Obesity
Memory
Menarche
Menopause
Muscle Performance *
Non-ABO Blood Groups *
Norovirus Resistance *
Odor Detection
Pain Sensitivity
Persistent Fetal Hemoglobin
Photic Sneeze Reflex
Prostate-Specific Antigen
Reading Ability
Refractive Error
Resistance to HIV/AIDS *
Response to Diet and Exercise
Sex Hormone Regulation
Smoking Behavior *
Tuberculosis Susceptibility

***Disease Risk (100)***

Abdominal Aortic Aneurysm
Age-related Macular Degeneration *
Alcohol Dependence
Alopecia Areata
Alzheimer's Disease *
Ankylosing Spondylitis
Asthma
Atopic Dermatitis
Atrial Fibrillation *
Atrial Fibrillation: Preliminary Research
Attention-Deficit Hyperactivity Disorder
Back Pain
Basal Cell Carcinoma
Behçet's Disease
Bipolar Disorder *
Bipolar Disorder: Preliminary Research
Bladder Cancer
Brain Aneurysm
Breast Cancer *
Breast Cancer Risk Modifiers
Celiac Disease *
Celiac Disease: Preliminary Research
Chronic Kidney Disease *
Chronic Lymphocytic Leukemia
Chronic Obstructive Pulmonary Disease (COPD)
Cleft Lip and Cleft Palate
Cluster Headaches
Colorectal Cancer *
Creutzfeldt-Jakob Disease
Crohn's Disease *
Developmental Dyslexia
Endometriosis
Esophageal Cancer: Preliminary Research
Esophageal Squamous Cell Carcinoma (ESCC) *
Essential Tremor
Exfoliation Glaucoma *
Follicular Lymphoma
Gallstones *

Generalized Vitiligo
Gestational Diabetes
Glaucoma: Preliminary Research
Gout
Hashimoto's Thyroiditis
Heart Attack *
High Blood Pressure (Hypertension)
Hodgkin Lymphoma
Hypertriglyceridemia
Intrahepatic Cholestasis of Pregnancy
Keloid
Kidney Disease
Kidney Stones
Larynx Cancer
Lou Gehrig's Disease (ALS)
Lung Cancer *
Lupus (Systemic Lupus Erythematosus) *
Male Infertility
Melanoma *
Melanoma: Preliminary Research
Multiple Sclerosis *
Narcolepsy
Nasopharyngeal Carcinoma
Neural Tube Defects
Neuroblastoma
Nicotine Dependence
Nonalcoholic Fatty Liver Disease
Obesity *
Obesity: Preliminary Research
Obsessive-Compulsive Disorder
Oral and Throat Cancer
Osteoarthritis
Otosclerosis
Paget's Disease of Bone
Parkinson's Disease *
Parkinson's Disease: Preliminary Research
Peripheral Arterial Disease
Placental Abruption
Polycystic Ovary Syndrome
Preeclampsia
Primary Biliary Cirrhosis
Progressive Supranuclear Palsy
Prostate Cancer *
Psoriasis *
Restless Legs Syndrome *
Rheumatoid Arthritis *
Schizophrenia
Scleroderma (Limited Cutaneous Type) *
Selective IgA Deficiency
Sjögren's Syndrome
Squamous Cell Carcinoma
Stomach Cancer (Gastric Cardia Adenocarcinoma) *
Stomach Cancer: Preliminary Research
Stroke
Tardive Dyskinesia
Thyroid Cancer
Tourette's Syndrome
Type 1 Diabetes *
Type 2 Diabetes *
Ulcerative Colitis *
Uterine Fibroids
Venous Thromboembolism *

**Navigenics' Test Panel:**

(Available at: http://www.navigenics.com/visitor/what_we_offer/conditions_we_cover/ [last accessed 15 April 2011])

***Health Conditions (28)***

Abdominal aneurysm
Alzheimer's disease
Atrial fibrillation
Brain aneurysm
Breast cancer
Celiac disease
Colon cancer
Crohn's disease
Deep vein thrombosis
Diabetes, type 2
Glaucoma
Graves' disease
Heart attack
Hemochromatosis, HFE-related
Lactose intolerance
Lung cancer
Lupus
Macular degeneration
Melanoma
Multiple sclerosis
Obesity
Osteoarthritis
Prostate cancer
Psoriasis
Restless legs syndrome
Rheumatoid arthritis
Sarcoidosis
Stomach cancer, diffuse

***Medications (12)***

Abacavir
Beta blockers
Carbamazepine
Clopidogrel
Floxacillin
Fluoracil
Irinotecan
Simavastatin
Statins
Succinylcholine
Thiopurines
Warfarin

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