VOLUME 23 NUMBER 4 AUGUST-SEPTEMBER 2010

# GENEWATCH

THE MAGAZINE OF THE COUNCIL FOR RESPONSIBLE GENETICS • ADVANCING THE PUBLIC INTEREST IN BIOTECHNOLOGY SINCE 1983

## DIRECT-TO-CONSUMER GENETIC TESTING


ISSN 0740-9737

FEATURES

How Berkeley Came to Abruptly Change Its Genetic Testing Program / Jeremy Gruber

In Their Own Words: Genetic Testing Company 23andMe

Biolab Safety: A View From the Inside / Nancy Connell

# GeneWatch

**AUGUST-SEPTEMBER 2010**
**Volume 23 Number 4**

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*GeneWatch* is published by the Council for Responsible Genetics (CRG), a national, nonprofit, tax-exempt organization. Founded in 1983, CRG's mission is to foster public debate on the social, ethical, and environmental implications of new genetic technologies. The views expressed herein do not necessarily represent the views of the staff or the CRG Board of Directors.

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Cover Art
Sarah Kim




# Editorial

Sam Anderson

*GeneWatch* is a unique publication. We cover controversial issues, but we toe a difficult line between strictly objective journalism and single-minded advocacy. Just to left of this editorial, you'll find the fine print: "The views expressed herein do not necessarily represent the views of the staff or the CRG Board of Directors." Except, of course—as in this issue—when those people are contributing articles of their own.

The purpose of each issue of *GeneWatch* is not to simply report what's happening out there, nor is it to tell you what you ought to believe, even if some of the pieces on the following pages fall into those descriptions. As I see it, if you read an issue of *GeneWatch* front to back, you ought to have learned something; most importantly, you ought to have thought. If you read every page of *GeneWatch* and your preconceived opinions have not been challenged, we came up short. If you can read the entire issue and never find yourself in disagreement with an author, we haven't done our job.

That job might be more difficult if our Board of Directors held monolithic views. While CRG has published position papers on everything from gene patents to biocolonialism, opinions within the organization are nuanced to say the least. This issue—Direct-to-Consumer Genetic Testing—is a prime example.

You will find several articles by CRG Board members in the following pages, and you will hardly find a united front. Sheldon Krimsky targets the risks of allowing companies to market genetic tests to consumers without meaningful regulation; Paul Billings defends DTC testing as a tool to empower consumers to take a more central role in their own health care; Robert Green, with Jordan P. Lerner-Ellis and J. David Ellis, balances the potential risks and benefits and concludes that we simply don't have all the answers yet. CRG has historically taken a quite critical view of DTC testing, but as evidenced by the highly informed views of our own Board members and other contributors in this issue, such a complex topic cannot be boiled down to a thumbs up or thumbs down. It's easy to just tell someone what they ought to believe—which is why you won't find us doing it.

And if you've read this far and are still wondering "What exactly is direct-to-consumer genetic testing?" … well, I'm afraid you'll just have to read on. Go into it as a blank slate. Think about where you stand. And let me know if you we made it too easy for you.

## What do you think?

GeneWatch welcomes all comments, as well as letters to the editor for inclusion in upcoming issues. Please email anderson@genewatch.org if you would like to submit a letter (200 words or less, please) or with any other comments or queries.

## Featured artist

***Sarah Kim*** *is a graduate of Massachusetts College of Art and Design who enjoys working on any and all kinds of illusration. You can see more of her work at* www.skimilkart.com. *This is Sarah's fourth* GeneWatch *cover.*

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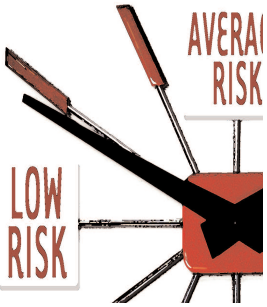
CRG played a crucial role in putting the brakes on UC Berkeley's plan to gather DNA from incoming students (p. 4)




"These companies want to have it both ways. Pick one or the other: it's either medically important or it isn't." (p. 8)

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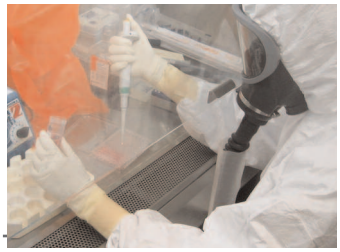
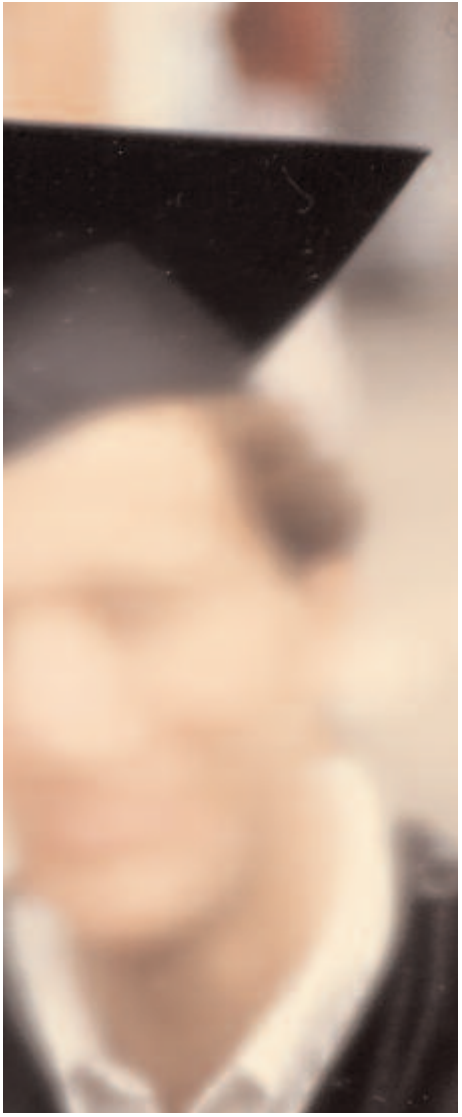


Nancy Connell knows a bit about safety in biolabs - she runs one (p 22)

A killer is found through a familial DNA search—but the technique remains highly problematic (p. 24)

# Lessons Learned: How Berkeley Came to Abruptly Change Its Genetic Testing Program

*By Jeremy Gruber*



Last month, the University of California, Berkeley changed course after months of intransigence and made significant changes to their controversial "Bring your Genes to Cal" freshman genetic testing program. The most prominent modification was the elimination of any individually identifiable analysis of student DNA. While this change of course appeared abrupt, it was the result of several months of significant and mostly behind-the-scenes work. The lessons learned from successfully pressuring the University to revise its program can provide a blueprint for future successes in steering the development of biotechnology towards the advancement of public health, environmental protection, equal justice, and respect for individual rights.

In May of this year, the University of California, Berkeley announced that it would be sending incoming freshman a cotton swab with which to send in a DNA sample to be tested for three gene variants that help regulate the ability to metabolize alcohol, lactose and folates as part of a program for the class of 2014 that would focus on genetics and personalized medicine. The announcement, including rough details of the program, brought swift condemnation from a number of quarters for the lack of due consideration for issues ranging from the privacy protections for the DNA samples and the data generated from them to issues of improper informed consent and conflicts of interest. Noted professors at Berkeley, from Kimberly Tallbear, Troy Duster, Charis Thompson and David Winickoff to Nancy-Scheper Hughes, Paul Rabinow and Laura Nader, as well as academics outside Berkeley, such as Hank Greely at Stanford, George Annas at Boston University and Debra Geenfield at UCLA all organized, and raised their voices within and without the university (and continued to speak out during the course of the summer). Organizations such as the Council for Responsible Genetics (CRG) and the Center for Genetics and Society issued serious point by point critiques of the program as well as brought public attention to the issue through significant media coverage during the first few weeks following the program's announcement. Many other members of the public and media spoke out as well.

Unfortunately, as is often the case, the initial outcry was not enough. While the University met with many of their academic critics, it failed to seriously consider and ultimately rejected their concerns. The media attention ran its course. Having weathered the criticism, indeed seemingly enthralled by it, Berkeley became even more dismissive and convinced of the virtue of its program.

And that is where the story would likely have ended, had many critics of the Berkeley program not urged the Council for Responsible Genetics to dig deeper. Raising your voice and taking a public position on an issue is the easy part of advocacy work. Seldom do organizations like ours have the resources to roll up their sleeves and conduct the incredibly time consuming and unglamorous work that is generally required to truly move an issue forward. Fortunately for us, we had an incredibly bright and energetic intern assisting us for the summer and there was no greater motivating factor than Berkeley's arrogance!

With our charge of halting this highly problematic experiment, CRG began a multi-prong advocacy plan. We began building a loose coalition of organizations to work on the Berkeley program. We had learned our initial lesson, that a group of organizations and individuals focused exclusively on biotechnology issues was insufficient to affecting change on its own. This time we recruited a much larger and varied group of organizations, ranging from civil rights and privacy groups such as the American Civil Liberties Union (ACLU), Electronic Frontier Foundation (EFF), Privacy Rights Clearinghouse and World Privacy Forum to consumer protection groups such as Consumer Watchdog as well as more focused organizations such as the Alliance for Humane Biotechnology.

We filed a number of public records requests with Berkeley under California's Sunshine Act, similar to the federal Freedom of Information Act, in an attempt to learn more details about the program, including information regarding the program's undisclosed funding source. Berkeley often delayed, and in some cases failed to comply with our requests, necessitating us to file a formal complaint with the Fair Political Practices Commission (which had enforcement authority over some of our requests) that resulted in a rare rebuke to the University. We also sent out a staggered series of press releases to the media with new information as we discovered it, keeping the issue on their radar.

We conducted a significant amount of legal research in our attempt to stop the program from moving forward, evaluating every facet of Berkeley's plan to look for opportunities for a legal or regulatory challenge. This research resulted in an extensive memorandum outlining Berkeley's potential regulatory and legal breaches and the opportunities

for legal action, ranking them in terms of likelihood of success. The strongest opportunity for challenge that we identified was in the California Business and Professions Code which regulates clinical laboratory licensure. Genetic tests, the results of which are reported back to the individual, are considered clinical laboratory tests by the California Department of Public Health (DPH) pursuant to the Code. Therefore, any lab conducting such tests must first obtain a license from the DPH. Through our public records requests, we determined that Berkeley had plans to conduct genetic testing of incoming students at the Genetic Epidemiology and Genomics Lab at the School of Public Health. We discovered that neither the lab (nor its Director or technicians), had any clinical laboratory licenses from the DPH. We further determined that in fact the only lab certified for this work was the campus health clinic which was insufficiently equipped to perform this type of testing. We further determined that no licensed medical professionals were involved in the program, as is also required by the Code.

In the course of researching our memorandum, we had obtained copies of letters sent by the DPH to several in state direct-to-consumer genetic testing companies a couple of years earlier that warned them of the requirement of proper clinical lab licensure. As the letters were signed, it was relatively easy to identify the appropriate individual to contact at the Department of Public Health with our findings. While the DPH confirmed that our analysis was a correct interpretation of the regulatory requirements, the Department seemed wary of making public comments before having an opportunity to fully investigate. Given that the University would only violate California law upon the actual testing—not yet performed at that time—it was too early for us to argue Berkeley was operating illegally.

Then we caught a lucky break. Assemblyman Chris Norby, a moderate Republican in the California legislature, introduced a bill (AB 70) that, if enacted, would essentially shield the state from any lawsuits as a result of Berkeley's (or any other public universitys') genetic testing program. The costs of any lawsuit would be borne by the individual university's general funds. While highly unlikely to pass, the bill proved an invaluable tool to renew media and public attention on Berkeley's program. We formed a close relationship with the sponsor's incredibly dedicated staff and began working closely with them on both substance and strategy.

With this new platform, we drafted multiple organizational sign-on letters with the help of our coalition partners both in support of AB 70 as well as urging the legislature to force a more general accounting of the Berkeley program. With these letters in hand, the ACLU became an essential ally in using its deep connections in the legislature to open doors for multiple meetings between themselves, CRG and EFF with staff in both the Senate and Assembly. Both the ACLU and EFF also assisted in broadening our analysis. The meetings created the necessary pressure to hold a hearing on the Berkeley program. The Alliance for Humane Biotechnology used its connection with the chairman of the committee holding the hearing to weigh in as well. CRG worked closely with staff to identify those individuals who could provide testimony beyond that narrowly offered by the representatives from Berkeley including Professors Greely and Scheper-Hughes. Lee Tien from EFF and myself representing CRG also testified at the hearing. Perhaps most importantly, the California Department of Public Health was called to testify. The added pressure on the agency was the final piece we needed.

Just prior to the hearing, the Governor's office contacted the DPH and ordered them to issue a statement at the hearing, rather than testify. Nevertheless, their statement reflected our initial analysis and the hearing elicited a promise from Berkeley, still unconvinced that the DPH was serious, to abide by the agency's interpretation. A meeting between DPH and Berkeley later that day convinced them that the agency was indeed serious. Berkeley hastily called a press conference the next day to announce significant changes in the "Bring Your Genes to Cal" program, bringing a media firestorm even larger than the one initially covering the announcement of the program. While some elements of the program have proceeded, it's safe to say that most institutions considering a genetic testing program in the future will remember Berkeley and invest far more effort into crafting an ethical and legally compliant protocol.

We learned many things from this small success. We learned that a successful advocacy effort requires many hands and diverse talents and that to actually be effective on our issues we need to continue to build relationships and alliances with organizations that do not exclusively work on biotechnology issues, ranging from the civil rights and privacy communities to the organized labor, disability, patient, consumer protection and environmental communities, to academia and beyond. We need to build strong relationships with legislators and other policy makers as well as the media. We learned that legislation, even when unsuccessful, can provide a valuable tool to bring attention to and impact our issues. And most importantly we learned that there is no substitute for rolling up your sleeves and doing the type of hard work that often goes unnoticed and is usually unsuccessful. With hard work (and a lot of luck!) we can successfully steer biotechnology development toward advancing the public interest. ■■■

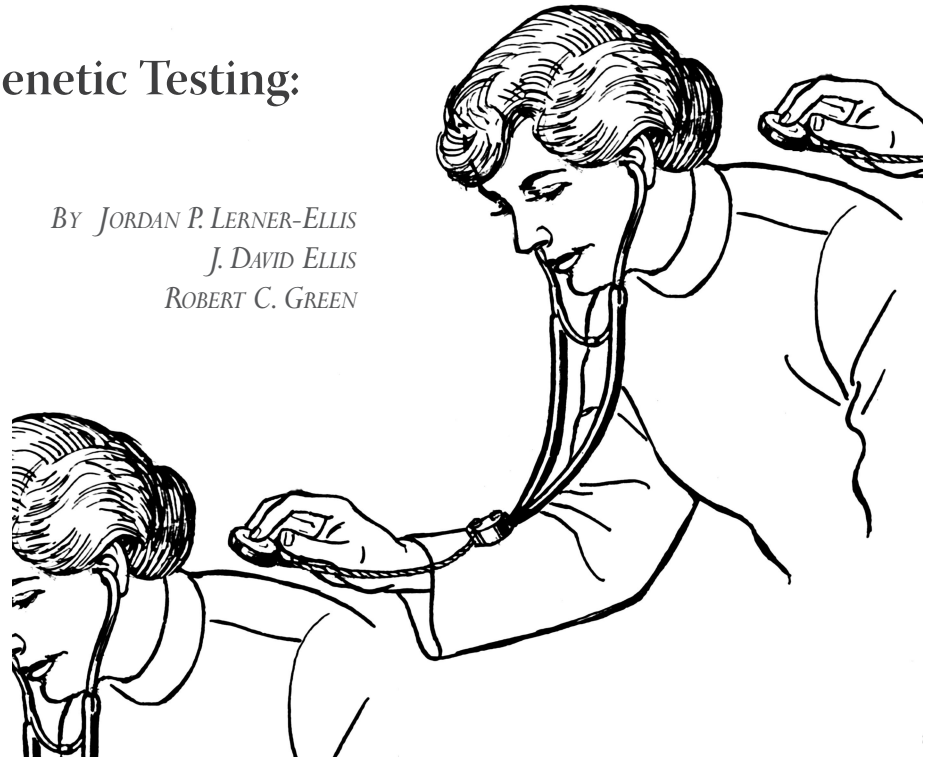
***Jeremy Gruber**, JD, is the President of the Council for Responsible Genetics.*

The Council for Responsible Genetics has launched a new blog: *Genetic Watchdog.* Watch for regular news and commentary as recorded by CRG staff, board members, and friends, and join the discussion by leaving your own comments. You don't have to wait for the next GeneWatch to keep up with the latest events in biotechnology and ethics!


The blog can be found at: http://www.councilforresponsiblegenetics.org/Blog.

# Direct-to-Consumer Genetic Testing: What's the Prognosis?

*By Jordan P. Lerner-Ellis*
*J. David Ellis*
*Robert C. Green*



Genetics has been making news lately, in large part because of the growing pains of a new and controversial industry: direct-to-consumer (DTC) genetic testing. DTC genetic testing raises questions involving privacy, how medical tests should be ordered and understood, who should regulate access to genomic information, and how individual consumers will understand and act upon such information.

DTC genetic testing has been around on a small scale for some years, but began in a new form in November, 2007 when three companies (23andMe, Navigenics and DeCodeMe) launched their genome-wide scan services within days of each other. Suddenly, individuals could send in a sample of their DNA and receive ancestry information or a wide variety of medical risk information based on the latest discoveries in genetics. In October 2008, TIME magazine recognized the 23andMe personal genome service as "Invention of the Year." Celebrities turned over samples of their DNA at trendy and well publicized "spit parties."

Non-medical services, like ancestry testing, provoked few criticisms. The same was not true of medical risk reporting, which was immediately criticized on two counts. Firstly, the companies were reporting in most cases on DNA variants of common diseases, discovered through statistical comparisons in genome-wide association studies. While these associations were well-established for large populations, they typically accounted for only a tiny fraction of total disease risk. Genetic testing of this kind was hard to justify for an individual, since it provided no clearly useful information to either the patient or the health care provider.

Secondly, it seemed possible that other risks, like family history and lifestyle-currently much better predictors of common disease-might be de-emphasized to the detriment of the DTC genetic testing consumers. Thus, a customer who was obese and had a strong family history of type 2 diabetes might well receive a low genetic risk score for the disease. To be fair, the leading companies have taken care to be accurate on their websites as to the modest effects of genetic risk information, and the importance of other risks.

By 2009, the DTC controversy revolved around conflicting visions of the future of personalized health care. To its supporters, DTC genetic testing offered private, scientifically supported and personalized information about the state of one's health-away from the intrusive gaze of insurance companies, freed from the paternalistic intermediation of harried and often uninformed clinicians seeking to preserve their economic advantage in an already dysfunctional health care system.

To its detractors, DTC genetic testing was exploiting widespread misunderstanding of genetic determinism to market common DNA risk variants that were poorly understood by the scientific community, and provided little useful information to consumers. DTC genetic testing was simply the latest in an unending series of health-related pseudo-interventions, ranging from colonics to nutraceuticals, for the privileged who could afford the extra cost. And the major challenge was to keep conventional medical practitioners from taking it seriously, lest the cost of medical testing be driven up in response to dubious genetic "risks."

Fast forward to 2010 and the controversies have evolved, but by no means disappeared. For one thing, DTC companies have expanded their offerings to include the identification of variants associated with rarer, more highly penetrant diseases, as well as carrier states. Examples include BRCA1, cystic fibrosis, PKU and Tay-Sachs. These disorders are more "fully penetrant" because if an individual carries mutations, he or she will either have the disease or be at high risk to develop the disease. Thus, the nature of the information being offered in the DTC genetic testing space is changing. Such changes have the potential to make the test results medically relevant for a small number of people. But this may also increase the potential for public misunderstanding, since companies will now be offering clinically meaningful rare DNA variant information alongside clinically less relevant, common DNA variant information.

Another disruptive development this year concerns the Food and Drug Administration's (FDA) regulatory actions. In May, 2010, DTC genetic testing almost went retail when the Walgreens drugstore chain announced it would stock $30 DNA collection kits for the DTC company, Pathway Genomics. The attempt to go to market was blocked at the last moment, and the controversy triggered new scrutiny and new revelations.

This summer the FDA decided to investigate the use of what it calls laboratory developed tests (LDTs), which had previously been unregulated.[1] The agency's main concern was focused upon genetic tests intended for use without medical supervi-

sion. FDA scrutiny has grown for several reasons, among them greater complexity of genetic testing, the role of labs located far from the primary care setting, the involvement of profit-making firms and the focus on poorly understood genetic risks for common diseases. The FDA notes that patient risks include "missed diagnosis, wrong diagnosis, and failure to receive appropriate treatment."

The agency later announced it was holding public meetings to gather stakeholder views on LDTs. As shown through the diverse testimony presented at its July public meetings[2], clinicians, researchers, advocates and business executives are far from united on the issue of whether or how to regulate genetic tests. During the July hearings, the General Accounting Office (GAO) made a surprise announcement that it had surreptitiously taped telephone conversations between investigators and representatives of the DTC testing companies. The GAO played the tapes on the record, and exposed a number of inaccurate statements made by company representatives.

It is worth noting that the proposed oversight of marketplace behavior will not necessarily ensure that the services in question will improve in accuracy or prognostic value. These goals are not often achieved through regulation, and physicians are not necessarily the best gatekeepers to determine the pros and cons of ordering genetic tests. Moreover, although commercialization has brought these regulatory concerns to the forefront, the development of innovations in genetics is clearly benefiting from the energy and imagination of the biotechnology and DTC testing industries. It may be that the interplay of commercialization and scientific innovation that is represented in the DTC genetic testing industry will prove to have long term value to society. The FDA is thus keeping a close eye on how innovation will be affected by its actions.

The Human Genome Project, completed in 2003, is rightly regarded as one of the great scientific achievements of our generation, well worth its $2.8 billion cost. But what scientists have achieved in the intervening years is every bit as significant: new technologies that have reduced the cost of DNA sequencing to one one-hundred-thousandth of what it was originally. It is considered inevitable that within the next 5 years, whole genome sequencing will be available to any individual for under $1,000! As it turns out, the big challenge for the future will not be the sequencing technologies, but the cost and difficulty of interpreting the huge amounts of data they generate.

Therein lies the dilemma for scientists and regulators. On one hand, the DTC testing companies may continue to be innovators in the interpretation of personal genetic data. On the other hand, the companies concerned will have to make a concerted effort to develop and refine precautionary measures covering a wide range of medical and ethical issues. Many unsettling results can turn up as part of an otherwise routine screening. A child might, for example, be found to have a variant associated with one disorder, say autism spectrum disorder-and the very same variant might later be determined to cause a separate neurodegenerative disorder. How will this development be reported and explained to the consumer? What procedures if any should be in place for tracking individual customers long after they've ceased doing business with the testing company? Examples abound of the challenges created by incidental and unexpected findings, and there may be no ready answers. While informed consent is the universal goal, making it work universally is not a simple matter.

Some experts suggest the crucial problem with DTC testing is lack of supervision by qualified medical personnel. Medical supervision may often be desirable, even essential. But there is another perspective here. Even the experts, including medical geneticists, continue to struggle with incomplete and incompatible genetic databases, poor risk models and disagreements over interpretation. Moreover, many primary care physicians are not well versed in genetics and may not know what kinds of tests their patients need. In other words, it is unrealistic to expect that medical supervision in and of itself will turn DTC tests—or any genetic tests—into accurate and reliable tools.

Even the experts, including medical geneticists, continue to struggle with incomplete and incompatible genetic databases, poor risk models and disagreements over interpretation.

In summary, difficult questions face medical professionals and members of the public in their attempts to evaluate genetic tests. What does a set of genetic results actually reveal? How will they help promote medical care? And what difference will testing make to the individual's quality of life? These are not theoretical questions. Right now many in the testing business are raising the public's expectations by making suggestive statements like this one from a company Web site[3]: "Let your DNA help you plan for the important things in life."

Given its mandate, the FDA will have to devote its attention to high-profile issues, especially patient safety, while encouraging innovation as best it can. Even then, the regulator can only do so much to manage public expectations, and rising consumer demand for inexpensive tests is certain to be a strong market mover as this debate unfolds. Over-regulation of a service that consumers want could simply drive such services offshore where they could operate over the internet with impunity. In any case, no amount of market regulation can take the place of well designed and well-funded research that will help geneticists and other scientists understand the complexities of the human genome in the service of better medical care.

Do customers of DTC genetic testing services really understand what they are purchasing? Do they understand the results? Do they consult their physicians about the information? Are unnecessary medical tests ordered or are valuable health lessons learned from the overall experience? At the present time, we simply do not have all the answers. The National Human Genome Research Institute (NHGRI) has recently funded a proposal to implement the first "before and after" survey of DTC genetic testing in order to better understand these questions. ■■■

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***J. David Ellis**, PhD, a consultant in public policy and regulatory affairs, teaches Communication Studies at York University in Toronto.*
***Robert C. Green**, MD, MPH professor of Neurology, Genetics and Epidemiology at Boston University Schools of Medicine and Public Health, and Fellow in Genetics, Harvard Medical School, will be co-directing the NHGRI study beginning in October 2010, in conjunction with Dr. Scott Roberts of the University of Michigan. He is a member of the CRG Board of Directors.*

# The Broken Clock: Accuracy and Utility of DTC Tests

## An interview with Professor James Evans

***James Evans**, MD, PhD, directs the Clinical Cancer Genetics Services at the University of North Carolina. He delivered testimony at the July congressional hearings focusing on a Government Accountability Office (GAO) investigation which criticized DTC genetic tests as "misleading and of little or no practical use to consumers."*

**How did you get involved in the GAO report hearings?**

They called me a year or two ago. They told me that they were concerned about some of these direct-to-consumer testing companies' offerings, and I have some concerns as well. I don't think that the sky is falling because of the existence of these things, but I have some concerns. My biggest concerns have to do with the false claims that are made by these companies and the fact that we don't really know how to interpret this kind of information.

So the GAO was looking to design a way to investigate some of these concerns, and I think that the strategy they ultimately took was a good way of investigating and illustrating that we are not ready to interpret this information with any degree of reliability. Then there is a second question: Even if we were able to interpret these results reliably, would it tell us anything of any real significance?

They investigated that first question and eloquently and elegantly demonstrated that we are not ready to interpret much of this data. There's just no way of reconciling claims that it's usable information with the fact that reputable companies conduct analyses on the same DNA and come up with radically different interpretations. There's no way to reconcile that information with claims that it's ready for prime time.

What the GAO did not investigate—and really could not investigate, I think—was the other issue. The question that remains is: Even if there was consistency, and we learned to interpret it, would it provide any utility to patients? And the answer to that, I think, is largely a resounding no.

**Industry critics have claimed that the GAO's methods were not scientific. Do you share any of those concerns?**

It's an interesting criticism, because they actually did an elegant experiment; it was entirely scientific. They had, really, the ultimate control. They took the same sample to different companies and simply presented the results: for the same exact sample, one company says the individual has an increased risk of prostate cancer, one says he has an average risk, and one says he has a low risk. One of them is right, but it's a little like the broken clock which is right twice a day.

We have no idea, as that experiment readily demonstrated, how to interpret some of this genetic information. So the idea that the report was not scientific is, I think, a rather silly accusation. They did an experiment, and the results speak for themselves.

**In your testimony you took issue with the marketing claims made by DTC testing companies. Are there any specific claims that you see commonly made which you find especially egregious?**

Yes. The three big players in this field, the top strata of these companies, are doing a fine job of telling you reliably which nucleotide you have at a given position, but all of these companies make implicit and explicit claims that the information will improve your health. All you have to do is look at their home page on their websites, look at their advertising, and they all make some claim along the lines of "Understanding your genes will be a roadmap to better health" or "Take control of your future with genetic analysis." They are all making explicit or implicit claims that knowing your genetic

information will improve your health; and, frankly, there is no evidence that this is the case.

They spout platitudes that, for example, people will be motivated to lose weight or live a healthier lifestyle. Firstly, there is little evidence that this is the case; secondly, even if this is the case, if somehow genetic information has some magical properties that make it particularly motivating, then we have a bigger problem: it is arithmetically guaranteed that for everyone who has increased risk of a condition, there are an equal number with decreased risk. If this information is actually so motivating, we run the significant risk of altering people's behavior for the worse. And frankly, the magnitudes of the risk shift that they are giving people are practically meaningless. Finding out that you are at a twofold or a fifty percent risk of heart disease over the general population is essentially meaningless since these are common diseases that we remain at significant absolute risk for whether or not we are at some relatively decreased genetic risk.

I don't have a problem with the public gaining access to information about their own genes. ...

**So you are concerned not only about the possibility of false reassurance, but even reassurance that isn't necessarily false.**

Exactly, it may not even be false! In other words, I might tell you that you're at a 50% risk of heart disease over the general population, but that relative risk is rather meaningless. You are still at a high risk for heart disease simply because it is a very common malady. Millions of people out there who are at relatively "low risk" for heart disease end up dying of it!

**Because of environmental factors?**

Yes, and because it's simply a common disease. But what you're getting at is exactly right: genetics is only one small part of our risk for most of these diseases. Therefore, even if we understood completely the genetic risk for diabetes and heart disease and cancer, we still would be left with a huge amount of uncertainty because the causation of these maladies is multifactorial.

My other gripe is that in the results they send to the consumer, some of these companies mix pure entertainment—like "Do you have thick earwax?"—with a tiny subset of information that is very medically meaningful. A small percentage of the information they give, like BRCA1 and 2 (relating to risk of breast cancer), and LRK 2 status (relating to risk of Parkinson's disease), are very predictive, and in the right circumstances have important medical implications. And yet they're being dumped into this big pot with all kinds of tests that are purely of entertainment value and some tests that are misrepresented as being medically useful when they are not.

I don't have a problem with the public gaining access to information about their own genes. I'm not so paternalistic as to say you can't have the information in your genome. What I do feel strongly about is that people shouldn't be lied to about the significance of that information, and that people should be able to be assured that the claims that are made are accurate and that their privacy will be protected.

**Do you think that the whole concept of the way these tests are marketed clings to the old concept that your genome can tell you everything about yourself?**

I think what's happened is that there's an understandable impatience to apply all of this wonderful, cool genetic technology to medical care. There's a seductive appeal to thinking that because we understand some things about the genome, we now understand a lot about its role in health and disease. The difficult and the sober reality, however, is that we don't have a very good grasp of precisely how to relate your genetic information to your health. That's going to be the work of many years. What we need to do before we just start willy-nilly selling this idea to people is to find evidence of what's real and what's not, what works and what doesn't. All I ask is that we have data that back up the things that we introduce into the realm of patient care.

And these companies want to have it both ways. They implicitly and explicitly make claims about the health value of this information, and yet on every page of their results, they say "this isn't medical advice." Pick one or the other: it's either medically important or it isn't. And I would say it is not, demonstrably, as the GAO report really pointed out.

**Since there are plenty of traits tested where there is not a lot of utility, do you think there are traits which are useful for consumers to know about?**

You bet. And I think that there may well be reasons that a patient might want to pursue various tests in what we consider a non-traditional environment. For example, DNA Direct for many years has offered BRCA testing. I've never had any problem with what they do. They don't misrepresent what they offer, and importantly, they have genetic counselors available to talk to customers about the meaning of their results. I haven't looked at their website in a while, but for many years they offered tests that arguably were medically valid tests, with real medically important results—and they didn't conflate entertainment with medical information.

I think there are ways of doing this that are reasonable and responsible, but I don't think companies like 23andMe are doing so.

**Going back to different companies' radically different interpretations of the same DNA sample in the GAO report: do you know of a reason that the interpretations would be so different?**

I think there are several reasons. Now, the reason that the companies will give you is only part of the truth. They will tell you the problem is that one company did nine variants and another company did fourteen variants. The reason that explanation isn't the whole story, and the reason that settling on everyone testing the same twelve variants isn't a valid response, is the following: We still don't understand how to aggregate these independent risk factors into a net risk score. Genes interact with each other in ways that we are only dimly beginning to glimpse, and genes interact with the environment. It is entirely possible that you might have variant A, B and C and have an increased risk for a condition, but a person who has variant A, B, C and D is actually at decreased risk because of the interaction of variant D with variant B.

... What I do feel strongly about is that people shouldn't be lied to about the significance of that information.

Secondly, genes interact with the environment. It could well be that an individual who has variant A, B and C, who should be at increased risk, is actually at average risk in the right environment—because those genes and our physiology interact with our environment.

So the reason that they come up with dif-

*Continued on page 14*

# Consumer Genomics and the Empowered Patient

## Genetic testing can help consumers become more knowledgeable and independent actors in their own health care

*By Paul Billings*

My medical school classmates, Harvard physicians Jerome Groopman and Pamela Hartzband (who are married to each other), have railed recently against too much "cookbook" medicine.[1] They have cogently argued that care of patients is an art; it may not be adequately represented in computer algorithms, treatment guidelines or glib quality assessment reports. They have supported the import that the professionalism, experience and expertise of physicians can bring to interactions with patients. This art in the practice of medicine yields many—and, Groopman and Hartzband would argue, necessary—variations.

But sadly this necessary art can account for a multitude of sins. From frank medical paternalism, like withholding key facts from dying patients, to unacceptable variance in interpretations of pathology or radiology data, to even the provision of unnecessary or harmful treatments, variability or artfulness in medical practice can be wasteful and deadly. How do we improve care and get the most out of the trust sick people place in their doctors?

One way, it seems to me, is to make patients and healthy citizens more knowing and independent actors in the health care system. Professional norms demanding real-time honesty with patients, medical malpractice suits, and the internet have all improved the power of patients in the doctor/patient relationship—and, I would posit, the quality of medical care provided. Measuring this change using outcomes like change in clinical outcome status could be very difficult at present, even if I am right!

If one's health and the management of illnesses are in fact one of the more basic personal responsibilities, then allowing people to pursue issues of prevention or disease treatment in whatever way they see fit could be reasonable. In such a model, government's role is to ensure honesty in the representation and claims of safety or effectiveness, while physicians act as solicited providers of expert opinion. The empowered and knowledge-armed citizen is a key agent for the improvement of all aspects of health care and illness prevention.

That is why I founded in 1999 one of the first direct-to-consumer (DTC) genetic information companies (GeneSage Inc) and why I generally support efforts to expand this knowledge and service channel now. I fundamentally believe that we all have the right to know and test things about our bodies, unhindered by physicians gate-keeping those activities. Naturally if someone else is paying for those services (a government, employer or private insurer, for instance), they may have some input into or influence on what they pay for; but the underlying "right to health" (as Franklin D, Roosevelt put it) lies with each of our fellow citizens and should allow for a wide range of affordable activities.

Because there is so little known about exactly how most of the human genome impacts traits and participates in disease, many of the early entrants into DTC genomics have made overly optimistic, exaggerated or false claims. This is, of course, true as well for all the physicians who have proffered misinformed advice for decades in the field. Some of the practices that are offered (DTC or otherwise) or that were noted in the recent Government Accounting Office investigation are bogus and should be curtailed. For instance, except in certain rare circumstances (for example, people with PKU should avoid phenylalanine), there is no genomic test for the right diet or exercise program that will yield better personal health. We may never see the day when attaching our DNA profiles to the grocery list as we head to the supermarket is a good idea!

But if someone wants to obtain a test that MAY identify a risk for disease or a susceptibility to a drug reaction, they should be able to do so without a physician's intercession. Those ordering such a test in person or from a website ought to have access to reliable and accurate data about what information the test may convey. They need to have a reasonable expectation of the quality of the lab that will conduct the test with access to easily understood lab performance data. Governments, professional societies, and good market practices should ensure those conditions are present. In fact, several states now allow consumers to order medical tests without a doctor's prescription.

23andMe and Navigenics are both companies I know and have advised. The tests they offer are pretty much "state of the art" in terms of assessing the genes of the human genome. Soon these companies or others will offer affordable sequencing assays of all the DNA in the human genome. It will be possible for many people to know exactly what nucleic acid sequences reside in the nuclei of most of their cells. Of course, the meaning of the huge preponderance of this data for an individual's health or disease development will take much longer to establish, and will ultimately be individualized, primarily by each of us. But as that knowledge

becomes available—unevenly, influenced in many ways, and with continued debate—some people will want that information, and so-called expert debate should inform but not stop them.

In general, the prominent commercial entities in the DTC genomics marketplace provide understandable information, are dedicated to support and participate in important research to make the field better, and engage in good clinical practices. Others do not and should be identified and shunned by consumers as well as scrutinized by legally designated regulators from HHS and FTC (but not Congressional witch-hunts). In my view, more knowledge and more highly empowered, well-informed independently acting consumers are needed to push improvements in genomic medicine and in all aspects of health care. DTC genomics is part of that. How medical care is ultimately personalized should be a topic that individuals acting as citizens, consumers, patients and in other roles actively control. ■■■

***Paul Billings** is a long-serving member of the CRG Board of Directors, a member of the HHS Secretary's Advisory Committee of Genetics, Health and Society, and in October will become the Chief Medical Officer of LIFE Technologies, a provider of tools and reagents for research and healthcare.*

# Not What the Doctor Ordered

## Direct-to-consumer marketing of genetic tests poses too many risks to go underregulated

*By Sheldon Krimsky*

The marketing of genetic tests to consumers is following a path similar to direct-to-consumer marketing of prescription drugs. And while there are good reasons for the Food and Drug Administration to rescind the rule on prescription drug advertising, there are greater risks to consumers in DTC marketing of genetic tests.

Here are some reasons. First, drug companies cannot advertise drugs that have not been approved by the FDA. Recently, it was reported that Allergan, the maker of Botox, agreed to pay $600 million to settle charges that it illegally advertised the drug for unapproved uses. Genetic tests, however, do not have to be federally approved or validated. The tests may or may not do what the companies claim they can do. Consumers have no recourse.

Second, most physicians are not familiar with the validation criteria, sensitivity, or reliability of genetic tests. They depend upon the interpretation by the company. If people take prescription drugs—whether or not they are marketed DTC—which turn out either ineffective or produce an adverse effect, they can discuss it with their doctor. There are often substitutes that can be used, and adverse effects can be reported to the FDA and to the company.

Genetic tests, on the other hand, are often patented. There are rarely second opinions or the possibility of retests by another company. The test for the breast cancer mutations BRCA1 and BRCA2 was for years controlled by one company, Myriad Genetics. The successful initial lawsuit by the American Civil Liberties Union challenged the patent on BRCA, and the appeal will determine whether other companies can use the DNA sequences of BRCA mutations for their own tests.

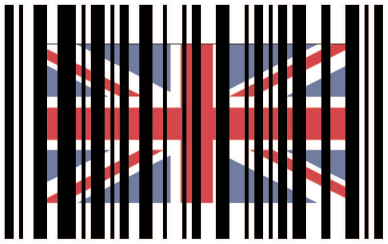
Third, it is easy for DTC advertisers of genetic tests to overstate the significance of the test result, particularly those tests for which reliability has not been certified and standardization has not been set by a professional genetics association. Consumers of DTC genetic tests are on their own in what they purchase (caveat emptor) and what they read about the product claims (caveat lector).

Fourth, in many cases DTC genetic tests create "needs" based on fears and false hopes. While a mutation may have some meaning in the context of a person's lifestyle, past history, or family health, the range of reliable interpretation and uncertainty associated with the consequences of having those mutations can be quite large. These tests circumvent genetic counselors who can advise people about whether they need such a test. Without the help of a trained genetic counselor, DTC genetic tests may induce severe psychological stress.

Finally, consumers cannot be certain about what happens to the information collected by genetic testing companies or whether that information can come back to haunt them. For example, if consumers who engage in DTC genetic testing are ever involved in litigation—say in a disability claim—they can be cross-examined about the test, however poor its reliability or the likelihood of it yielding a false positive result. ■■■

***Sheldon Krimsky** is Chair of the Board of Directors and a founder of the Council for Responsible Genetics. He is a Professor of Urban and Environmental Policy and Planning at Tufts University.*

# DTC Genetic Testing: A UK Perspective



*By Helen Wallace*

The recent investigation of direct-to-consumer genetic testing companies by the US Government Accountability Office has highlighted a debate about gene test regulation that has been ongoing on both sides of the Atlantic for well over a decade. While the issues raised in the debate have been similar in all countries—focusing on the quality of tests and their interpretation and issues of privacy and discrimination—there are also significant differences.

**Historical context and the current market**

Concerns about DTC genetic testing are not new, although they have drawn the attention of a much wider audience since the highly-publicized launch of 23andMe and DeCode's online gene test services in 2007. As Stuart Hogarth describes in a recent article, the US Task Force on Genetic Testing first warned in 1997 that the rapid pace of commercialization of new genetic tests would one day outstrip any capacity for oversight.[1]

In the UK, a commercially unsuccessful DTC service for cystic fibrosis carrier testing was launched in 1995, leading to the launch of a UK Code of Practice in 1997. This was followed in 2002 by the first attempt to market a panel of genetic tests associated with dietary advice in British high street stores. Sciona, the UK company responsible for the tests, moved to Boulder, Colorado in 2003, citing adverse publicity about its products. Sciona later became the main subject of the first GAO gene test investigation, published in 2006, and ceased to trade in 2009. In the meantime, a succession of other small companies entered the market. In the UK, this included both US and UK companies, marketing via the internet, private medical practices and alternative healthcare providers, all making unsubstantiated or misleading claims.

Beginning in 2003, the UK advisory body, the Human Genetics Commission (HGC), issued two reports raising concerns and proposing voluntary guidelines and additional oversight for DTC genetic tests, but in practice it abandoned the 1997 Code of Practice established by its predecessor committee, arguing that it had only an advisory role, not a regulatory one. The Medicines and Healthcare Regulatory Agency (MHRA), which could have regulated the tests, instead became a member of the Ministerial Medical Technologies Strategy Group, a body co-chaired by government and industry with the aim of promoting a shift to 'early health' in the UK National Health Service (NHS) (including genetic screening and pre-symptomatic treatment) and resisting regulation on the grounds that it would stifle innovation.[2] The net result is that no action has been taken to prevent misleading marketing, either by the authorities or the companies themselves, although the HGC has recently published a further voluntary Code of Practice.

In 2008, a Sunday Times investigation revealed significant discrepancies in genetic risk predictions provided to the journalist by 23andMe, DeCode Genetics and the UK company Genetic Health.[3] This report highlighted that 'genetic information' is actually an interpretation of a DNA sequence that may differ substantially depending on what is tested and the assumptions made. The investigation covered not only tests being marketed DTC via the internet but also misleading claims being made about gene tests sold via doctors in private healthcare clinics.[4] An investigation of DTC genetic tests by the European Technology Assessment Group (ETAG) also raised serious concerns, including poor quality of information, lack of counselling and the testing of children.[5]

The leaders in the gene test market all remain loss-making companies, with a small customer base, and DeCode Genetics has declared bankruptcy.[6] There is anecdotal evidence that, rather than being 'early adopters' in an expanding market, many of their customers may represent a clique of true believers—many working in the industry—plus the professionally curious (ethicists, social scientists, geneticists and journalists), in a sea of more skeptical consumers who remain to be convinced.

Although these companies undoubtedly have customers in the UK and elsewhere in Europe, the market is likely to be a small fraction of the total number of tests sold. More limited marketing efforts than in the U.S., plus less consumer interest and trust in commercially provided health information, may both play a role.

However, there is also evidence that access to customers within the UK National Health Service (NHS), via a public-private partnership would be attractive to many gene testing companies. In particular, companies are interested in accessing biological samples for research purposes and some-including 23andMe-then advocate feeding back unvalidated research results to research participants. There has been an ongoing dispute within the UK regarding the extent to which DNA samples and electronic medical records stored within the NHS might be accessed for such research without consent.[2] Whilst the British public is supportive of medical research, there is little support for abandoning consent or for widespread data-sharing with commercial companies, who are commonly presumed to be more interested in profiteering than in improving health. There are also significant privacy concerns.

**Role of publicly-funded health services**

On the one hand, some policy-makers and advisors have argued that the publicly-funded NHS has a key role to play in driving the supposed genetic revolution in healthcare. From this perspective, the NHS is a unique resource to mine genetic and other healthcare data from the entire UK population and make predictions regarding genetic susceptibility to common diseases. In this vision of the future, DTC genetic tests would form part of a shift to a new system involving greater use of public-private partnerships in the NHS, including a major shift to 'pre-symptomatic' treatment and the possibility of individuals making top-up payments for extra tests and treatments. A major expansion in the drug and healthcare market is expected as a result.[2]

On the other hand, many medical professionals remain skeptical of the value of genetic susceptibility testing and concerned about unregulated DTC testing impacting on taxpayer-funded services by requiring

costly, time-consuming and medically unnecessary follow-up. The adoption of meaningless or misleading tests within the NHS itself is also likely to be resisted by professionals anxious to maintain standards of care as well as by the need to procure cost-effective public services. There is strong support for only introducing tests which make a difference to health outcomes, i.e. which would alter advice or clinical management, or which significantly reduce uncertainty for people at high risk of a familial disorder. Until recently, this view was in conflict with political pressures, particularly in the UK, to move as quickly as possible to whole genome screening of the general population on the grounds that this would stimulate a new biotech economy. However, economic realities and a change in UK government, combined with greater sensitivity to privacy concerns, means that there is now less political enthusiasm for introducing innovations without assessing health outcomes and cost-effectiveness.

Thus, the debate about genetic testing within the EU is focused on protecting and improving existing genetic testing services and preventing DTC tests from undermining either these services or health services more broadly.

The Eurogentest Network of Excellence was funded by the European Commission from 2005 to 2010 with the aim of establishing harmonized, quality genetic testing services in Europe.[7] It has done much to improve laboratory accreditation, survey existing services, involve patients and issue guidelines. A recent Eurogentest book includes extensive discussion of the need to evaluate the clinical validity, utility and cost effectiveness of tests.[8] Whilst opinions on the role of regulation vary, there is consensus on the need for such assessments before new tests are introduced into publicly-funded European health services. At the same time, there is considerable skepticism that tests for genetic susceptibility to common, complex diseases—as opposed to tests for rare disorders or predisposition to rare familial forms of common disorders—will prove of much clinical value.

A recent UK report, based on five expert workshops, whilst recognising enormous progress in genomic science, concluded that: "the importance of genomics for the prediction and prevention of common complex diseases has been overestimated (though there is little doubt about its potential to provide a better understanding of disease mechanisms)."[9] The report found that genomic medicine should focus on diagnostic and cascade testing (screening family members) for single gene disorders and inherited subsets of complex disease, plus the use of specific pharmacogenetic tests to predict and monitor individual drug response. The report also advocated a media strategy "which focuses on 'myth-busting' (rather than creating further hype around genomics) without undermining research."

Eleven professional genetics societies in France have gone further by issuing a statement criticizing the underlying theoretical basis for calculating risk of common diseases based on multiple genetic variants and concluding: "While genome wide studies provide an essential contribution to scientific knowledge of multifactorial diseases, the isolated use of information provided by them lacks any capacity to predict future onset of those diseases. It leads to an erroneous perception of the risk for the individual."[10] This statement reflects increasingly widespread doubts about the scientific basis of this approach to health.[11] It is currently being discussed within the European Society for Human Genetics (ESHG).

Although the value of pharmacogenetic testing in specific circumstances is widely recognized, European medicines regulators and clinicians have also preferred the approach adopted by US medical insurers of waiting for more convincing data from clinical trials before such tests are introduced: for example, in the context of prescribing warfarin.[12]

**Regulation and the single European market**

Healthcare is the responsibility of the individual member states of the European Union, but the EU also creates a free market for the delivery of people, goods and services, which requires the harmonization of quality standards. In theory, standards for genetic tests are covered by the In-vitro Medical Devices Directive (IVDD). However, the IVDD is widely regarded as inadequate, having failed to keep up with developments in science, technology and marketing, and is also interpreted in widely different ways in different member states. One overarching problem is that genetic tests are classified as 'low risk', meaning that the manufacturer has sole responsibility for ensuring its own compliance and awarding itself the 'CE mark' that allows it to trade. In addition, some member states (especially the UK) interpret compliance as requiring only demonstration of analytical validity, not clinical validity. There is also a lack of clarity about whether genetic susceptibility tests are categorised as medical tests under the Directive, and about whether some laboratory-developed tests should be covered by the provisions. These difficulties of interpretation mean that even the self-assessment of health-related genetic tests is lacking in many cases. Thus, regulation is weaker than in the U.S., where only laboratory-based tests, not tests sold as manufactured kits, have escaped FDA oversight. The IVDD is currently undergoing a long process of revision and a current consultation is seeking views on these issues.[13]

In the meantime, legislation covering genetic tests has been introduced at the national level in some countries (although not the UK). For example, Germany has established a commission to evaluate genetic tests and requires counseling to be provided by a suitably qualified medical professional unless the subject has waived the offer of such counseling in writing.

There is considerable skepticism that tests for genetic susceptibility to common, complex diseases will prove of much clinical value.

The situation in Europe is further complicated by the role played by the European Convention on Human Rights and Biomedicine, which was adopted by the Committee of Ministers of the Council of Europe in 1996 and opened for signature in Oviedo, Spain in 1997. The Council of Europe has a wider membership than the EU: thirteen member states of the EU have ratified the Convention, obliging them to ensure that their national legislation conforms to its provisions. An additional Protocol on Genetic Testing, adopted in 2008, has to date been ratified only by Slovenia, but includes important provisions requiring states to ensure that genetic tests meet criteria of scientific and clinical validity, laboratory quality assurance and clinical utility, and that appropriate counselling is provided.[14] Bringing the IVDD into line with the Protocol, as well as with the OECD's Recommendations on Quality Assurance in Molecular Genetic testing, would allow a consistent approach to gene testing across Europe and protect consumers from misleading claims.[15] This approach has been supported by the ESHG in its recent policy on DTC genetic tests.[16]

*Continued on page 24*

***The Broken Clock***
*Continued from page 9*

ferent results is that we don't know how to come up with a single net risk estimator from these variants. We just simply don't know enough at this point.

One of the things that was left hanging after the testimony was an idea that the industry would love to have you believe: "If we could all just get together and agree on standards, it would be fine." No, what would happen is you would all agree on standards and we would see the same risk prediction from all the companies …but that doesn't mean it's correct!

**How much of this do you think could be solved just by having a genetic counselor involved throughout the process?**

That's part of the solution, that the individual who avails themselves of these tests would have a first responder who could give them information. That probably isn't all of it, though. As we learned from the GAO report, people can get told all kinds of different things, especially when there are conflicts of interest that are swaying people to give certain kinds of advice.

If 23andMe would just have a line that people could call, that would go a long way toward alleviating some of my concerns. But it doesn't relieve all of them, because I still think the claims that are being made in their advertising are simply wrong. And that seems to me something that doesn't necessarily require further regulation; it requires the FTC to enforce truth in advertising.

Can I say one other thing that I didn't get a chance to say during my congressional testimony? One of the things you will hear from these companies at first sounds quite convincing. Cholesterol and blood pressure confer only subtle relative risks for heart disease; so they'll say, "High cholesterol only confers a 1.4 relative risk on somebody for a heart attack and this is similar to the degree of risk conferred by genetic variants." And that is true. But what they fail to discuss is that your doctor doesn't check your cholesterol because they are primarily seeking predictive information. Your doctor checks your cholesterol because they can change your cholesterol. They aren't doing it just so they can say, "Oh, you're at increased risk for a heart attack. Have a good day." They're checking it because they can do something about it. And that puts it in an entirely different category than these direct-to-consumer genetic tests. □□■

# False Reassurance

## There is cause for concern in the way DTC companies test for Tay-Sachs disorder

*Statement and comments by Adele Schneider*

***Adele Schneider**, MD, is Director of Clinical Genetics at the Victor Center for Jewish Genetic Diseases at Albert Einstein Healthcare Network in Philadelphia. She was invited to speak at the July FDA hearings on consumer genetic testing (statement printed at right).*

**Are very many direct-to-consumer genetic testing companies trying to tell people whether they are a carrier for Tay-Sachs?**

Many of them are, because the test has been around for a long time, it's a severe disease, and people know about it. It fills all the criteria for an important disease that you would want to screen out of the community. The detection rate, if you do it with enzymes, is good. If you do both the enzyme and DNA test, the detection rate is 98%; but if you only do the DNA, it's 88.6%. The DNA test is looking for specific mutations in the Jewish community, but the Jewish community is not monolithic—the demographics have changed, so you can't just test the DNA.

**And I assume none of these genetic testing companies have an option to include the enzyme test?**

The ones that are direct-to-consumer do not, because they're using saliva and they would need a blood sample.

**I haven't seen the results that they provide, but how do the companies only using saliva samples frame the results?**

They say in the report that if you are negative, your risk is reduced—they're careful about that. If you're a carrier, they tell you that. What I'm concerned about is them saying your risk is reduced for Tay-Sachs when it may not be, because they didn't do the proper test.

With enzyme and DNA testing, you're going to pick up 98% of the carriers. There's that 2% residual risk, at which point your risk is so significantly reduced that you pretty much ignore it. If your residual risk is 25%, it means that one out of four people who was told that their risk is reduced in fact doesn't have a reduced risk. So it's important for people to understand, and to get counseling.

It's like if you had an X-ray and a beautician read it. You're not dealing with the people qualified to tell you about it—you're dealing with business people. If you look at the staffing of many of these direct-to-consumer labs, their lab directors are not resident lab directors and are often in other parts of the country. There is usually a PhD geneticist somewhere around, and the rest are business people.

**And there's the concern about conflict of interest …**

Oh, there are a lot of conflicts of interest. All of these companies have people out there who have good reputations, speaking on their behalf, who are on their payroll. To the person on the street, it looks great when a Harvard guy or a Yale guy says, "This is the bee's knees, we really love this test, it found out that we were carriers." That's great, but does this person really understand what they are saying? And how many bucks are they being paid to say it?

**You mentioned in your FDA statement that you too often have been on the other side of calls from people who ordered genetic testing without seeking counseling. Can you think of any examples that stick out to you?**

There was a woman who called us one afternoon and said, "My doctor did my cholesterol and breast cancer gene testing and I'm positive. What do I do?" They had just said, "Let's get your cholesterol, and let's just get your breast cancer gene while we're about it." No counseling. This is a woman whose life is turned upside down, and there's no one to explain it to her.

This happens all the time. Every geneticist has had to deal with something like that. And then we get the flipside: "My doctor didn't look at my results and told me they were fine." And they weren't fine.

**You've had cases where the doctors did not even look at the results?**

Yes. Babies get born with recessive diseases now and then where the mother was screened, the doctor told her she was fine, and when we go back and look, the results were positive. And the doctor says, "You know, I'm so busy—they're usually normal, so I assumed they would be normal."

**Is it a matter of it being difficult for doctors to interpret?**

It's a matter of the doctor not being thorough. That's why genetic counseling is so much better, because genetic counselors are thorough beyond words.

**And they know exactly what they're looking for.**

Exactly. And anybody who gets their screening done with a genetic counselor is going to know that the counselor double and triple checks things.

**Are you finding that more people are going to genetic counselors?**

A little bit. In obstetric practices it's becoming somewhat more common, but still most doctors don't really know about genetic counseling, and in places where you don't have large medical centers, often there are cities that do not have a genetic counselor. Tulsa, Oklahoma doesn't have one, though they're hiring one soon. There's a geneticist who could do it, but it's not the same as living in Philadelphia or Boston where there are hundreds of genetic counselors. ■■■

Adele Schneider, from a statement made at public meeting on oversight of laboratory developed tests, Sponsored by FDA, July 19-20, 2010:

Too often I have been on the other end of phone calls from a patient whose primary care provider ordered genetic testing without providing genetic counseling and have had to "pick up the pieces" under emergent conditions explaining to a distressed person what their test results might mean. I am concerned that companies offering direct-to-consumer testing are not necessarily obligated to obtain informed consent from customers or to include an appropriately trained medical professional in the testing process. As a result individuals who are tested may not understand the test results, may take no action when one would be beneficial and fail to take steps to prevent a problem. This might be a missed opportunity to provide good preventive care if the interaction bypasses the person's medical providers.

Some DTC companies test for the BRCA 1 and 2 mutations that occur at greater frequency in the Ashkenazi Jewish population, without counseling or adequate/meaningful informed consent. It is also possible for a minor to order testing from these online companies. Since the first principle of medical care is to "do no harm," these practices would seem to be counter to the medical model of helping patients and not doing anything that might cause unnecessary distress or harm.

Laboratories offering DTC testing may expose the public to harm in several ways. First, the failure to provide adequate guidance in test selection and proper counseling about the benefits and limitations of test results may lead to lack of recommended medical care or unnecessary medical care that would have been avoided if genetic counseling was part of the process. Test results provided by DTC companies are often not offered in a format that the average individual can understand as was noted in an article in the May 2010 issue of Genetics in Medicine. Many do not provide a health professional to explain the results. Regulation is needed to ensure that the tests are reliable and clearly explained and results provided with the help of a medical professional.

Second, there are few laws that require DTC companies to protect the privacy or confidentiality of consumer information, and some companies require consumers to consent to the research use of their samples as a condition of testing. When IRBs approve a study using DNA it has to be clear what is done with the remainder of the sample. Similar consumer protection should be provided by labs offering DNA testing.

Third, the clinical utility of many of the tests on the DTC panels has not been established. Some panels have large numbers of tests with detection rates below 10%. That is not really a useful test but makes for good advertising (as in—"we screen for over 100 disorders") but this is not "truth in advertising" and is misleading the public. I would ask that regulatory agencies and perhaps the national medical organizations clarify what detection rate constitutes a valid test, so tests in these panels actually provide useful information for the person tested. Finally, DTC test companies fail to disclose clear conflicts of interest—such as the use of paid advisors as spokespeople without disclosing their financial relationships to the company on the website.

As the medical director of a Jewish genetic disease screening program I have a specific concern relating to Tay-Sachs disease. Since the Hex A enzyme assay became available in the 1970's over 1 million people have been screened for TS disease and the incidence of the disease in the Ashkenazi Jewish community has fallen by 90%. The optimal screen for TSD is an enzyme assay with the DNA test and this has a 98% sensitivity. The enzyme assay has to be done on blood. The DTC companies are testing for TSD with DNA only (using saliva), looking at a small number of mutations that are known to be present in a homogenous Ashkenazi Jewish population. With intermarriage and adoption, the AJ gene pool is no longer homogeneous and in a recent study we published in the American Journal of Medical Genetics, we showed that if you omit the enzyme assay you will miss 11.4% of AJ carriers who do not have one of the common AJ TSD gene mutations.

My fear is that members of the public, believing that they are obtaining good medical care, will be tested by one of these DTC panels and will be falsely reassured that they are not TSD carriers when in fact their carrier status has been missed because HexA enzyme was not included in the assay. I fear that in the next year we will see an increase in births of babies with TSD to people who tried to get proper screening but instead were deceived by a DTC company that failed to disclose that the TSD screening it provided was inadequate to rule out TSD carrier status.

# In Their Words: 23andMe

## with Anne Wojcicki and Ashley Gould

*23andMe is a personal genomics company based in Mountain View, Cal.* ***Anne Wojcicki*** *is co-founder of the company and* ***Ashley Gould*** *is 23andMe General Counsel.*

**Direct-to-consumer genetic testing has received a lot of government and media attention recently. Are you satisfied with how they have portrayed the industry and the technology?**

We believe that ultimately the attention is useful in that we expect the industry to evolve and improve on the basis of constructive feedback. We think there is a good deal of misunderstanding of the technology we use and our scientific processes. We have been working and will continue to work to set the record straight in this regard.

**The recent GAO report on DTC testing was highly critical of the industry and recorded some eyebrow-raising conversations between fictional customers and representatives from genetic testing companies, including 23andMe, and found a number of accuracy problems. How do you respond to the report's accusations?**

The "eyebrow-raising" conversations were not in fact related to 23andMe, but other companies in the DTC space. We suggest that anyone looking for the facts read our blog following the GAO report and congressional hearing. As our blog explains, we do not agree with the accuracy accusations. Our processes have always been transparent, and the bases for our risk estimates are no exception to this transparency.

**In the wake of the GAO report, what new FDA regulations are you preparing for? How would you like to see FDA handle regulation of the DTC testing industry?**

We are currently working closely with the FDA and will provide updates as new developments arise.

**Do you believe consumers can generally interpret their DNA test results without talking to a genetic counselor or doctor?**

Our data indicates that consumers are quite capable of this, yet we are a data-driven company and there are ongoing independent studies assessing this question. When these studies are published the resulting data, and data that is continually collected, should provide additional insight into this question. Our goal is for customers to understand what there is to know about their DNA; in this regard, as you may know, in June of this year we launched the ability for our customers to contact independent genetic counselors informed about our service. We look forward to learning from published studies and incorporating any changes that will improve customers' understanding.

**Why doesn't 23andMe include consultation with a genetic counselor as part of the 'Health Edition' DNA testing service?**

We believe an individual has the right to decide if they would like to interact with a genetic counselor. As previously noted, in June we announced a partnership with Informed Medical Decisions, Inc., a national network of genetic counselors.

**How much clinical utility can really be gleaned from results regarding health concerns with highly significant environmental components, such as heart disease?**

The answer depends on the report—as we note that some reports have higher environmental components than others. Knowledge about genetics and its impact on health is constantly evolving. We work to make this point very well understood in different ways, from our agreement with our customers noting risks and considerations in obtaining our service (See Section 5 of our TOS which is presented to each customer and is on every page of our website), to our online genetics videos. Contributing to the knowledge and understanding of the meaning of genetics through our research was a large part of the reason 23andMe was founded. Despite the ongoing understanding of many aspects of our DNA, there are many well founded and well accepted associations with published correlations to health conditions. Our objective is to present our customers with what science can tell them about their DNA and provide digestible context for that information.

**What safeguards does 23andMe have in place to prevent surreptitious testing?**

The saliva collection device used by 23andMe requires a sizeable sample that can take anywhere from 5 to 20 minutes to collect. 23andMe also requires that each customer agree to specific representations, including that the saliva provided is their own. To date, we have never received a complaint or logged a concern about surreptitious testing. ■■■

# Genetic Counselors: Don't Get Tested Without One

## An interview with Elizabeth Kearney, President of the National Society of Genetic Counselors

**Is there a brief definition that you give people when they ask "what is a genetic counselor?"**

If I'm meeting somebody and they ask me what genetic counselors do, I tell them that genetic counselors work with families or individuals who are either at risk for or have a genetic condition, we take their family and medical histories, and we help assess what their chances are for that condition; we go over whether there are tests available and what is good and bad about that testing; and if there is a diagnosis, we explain what it means and connect them with the support that they need, whether it be medical professionals or a support group.

**Are there certain scenarios when you would tell someone not to get a test?**

If someone doesn't have a history that would predispose them to a condition, we really want to understand their reasoning for getting a test for it. Part of it is a matter of spending our health care dollars wisely. Obviously if someone wants to pay for it out of pocket, understanding that this information may not be as impactful as they were hoping, that's one thing. The more typical scenario genetic counselors deal with is when we are billing insurance, so we have to be careful to consider whether someone really has a risk that justifies using health care dollars to assess it.

The second part of it is the psychosocial element. If somebody really wants to have testing done, we want to ask them some questions about why, and why now? I had a patient who wanted to be tested for Huntington's disease six months before she was getting married. It was totally medically appropriate—her father had been affected—but she was six months from getting married, so I asked her: Why now? Would this change anything for you? And after that discussion, she thought about it and decided that now wasn't the time.

**A good deal of attention has been drawn to direct-to-consumer genetic testing recently on Capitol Hill, from the GAO report to FDA and congressional hearings. Do you think the attention is steering the conversation in the right direction?**

I think the positive thing that's coming out of all of this is that it's engaging people. I believe that more consumers and more physicians are aware of the availability of genetic testing, and I hope that they are learning about some of the possible benefits and drawbacks of obtaining genetic information. So I see that as a positive outcome. Genetic counselors work primarily with patients and obviously we care a lot about people having access to genetic information, so a real benefit that has come out of this for patients is that they probably are more aware and might be more likely to inquire about genetic testing to help them.

From the NSGC's perspective, I think it is most important for people to know that they have the opportunity to meet with a genetic counselor before they have testing, to determine if testing is right for them, to find an appropriate test, and to have support interpreting the results if they decide to have testing. So the benefit of all this is that it started a conversation, and I see that as fundamentally a good thing.

**Do you find that many customers of direct-to-consumer genetic tests are coming to genetic counselors first?**

There has definitely been an increase in recent inquiries, but I don't know whether it has been more frequently before or after the test. I certainly know of situations where people have contacted genetic counselors after the fact.

One example is a woman who'd had carrier testing for a number of genetic disorders and was found to be a carrier of Alpha-1 antitrypsin deficiency, a condition which results in early lung problems and basically causes emphysema even if the person is not a smoker. You have to have two copies of the gene in order to be affected, and this individual had only one copy. She had not had any genetic counseling beforehand, and she called the genetic counselor in a panic and thought that she was at risk for the condition.

**So the report wasn't clear about the difference between being a carrier and actually being at risk for the condition?**

Exactly, so she thought that being a carrier would mean she could be affected by those symptoms. It's an example of the value of meeting with a genetic counselor beforehand. A genetic counselor will ask why you want to have the test, go over which tests are right for you, and explain what you can learn and what you won't learn from it. If you still want to go ahead, that's fine, and you already have a relationship with that counselor and can call them up right away and go through the results and not have to go through that period of panic.

**Would you be concerned about a conflict of interest if customers go to a counselor on the DTC testing company's payroll instead of an independent genetic counselor?**

I think it's obvious there's some inherent conflict of interest. That doesn't mean that someone who is a board certified genetic counselor who works for a company cannot provide good care to a patient, but it's important to look at the incentives and how those counselors are evaluated … but I think it's fair to say there is some potential inherent conflict of interest, and patients could avoid all of that if they contact a genetic counselor who is not affiliated with the company.

**Is there a best practice scenario you can point to where genetic counselors are working together with test providers to reach the best outcomes for patients? Is there a model already in place?**

If you look at more classic genetic testing—testing for single gene disorders like cystic fibrosis, sickle cell, and Tay-Sachs disease—a lot of laboratories work with the requirement of having a provider involved and they have close relationships with genetic centers. For example, academically based labs will often have a genetic counselor based in the lab, primarily to get in touch with a provider if something doesn't look right. For instance, there may be a question as to whether the patient is really ordering the right test, and those genetic counselors

who work in the lab might get back in touch with whoever ordered the test and advise them about whether this is the test that they really want. In this model the genetic counselor is in a sense the gatekeeper for the appropriateness of testing.

**Is there any particular trait or set of traits being routinely oversold in terms of utility for patients? Put differently, is there a test or area of testing where you think a genetic counselor is most needed?**

One of the areas of concern is when someone is ordering the wrong test. One problem is simply that ordering the wrong test is a waste of money; but the more significant concern might be around not integrating information from genetic testing with medical and family history.

I would use diabetes as an example. Suppose somebody has a family history of diabetes and they are wondering about their own risk of developing diabetes, and they have a test result that shows they have decreased risk over the general population—but they have a family history of diabetes, and maybe it's even a woman who has had gestational diabetes during a pregnancy. A genetic counselor would look at all of that and integrate it, and tell that patient that while the test result was reassuring, most likely the genetic factors responsible for the diabetes in your family are not those that were tested in this particular test. That's an example of when a test is misinterpreted as being sufficient information on its own, when you really want to integrate it with family and medical history.

**Has the profession of genetic counseling changed as more direct-to-consumer genetic tests have been introduced?**

Actually, I don't think that the practice of genetic counseling has changed that dramatically. The model for how we care for a patient is the same whether we're testing for single gene disorders or whether a patient is coming to a genetic counselor with a report from a direct-to-consumer lab. I also think that it's a pretty small percentage of the population that's pursuing direct-to-consumer testing without the provider involved. So I really don't think that, as of yet, it has influenced the practice of genetic counseling very much. □□■

# DTC Genetic Testing: Consumer Privacy Concerns

*By Jeremy Gruber*

DNA provides a rich digital source of medical information; as a result it has great scientific value. But it is also ripe for data sharing and has significant commercial value as well.

Purchasing genetic testing services in an online commercial marketplace raises significant privacy concerns, as consumers may turn over their DNA and other personally identifiable information to companies without a clear understanding of the privacy risks and without clear guidance as to their legal and regulatory rights in this area.

There are currently no clear guidelines on the ownership of genetic material and the information derived from it, nor are there clear guidelines with respect to the protection of customer privacy by the direct-to-consumer genetic testing industry. Indeed, consent forms and privacy policies vary widely within the industry and without standards can be unclear and often subject to change.

There are three specific areas where significant privacy concerns arise:

**1) Controls on DNA Submitted by Customers**

Current practices related to ensuring that customers are submitting only their own DNA are insufficient. At present, commercial personal genomics companies do require customers to confirm they have the legal authority to submit DNA samples, yet such statements are not clearly and conspicuously posted but rather often hidden within larger privacy and consent documents which are often visible to the consumer only after the registration process has begun. Moreover, they do not explicitly warn customers of the possible issues raised by submitting another individual's DNA for analysis.

Considering how simple surreptitious collection of individual DNA can be, it is not hard to imagine how political, social and personal motivations could compel the improper submission of DNA samples. This is a particular concern since most of these companies allow for an individual to purchase multiple testing kits per order. Yet, few controls are offered beyond such statements to ensure that customers are actually complying with this requirement. No offer of proof is requested beyond the statement. This could easily be included as part of the sample submission process.

**2) Security of Genetic Information**

Customers are often not limited to providing a DNA sample as part of their participation in the personal genomics marketplace. They are also offered a variety of surveys, blogs and other tools where they can provide personally identifiable information. Whenever identifiable DNA samples are collected and stored, there is a high risk that violations of genetic privacy will follow. The methodology by which this information is secured is essential, yet without standards and oversight we still know very little beyond the assurances of the industry as to what specific controls are used.

Moreover, the privacy policies of DTC companies are not subject to the health privacy regulations issued pursuant to the Heath Insurance Portability and Accountability Act (HIPAA) and there few state and federal privacy laws that apply. It is essential that personal information should be protected by security safeguards appropriate to the sensitivity of the information.

Safeguards should include physical, technical and administrative measures to protect information and biological samples from unauthorized access, use, disclosure, alteration or destruction.

Almost all DTC company privacy policies make statements about security safeguards, though the degree of detail varies substantially. Mistakes and other breaches of security are not uncommon. Just this summer, the DTC company 23andMe accidentally sent data of up to 96 individuals to the wrong customers.[1]

There is also no transparency as to the degree to which personally identifiable health information is de-identified. As the ability to share, store, and aggregate genomic data progresses, the capability of keeping this data anonymous becomes increasingly important. Because an individual's genetic information is so personal and specific, it is vital to protect it from any unwarranted access or use. There have been several instances where de-identified data has been re-identified and personal information linked back to its owner. One such study[2] achieved re-identification of DNA data and established identifiable linkages in 33-100% of surveyed cases, which focused on eight gene-based diseases. The researchers used anonymized DNA database entries, and related the information to publicly available health information despite the fact that the database did not include any explicit identifiers, such as name, address, social security number, or any other personal information. Because not all de-identification techniques adequately anonymize data, it is important that the process employed by the industry is robust, scalable, transparent and shown to provably prevent the identification of customer information.

**3) Third Party Disclosure of Customer Data**

One significant unresolved issue relating to the DTC industry is exactly who owns the customer's data. Most DTC companies do not explicitly address this issue in their privacy policies. If the DNA sample and other information submitted by the customer are the property of the company, the company is free to sell or otherwise transfer that information to a third party.

Many DTC companies have adopted this approach as part of their business model without sufficiently explaining to customers the extent to which this may occur, what type of data is being transferred and the potential negative consequences. For example 23andMe has partnerships with the Swiss firm Mondobiotech and the Parkinson's Institute and Navigenics is conducting studies with the Mayo Clinic and Scripps Institute.

Moreover how such information is to be treated upon sale of a company or if a company enters bankruptcy proceedings, particularly when the entities potentially acquiring such information have significantly less strict privacy standards, is less than clear and is certainly not expressed to customers.

Most DTC companies do not ask for specific consent for these purposes. Some companies are moving in the right direction. 23andMe has recently begun asking for specific consent for participation in published research. However, they note that even by refusing to participate,

> we may still use your Genetic and/or Self-Reported Information for R&D purposes…which may include disclosure…to third-party non-profit and/or commercial research partners who will not publish that information in a peer reviewed scientific journal.[3]

The degree to which these types of partnerships and others have proliferated within the industry is still largely unclear. What is clear is that it is essential that affirmative written consent must be required before DTC companies can use any customer generated genetic information in this way.

There is currently very little guidance on how consumers can protect their privacy. For example, the US Federal Trade Commission gives the following advice to consumers who are considering DTC genetic tests:

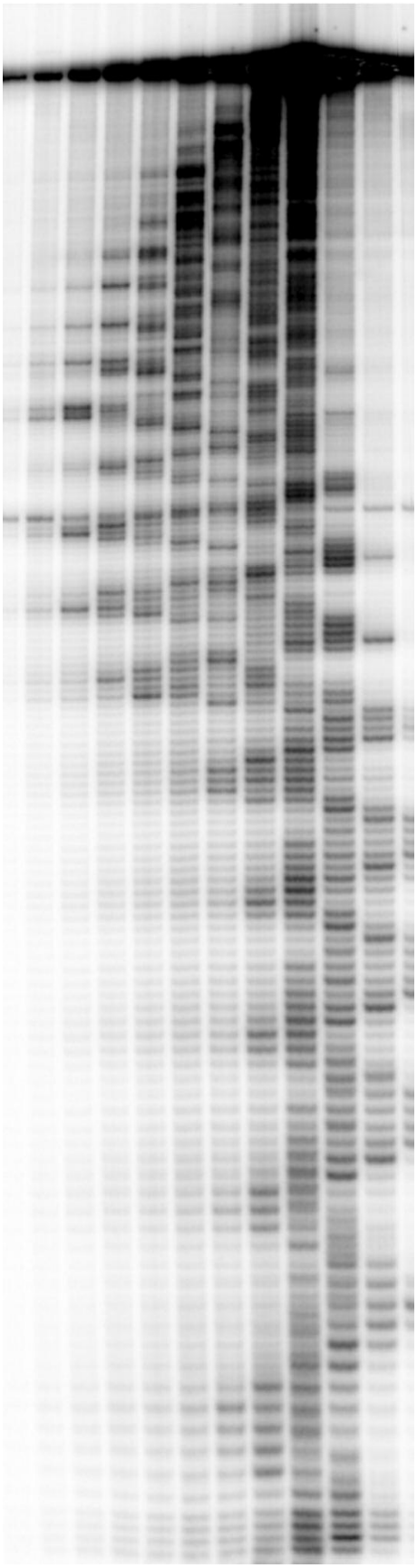
> Protect your privacy. At-home test companies may post patient test results online. If the website is not secure, your information may be seen by others. Before you do business with any company online, check the privacy policy to see how they may use your personal information, and whether they share customer information with marketers.[4]

Such advisories are hardly satisfactory to ensure consumer privacy is protected.

It is essential that Congress, the Food and Drug Administration, the Federal Trade Commission, and the Centers for Disease Control all work together to help set privacy standards for the direct-to-consumer genetic testing industry and ensure that all issues regarding industry practice are adequately supervised to ensure compliance. ■■■

*This essay is a modified excerpt from testimony offered at the FDA public meeting on "Oversight of Laboratory Developed Tests 'Direct to Consumer Genetic Testing'" in Silver Springs, Maryland on July 20, 2010.*

***Jeremy Gruber**, JD, is the President of the Council for Responsible Genetics.*



# *The $1,000 Genome*: Caveat Emptor

*By Andrew D. Thibedeau*

We will dispense with the starry heavens and so convert to right use from uselessness that natural indwelling intelligence of the soul.[1]
-Plato, *The Republic*

In his forthcoming book, *The $1,000 Genome*, Kevin Davies casts an uncritical gaze at corporate biotechnology, offering little more than a protracted puff piece on speculative technology. He populates his narrative with the leading lights of that industry, celebrating their innovation and avarice in equal measure. Davies's dramatis personæ—reading like a Who's Who of the biotech industry—is almost exclusively comprised of "life sciences" entrepreneurs and their pet firms. Throughout, his haphazard style elides these market participants with the market discourses each produces, promoting the view that they are all one in the same feature in the production of a "personalized" biomedical future. The future of biomedicine has its enemies, however, and first among them are pseudojournalistic partisans who think their love of biotech capital translates into some kind of knowledge. The $1,000 Genome is much like the "personal" biotechnology industry it chronicles, ultimately looking to capture market share in the name of health and market genetic misinformation in the name of truth.

Davies offers the telling story of Jonathan Rothberg, founder of CuraGen Corp., 454 Life Sciences Corp., Ion Torrent Systems, Inc., Clarifi Corporation, and RainDance Technologies Inc. Rothberg—DNA sequencing pioneer and architect of hundred-million dollar profits—is also the father of a child born with tuberous sclerosis, a hereditary condition in which the brain, skin, and major organs become covered with small tumors.[2] Faced with his daughter's illness, Rothberg's "typically audacious" response was to found the Rothberg Institute for Childhood Diseases, "a non-profit organization dedicated to finding a cure for children suffering from Tuberous Sclerosis."[3]

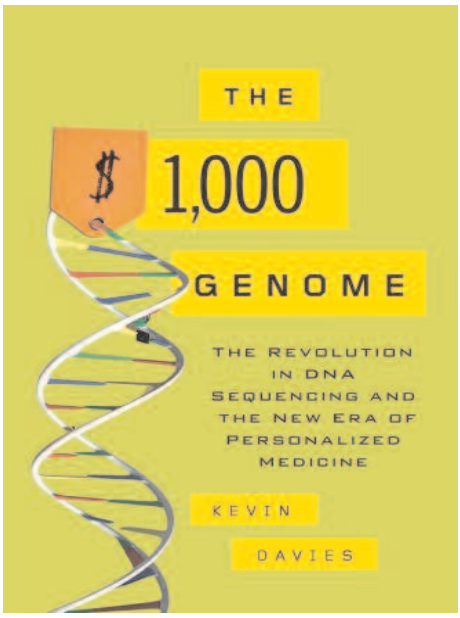
In addition to his foundation, at his eleven-acre ocean-side home Rothberg also commissioned the mammoth Stonehenge-like sculpture entitled the "Circle of Life." He built it "for [his] kids," Davies writes, "as if it was [sic] entirely routine to import 700 tons of Norwegian granite and sculpt, polish, and arranged it according to celestial factors on one's own oceanfront property."[4] The giant stones are arrayed according to the birthdays of Rothberg's children as well as other astrological "events." "Think of the Circle of Life as a complex watch," its creator Darrell Petit is quoted in Stone World magazine, which "demonstrates that these structures can function as powerful astrological instruments with substantial predictive abilities."[5]

Rothberg's sculpture is like Rothberg's foundation, which is like any of Rothberg's biotechnology companies—all of which are like Rothberg himself: a perfectionist "biotech impresario" who nevertheless reminds Davies of "a boy trapped in a man's body."[6] Whether intentional or not, this insight captures the doubly-capricious ideology that unites Rothberg and his biotechnology businesses and that is metaphorically expressed in his sculpture the "Circle of Life," namely: that DNA can be thought of as "a complex watch" that, upon the expenditure of adequate capital, can "function as a powerful ... instrument with substantial predictive abilities." In other words, human traits and diseases can be analytically reduced to genetic causes. Davies shares this misleading misperception. "[M]ost human disease ... such as heart disease, diabetes, obesity, and cancer," he writes, are "caused primarily by common DNA variants."[7] Naïve at best, this essentialist view of genetics—a kind of genetic astrology—is the tacit assumption lying behind the characters and companies Davies chronicles.

The future of biomedicine has its enemies, and first among them are pseudojournalistic partisans who think their love of biotech capital translates into some kind of knowledge.

"Genetics isn't just a science," Barbra Katz Rothman argues in her book Genetic Maps and Human Imaginations, "[i]t's a way of thinking, an ideology." "We're coming to see life through a 'prism of heritability,'" she writes, "a 'discourse of gene action,' a genetics frame."[8] It is in this "genetic frame"—with promises of horoscopes spun from strands of DNA—that direct-to-consumer (DTC) genetic firms like 23andMe, Navigenics, and deCODEme deploy genetic astrology as a marketing strategy. "When you go to a bar," Davies quotes Linda Avery, co-founder of 23andMe, "the pickup line could change from, 'What's your sign?' to 'What's your haplogroup?'"[9] Kari Stefansson, deCODEme co-founder and Executive Chairman, describes his company as providing "a service where people . . . are coming to us to learn more about themselves."[10] Of the two men behind Navigenics, Dietrich Stephan dedicated fifteen years of research "predicated on the belief that all human disease had a genetic component"[11] and David Agus "believes it will come down to ... gene X is up, gene Y is down."[12] "Know your CODE," Stefansson is quoted at the apex of his sales pitch: "[l]earn more about your ancestry, traits, and health risks."[13] In short: know yourself by knowing your genes.

As stone monuments and tabloid back-pages the world over attest, predicting the future is a seductive business. Moreover, the discourse situating those predictions in DNA is not new. In 1995 Dorothy Nelkin and M. Susan Lindee observed that "images and narratives of the gene in popular culture reflect and convey . . . genetic essentialism."[14] Then, as now, "genetic essentialism" represents a mode of biological reductionism resting on the fallacy that "reduces the self to a molecular entity, equating human beings, in all their social, historical, and moral complexity, with their genes."[15] In other words, "[g]enetic essentialism is the idea that the essence, the nature of a human being is defined by its genes."[16] The mass appeal of genetics, Nelkin and Lindee conclude, "lies partly in its image as a predictive science: a means to uncover predispositions."[17] It is precisely




**The $1,000 Genome: The Revolution in DNA Sequencing and the New Era of Personalized Medicine**
by Kevin Davies. Free Press (2010)

this image of genetics as horoscope that DTC corporations purposefully invoke. But in the search for meaningful predispositions, it becomes increasingly easy to collapse the distinction between statistical correlation and factual cause. The subtle but significant difference between the two is lost on Davies, who spends most of The $1,000 Genome playing interlocutor to corporate biotech—rarely if ever interposing critical distance between biotechnology marketing and his reader. One can only conclude that Davies's enterprise is not, as he claims, to document a genomic revolution, but instead to sell a particular narrative in which venture-capital biotech is savior to client and shareholder alike. The ease with which Davies allows essentialist discourses to dominate his subject matter belies his unambiguous predisposition toward industrial biotechnology, calling into question the merit of his entire work.

Davies asserts that the DTC genetics is about patient "empowerment" and "personalized" healthcare. Navigenics, deCODEme, and 23andMe all offer services that their financiers believe "will become part and parcel of twenty-first-century medicine."[18] Accordingly, a 2010 report of the Government Accountability Office found that the websites of these three corporations "contain a variation of the statement that their tests help consumers and their physicians detect disease risks."[19] In a series of protracted vignettes profiling various players on the biotech stage, Davies invokes genetic astrology in all but name as he recounts the services they offer. 23andMe "provide[s] the deepest dive into the genome," he writes, "presenting information on ancestry, traits ... carrier status for Mendelian disorders, and risks for common diseases."[20] "The basic goal," he quotes Stefansson, "was always to use genetics for preventative health care."[21] Navigenics also "focuses squarely on risk assessment for actionable, common medical conditions such as heart disease, cancer, and diabetes."[22] Davies's text documents yet denies how these firms traffic in medical prognostication.

Hence Davies reproduces the proclamations of DTC biotech, decrying any suggestion that their services are medical or predictive. "From the inception of the consumer-genomics industry," Davies assures his reader, "every piece of marketing collateral, Web site real estate, and legal document bearing a company logo stressed and reaffirmed the strictly educational, nondiagnostic nature of their genome-scanning services."[23] It is impossible to interpret this claim—by the DTC industry or by Davies—as anything but disingenuous. After conducting a clandestine investigation of fifteen DTC genetics firms, the GAO found that ten of them "engaged in some form of fraudulent, deceptive, or otherwise questionable marketing practices."[24] What sort of fraudulent practices? "Advertising for genetic testing on TV, in print, on the radio or via the internet," a recent British study concluded, "provide[s] simplistic explanations of genetics and exploit[s] existing anxieties and widespread misinformation about genetic determinism."[25] A paper published in 2008 in the Journal of Business Ethics identifies the same trend: "there has been a tendency on the part of many diagnostic companies to downplay the probabilistic nature of genetic information and to use deterministic language in their physician- and patient-oriented advertising and promotional campaigns."[26] Davies writes in the same determinist language, conflating cause and correlation without regard for the myths he thereby endorses.

And what of the medical utility of DTC genetics? "The test results we received," the GAO investigation concludes, "are misleading and of little or no practical use to consumers."[27] 23andMe Director Ester Dyson, quoted by Davies, agrees: "[i]t's fascinating. But medically useful? No."[28] One wonders what role useless genetic tests have to play in "the new era of personalized medicine." Remaining silent on this question, Davies maintains a legitimating façade of "personal" genetic knowledge; this is a paradox on the face of his text that irretrievably indicts its ultimate claim to legitimacy. In the same way, heeding well their legal counsel, every DTC marketing campaign is flush with fine print ceaselessly working to negate any claims made elsewhere. The DTC market that Davies describes is a contradiction: "[t]he explicit health claims and the small print disclaimers cannot both be true."[29] Again, Davies fails to register what other observers see plainly. Occupying a nether region between naïveté and complicity, Davies accepts DTC's talking points sans reflection, parroting them back at his reader. As such, his book is more akin to biotech puffery than explanatory prose.

The (pre)dominance of deterministic rhetoric in the public discourse surrounding genetic testing is worrying not simply because it is bad science. According to a 2010 study, "[p]ublic understanding of details pertinent to genetic testing generally appears to be weak."[30] In this context, appeals to genetic essentialism in DTC marketing must be understood as intentionally misleading. "Like its competitors, " Davies nevertheless claims, "Navigenics ... makes a good effort to communicate the dual role of genetics and environment ... in shaping individual risk of complex diseases."[31] If this were so, it is certainly not reflected in their advertising, where disease "is portrayed as a unitary phenomenon, something that can be resolved by genetic testing and appropriate medical treatment." Thus a return to Jonathan Rothberg's seaside Stonehenge: the center of gravity for both DTC genetics and *The $1,000 Genome* is the myth of the genetic horoscope. Fine print aside, Navigenics and its competitors are "exploiting a climate of genetic determinism and public anxiety to sell speculative technologies."[32] *The $1,000 Genome*'s myopic stance toward these aspects of its subject signals its ultimate failing. In the end, Davies is less concerned with the revolution of "personalized" medicine than he is with the astrological edifice constructed by those financial interests invested in the predictions of that revolution. ■■■

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# A View From the Inside

## Establishing and maintaining a Biosafety Level Three laboratory

*By Nancy Connell*

In the March/April 2010 issue of *GeneWatch*, Beth Willis of Frederick Maryland stated:

> We also know that high containment biodefense lab proliferation is a national policy problem that has to be addressed in Washington.

As the director of a Biosafety Level Three (BSL3) laboratory at a large academic medical center, I thought it might be useful to *GeneWatch* readers to hear some comments from the inside of one of those laboratories. I will describe our efforts to build a safe and collaborative environment in our containment laboratory, and the impact of increased regulations following the anthrax attacks and PATRIOT Act on our procedures.

Our respiratory infectious agent program was begun in 1999 with the construction of new Biosafety Level three containment space within existing laboratory space in our research building as part of the Center for Emerging and Re-emerging Pathogens (CERP) at UMDNJ-NJMS. The laboratory was designed for the study of the causative agents of tuberculosis and HIV-AIDS. The initial application was submitted before the year 2001, which was followed by unprecedented regulatory oversight. However, we had formed close ties and collaborations with the Emergency Response and Biosafety personnel at the university during the process of designing the lab.

Soon after opening in 1999, we received additional funding for work with bacterial and viral agents, some of which were considered potential biological weapons agents; such microbes are now termed "Select Agents." Consulting with our colleagues in safety and security, we instituted new procedures in the form of training programs and safety procedures. For example, we felt it was essential for safety reasons that two people be present at all times during work with dangerous pathogens such as Bacillus anthracis (anthrax) and Yersinia pestis (plague): we recognized that people can be tired, be distracted, make mistakes, and that having two people carrying out the experiments would serve as a internal check for errors and to prevent accidents. This "two-person rule" was later required to ensure security of the reagents, discussed below.

During the months immediately following the 2001 anthrax attacks, the scientific community saw a gradual increase in regulations and oversight for Select Agent work, mostly in the form of increased security and access control. The impact of these new rules was discussed in Dias et al, 2010[1], and also reviewed by Andrew Thibedeau in the March/April 2010 issue of GeneWatch. Further debate of the impact and efficacy of these regulations is outside the scope of this article. Note however that there are few differences in procedures between working with TB and anthrax in our laboratory.

Traditional lab safety and bloodborne pathogen training, mandated by the Occupational Safety and Health Association (OSHA), is provided to all laboratory workers. OSHA has identified within its array of standards for general industry those with specific application to laboratories, such as chemical safety/"right-to-know", hazardous waste and regulated medical waste handling, fire safety, personal protective equipment, and emergency procedures. The formats for trainings in many institutions are slides and lectures with a short quiz, but we wanted a more hands-on approach for our BSL3 safety training.

However, following the model of emergency responder training methods and with the involvement of our first responder colleagues, in 2002 we began to develop a series of exercises to test the efficacy of our training modules. These exercises range from tabletop format to full-scale scenario exercises involving representatives of departments and agencies at the level of the institution, the city, the county, and the State. We have as many as 100 people attending our exercises, both players and observers.

Experienced first responders are well seasoned in carrying out training exercises. We found that scientists and laboratory workers were unfamiliar with the format and purpose of an emergency response training exercise. The scientists felt anxious about the possibility of error. Many scientists are perfectionists and they struggled with the stress

of thinking that everything had to go exactly right. They were often defensive and sometimes critical of their colleagues. They were also unfamiliar with the incident command system procedures that drive emergency response to incidents such as those that might be experienced at our laboratories. So we learned to prepare them beforehand for how these exercises work, pointing out that they are designed to instruct us in what we do not yet know, and to discover what might not work. Our BSL3 staff are now required to complete awareness level incident command training (FEMA course ICS 100). The exercises are followed by long discussions that analyze in detail where the problems lie and what the solutions might be. After the first full-scale exercise, a real emergency occurred. A pressurized water pipe burst due to extremely cold temperatures on a Saturday evening, resulting in at least 6 inches of water in the BSL3 and throughout the CEP. The previous exercises helped staff to respond calmly to this crisis, without panic or confusion, allowing them effectively to carry out emergency procedures in this off-hours emergency. Similarly, we experienced a regional blackout, and the response to this crisis also went fairly smoothly.

We hold frequent "refresher" trainings to review protocols and introduce modifications that might be required by changes in CDC regulations. For our twice-yearly reviews, we have changed the format of the quizzes, created games and asked participants to lead discussions. All members of the laboratories, from staff workers to the Prin-

cipal Investigators, are involved. We held a hands-on demonstration for aerosol creation using fluorescent marker dyes so users could analyze their own technique. We have recently instituted an entirely new format: initially and once per year thereafter, the BSL3 manager and institutional biosafety officer will follow and observe each user as s/he carries out a protocol, including entry and exit procedures.

Finally, and perhaps most importantly, we strive to create a supportive atmosphere that leads to a secure and collaborative environment. In a punitive environment, there is the chance that an accident will go unreported; this is a most dangerous situation. It is essential to create an environment where if a mistake is an honest one, people trust that they will not be punished, be restricted from access to their experiments, lose their jobs or worse.

**Security training**

It was in the wake of the World Trade Center attacks and the anthrax letter mailings that security became an enormous issue in academic laboratories such as ours. All workers must comply with the terms of the USA PATRIOT ACT (Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2002) and other legislation (Public Health Security and Bio-terrorism Preparedness and Response Act of 2002). "Personnel reliability", as regulated by this and other legislation, has had an ever-widening effect on the process of science. The early and close relationship between law enforcement and our facility meant that in an operational sense, many security procedures were incorporated into the procedures in our laboratory from the very opening of the program. First and foremost, researchers must now be fingerprinted and submit to a background check by the Department of Justice before handling or accessing select agents. All refrigerators and incubators have locks and pin numbers, with two-person access. Most importantly, there are inventory requirements for Select Agents, so that samples are tracked from seed stocks and working stocks, accounting for every microliter of culture. Lab notebooks are always vital for researchers, but tracking agents and tubes is important to be sure there has not been a theft of an agent. If an inventory status cannot be resolved, and does not match the laboratory notebook, then that incident is treated as a theft, which requires reporting to the FBI and CDC. This type of reporting was new to scientists, and in the beginning there was no guidance as to the best way to record all this data. Inventories can add in a layer of anxiety in order to be sure that things are logged properly, since the repercussions can be severe. Now, several years after the introduction of inventory requirements, guidance has been given as to the preferred method of data recording, and many laboratories, including ours, have developed a system to reduce the time burden of this regulation. Note that this kind of oversight and tracking is modeling on the tracking of radiological material and its utility for replicating organisms has been questioned by many scientists (Casadevall and Imperiale, 2010).

**Ethics, dual use and responsible conduct**

Massive increases in funding over the past decade— over $50 billion between 2001 and 2009—have been directed towards civilian biodefense (Franco, 2009). An enormous amount of federal effort and capacity is now directed towards select agent research in particular and infectious disease research in general. The global proliferation of BSL3 containment laboratories has sparked safety and security concerns and is reflected in increased oversight of laboratory operations, as discussed above. Additionally, the concept of dual use research is receiving increasing attention around the world (Selgelid, 2009). Dual use research of concern is research that is conceived for the purpose of healing or helping human kind but which can be used in the development of dangerous technologies for malevolent purposes. Our research program focuses on bacterial Select Agents, and the experiments we perform with these organisms are intrinsically dual use, in view of their potential—and in some cases, historical—development as bioweapons.

Over the past fifteen years at our institution, we have developed a number of avenues for introducing the concept of dual use research to the university community (Connell and McCluskey, 2010). The first is through the federally mandated "Responsible Conduct of Research" education of National Institute of Health (NIH)-sponsored trainees . The second route is through the Institutional Biosafety Committee, originally mandated by the NIH in the 1970's to review experiments involving recombinant DNA and since expanded to include infectious agents. The third avenue is the laboratory safety training mandated by the Occupational Safety and Health Association for all laboratory workers. The fourth route is through a robust biodefense "certificate" academic curriculum, open to all students at the university regardless of program (PhD, MS, MD, nursing, etc). We are in the process of designing and implementing a fifth approach using an institutionally based "train-the-trainer" system of intercalating dual use awareness into individual academic departments through periodic seminars and discussion groups. Of course, there is some apprehension in the scientific and security communities that identifying inherently or potentially dangerous research will have the negative effect of directing attention to possible "recipes." In other words, increasing awareness of potential dangers might lead, paradoxically, to the actual creation of such perils. These and other debates in the field of dual use ethics (Rappert, 2007; Segelid, 2009) are beyond the scope of this discussion, but most would agree that scientific inquiry and its dissemination must be allowed to continue.

**Conclusion**

The transition from basic microbiology laboratory to biocontainment laboratory is a complex process of learning new regulations, increased training and responsibility, and incorporation of new practices and procedures. Maintaining a containment laboratory is an ongoing process: regulations change and security requirements differ among funding agencies, but most importantly, we recognize continuous monitoring in emergency response and safety training in an emotionally safe environment. As the biomedical research enterprise becomes increasingly complex with regard to policy and regulation, the Biosafety Officer plays a pivotal role, coordinating the needs of the workers, the requirements of the regulatory agencies and the needs of the institution. In turn, the cooperation of the PI with the biosafety officer is also vital; the PI can set the atmosphere for the laboratory and can also foster in post doctoral fellows, technicians, and students an appreciation of the delicate balance of conducting good scientific experiments in as safely as possible. This balance between the scientists and the regulatory personnel is instrumental in developing a successful and safe Select Agent research program. ■■■

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*A UK Perspective*
*Continued from page 13*

**Conclusions**

In most European countries, including the UK, there is a total lack of regulation of DTC genetic tests, although a small number of countries have imposed national restrictions. Although the market for DTC tests is currently small, there is significant concern that misleading tests will impact adversely on patients and also divert healthcare resources from those in need to providing unnecessary follow-up tests and treatments to the 'worried well.'

In contrast to the USA, political enthusiasm for transforming health services to enable the genetic 'prediction and prevention' of common diseases appears to be waning within Europe (although it has not been abandoned). This is due to a more realistic view of costs, privacy implications, and serious doubts about whether the claimed health benefits would actually be delivered. Thus, economic realities and professional concerns are likely to restrict the adoption of genetic susceptibility tests by publicly-funded healthcare services for the foreseeable future.

Whether DTC genetic tests will be adequately regulated by revising Europe's IVD Directive is currently uncertain. However, an extensive market in unregulated tests in Europe looks increasingly unlikely as health services seek evidence of the validity and usefulness of tests before their introduction. Responsible companies may find their best hope of survival lies in focusing on developing and refining tests which actually improve health outcomes for members of the public. This requires a very different business model from that being followed by the current market-leaders. Instead of treating whole genome sequencing as inevitable, it implies a focus on specific tests for use in high-risk families or prior to prescribing certain drugs. To succeed in the European market, it seems likely that in the future companies will need to demonstrate that their products provide benefits to health. In turn, this implies revisiting the underlying basis of long-standing but unsubstantiated claims about the genetic 'prediction and prevention' of common diseases in the general population.[17] ■■■

***Helen Wallace** is Director of GeneWatch UK, a research and public interest group that investigates the environmental and social impacts of genetic science and technologies.*

Topic update

# DNA Profiling Is Tested in California

## It worked to track one Los Angeles killer, but familial DNA searching is still a highly flawed tool

*By CRG Staff*

For almost thirty years, the Los Angeles Police Department was stumped by the killings of mostly poor black women by a serial killer known as the "Grim Sleeper." Then police used DNA taken from one of the crime scenes and cross-referenced it with the DNA of convicted criminals utilizing a controversial new technique called familial DNA searching. Familial DNA searching operates off the principle that when there is a partial (not exact) DNA database match to a crime scene sample there is a likelihood that the sample comes from someone related to the perpetrator.

They hit with a close match, a man who had been convicted of a felony weapons charge. The convicted man's father then came under suspicion. DNA was lifted from a slice of pizza from the father. When that was found to match evidence from the killings, Lonnie David Franklin Jr., 57, was arrested and charged with 10 counts of murder and one count of attempted murder.

Familial DNA searches target potentially millions of individuals that police know are innocent and therefore have raised serious civil rights and privacy concerns. In particular, the technique has raised concerns that DNA testing will fall disproportionately on the shoulders of black and Latino populations and lead to even greater racial disparities in the criminal justice system, which arrests and imprisons vastly more African-American and Latino men than other groups (who are therefore more likely to appear in DNA databases). Considering that familial DNA searches have very low success rates—it had been tried unsuccessfully several times before in California—the practice appears disproportionately out of touch with democratic values.

The irony, here, is that Lonnie David Franklin Jr. is a convicted felon and should have been in the database himself to begin with and arrested as a result. The fact that he wasn't is indicative of the already overtaxed and underfunded forensic systems. Without restraints—there are currently no statutory limitations on familial DNA searches—there are no guarantees that any safeguards used in this particular case will be replicated among the many police departments that will use this technique once it is legitimized.

Singular cases make bad precedent. As the collection of DNA by law enforcement officials has greatly expanded over the last decade, we need a much larger national discussion before sanctioning familial DNA searches for widespread use. ■■■

# Fishy Business at the FDA

## Genetically engineered salmon carries a boatload of problems

*By Eric Hoffman*

The U.S. Food and Drug Administration announced on August 25 that it is considering approval of a genetically engineered (GE) salmon for human consumption, which would make it the first GE animal to enter the food supply. FDA only gave the public a few weeks to respond to this announcement and to analyze their data even though they have had this application on their desks for over ten years. This data revealed that these modified fish pose a variety of threats.

The GE salmon, created by a corporation called AquaBounty, is engineered to grow twice as quickly as its non-engineered counterparts—and that's cause for concern. If the GE salmon escapes from aquaculture farms where it is raised and enters the open ocean, it could contaminate natural populations with its genes and weaken salmon populations. Of particular concern is the survival of natural Atlantic salmon, which are already listed as endangered. Indeed, research published in a report by the prestigious National Academy of Sciences indicates that a release of just 60 genetically engineered salmon into the wild could lead to the extinction of a natural population of 60,000 salmon in less than 40 fish generations.

AquaBounty claims their fast-growing fish would be contained and will not escape into local waterways. One not need look further than the Asian carp in the Great Lakes to know that even the best containment systems fail. Natural disasters, wear-and-tear and human error can all lead to breaks in AquaBounty's containment systems and escaped genetically engineered salmon in our waterways.

The company also claims that their fish will be sterilized, but even their own data admits that up to 5% of the eggs may remain fertile.[1] AquaBounty claims to have orders for 15 million eggs.[2] That means that right off the bat we may have up to 750 thousand fertile fish that can escape and wreak havoc on the environment. Even more troubling is the fact that AquaBounty will still need fertile males and females to fertilize their genetically engineered eggs.

Human health is a pressing concern as well. One consequence of government approval of the genetically engineered salmon would likely be the use of even more antibiotics in aquaculture, increasing opportunities for drug-resistant bacteria to develop. Farmed salmon are given more antibiotics than any other livestock by weight[3], and the GE salmon could require even more antibiotics, since AquaBounty's fish would be less fit, making them even more susceptible to disease.

In addition, scientists have raised concerns about how physical properties of genetically engineered animals could make them unsafe to eat, but neither AquaBounty nor the federal Food and Drug Administration have made the GE salmon available to independent experts for safety testing. It is irresponsible for the FDA to say these fish are safe to eat without such testing.

AquaBounty's plan for raising these fish was designed with the intent of avoiding U.S. environmental law. They plan on fertilizing the eggs in Prince Edward Island in Canada, shipping them to Panama to be raised and processed, and then shipped back to the U.S. to be eaten. Despite open claims that they will expand their operations to the U.S. and other countries, the FDA is refusing to look at the cumulative harms their commercial operation will have on the environment.

Fortunately, a final decision by the FDA has not been made, and citizens are rising up to pressure the FDA to reject the genetically engineered salmon. 171,645 comments from the public were submitted to the FDA demanding that this fish not be approved for human consumption. In addition, letters signed by over 300 environmental and public health organizations, chefs, restaurants, and tribal communities were submitted telling the FDA to deny approval of the GE salmon.

On September 16, Friends of the Earth, Food and Water Watch, the Center for Food Safety, and Ben and Jerry's organized a demonstration about the salmon in front of the White House. At the demonstration, CEO of Ben & Jerry's, Jostein Solheim, explained why his company is against the GE salmon. Once the door is opened, he explained, the FDA is prepared to approve a number of genetically engineered animals and Ben & Jerry's does not want a genetically engineered dairy cow to be next. In protest, they announced the symbolic renaming of their famous "Phish Food" ice cream to "Something's Fishy" and passed out coupons for free ice cream to rally participants.

And on September 20, the public was allowed to testify before an FDA committee considering the GE salmon application. Friends of the Earth wrote comments to the FDA, which were signed by twenty other organizations in the U.S. and Canada, highlighting the environmental threats posed by approval of this genetically engineered salmon. We called on the FDA to conduct a comprehensive and independent environmental impact review before any decisions on approval are made.

The FDA committee recognized problems in AquaBounty's plans and requested that more studies be conducted before this fish is approved. The company's studies on health safety were poorly designed and their sample sizes, sometimes as low as twelve fish, were way too small to guarantee safety.

Members of the committee also expressed concern that not enough evidence exists to show these fish will be safe if they escape into the environment. The committee's only expert on fisheries, Dr. Gary Thorgaard, called on the FDA to conduct an Environmental Impact Statement—a comprehensive review of all the environmental risks—a sentiment echoed by other members of the Committee. If the FDA takes this call to heart, it will allow time to fully analyze the environmental and health risks instead of trying to rush the process through as the FDA is currently attempting. ■■■

***Eric Hoffman** is Biotechnology Policy Campaigner at Friends of the Earth, an international grassroots environmental network.*

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