Patenting and Personal Genomics: 23andMe Receives its First Patent, and Plenty of Questions

by Dan Vorhaus

Earlier this week 23andMe, the Silicon Valley-based personal genomics company, was awarded its first patent: US Patent Number 8,187,811, entitled "Polymorphisms associated with Parkinson's disease".

23andMe co-founder Anne Wojcicki announced the issuance of the patent via a post on the company's blog late Monday evening, attempting to strike a tenuous balance between her company's oft-championed philosophical devotion to providing individuals with "unfettered access to their genomes" and its desire to commercialize the genomic information so many of those very same individuals have shared, free of charge, with 23andMe. With its new patent, 23andMe also injected itself into the middle of what Wojcicki herself described as the "hot debate" surrounding the patentability of "inventions related to genetics." Wojcicki's announcement appeared to catch more than a few of the company's customers by surprise, sparking concern about the company's intentions on 23andMe's blog, Twitter and elsewhere, along with rapid and pointed commentaries from Stuart Hogarth and Madeleine Ball, among others.

Of the various questions asked of and about 23andMe and its new patent, these may be the three most common: *Where did this patent come from, and why didn't I hear about it before? What does 23andMe's patent cover? How is 23andMe going to use its patent?* Let's take each question in turn.

1. Where did this patent come from, and why didn't I hear about it before? Just over three years ago, 23andMe announced that it was launching its Parkinson's Disease Genetics Initiative in collaboration with The Parkinson's Institute and Clinical Center and The Michael J. Fox Foundation. In the years that followed, the company regularly touted (see, e.g., here, here, here and here) the scientific progress that it was making, frequently crediting its novel research model which leveraged an engaged customer base willing to freely share not only personal genetic information but also the medical and family history, lifestyle, environmental and other phenotypic data so critical to untangling the complex relationship between genes, environment and traits.

Indeed, in a paper published last summer in *PLoS Genetics* in which 23andMe confirmed several existing genetic variants associated with late-onset Parkinson's Disease (PD) susceptibility and identified two new variants, 23andMe's research was newsworthy less for its scientific contributions to the understanding of PD than for its validation of the company's research model. As Chuong B. Do and his 23andMe colleagues wrote, their research:

…illustrates the ability of web-based methods for enrollment and data collection to yield new scientific insights into the etiology of disease, and it demonstrates the power and reliability of self-reported data for studying the genetics of Parkinson's disease.

But for all of the digital ink that 23andMe spilled in the past three years in highlighting both its scientific progress and the broader utility of its web-based research platform, the company maintained a persistent public silence with respect to its concurrent pursuit of intellectual property protection[1] (23andMe's first provisional patent application was filed in late 2009, the same year it launched its PD initiative).

To be clear, it's not as if it was a secret that 23andMe was pursuing a PD-related patent. After all, in keeping with the Constitutional aims underlying the United States patent system, patents and patent applications, and the inventions they purport to describe, are matters of public record. Accordingly, 23andMe's patent application, which was filed November 2010 and published June 2011, had been publicly available for nearly a year before the final patent issued, and had during that time been a topic of discussion at academic conferences, in blog posts and in private industry conversations.

Still, with more than a half million other patent applications published by the PTO in 2011, and most of 23andMe's customers having lives and careers outside of personal genomics, the odds were very good that the vast majority of the company's customers were never going to learn of its patent plans until 23andMe itself made an announcement.

Which brings us to Monday evening and to our second question.

2. What does 23andMe's patent cover? One of the oddest aspects of 23andMe's press release was how vague it was in describing the nature of the company's patent, along with its failure to provide a patent number or, better yet, a copy of or link to the patent itself.[2]

Here's what co-founder Anne Wojcicki wrote instead:

Our patent, "Polymorphisms Related to Parkinson's Disease" is expected to issue on Tuesday, May 29, 2012. This relates to our discovery of a variant in the SGK1 gene that may be protective against Parkinson's disease in individuals who carry the rare risk-associated LRRK2 G2019S mutation.

Saying that the patent "*relates to* our discovery of a variant" (emphasis added) in a Parkinson's disease gene does not give a reader a very good sense at all of the specific invention covered by 23andMe's patent. That requires a review of the patent itself, which is available from both the PTO and the GLR, and in particular the "Claims" section where the invention itself is described.

Claims in 23andMe's Issued Patent. The claims section itself is fairly short but, for our purposes, we can shorten it further by focusing on the four key claims, which read as follows:

1. A method for screening a human subject for susceptibility to Parkinson's Disease (PD), the method comprising: obtaining a nucleic acid sample from the human subject; determining which allele is present in the sample at the polymorphic nucleotide position of SNP rs10513789 (SEQ ID NO: 1); and identifying the human subject as having an increased risk of developing PD if the subject has a T at the polymorphic nucleotide position of rs10513789 (SEQ ID NO: 1).

5. The method of claim 1, further comprising determining which allele is present in the sample at one or more of the polymorphic nucleotide positions selected from the group of SNPs consisting of rs6599389 (SEQ ID NO: 2), rs873785 (SEQ ID NO: 3), rs11248060 (SEQ ID NO: 4), rs6812193 (SEQ ID NO: 5), rs4130047 (SEQ ID NO: 6), rs7451962 (SEQ ID NO: 7) and rs4397141 (SEQ ID NO: 8).

6. A method for generating a prognosis of a human subject's susceptibility to Parkinson's Disease (PD), comprising: obtaining a genomic sample from said human subject; analyzing the genomic sample to determine which allele is present in the sample at the polymorphic nucleotide position of SNP rs10513789 (SEQ ID NO: 1); storing the determined allele of the sample in a database that includes a set of information related to said subject; correlating the determined allele with an association between the alleles of rs10513789 (SEQ ID NO: 1) and susceptibility to PD in the database; generating a prognosis of the subject's susceptibility to PD based on the correlation; and communicating the prognosis of susceptibility to a medical practitioner.

7. The system of claim 6 wherein the set of information related to said subject comprises family medical history, diet, exercise and medical history of said subject.

To put it in slightly simpler terms, 23andMe's patent claims a method of (a) screening human subjects for PD susceptibility based on examining variations at eight separate positions in the human genome[3] and (b) generating a separate prognosis for PD susceptibility developed by considering genetic variation[4] alongside family medical history, diet, exercise and medical history, and then communicating that prognosis to the subject's doctor.

Or, to simplify even further, this is a patent on one particular method of predicting susceptibility to Parkinson's Disease.

The Past and Future of 23andMe's Patent. It is important to note that everything we've said so far describes only the *present state of this single patent* as presently granted to 23andMe. The company has indicated that it will "continue to pursue patents that we believe will eventually benefit us all," but has not publicly expounded upon what, specifically, that might entail.

As for 23andMe's first patent, the patent that was issued earlier this week is substantially narrower than the patent that the company sought 18 months ago, as we can see by comparing the claims section from 23andMe's published patent application (2011/0130337) to that of the issued patent (8,187,811)[5]. In particular, (i) the range of genetic variants covered by the patent has been narrowed, (ii) the claims on primers designed to specifically hybridize to the identified genetic variants have been removed completely and, likewise, (iii) an attempted claim for "a kit for diagnosis or prognosis of PD" based on the identified genetic variants has vanished in its entirety.[6]

Also gone is claim 10 of 23andMe's original application, which was clearly the application's most ambitious claim, and comprised "a method for treating or preventing the development of PD" by "administering to a subject suffering from or identified at risk for PD an agent that modulates expression or activity of a protein" influenced by the one of the identified genetic variants.

The fact that 23andMe's patent application was narrowed so significantly should come as no surprise. Despite persistent claims that the PTO's review process is inadequate to the task, producing questionable and/or overly broad patents (see, e.g., here and here), it does result in the limiting (and even outright rejection) of numerous patent applications.

Likely of particular interest to the PTO in reviewing (and ultimately narrowing) 23andMe's patent application, as co-founder Anne Wojcicki noted in her announcement of the company's own patent, is the ongoing question "of whether innovations related to genetics can be patented," which Wojcicki acknowledged remains a "hot debate as evidenced by recent rulings related to Prometheus and Myriad patents."

As background, this past July, in *Association for Molecular Pathology v. USPTO* (aka the *Myriad* gene patent litigation), the Federal Circuit held unanimously[7] that Myriad Genetics' claims on a method to assess cancer susceptibility by examining genetic variations in the BRCA1 and BRCA2 genes were invalid. The court found that Myriad's claims "recite nothing more than abstract mental steps necessary to compare two different nucleotide sequences" and, therefore, do not constitute patentable subject matter.

Next, in March of this year, the Supreme Court reached a similar conclusion, also unanimously, in its opinion in *Mayo Collaborative Services v. Prometheus Laboratories*, holding that Prometheus Laboratories' claims to methods of administering drugs to treat an autoimmune disease reflected a law of nature and did not constitute a patentable invention. As Justice Breyer put it:

If a law of nature is not patentable, then neither is a process reciting a law of nature, unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself. A patent, for example, could not simply recite a law of nature and then add the instruction "apply the law." Einstein, we assume, could not have patented his famous law by claiming a process consisting of simply telling linear accelerator operators to refer to the law to determine how much energy an amount of mass has produced (or vice versa). Nor could Archimedes have secured a patent for his famous principle of flotation by claiming a process consisting of simply telling boat builders to refer to that principle in order to determine whether an object will float.

Both the *Myriad* and *Prometheus* opinions discussed above were published subsequent to the filing of 23andMe's patent application in November 2010, and there should be little doubt that each played a role in the PTO's review and narrowing of the PD-related claims 23andMe initially sought.

As for the future of 23andMe's current patent, there remains the possibility that its claims will be further limited, or even invalidated entirely, by

way of one or more post-grant challenges to the breadth and validity of those claims. Last September, Congress passed the Leahy-Smith America Invents Act (aka patent reform legislation) and, in the process, revised and expanded the options available to third parties to challenge patents following their issuance by the PTO. With relevant litigation still pending (for example, *Myriad* is currently awaiting additional review at the Federal Circuit level following its remand from the Supreme Court) and the options for would-be challengers of 23andMe's patent bolstered by the recent patent reform legislation, the future of 23andMe's patent is far from secure.

Of course, with the cost of challenging a patent, whether through the PTO or in court, typically starting at six figures and rising rapidly from there, whether any would-be challengers to 23andMe's patent actually emerge depends almost entirely on the answer to our third question.

3. How is 23andMe going to use its patent? Patents are frequently mischaracterized as granting the inventor sole ownership and control of the claimed invention. In fact, patents provide a more limited right to exclude others from making, using or selling that invention. As a practical matter, this means that many patents covering (or arguably covering) many "inventions" are never enforced, with actual and potential infringement of untold patents happening every minute of every hour of every day.

The rubber meets the road when a patent holder — or the assignee, purchaser or licensee of the patent — seeks to prevent what it believes to be an infringing use of the covered invention, which can include suing or threatening to sue the alleged infringer. Inventors profit financially from the patents they awarded primarily in one of two ways: either by (i) exercising their right to exclude others from using the invention (as Myriad Genetics has done in using its patents on breast cancer genes to develop a lucrative diagnostic product) or (ii) sharing that right with others in exchange for a fee (i.e., licensing).

23andMe, while arguably one of the most successful personal genomics companies in terms of consumer uptake and public exposure, is still a business struggling to find its way to profitability. Co-founder and CEO Anne Wojcicki explicitly acknowledged as much in a note sent to customers in early May[8] to clarify yet another change in the company's pricing structure. "We are not profitable yet," Wojcicki wrote, "and we need to continue to develop our business model."

23andMe has been working on achieving profitability for a while now, having raised more than $50 million in investor funding (in addition to the tens of millions contributed by Wojcicki, her husband, Google co-founder Sergey Brin, and others to Parkinson's Disease research with which 23andMe is involved, with some of those dollars flowing back to 23andMe) since the company was founded more than five years ago.

Naturally, then, 23andMe is exploring all available avenues as it seeks to find a sustainable business model that will return, and ideally multiply, the money its investors have handed to it over the past half decade, including pursuing patents on the results of the research it conducts with the assistance of its customers.

Still, the company's patent announcement prompted plenty of questions, in part because of the unmistakable tension in Wojcicki's statement between the company's need to demonstrate a commercially viable business model and its desire to provide the public with affordable, unfettered access to their genomes, at times seeming to vacillate between the two.

"If the follow up work we are now doing with the Scripps Research Institute and the Michael J. Fox Foundation looks promising and moves towards drug development," Wojcicki wrote, "the patent will be important for a biotech or pharmaceutical company to pursue drug development." In the very next sentence, however, Wojcicki emphasized that 23andMe believes "patents should not be used to obstruct research or prevent individuals from knowing what's in their genome. We believe that everyone has a right to know their genomes — their sequence of As, Ts, Cs, and Gs — and should be able to access them should they want to."

A diagnostic patent such as the one issued to 23andMe this week may one day be valuable to a pharmaceutical or biotechnology company, although in all likelihood it would first need to be paired with other, stronger patents more directly applicable to a targeted and commercially protectable diagnostic or therapeutic product. But to the extent that 23andMe's first patent does one day come to represent a commercially valuable asset, as opposed to a scientifically important discovery or invention (depending on your point of view), its value is most likely to rest with its ability to help the party controlling the patent (whether 23andMe or a future pharmaceutical or biotechnology acquirer) prevent others from using the patent invention, in this case a method for predicting PD susceptibility.[9]

That unavoidable tension helped to spur a flurry of concerned comments in response to 23andMe's patent announcement, including the following:[10]

- *Why were we not explicitly told that 23andMe would be pursuing patents on research involving its customers?* [Holly Dunsworth]

23andMe responded by pointing to sections of its terms of service and research consent document that referenced its "intent to pursue intellectual property rights." The references in those documents to the company's commercial plans are vague and conditional, with the most explicit showing up in Section 5 of the 23andMe consent document, which states that "***if*** 23andMe develops intellectual property and/or commercializes products or services, directly or indirectly, based on the results of this study, you will not receive any compensation." (emphasis added)

- *How does a patent on a method of determining susceptibility to Parkinson's Disease (i.e., a diagnostic patent) drive the development of a therapy?* [Stuart Hogarth]

In response, 23andMe reiterated Wojcicki's original comment that "if our continued research on SGK1 offers promise, the patent may be crucial for a pharmaceutical company to take the next step and begin drug development," which is arguably not much of a response. As mentioned above, the likelihood of the patent as issued being "crucial" to the development of a PD therapy seems slender indeed, but recall that claim 10 of 23andMe's original patent application, which was explicitly therapeutic in nature, was not allowed by the PTO.

- *If 23andMe's core beliefs include an individual's right to unfettered access to his or her own genetic data, why hasn't the company publicly committed to using and/or licensing its patent only in accordance with those beliefs?* [E.g., Madeleine Ball, Stuart Hogarth, Dave Mackey and Carl Lumma]

In response, 23andMe reiterated its general philosophy regarding genetic access and patents, but stopped well short of publicly imposing restrictions on how it will use or permit others (including its sought after pharmaceutical or biotechnology partners) to use its patents. As Madeleine Ball notes, prominent technology developers, including Red Hat and Twitter have public policies limiting their enforcement of certain patents. In addition, fellow personal genomics company Navigenics has long maintained a written policy promising to license on a non-exclusive, non-discriminatory basis any gene patents it may acquire (although Navigenics' own policy appears to explicitly exclude diagnostic patents of the type issued to 23andMe).

In addition to the important questions above, here is one more:

- *Why has 23andMe not been more aggressive in trying to engage its customer base as a partner in its for-profit endeavors?*

Rather than continuing the struggle to strike the elusive balance between encouraging individuals to freely give of their genomic and phenotypic data in the name of scientific progress and urging investors to open their wallets wide on the promise of future corporate profits, why not seek to align the two goals by finding a way for 23andMe's customers to share more directly in the company's success. As one example, last spring in the journal *Science*, Mitchell *et al.* proposed a novel approach to genomic biobanking based on the trade secret model. After interviewing biobank volunteers, the authors concluded that many healthy participants already understand their participation (contributing genetic information, medical records and other data, answering surveys and questionnaires, etc.) in terms of an exchange, and some in explicitly financial terms. 23andMe could seek to invest their customers and research participants directly in the company's ongoing success by promising to share a (likely small) portion of the financial proceeds it realized from research and/or commercial partnerships built upon customer-provided data.

While even a nominal sharing of corporate profits might be the most direct way to ease the tension between soliciting already-paying customers to provide additional data from which 23andMe seeks to profit, as Mitchell *et al*. note, "the trade-secret model does not require that an exchange take the form of money." In addition to sharing data with its participants and involving them in the identification of research targets, two things Mitchell and his colleagues suggest and 23andMe has already embraced, the company could take other steps to more clearly align its own interests with those of its customers, including joining the growing movement to promote expanded access to scientific research. Rather than embracing its scorpion nature and erecting walls around its data, it could embrace openness instead, and commit not only to publishing its own research in an open access format but to requiring its commercial partners to do the same as a condition to their receiving access to data supplied by 23andMe's customers.

Taking a step back, it is hardly surprising that 23andMe appears to be unsure, at this point in time, as to how exactly it intends to use its newly issued patent. Given the continuing shifts in the company's business model and the company's uncertainty as to what value, if any, outside parties will place on the patent (or 23andMe's future patents) now or ever, 23andMe has a clear interest in keeping its options open. It is also not surprising that the company is proud of earning its first patent, which represents an important and validating milestone for a young company.

What *is* surprising is that 23andMe appears to lack a coordinated plan for positioning its patent — a relatively pedestrian diagnostic method patent that, if it ever becomes valuable enough to be challenged, might not survive the challenge — as clearly of secondary importance to what is, at least in this author's view, unquestionably the company's most valuable asset: an engaged, enthusiastic and growing community of customers-qua-research-participants who, provided 23andMe can keep from alienating too many of them, represent something much more unique, and inventive, than US Patent number 8,187,811.

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[1] 23andMe's first provisional patent application was filed in late 2009, the same year it launched its PD initiative. Provisional patent applications are not examined by the PTO and, unlike patent applications, are not published.

[2] In a comment on its blog post two days later, 23andMe did provide the patent number (8,187,811), although not a direct link.

[3] The first genetic variant — a single nucleotide polymorphism or SNP — is identified in claim 1 by its "rs" or "**r**eference**S**NP" number 10513789; the other seven variants are identified in claim 5.

[4] Only the first of the eight SNPs (rs10513789) was allowed in claim 6 (the method for generating a multi-factorial prognosis and communicating it to a subject's doctor), which represents a narrowing of what 23andMe sought in its original application.

[5] Text in black represents overlap between the application and the issued patent. Text that is blue and underlined represents new text in the issued patent that did not appear in the patent application. Text in red that has been struck through represents text from the patent application that does not appear in the issued patent. And text in green represents text from the patent application that appears in the issued patent but has been moved, with the strikethrough portion representing where that that text appeared in the application and the underlined portion represent where that text appears in the issued patent.

[6] See claims 2 (related to rs11755699), 6-8 (related to primers) and 9 (related to a diagnostic kit) of the 23andMe patent application.

[7] While the opinion was not unanimous in its entirety, on the question of the validity of Myriad's diagnostic method claims the panel held 3-0 that those claims were invalid.

[8] The note was sent to customers on May 8, 2012, ~~although for reasons unknown it has been given a publication date of January 8, 2012 on~~

~~23andMe's corporate blog~~and is available only to customers who are logged in to their accounts. A 23andMe representative clarified that the January 8, 2012 post represents a separate communication by the company, also regarding customer pricing models.

[9] There are other ways in which 23andMe's patent could be valuable, including as a bargaining chip in future discussions to create patent pools or similar resources designed to prevent patents from impeding the development and provision of personalized medicine. However, this is not an angle that 23andMe has emphasized, preferring instead to focus on the potential direct commercial value of its patent.

[10] The questions are presented in a combined, condensed and paraphrased format for clarity, with a link provided to the original comment or post.