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CASE STUDY

A Family Experience of Personal Genomics

Manuel Corpas

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Abstract This article presents a personal journey of a close-knit family from Málaga, Spain who engaged with direct-to-consumer (DTC) genomic testing. Whilst the testing was initiated by one member of the family who works as a genome bioinformatician, none of the remaining family had any prior experience with DTC genetic testing. A thoughtful account, written in the first person, is offered on the experience of genome testing across the various members of the family together with a reflection on how it felt to be a custodian of the 'family genome'. The way the family processed their genome information is explored and the difficulties and challenges that resulted are discussed. Whilst there is a wealth of literature that describes how families communicate information surrounding single genes, there is very little which explores the experience of communication about whole, shared genomes. The experiences described in this paper provide an insight into this new territory.

Keywords Direct-to-consumer genetic testing · Family communication · Genotype · Whole family genotyping · Custodian of genetic information · Consent · Genetic risk

Introduction

Direct-to-consumer (DTC) genomic testing is a new field of commercial activity available to the general public. It is possible for a person to find out certain genetic predispositions pertaining to health, ancestry and sensitivity to medications via one apparently simple test. To carry out a test, all that is needed is a saliva sample, credit card payment and postal instructions. Genotype data is delivered via a password-protected account within a matter of weeks. The genotype interpretation is presented in terms of relative and absolute risk of developing an associated phenotype. An ancestry-finding tool may also calculate the likely geographical origin of the DTC customer. Recipients of such genetic information add their own personal interpretation to what this means for themselves and their family. Without any input from a health professional they are free to make their own choices about how this is internalized and how they may wish to affect health decisions.

M. Corpas (✉)
Cambridge, United Kingdom
e-mail: mc@manuelcorpas.com
URL: http://manuelcorpas.com

My Genotyping

I work at a leading institution for genome research that has exposed me to the latest advances in genomic technology. My research interests include the development of bioinformatics tools and methods for interpretation and visualization of personal genome data. Direct-to-consumer (DTC) genomic testing is now available via a whole host of companies at an affordable price. Given my specific interest in genomics I felt compelled (in my own time) to try out a commercial DTC test; not only did I want to find out more about my own personal genome but I wanted to be able to experiment with the data and, if possible, research the results I got.

Six weeks after sending off a saliva sample I was able to see my results through my personal account on the company website. I viewed the analysis in excited anticipation but soon felt strangely disappointed on a scientific level. Although relieved (and, on reflection, increasingly so) that I was not subject to any major health risk, still the scientist in me was disappointed that I did not seem to have any

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'exciting' findings. These two conflicting reactions to my results really brought home to me that I hadn't thought enough about what I would do if there had been a significant predisposition to a serious, life-threatening condition. Even though there were many explanations made by the provider about the potential to reveal such information, prior to testing I found it difficult to consider potential scenarios when I did not know what would be relevant to me. What motivated me to have this test done was a desire for understanding more of myself and I didn't feel pessimism about what the results might contain. I suspect that this isn't unusual for customers of DTC testing. I wondered whether this is because the sheer volume of potential data that will be explored somehow makes it easier to not feel too attached to any particular type of finding. No health professional was available for me to share experiences of how other people handled this information; I had no pointers from anyone that having contradictory 'emotions' about any of the information was appropriate. I just tackled it in a very rational and scientific manner.

In addition to not having much prior thought about how the data might impact on me, once I did receive my results I felt that the actual data provided could be expanded. I also felt a lack of connection between myself as a person and what I was seeing in the results. I saw a series of illnesses I had never heard of for which I had either a minimal disease risk or a low relative risk. I was frustrated because I was not sure of how this could be of any relevance to me as an individual, possibly because of the volume of information provided. It seemed that the influence these results could have in my normal life would be minimal. I thus decided to gather more information relating to my area of expertise: gene names, OMIM diseases and known regions of variation. I wondered if having somebody to talk it through it would have made me more aware of the value of this information.

There are many free databases and resources online and I wanted to know more by interrogating my genome data using these. I co-developed a new data visualization and integration system (Jimenez et al. 2011). The hope was that this tool would allow me start making discoveries about my own genome by combining my genotype information with online resources looking at known genes, variable regions and cancer mutations. I wondered if this might allow me to feel more connected to the data, by being able to see it within the context of chromosome locations and neighboring genes.

According to my results I have a 28.1% lifetime risk of developing prostate cancer as opposed to a 17.8% average risk in males. This risk is calculated by analyzing the genotypes of 12 SNPs. The SNP marker *rs10993994* shows the greatest risk among the 12 reported markers and is located in 10q11, near the *MSMB* gene. The alleles (TT) have been shown to affect its expression levels, decreasing its cancer suppressor function (Lou et al. 2009). Having no history of prostate cancer in close relatives, I wanted to find more information about this SNP. After doing an extensive analysis, I felt more confident the prostate cancer risk figures I had been given were correct. However, I then became curious as to where my TT genotype had come from and started to wonder if my family would also be interested in being genotyped. I approached my dad, mom, sister and maternal aunt and asked them if they would like to have a whole genome test.

Family Genotyping

We talked within the family about what the genotyping testing would be for. My family understood that the results could provide information about their health; they were excited to find out if they were at risk of any particular conditions. In our culture (we are from Málaga in Spain) it is normal to share personal information within families, therefore it felt very culturally acceptable for us to talk about shared family (genetic) information and no-one was concerned that in effect, we were taking part in a group consent process. It felt natural to us to discuss the issues in this way and whilst I accept that in other cultures a consenting process might be centred more around an individual, for us, this became a group decision and a group project. I also double-checked that my family were happy for me to share their genomic results with them (and thus see them before they did) and also made sure that they were OK for me personally to analyze their genomic data. All consented willingly.

The process of providing my relative's samples to the DTC testing company was not difficult – all I needed to do was add them onto my online account with the DTC testing company, pay the fee and collect the saliva samples from my relatives which I then posted in bulk. I didn't need to undertake any difficult processes to demonstrate that informed consent had indeed been gathered from my relatives. In effect, I became the custodian of the family genotypes. Whilst at the time this felt sensible, as I was the one who had initiated this exercise, I felt a heady level of responsibility.

Having a complete genotype for all my family opened the door to asking important questions about the pattern of inheritance of specific disease-causing SNPs. It also meant that as a consequence, I would have to deal with the more personal and emotional aspects of how my family felt about this information. Such issues are familiar territory to clinical genetic health professionals but they were completely alien to me. What had started out as an interesting academic exercise to explore where my prostate cancer SNPs had come from turned into a poignant exchange between family

members as they put their own values and meaning to their genomic data.

Once the family genotyping was complete, the results were sent directly to our, now shared, online account, accessible to all of us. I did find this somewhat puzzling, given the huge level of care that health professionals and scientists take to protect patient identity and personal information. Fortunately there were no major surprises. On receipt of each report, I excitedly approached my family, eager to share with them details about who had what. Then it hit me – how would I explain any high-risk results to my own mother? As I thought about what words to use, it suddenly occurred to me - would my family remember the issues we discussed before testing? Would they appreciate the fact that I had information about their potential future health? Although I had obtained informed consent from all of my relatives I felt the burden of explaining the results to them. I had no past experience that told me whether they would feel comfortable with knowing their genetic risks or would rather prefer not to know. I felt burdened by the fact that my family might not share the same skepticism about the results as I did; I was concerned that they may not have appreciated that current SNP genotype interpretation methods are still at a primitive stage. I tried to explain this in lay language to them.

The Defining Moments

The most defining moment during this whole process occurred when I received the results back for my aunt whom I knew had previously had two episodes of venous embolism. The genotype results showed that she had a ~30% probability of developing venous thromboembolism (VTE), as opposed to the 9% typical risk. She had been predicted to have a 300% increased risk of developing this pathology based on the delivered genetic test results. Although it has been argued in the literature that 'the validity for predicting VTE has only weak clinical utility' (Segal 2009), test results yielded a higher risk prediction for this condition in a person who had suffered it twice. Seeing VTE ranked as the highest in a long list of conditions made it seem like a significant result. I had also *bought* the test, with an expectation of gaining an increased awareness of our family's health and on some level I realize now that I wanted to see an actual result that meant something. There is also something about buying a service, investing in it, that you want it to deliver in the way the marketing promises (I wanted to 'increase awareness', 'gain insight', 'plan for the future', 'empower prevention', 'prolong health', have a 'healthier future' – all messages received from the various DTC company websites). On reflection, I realize that 30% risk meant that there was a 70% chance of the VTE not occurring but there was something about the way the data was presented that made me feel it had a greater significance than perhaps it did. In addition to this, my aunt had already had a VTE, twice, and so this added more credibility to the result, i.e. I was confronted with a prediction that did make sense clinically. This was double edged – I felt a real intellectual satisfaction that there were some genomic results that offered an explanation to a clinical fact, however, I also grappled with how I would actually communicate this to my relative. Would she be pleased to learn this new information? I realized I didn't know what her existing perceptions were of her VTE, would this new information contradict these? Would it be unsettling?

As the gatekeeper to my family's genomic information it meant that I was not only responsible for what information I told them but also *how* I told them. I am aware of what genetic counseling is and thus knew that there was a great importance in communicating the scientific information in an appropriately sensitive manner. However, I was unsure exactly how to do this. I did not want to do or say anything that could in any way harm any member of my family or affect their feelings: I was uncomfortably aware that I was not trained to do genetic counseling. Whist I felt I was able to talk to them in a scientific manner, distancing myself from the person and focusing on the facts, this approach clearly was not the one I thought was the most appropriate. At that moment of realization, I made the decision to get some advice first from colleagues at my Institute who helped me to think through how I might share the results.

Once I had done some rehearsal on the questions I was going to ask my family members I started by calling my parents first (we live in different countries now and so a phone call was the most natural way to communicate). I told them that I had their results of the genome testing and asked them if they wanted to talk through these; they sounded interested and so I began by reminding them of what the testing had involved. I was acutely aware of the words I used, I did not want to overload them with too much science but at the same time felt a responsibility to warn them again that their results related to many different areas of their health. I found myself oscillating between the roles of 'expert or professional' and son. I wanted to be able to explain the results in a scientific manner but also I wanted to acknowledge that talking about their health had emotional connotations for us all. I also did not want to overload them with technical jargon but I did want to clearly explain what the testing had revealed (together with the limitations of the interpretations). I tried to give them the analogy of a very extensive blood analysis. 'Imagine', I said, 'that you perform an extremely detailed blood analysis, where doctors measure thousands, millions of things. The doctors will find some things that are reassuring to know about your health and other things that you might not like'.

I had no idea how they would react. They knew what the testing was for as we had discussed it extensively before

they provided their samples. However, I wondered if they would feel differently now that I was ready to give them their results. They are a very affable, placid and generally laid back people in their retirement age. My mom decided, after careful consideration, that she did not want to know her results. My father said 'yes' immediately. I told my father that he had an apparently small increased risk of developing prostate cancer, rheumatoid arthritis, restless legs syndrome and decreased risks for developing psoriasis, melanoma, Parkinson's disease. Examining my father's genomes together with mine I could clearly see that there were significant differences. Moreover, these differences suggest that some genomes have a greater number of increased risks for certain diseases than others. We compared our genomes and discovered that at the time he had fewer reported risks than I did. We remarked that based on these results he was genetically 'fitter' than me. The truth is that, as someone who knows him really well, my father looks 10–15 years younger than his real age. Can this be explained from the observed genotype? Probably not, but we all enjoyed lamenting over this.

At this point my mom changed her mind and said that she really wanted to know her results, whatever they might be. I told her that she had an apparently small increased risk of developing coronary heart disease, rheumatoid arthritis, lupus and a reduced risk of developing restless legs syndrome, melanoma, multiple sclerosis and again, when comparing her genome to mine, she had fewer raised risks than me and thus we concluded that her genes were 'fitter'. She instantly said, as a caring mother to her son, that she wished she could swap her genome with mine! I reassured her that I did not blame her for any trait I have inherited. After this initial discussion, we went through the individual results for my parents in greater detail. They were fascinated and appeared to enjoy the comparisons we could make between us. The health related information was received with interest rather than trepidation and we bonded as a family as we discussed our shared traits and who had inherited what from whom.

Next, I phoned my sister and then my aunt. As with my parents I explained again what the testing had been for and asked them to confirm that they wanted to hear their results. My uncle, who is not a blood relative and did not take a genetic test, was also present during the call to my aunt. He was very interested to hear about his wife's results and requested to have a genome test done for himself as well. I talked to my aunt about her genetic VTE risks. She did not show any particular emotion or relief when I mentioned this result to her. I do not think my conversation changed her perceptions of what had caused her to suffer VTE. She has not used this new-found knowledge to alter the clinical management of her condition and her results have not been communicated to her GP. She has also not shown any signs of worry as a result of her DTC test results. Based on my personal knowledge of her, I do not think that a discussion face-to-face would have changed her reaction to her results.

Who has the Fittest Genome?

Something I did not expect was that amongst the members of my family there was a kind of competition about whose genome was 'the best'. Soon it became a game and we joked about it. All members were interested to know how their genome ranked compared to others. As the information gatekeeper I did not feel that revealing whose genome had the fewest number of reported risks was appropriate. I did reveal that dad's report looked quite good but I didn't want to share who had the greatest number of reported risks. I did not think that this information would do any good to anyone and, if anything, it could potentially do more harm than good. However, what struck me was how easy it should be to create a ranking system that balanced out the number of increased versus decreased risks of various conditions. It was blatantly obvious to me, looking collectively at the family genotypes, that some members of the family appeared to be luckier than others in terms of genetic risk. Of course these rankings would change as new findings and knowledge are added to the literature body. Nevertheless, this made me feel uneasy as, taken to a logical extreme, it becomes easy to draw eugenic conclusions about who could be perceived as genetically superior. I suddenly had a sense that whole genome analysis, whether it be via DTC testing or via routine healthcare, certainly makes it easier than ever before to make value judgments about who has a 'fitter' genome.

Researching Family Genotypes

After our family had been genotyped and we discovered that there were no significant health risks nor surprises in the current analysis of the data, I asked them if they would allow me to research our data in more depth and potentially publish my findings. They unanimously consented to this. In fact, my father said 'we would like to share our genetic data with the world' and my mother said 'do whatever you need to do with it so that we can know more about ourselves'. After much deliberation, I have decided that I would use their data for further analyses. We appreciate that on further analysis, new information about our family may be revealed, but as yet, neither myself nor my relatives are particularly concerned about any possible negative finding this may provide us with, we just want to learn new information and we are not frightened of this. What is most important to me is that we have discussed this and made a

collective and supportive decision to embark on uncharted territory.

Having the genomes of my family for research allowed me to start finding things about myself. The first thing I did was to establish how I inherited my TT genotype for the rs10993994 SNP. I learnt that my mom and dad both have CT for the genotype of this SNP. So in fact I was unlucky enough to inherit one T from each parent. My sister was luckier (well, apart from the fact that she does not have a prostate!) the genotype she inherited, CT, is not the one that has been related to the greater health risk. My aunt inherited CC.

Navigation and investigation of my family's genomes would not have happened without the myKaryoView tool. After downloading the data for the other family members, I was able to put them in a format that can be easily queried via myKaryoView. With the consent of all family members involved in this DTC analysis, our experiences are being shared regularly as a series of blog entries (Corpas 2011). For example, we have described that we all come from a very homogeneous genetic background (100% European) and that we have been (as we know) living in the same part of Southern Spain for generations.

Sharing these experiences with the rest of the world is certainly a brave step that takes us all as a family to new horizons. Although up to date the information provided by our DTC reports has not revealed any nasty predictions about our genotypes, we are aware that we may discover findings that were not initially reported. However, we still believe that we can gain a lot more than lose by sharing our experiences with the world. Mining this information has the potential to help us understand our ancestry, our future health and ourselves. As a family, we believe that embracing whatever information may be derived from these experiments will ultimately add value to our lives. Notwithstanding, we also respect other points of view and are aware that other people may not share these thoughts.

Discussion

I expected to have all the information and support I needed from my DTC provider; it was only after I had communicated the results to my family that I started to wonder if the experience should have been different. I began to explore what could have been available had genetic counseling been offered as part of the process. In retrospect I would have appreciated some suggestions on how I might be able to communicate the results to my family. Perhaps by meeting with someone face-to-face or even talking on the telephone could have meant that sharing the predicted genetic risks might have felt less burdensome. Also, the sheer volume of results meant I also did not feel connected to them, i.e. they just did not seem relevant to me. It is possible that I could have developed more of a personal relevance if I had the chance to talk directly with someone who could advise me. Therefore, what I would have done differently, if I was embarking on genotyping again is: 1) explore the communication literature more in depth, 2) look for the advice of a genetic counselor and 3) apply the skills learnt from 1) and 2) to help prepare my family better prior to sample collection.

In terms of recommendations to DTC companies offering genetic testing, I would emphasize the need for some clear pointers or guidance for psychological translation and communication of results to loved ones, especially if there are customers of the same family. Indeed the DTC process appears to be mainly focused on the individual rather than the family. Personally, I did not have any issue with interpreting the results for myself (after all I work as a genome bioinformatician); the problem arose when my family became involved. Having the opportunity to discuss my results with someone who understood genomics but also how to communicate relevant genetic findings would have been enormously valuable.

For DTC customers I would suggest extreme caution in interpreting the results. Many DTC companies stress the fact that the information they provide should not be used for any diagnostic purposes and that many of their results are offered purely for information purposes. I think this is an unrealistic expectation as customers are still confronted with multiple health messages about the value of testing in the pre-test marketing. Some of these messages can be very convincing, even to someone who understands the limitations of the interpretations; it is still very easy to become drawn into believing the information provided. The slick presentation of the data, based on rigorous scientific methods, also provides a sense of credibility. Whatever is being shown is very professional (and thus one feels it must be trusted). Despite the disclaimers, it is easy to feel that the findings truly relate to health and that action can (and should) be taken.

Conclusion

Analyzing my own family's genomes has been a completely different experience than analyzing my own. Assuming the role of custodian of the 'family genome' has been an unexpected and particularly burdensome part of the whole experience, particularly communicating DTC results to my family. I would not expect the experiences reported in this paper to be necessarily conclusive but simply a probing insight into this promising field, still in its infancy. To my mind, instead of heavily regulating services offered by DTC companies, educating the general public about the real capabilities for diagnosis and prediction remains the most useful policy. It is impossible to provide a full explanation

of all potential risks before the analyses are undertaken. However, once results are back, delving into the depths of one's genetic past, present and future can begin. Personal genome analyses are likely to be of greater importance in years to come, not just having a tremendous impact in clinical genetics, but also the way we think about medicine and health care in general.

Working at the cutting edge of genetics and bioinformatics has allowed me to be in a pioneering position, which led me to wanting to improve the understanding of myself and my family utilizing DTC genetic testing. I could experience first hand that it is not the same dealing with one's own genome as it is to that of a loved relative. Even when having full consent to share our experiences, I feel a huge responsibility in the way I handle the results and share them. Based on the health risks reported by the provider there was a general feeling that genotypes could be ranked according to their fitness as calculated by reported risks. Telling my family the results for these analyses was a defining moment for me. For a serious illness such as VTE, I was able to reassure a tested family relative who suffered from this disease that its original cause may have been genetic, not necessarily poor diet choices or lifestyle. More importantly, my family's reactions before and after disclosure of their genetic personal information led to unexpected behavioral patterns, such as being curious about whose genome ranks best in terms of the predicted risks. This opens the door to a new realm of ethical questions that were not so obvious before the appearance of genetic tests for the masses.

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References

Corpas, M. (2011). Manuel Corpas' Blog. from http://manuelcorpas.com

Jimenez, R. C., Salazar, G. A., Gel, B., Dopazo, J., Mulder, N., & Corpas, M. (2011). myKaryoView: A Light-weight Client for Visualization of Personal Genomes. *In Review*.

Lou, H., Yeager, M., Li, H., Bosquet, J. G., Hayes, R. B., Orr, N., & Kraft, P. (2009). Fine mapping and functional analysis of a common variant in MSMB on chromosome 10q11. 2 associated with prostate cancer susceptibility. *Proceedings of the National Academy of Sciences, 106* (19), 7933.

Segal, J. B. (2009). *Outcomes of genetic testing in adults with a history of venous thromboembolism*: Johns Hopkins University. Evidence-based Practice Center. Agency for Healthcare Research Quality, United States.