Published in final edited form as:
Per Med. 2011 November ; 8(6): 651–657. doi:10.2217/pme.11.62.

You never call, you never write: why return of 'omic' results to research participants is both a good idea and a moral imperative

Misha Angrist
Duke University Institute for Genome Sciences & Policy, Durham, NC 27708, USA, Tel.: +1 919 684 2872, misha.angrist@duke.edu

Abstract

The rapid emergence of whole-genome and whole-exome sequencing of research participants has helped to revive the debate about whether genetic and other 'omic' data should be returned to research participants, and if so, which data, under what circumstances and by whom. While partial disclosure of such data has been justified in cases where participants' lives and health are threatened, full disclosure appears to remain beyond the pale for most researchers and bioethicists. I argue that it should not be and that the objections to full disclosure short-sightedly favor near-term considerations over long-term benefits. Return of genomic data to those who want it, even if a difficult undertaking and even if the meaning of the data is unclear, engages participants in science and the research enterprise, and positions them to be better stewards of their own health and wellbeing.

Keywords

biobanking; genomic data; research ethics; return of results

For decades scientists and ethicists have debated the merits and risks of returning and withholding research results from research participants (I will use 'participant' rather than 'subject' throughout). Recently, those questions have become more acute for genetic data in particular as the cost of DNA sequencing continues to nosedive [1]. Research studies of whole genomes and whole exomes of potentially identifiable people are suddenly everywhere [2–9]. Thus, even though a given study might be focusing only on the genetic basis of, say, Crohn's disease or epilepsy, a researcher might find that she has every participant's and every control's complete 'cellular hard drive', that is, his or her full set of protein coding sequences and all the variation therein, at her disposal. What's a principled principal investigator (PI) to do?

In two recent papers, Bredenoord and colleagues provide a useful overview of the various points of view about whether genetic data should be returned to research participants, and if so, which data, under what circumstances and by whom [10,11]. The authors note, as I have [12], that there is no consensus on the issue. They argue forcefully for a middle ground, citing the 'rule of rescue' (i.e., if one sees something life-threatening and actionable in a genome, then one has a moral duty to say something to the person whose genome puts him/

Financial & competing interests disclosure
The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.
No writing assistance was utilized in the production of this manuscript.

her at risk [13]) as a reason to disclose. Conversely, they view full disclosure of whole-genome data with contempt:

> *"No disclosure is unethical because it fails to adhere to the rule of rescue, whereas full disclosure is nonsensical (at best) because it could imply disclosure of all raw sequencing data…"* [10].

In this paper, I will attempt to defend the 'non-sensical'. I will address each of the objections to return of research results. I will argue that return of such results to the participants who give their time, private information and biological materials – to say nothing of their tax dollars – is not only a moral imperative, but is in researchers' own best interests.

Before proceeding, a point of clarification: I advocate full disclosure only to those research participants who actually want to see or have access to their data. The decision to see one's results should be a mutually agreeable transaction and favor individual autonomy; thus, it should be purely opt-in.

Disclosure promotes the therapeutic misconception

While the concept remains somewhat nebulous [14], for my purposes the therapeutic misconception can be defined according to Matutina [15]. It is essentially the notion that, if investigators are not careful, research participants will confuse research with treatment; believe they will receive physical benefits from study participation; and fail to sufficiently acknowledge altruism as a motive for participating in research [15].

This is arguably the most paternalistic and hypocritical objection to return of genetic results. In part, the hypocrisy stems from the relentless selling of the Human Genome Project and its fruits to the public health by the genomic research community over the last two decades. These included holding out 'the prospect that our children's children will never die of cancer' [16], the certitude that 'our fate is in our genes', [17] and the prediction that by 2020, 'the [drugs] we use today will be relegated to the dust bin' [18]. There can be little doubt that this sort of rhetoric was instrumental in the inflation of 'the genomic bubble' [19]. One might further argue that whatever damage was done to public faith in genomic research by these pronouncements has been exacerbated by a recent wave of backpedaling, wherein some of the same high-profile and once wildly optimistic genomicists conceded that these expectations were 'probably unrealistic' [101] and indeed, that 'we have learned nothing from the genome' [20].

Thus, the seeds of the therapeutic misconception were planted and fed at a macrolevel by genome researchers themselves – at least until the limits of the data became incontrovertible. But so too have research participants' 'unrealistic' desires for cures been nurtured at the microlevel. I serve on my university medical center's institutional review board (IRB), the body charged with protecting research participants from harm and, among other things, making clear the critical and oft-cited distinction between research and clinical care [21]. Why then does virtually every single consent form that comes before our IRB include a section titled 'who will be my doctor on this study?' that then provides participants a reassuring answer to this question along the lines of: 'Dr Welby will be your doctor on this study. He will be in contact with your regular doctor and afterwards if necessary'. Is it any wonder that participants conflate research with clinical medicine?

Research participants want to know that someone is looking after them. If they are in a healthcare setting being asked to sign documents fraught with healthcare language related to their phenotype, I'm guessing the chances are pretty good that many of them are not making a meaningful distinction between research and healthcare. Is this a reason to deny them access to data about themselves?

Disclosure rests on a mistaken interpretation of autonomy

A mistaken interpretation of autonomy is simply the idea that if an investigator puts his cards on the table up front – 'there is no *quid pro quo* and you should know that I am not sharing anything with you' – then he is not violating research participants' autonomy.

Insofar as it goes, this is legitimate: 'caveat guinea pig'. But it also reeks of the legalistic, liability-mitigation approach that has come to characterize so many informed consent documents these days [22]. And I would argue that many of the grassroots 'citizen science' research and healthcare initiatives that have sprung up in recent years – including PatientsLikeMe [23,24], DIYbio [25] and the broader e-patient movement [26], among others – are to some degree a reaction against exactly this type of arm's length treatment of research participants.

Of course not every PI behaves with such institutionalized aloofness. A few years ago, the urologist and prostate cancer geneticist William Catalona had a falling out with his employer, Washington University (WashU) in St Louis, MI, USA. He took a job at Northwestern University and asked WashU to transfer the 10,000 research samples he had collected to his new laboratory in Illinois. WashU refused, arguing that the samples belonged to the institution (WashU) and not to the investigator (Catalona). Catalona then asked the 10,000 people from whom the samples had come to write letters to WashU and ask that their samples be transferred to Northwestern. A total of 6000 complied with this request [27–29]. The fact that Catalona ultimately lost his legal battle with WashU and his patients/participants had their samples anonymized against their wishes are, in my view, tragic and shameful outcomes of this story [12], but not relevant to the present discussion. The point is, 6000 people who had already given of their time and tissue went to bat for Catalona and took part in a letter-writing campaign on his (and arguably their own) behalf. Such efforts are less indicative of a formal contractual relationship between business associates or an effort by a researcher to indemnify himself and more illustrative of a true abiding partnership between researcher and research participants.

As Hank Greely has so eloquently pointed out, researchers who proactively engage their participants, respond to their queries and make themselves available, are not merely being nice people, they are keeping these people – taxpaying citizens – invested in the research enterprise [30], financially, intellectually and emotionally. At the risk of underplaying altruistic motivations, one can imagine investigators willing to go this extra mile outcompeting those who are unable and/or unwilling to do so in the marketplace for research participants. The Personal Genome Project (in which I participate) returns all 'omics' data to participants. I suspect this fact has a lot to do with why nearly 14,000 would-be participants have registered at the Personal Genome Project (PGP) website [J Bobe, Pers. Comm.].

Disclosure would pose an untenable burden on research infrastructure

Let's be clear: returning research results is not a trivial exercise. When I was a human genetics graduate student studying Hirschsprung disease in the 1990s, one day our PI announced that we were going to jump through the necessary bureaucratic hoops to become certified in accordance with the USA Clinical Laboratory Improvement Amendments of 1988 (CLIA) [31] so that we could return results to research participants. As the CLIA-certification process dragged on, I was frequently annoyed at the Kafka-esque paperwork and constant disruptions – wasn't earning a PhD hard enough already? Nor did I understand why our research laboratory needed a genetic counselor on staff to talk to the families we were studying – weren't those resources better spent on *Taq* polymerase and plasmid preps?

A total of 15 years later I can see that my advisor, Aravinda Chakravarti, was both compassionate and prescient in ways that I was not. Like William Catalona, he understood that it was not only NIH that buttered his bread, but ordinary people who had had the misfortune of having heritable diseases strike their families and were generous enough to subsidize his research with their biological materials. Yes, my advisor was in the business of generating generalizable knowledge, but he recognized that the people from whose tissues that knowledge derived ought to be, at the very least, kept in the loop, particularly when they were found to carry high-risk alleles and were still in their reproductive years.

In addition, what about CLIA? Aren't there 190,000 CLIA-certified laboratories [32]? Is it really such an insurmountable hurdle? And if it is, perhaps research laboratories can partner with CLIA-certified clinical laboratories in ways that are financially feasible for both. Indeed, my collaborators at Duke involved in whole-exome sequencing have done exactly this (although the larger question of return of genomic results remains the subject of ongoing discussions). We might also encourage IRBs to encourage investigators to make provisions for return of results. This could give participants the option to pursue CLIA-certified testing on their own should highly suspicious alleles arise in incidental findings. Most such alleles will be of unknown significance, but presumably their significance will not be unknown forever.

The inevitable objection to such allowances is that they will lead to 'a raid on the medical commons', [33] further driving up healthcare costs in pursuit of innocuous variants hiding in 'the incidentalome' [34]. Perhaps large-scale return of results will indeed result in this type of scenario. But before slamming the door, shouldn't we make the same demand of the return-of-results nay-sayers that critics of personal genomics so frequently do, that is, 'show me the data' [35–40]? Large-scale results thus far suggest that such a 'raid' on healthcare resources is an unlikely outcome [41,42].

It's also fair to ask whether the interpretation of research results will necessarily be laid at the feet of the medical and research establishments. There is a growing array of public and commercial resources for genome interpretation, many of which are quite sophisticated, yet do not subsist on public largesse [43–46]. To pretend that CLIA-certified testing and analysis are still the only game in town seems a bit naive this late in the day.

Disclosure is not feasible

In this context 'feasibility' encompasses several things. First, research participants vary widely with respect to their knowledge and understanding of genetics and genomics. To educate them about experimental findings may be a trivial task in some cases and a monumental one in others. How can a PI be expected to address such a heterogeneous group? Second, since most whole-genome data are thus far 'meaningless', why bother? And when they do become meaningful – say, next week – does this obligate the PI to educate the participants all over again? Finally, is it fair to expect scientists to be communicators at all? Even if they have the desire to share their findings with the lay world (a big if), don't they lack the training?

What I am calling for is not individualized classroom education of participants, but rather, clear and regular written communication in plain language about general findings and, if possible, each participant's data. Given the uncertain and ephemeral nature of research funding, it is not realistic to expect periodic, individualized updates for an indefinite period akin to direct-to-consumer genomics companies, whose business models can incorporate monthly subscription fees for periodic revision based on new findings in the literature [47]. The object is not to hold research participants' hands *ad infinitum*, but to maximize openness and transparency. This is in part why Steven Brenner's idea of a 'Genome Commons' is so

compelling: it would be open to all and could presumably exist independent of the vagaries of massive public funding [48]. Could a lay person use it? Perhaps not right out of the box, but couldn't such a resource reside along a continuum with other genetic databases meant for public consumption such as a genetic testing registry [49] and SNPedia [12]?

As noted in previous sections, the citizen science community has already begun to take it upon itself to develop tools for parsing genetic data. In the case of participants in the PGP, true understanding of such data is more likely to occur because of the exam that is required as part of the PGP consent process [50]. But even if raw data were returned without any sort of barrier or mediation, I would argue that that would be a more responsible act than return of no data, because it would respect participant autonomy and make it possible for the most relevant party to exert control over her own data.

As for whether genetic and genomic scientists should be in the communication business at all, the question is moot: they already are, even if they don't realize it. We can bemoan the very real public skepticism about evolution [51] and general deficiencies in science literacy [52,53], but those of us who feed at the public trough cannot afford a "failure to communicate" as stated by the character Luke in the film, *Cool Hand Luke*. It is incumbent upon academic institutions to train their researchers to explain their findings. And indeed, many in the genetics community insist that they want to engage the public [54]. Is there ever a more ready-made opportunity than the one in every PI's own backyard, that is, their cohort of research participants?

Disclosure has harmful consequences

Telling someone what alleles they carry, the harmful consequences argument goes, can be psychologically damaging [55]. It can bring unwanted surprises [56]. It can lead to unnecessary procedures [35]. It can jeopardize one's chances of getting insurance [57].

It is not clear to me how broadly applicable these conclusions are; the data tend to be sparse. What is clear is that each is rooted in genetic exceptionalism, that is, the idea that the 'immutable' nature of DNA and its perceived role in shaping human identity warrants a paternalistic, hands-on approach so as to protect people from their own genetic selves, a standard that is not demanded by other types of health information [58,59]. Recent data suggest, however, that even for relatively deterministic susceptibility mutations for late-onset disorders such as hereditary breast cancer and Huntington's disease, disclosure is unlikely to produce long-term negative consequences for those who desire such information [60–62]. Indeed, the work of Green and colleagues has demonstrated that disclosing these sorts of genotype results can sometimes have a salutary effect [63,64]. In addition, the insurance risks, at least thus far, remain almost entirely hypothetical [65,66]. The 2008 US Genetic Information Nondiscrimination Act, which has health insurance and employment protections in place (but also many loopholes), has yet to be tested in court [67].

Strangely, the risks and benefits of the *status quo* are rarely if ever discussed. What, one wonders, are some of the harmful consequences of nondisclosure? A compelling argument can be made that in the USA in the late 1970s, it was obstetricians' failure to refer women over the age of 35 for amniocentesis and the subsequent spate of wrongful birth litigation that prompted the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics to insist that its members offer prenatal diagnosis or referrals to prenatal diagnosis [68,69]. Similar litigation has touched the largely unregulated sperm banking industry [70,71]. Given these precedents, it is not hard to imagine a research participant in a genetic or genomic study conceiving a child with a hereditary disease, the higher risk for which might have been anticipated.

Conclusion: what's different this time?

I often liken the human genome to a savings bond. When we get it, we overpay. Eventually – barring an economic meltdown (or a genomic bubble [19]) – it matures. For most of us, the return on investment will be low. But for a few of us, the return on investment will be substantial. This is exemplified by the recent case of a gravely ill young boy in Wisconsin whose genome sequence revealed an X-linked mutation that made him a candidate for a subsequent cord-blood transplant that probably saved his life [72,73]. If a researcher already has such data in his/her possession, then it is an easy call to return it and act upon it. Indeed, the rule of rescue demands it.

But if the meaning of the data is obscure, as is true for most genomic data, then the rule of rescue does not apply. So why bother returning the information? The answer is because the rule of rescue could apply tomorrow. How many of the more than 100 surgeries the Wisconsin boy endured in infancy [72,73] could have been obviated had his genome sequence been known and readily available and shepherded by those most invested in his health, that is, his parents?

Research data and information found on the internet can be dubious indeed. But how many instances of parents using social networking to improve, if not save their children's lives do we need before we recognize its potential power for positive health outcomes [74]? If it were our loved one's research data, presumably we would want to have it in our possession or otherwise easily accessible and not be in the position of having to track it down and unearth it years later.

The other broad reason researchers should return data to participants in their studies has to do with culture change. One aspect of this is the inexorable and ongoing tide of social media, information sharing and crowd sourcing in Western culture. To exclude human research participants' data from this movement seems unrealistic at best and toxic at worst.

The second cultural aspect is that, for all of the time and hassles involved, returning results is a generous act. It is the right thing to do and as such can be expected to produce a tangible return on investment in the form of participant goodwill and support for research. Recent community-based participatory research in environmental biomonitoring strongly suggests as much [75,76]. Thus, if one cannot return results for his participants, he should do it for himself.

Future perspective

I cannot presume to know whether large-scale return of results will become a reality. At present, one could argue that few near-term incentives exist for researchers to take it upon themselves to return participant data. But the cost of generating DNA sequence data continues to decline, while social networking and its application to science and health continues to explode. Thus, I suspect that initiatives such as PatientsLikeMe, whose membership now exceeds 100,000 [77] and has embedded routine sharing of results in its operations [23,24], are already giving us a glimpse of the future.

Executive summary

- The issue of returning research results has become more acute with the proliferation of human DNA sequencing studies.
- Bredenoord and colleagues outline some of the objections to full disclosure of research results, which I rebut because in my opinion, they are paternalistic, not necessarily in participants' best interests and deny

participants their autonomy, one of the foundational tenets of postwar bioethics.

Disclosure promotes the therapeutic misconception

- One objection to return of results is that it encourages participants to conflate research with healthcare. I argue that this conflation already occurs and that it is disingenuous to pretend otherwise.

Disclosure rests on a mistaken interpretation of autonomy

- This argument holds that if an investigator offers no *quid pro quo*, then participants will not have dashed expectations. I argue that this legalistic approach misses the point; those researchers who do assume the burden of returning results will reap the rewards *vis-à-vis* enrollment.

Disclosure would pose an untenable burden on research infrastructure

- Many investigators are unable and/or unwilling to acquire the necessary clinical credentials to return research results. I argue that the Clinical Laboratory Improvement Amendments of 1988 certification is not an insurmountable hurdle and that return of clinically relevant (or even interesting) results offers residual benefits in the form of abiding relationships with the groups of people one studies.

Disclosure is not feasible

- Scientists can be reluctant to educate or otherwise communicate with the public about their findings. I argue that these are part of the job description. Interacting with the public – especially the public as represented in one's research cohorts – is a moral responsibility and in scientists' own best interests.

Disclosure has harmful consequences

- Critics of the return of research results worry about research data distressing participants; prompting them to take drastic action; and suffering genetic discrimination. I argue that there is little data to suggest that these things are happening in the USA and that to deny research participants access to their own data (if they want it) is to deny them their autonomy.

Acknowledgments

The author thanks Barbara Prainsack, Dan Vorhaus, Daniel MacArthur, Sharon Terry, Paul Wicks, Leila Jamal, Sara Katsanis and Bob Cook-Deegan for helpful discussions; and anonymous reviewers for helpful comments.

The author's work is supported in part by grants from the National Human Genome Research Institute (2P50-HG003391-06) and the Ewing Marion Kauffman Foundation (#20110316).

Bibliography

Papers of special note have been highlighted as:

▪ of interest

▪▪ of considerable interest

1. Glenn TC. Field guide to next-generation DNA sequencers. Mol. Eco. Res. 2011; 11(5):759–769.

2. Tsurusaki Y, Osaka H, Hamanoue H, et al. Rapid detection of a mutation causing X-linked leucoencephalopathy by exome sequencing. J. Med. Genet. 2011; 48(9):606–609. [PubMed: 21415082]
3. Kitzman JO, Mackenzie AP, Adey A, et al. Haplotype-resolved genome sequencing of a Gujarati Indian individual. Nat. Biotech. 2011; 29:59–63.
4. Bolze A, Byun M, McDonald D, et al. Whole-exome-sequencing-based discovery of human FADD deficiency. Am. J. Human Genet. 2010; 87:873–881. [PubMed: 21109225]
5. Bonnefond A, Durand E, Sand O, et al. Molecular diagnosis of neonatal diabetes mellitus using next-generation sequencing of the whole exome. PLoS ONE. 2010; 5:e13630. [PubMed: 21049026]
6. Tong P, Prendergast JG, Lohan AJ, et al. Sequencing and analysis of an Irish human genome. Genome Biol. 2010; 11:R91. [PubMed: 20822512]
7. Rios J, Stein E, Shendure J, Hobbs HH, Cohen JC. Identification by whole-genome resequencing of gene defect responsible for severe hypercholesterolemia. Human Mol. Genet. 2010; 19:4313–4318. [PubMed: 20719861]
8. Sobreira NL, Cirulli ET, Avramopoulos D, et al. Whole-genome sequencing of a single proband together with linkage analysis identifies a Mendelian disease gene. PLoS Genet. 2010; 6:e1000991. [PubMed: 20577567]
9. Pelak K, Shianna KV, Ge D, et al. The characterization of twenty sequenced human genomes. PLoS Genet. 2010; 6(9):e1001111.
10. Bredenoord AL, Kroes HY, Cuppen E, Parker M, van Delden JJ. Disclosure of individual genetic data to research participants: the debate reconsidered. Trends Genet. 2011; 27:41–47. [PubMed: 21190750] ▪ Frame for the discussion of what's at stake when individual genetic research results are returned to individuals.
11. Bredenoord AL, Onland-Moret NC, Van Delden JJ. Feedback of individual genetic results to research participants: in favor of a qualified disclosure policy. Hum. Mut. 2011; 32(8):861–867. [PubMed: 21538687] ▪ Frame for the discussion of what's at stake when individual genetic research results are returned to individuals.
12. Angrist, M. Here is a Human Being: At the Dawn of Personal Genomics (1st Edition). Harper, NY, USA: 2010. p. 341
13. McKie J, Richardson J. The rule of rescue. Soc. Sci. Med. 2003; 56:2407–2419. [PubMed: 12742604]
14. Kim SY, Schrock L, Wilson RM, et al. An approach to evaluating the therapeutic misconception. IRB. 2009; 31:7–14. [PubMed: 19873836]
15. Matutina RE. The concept analysis of therapeutic misconception. Nurse Res. 2010; 17:83–90. [PubMed: 20712237]
16. Lander ES. Genomics: launching a revolution in medicine. J. Law Med. Ethics. 2000; 28 Suppl. 4:3–14. [PubMed: 11244841]
17. Jaroff L. The gene hunt. Time. 1989; 133:62–67. [PubMed: 11659109]
18. Lesko LJ, Zineh I. DNA, drugs and chariots: on a decade of pharmacogenomics at the US FDA. Pharmacogenomics. 2010; 11:507–512. [PubMed: 20350131]
19. Evans JP, Meslin EM, Marteau TM, Caulfield T. Genomics. Deflating the genomic bubble. Science. 2011; 331:861–862. [PubMed: 21330519] ▪▪ Timely critique of 'genohype' and the damage it does to the genomics research enterprise.
20. von Bredow R, Grolle J. Spiegel interview with Craig Venter. Der Spiegel. 2010 July.29 ▪ Transcipt can be accessed at: www.spiegel.de/international/world/0,1518,709174-3,00.html
21. Skolnick BE. Ethical and institutional review board issues. Adv. Neurol. 1998; 76:253–262. [PubMed: 9408484]
22. Fost N, Levine RJ. The dysregulation of human subjects research. JAMA. 2007; 298:2196–2198. [PubMed: 18000206]
23. Wicks P, Vaughan TE, Massagli MP, Heywood J. Accelerated clinical discovery using self-reported patient data collected online and a patient-matching algorithm. Nat. Biotechnol. 2011; 29:411–414. [PubMed: 21516084] ▪▪ A clear and persuasive explication of the PatientsLikeMe model.

24. Wicks P, Massagli M, Frost J, et al. Sharing health data for better outcomes on PatientsLikeMe. J. Med. Internet Res. 2010; 12:e19. [PubMed: 20542858]
25. Cowell M, Bobe J. Straight talk with Mac Cowell and Jason Bobe. Interview by Prashant Nair. Nat. Med. 2009; 15:230–231. [PubMed: 19265814]
26. Orizio G, Schulz P, Gasparotti C, Caimi L, Gelatti U. The world of e-patients: a content analysis of online social networks focusing on diseases. Telemed. J. E Health. 2010; 16(10):1060–1066. [PubMed: 21070131]
27. Roche P. The property/privacy conundrum over human tissue. HEC Forum. 2010; 22(3):197–209. [PubMed: 20737193]
28. Rao R. Genes and spleens: property, contract, or privacy rights in the human body? J. Law Med. Ethics. 2007; 35:371–382. [PubMed: 17714248] ▪▪ Outstanding review of the legal landscape in the USA as it pertains to ownership of human biological materials; now slightly dated.
29. Andrews L. Who owns your body? A patient's perspective on Washington University v. Catalona. J. Law Med. Ethics. 2006; 34:398–407. [PubMed: 16789962]
30. Greely HT. The uneasy ethical and legal underpinnings of large-scale genomic biobanks. Ann. Rev. Gen. Human Gen. 2007; 8:343–364. ▪▪ Compelling arguments against de-identification in genomic biobanks: it does not work; and it impoverishes the data.
31. Rivers PA, Dobalian A, Germinario FA. A review and analysis of the clinical laboratory improvement amendment of 1988: compliance plans and enforcement policy. Health Care Manage. Rev. 2005; 30:93–102. [PubMed: 15923911]
32. Wagner, MM.; Moore, AW.; Aryel, RM. Handbook of Biosurveillance. Wagner, MM.; Moore, AW.; Aryel, RM., editors. Amsterdam, The Netherlands: Academic Press; 2006.
33. McGuire AL, Burke W. An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons. JAMA. 2008; 300:2669–2671. [PubMed: 19066388]
34. Kohane IS, Masys DR, Altman RB. The incidentalome: a threat to genomic medicine. JAMA. 2006; 296:212–215. [PubMed: 16835427] ▪ Possible reasons to be wary of access to one's entire genome.
35. Ransohoff DF, Khoury MJ. Personal genomics: information can be harmful. Eur. J. Clin. Invest. 2010; 40:64–68. [PubMed: 20055897]
36. Evans JP, Burke W, Khoury M. The rules remain the same for genomic medicine: the case against 'reverse genetic exceptionalism'. Genet. Med. 2010; 12:342–343. [PubMed: 20556868]
37. Khoury MJ, Coates RJ, Evans JP. Evidence-based classification of recommendations on use of genomic tests in clinical practice: dealing with insufficient evidence. Genet. Med. 2010; 12:680–683. [PubMed: 20975567]
38. Cho M, Wolpert M. Not yet in sequence: clinical, technical, ethical questions linger over personal genomics. Modern Healthcare. 2010; 40:24. [PubMed: 21137125]
39. European Society of Human Genetics. Statement of the ESHG on direct-to-consumer genetic testing for health-related purposes. Eur. J. Hum. Genet. 2010; 18:1271–1273. [PubMed: 20736974]
40. Henrikson NB, Bowen D, Burke W. Does genomic risk information motivate people to change their behavior? Genome Med. 2009; 1:37. [PubMed: 19341508]
41. Bloss CS, Schork NJ, Topol EJ. Effect of direct-to-consumer genomewide profiling to assess disease risk. N. Engl. J. Med. 2011; 364:524–534. [PubMed: 21226570]
42. Bloss CS, Ornowski L, Silver E, et al. Consumer perceptions of direct-to-consumer personalized genomic risk assessments. Genet. Med. 2010; 12:556–566. [PubMed: 20717041] ▪▪ Users of consumer genomics services do not become anxious about their results, but neither do they change their behavior.
43. Callaway E. The rise of the genome bloggers. Nature. 2010; 468:880–881. [PubMed: 21164454]
44. Dolgin E. Personalized investigation. Nat. Med. 2010; 16:953–955. [PubMed: 20823867]
45. Paananen J, Ciszek R, Wong G. Varietas: a functional variation database portal. Database (Oxford). 2010 baq016.

46. Terry SF, Terry PF. Power to the people: participant ownership of clinical trial data. Sci. Transl. Med. 2011; 3(69) 69cm3. ▪ Thoughtful discussion of how research participants can (and should) maintain control over their data.
47. Delevett P. Google-backed 23andMe hits major milestone: 100,000 users in DNA database. San Jose Mercury News. 2011 June.15
48. Brenner SE. Common sense for our genomes. Nature. 2007; 449:783–784. [PubMed: 17943102] ▪ Issues a much needed *cri de coeur* to the genomics community to begin to tackle interpretation of genes and DNA variants en masse.
49. Field A, Krokosky A, Terry SF. Answering the hard questions: the genetic testing registry and its request for information. Genet. Test. Mol. Biomarkers. 2011; 15:1–2. [PubMed: 21275651]
50. Lunshof JE, Bobe J, Aach J, et al. Personal genomes in progress: from the human genome project to the personal genome project. Dialog. Clin. Neurosci. 2010; 12:47–60. ▪▪ Explication of the ways and means of the Personal Genome Project.
51. Goldston D. The scientist delusion. Nature. 2008; 452:17. [PubMed: 18322497]
52. Calfee R, Bruning R. Science education: neglected. Science. 2010; 329:748. [PubMed: 20705830]
53. Alberts B. Prioritizing science education. Science. 2010; 328:405. [PubMed: 20413460]
54. Mathews DJ, Kalfoglou A, Hudson K. Geneticists' views on science policy formation and public outreach. Am. J. Med. Genet. Part A. 2005; 137:161–169. [PubMed: 16082707] ▪ Geneticists claim to care about public outreach.
55. Bradley AN. Utility and limitations of genetic testing and information. Nurs. Standard. 2005; 20:52–55.
56. Clayton EW. Incidental findings in genetics research using archived DNA. J. Law Med. Ethics. 2008; 36(2):286–291. 212. [PubMed: 18547196]
57. Kass NE, Medley AM, Natowicz MR, et al. Access to health insurance: experiences and attitudes of those with genetic versus non-genetic medical conditions. Am. J. Med. Gen. Part A. 2007; 143:707–717.
58. Bains W. Genetic exceptionalism. Nat. Biotech. 2010; 28:212–213.
59. Kakuk P. Gene concepts and genethics: beyond exceptionalism. Sci. Eng. Ethics. 2008; 14:357–375. [PubMed: 18335320]
60. Decruyenaere M, Evers-Kiebooms G, Cloostermans T, et al. Psychological distress in the 5-year period after predictive testing for Huntington's disease. Eur. J. Hum. Genet. 2003; 11:30–38. [PubMed: 12529703]
61. Schlich-Bakker KJ, ten Kroode HF, Ausems MG. A literature review of the psychological impact of genetic testing on breast cancer patients. Patient Educ. Couns. 2006; 62:13–20. [PubMed: 16242293]
62. Beran TM, Stanton AL, Kwan L, et al. The trajectory of psychological impact in *BRCA1/2* genetic testing: does time heal? Ann. Behav. Med. 2008; 36:107–116. [PubMed: 18787910]
63. Ashida S, Koehly LM, Roberts JS, Chen CA, Hiraki S, Green RC. The role of disease perceptions and results sharing in psychological adaptation after genetic susceptibility testing: the REVEAL Study. Eur. J. Hum. Genet. 2010; 18:1296–1301. [PubMed: 20664629]
64. Green RC, Roberts JS, Cupples LA, et al. Disclosure of *APOE* genotype for risk of Alzheimer's disease. N. Engl. J. Med. 2009; 361:245–254. [PubMed: 19605829] ▪▪ Landmark paper describing what happens when asymptomatic people learn about their genetic risk for late-onset Alzheimer's disease.
65. Pollitz K, Peshkin BN, Bangit E, Lucia K. Genetic discrimination in health insurance: current legal protections and industry practices. Inquiry. 2007; 44:350–368. [PubMed: 18038869]
66. Otlowski M, Barlow-Stewart K, Taylor S, Stranger M, Treloar S. Investigating genetic discrimination in the Australian life insurance sector: the use of genetic test results in underwriting, 1999–2003. J. Law Med. 2007; 14:367–396. [PubMed: 17355100]
67. Terry SF. Genetic information nondiscrimination act insurance protections issued. Genet. Test. Mol. Biomarkers. 2009; 13:709–710. [PubMed: 20001579]
68. Cowan RS. Aspects of the history of prenatal diagnosis. Fetal Diagn. Therapy. 1993; 8 Suppl. 1:10–17.

69. Cowan, RS. Heredity and Hope: The Case for Genetic Screening. MA, USA: Harvard University Press; 2008. p. 292

70. California. Court of Appeal, Second District. Johnson v. Superior Court. Wests Calif. Report. 2000; 95:864–879. [PubMed: 17225339]

71. Grady D. As the use of donor sperm increases, secrecy can be a health hazard. NY Times. 2006 June.6

72. Worthey EA, Mayer AN, Syverson GD, et al. Making a definitive diagnosis: successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease. Genet. Med. 2011; 13:255–262. [PubMed: 21173700]

73. Mayer AN, Dimmock DP, Arca MJ, et al. A timely arrival for genomic medicine. Genet. Med. 2011; 13:195–196. [PubMed: 21169843] ▪▪ Arguably the first use of whole-exome sequencing to guide acute pediatric care. The second paper includes a thoughtful discussion of all of the ancillary issues that were raised by this decision.

74. Kogan DC. How Facebook saved my son's life. Slate. 2011 July.13

75. Adams C, Brown P, Morello-Frosch R, et al. Disentangling the exposure experience: the roles of community context and report-back of environmental exposure data. J. Health Soc. Behav. 2011; 52:180–196. [PubMed: 21673146]

76. Morello-Frosch R, Brody JG, Brown P, Altman RG, Rudel RA, Perez C. Toxic ignorance and right-to-know in biomonitoring results communication: a survey of scientists and study participants. Environ. Health. 2009; 8:6. [PubMed: 19250551]

77. Mansell P. PatientsLikeMe bolsters trial recruitment efforts wi th BBK alliance. Pharma. Times. 2011 June.16

Website

101. US Public Broadcasting Service network. A decade on, human genome research yet to directly affect many patients. www.pbs.org/newshour/bb/science/jan-june10/genome_06-24.html