

Genomics, inconvenient truths, and accountability

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Recently, genetics and genomics have moved beyond the research lab and outside of the clinic into the daily life of modern citizens, where they have become consumer products. Direct-to-consumer (DTC) marketed genetic tests are probably the best known example, the ‘products’ being actually lab services (Prainsack 2013). DNA-based genealogy tests to find out more about one’s ancestry were among the first on the market.¹ Now that technology developments have led to the increasing availability of sophisticated but affordable tests, questions concerning genomics’ applications arise in a new context for individuals and families, and at a larger scale for communities and societies. While individual-centered, clinical and non-clinical use of genetic testing is booming, other areas of genetic research are also

¹ DNA Family Tree is known as the first service provider on the market. http://en.wikipedia.org/wiki/Family_Tree_DNA (accessed 29 October 2013)

changing, as can be seen in, for example, human anthropology and population genetics. New insights and, in particular, new technologies in genomic science are leveraging the broad field of biomedicine and they imply changed patterns of accountability in research. Therefore, established normative frameworks that refer to classical (human) genetics require careful inspection and they may need to be adjusted in order to be applicable to the new knowledge from the genomic sciences.²

We aim to contribute to that revision by reviewing some classical cases that challenge our thinking about ethics and accountability in the sciences in various disciplines.

We will examine the interaction between science, ethics and accountability in the field of genomics research and present several cases which highlight unresolved issues that can arise in the context of

²The genomic sciences include genetics. For reasons of readability we will further use ‘genomics’ in this text and use ‘genetics’ only if we specifically refer to this narrower field.

genomics research at the community and population level. Research findings concerning ancestry may heavily impact core concepts of identity, for individuals as well as for communities (Elliot & Brodwin 2002; Wolinsky 2006).

This does raise the question of whether groups – regardless of the decisions of individual group members - have the right to decline to learn the outcomes of scientific research. Such a right would be difficult to protect upon publication, and may at the extreme lead to calls for prohibiting the conduct of particular population-level studies that may convey unsolicited and unwanted insights.

We will analyse the accountability of scientists in the light of changing practices in the application of genomics research and the associated set of moral obligations. To that end, we first describe our view on the normative structure of accountability, in particular in the context of scientific research. Second, we present several examples of disputed or unwelcome findings in population genetics or ancestry studies from the

past decades and, thirdly, we analyse the case of population-level research among the Native American Havasupai community, to illustrate the changing patterns of accountability in genomics research in a distinct population, over a long time. We will ask what, if any, specific conclusions can be drawn from this case, and what wider insights we can take from it about the responsible conduct of research and the different ways of sharing information.

Science, ethics and accountability

What function does accountability have in the context of science today? And how does it relate to ethics?

In general, accountability has a crucial function in maintaining the standards of a discipline or a profession. Systems of accountability, with structures that codify the rules for both giving an account and holding to account, are in place in organizations of almost every profession (in the wide sense of the word) be it of lawyers, plumbers, physicians or

car mechanics. In the academic world, rules for accountability can be found at all levels of the organization: the university itself, the institutes, the research groups and labs, as well as in education and within student organizations.

Internal accountability, i.e. the maintenance of standards within the profession itself, can be distinguished from *external accountability* where professionals individually or collectively have to render account to public bodies or institutions or to specific other professions. The latter, external accountability at the interface of disciplines, professions and society is operationalised, for example, by funding bodies, science policy organizations and governmental research oversight bodies and also, obviously, by financial accountants.

Examples of internal accountability in the area of science include scientific review of research proposals and the process of peer review of publications. In many professions, certification of continuing education, professional licensing and disciplinary systems are internal

measures for quality assurance that set benchmarks for accountability.

This has led, however, to the rise of the *audit agenda* that, according to O'Neill, "... seeks to improve accountability by ever-more intensive monitoring, inspection and audit of performance." (ONeill 2002, p.131).

The improvement of accountability entails an increase of trustworthiness, but this comes at the price of a decrease of trust, a result which can undermine the very *raison d'être* of the profession.

Ethics review bodies represent a specific system of accountability, as they by definition hold researchers to account for the fulfilment of moral obligations in the design and conduct of research. In biomedicine and in behavioural research, ethics review has become an ubiquitous phenomenon over the past decades. The system has been implemented in a variety of forms that often exist next to one another and thereby set standards that may be in tension or even contradictory, resulting in rather unclear accountability structures. Moreover, we should ask ourselves to what extent institutionalized ethics review has

turned into an intrusive bureaucracy. This is another example of the 'audit culture' analysed by O'Neill, that originally was intended to improve accountability and secure trustworthiness (O'Neill 2002). In fact, however, although the audit culture was developed to restore trust, " ... its spread actually creates the very distrust it is meant to address." (Power 1994, p.10).

Accountability in science

External and internal accountability as described above are mostly procedural, but also relate to the concept of the 'good' that science pursues (Chadwick 2005). However, added to that, there is a type of accountability intrinsic to the scientific endeavour itself. In science, apart from the procedures, there is the key issue of scientific *content*.

Thorny issues in scientific accountability arise about the maintenance of standards that includes the research question and the scientific method, as well as the outcomes. There is a good that is internal to

science and, according to Serageldin, it includes rationality, creativity, the search for truth, adherence to codes of behaviour and, as he calls it, a certain constructive subversiveness (Serageldin 2008). Scientists can be assumed to have the obligation of doing *good science*, they can be held to account for the way in which they conduct research and for the quality assurance of the outcomes according to the standards of the profession. The recent flood of published misconduct cases shows that the procedural control mechanisms do work, at least *ex post* (Investigation Committee Bell Labs 2002; Institute of Medicine 2012; Levelt, Noort & Drenth Committees 2012) But, what *are* the standards for scientific content, and to *whom* are scientists accountable regarding the content of their work?

There is much discussion about method, in particular in the genomic sciences. Here, we want to look in particular at the object and the *outcomes* of research. Research findings and conclusions usually entail some truth claim. Also negative results of studies – where the

hypothesis that the study set out to test turns out to be wrong – can be reported as a true conclusion about the absence of evidence. Such negative outcomes tend to be underreported (Fanelli 2012). There can be, however, some very ‘inconvenient truths’ – from positive as well as negative outcomes – that may bring scientists into conflict not only with their sponsors and oversight bodies, but potentially also with their research subjects and their communities, or even society at large. The classical case of such an inconvenient truth is of course Galileo’s heliocentrism, based on the earlier findings of Copernicus, the truth of which was confirmed by Galileo through systematic astronomical observations (Galilei 2001). Sticking to his conviction about the scientific fact of the planet Earth orbiting the sun, in front of the Inquisition and the head of the Roman Catholic Church, resulted in lifelong house arrest for Galileo Galilei.

On the other hand, deliberate denial of scientific truth for political or religious purposes is not confined to the past. Recent examples are the

‘AIDS denial’ and the ‘creationism’ controversy. The ‘AIDS denial’ by president Mbeki of South Africa led to an estimated loss of more than 330,000 lives between 2000 and 2005 (Chigwedere et al. 2008). Mbeki denied that HIV was the cause of AIDS and blocked the provision of antiretroviral drugs to the South African population. He rejected the firmly established consensus of the scientific community about the causative role of HIV, and referred to the so-called Duesberg-hypothesis, claiming that the use of recreational drugs and of antiretroviral drugs are causes of AIDS (Duesberg et al. 2003). Another example, with great public and individual health impact, is the obstruction of the tobacco industry of the reporting of outcomes of studies on the risk of cancer – and other diseases – from environmental tobacco exposure (ETS, “second-hand smoke”) (Ong & Glantz 2000).

Serious conflicts arise when scientific findings, or particular interpretations of such findings, clash with public policy, as shown in the UK by the recent “Nutt-gate” affair. David Nutt, a professor of neuropsychopharmacology, was the chairman of the UK Advisory Council on the Misuse of Drugs (ACMD). In 2007 he published an article in the *Lancet* purporting to show that alcohol is the most harmful drug, before heroin and crack cocaine (Nutt et al. 2007). When he later compared the risk of harm from ecstasy to that of horse riding, he was sacked as chair of the ACMD (Nutt et al. 2009). As Alan Johnson, the Home Secretary, stated “He was asked to go because he cannot be both a government adviser and a campaigner against government policy”. In other words, it was denied that it was the scientific finding itself that was the problem. Further research confirmed the overriding harm caused by alcohol and in 2010 Nutt and colleagues published a refined version of their article of 2007, reaching the same conclusions (Nutt et al. 2010).

A typical example of religiously motivated denial of corroborated scientific knowledge is ‘creationism’. The anti-evolution ‘Creation science’ movement and its more recent subset of ‘Intelligent Design’ (‘ID’), that are particularly active in the United States, reject the theory and findings of evolutionary biology. Originating from the 1920s, the argument about ‘creation’ or evolution has been ongoing for nearly a century. The current battle – that has resulted in a considerable number of law suits – is actually about education policy and the unsuitability of theories grounded in religious beliefs for the science and biology classroom (Scott & Matzke 2007)³

Questioning established knowledge and raising hypotheses as to its falsification are essential features of the scientific enterprise – and include questioning scientific method itself, a discussion that meanwhile has reached the general media (Ioannidis 2005; Lehrer

³ On 3 December 2010, a settlement was reached with a family receiving \$475,000 in the case of Doe et al. v. Mount Vernon City School District Board of Education et al.

2010, p.52). The requirement of reproducibility of results is a further key characteristic (Diamandis 2010). It necessitates sharing of information, access to – the sources of – research data and unrestricted dissemination of findings. Scientific inquiry may shake long held beliefs on any topic in any area, on seemingly small but very fundamental issues in science itself (Boogerd et al. 2011), as well as on the ‘big’ questions in areas as remote as religion and cultural narrative. The latest developments in the biological sciences show that we are still sailing in uncharted waters and in particular the rise of synthetic biology presents us with what appear to be completely novel questions: we have moved from reading the genome to writing and editing genomes and are already “remaking ourselves and our world”(Church & Regis 2012, p.13). How far applications of molecular engineering, as, for example, genome editing or the use of synthetic DNA as a programmable material, challenge our conceptual and normative frameworks remains to be seen (Mali et al. 2013; Qi et al. 2013).

Genomics, truth, and accountability

Genetics and genomics regularly convey unwelcome messages and reveal inconvenient truths. They can range from non-paternity issues in classical clinical genetics to revealing information about ancestry and geographical origin of communities that is perceived as highly disturbing by the people in question. In both cases, the ethical, social and psychological implications are non-trivial.

What are the issues of professional and scientific accountability in this context? What of truth and truthfulness? In the first case, the professions of clinical geneticists and counsellors, well-aware of the realities of family relationships and of hereditary disease susceptibility, have established practical guidelines for dealing with such situations. Apart from that, they are in the role of health care providers – as physicians or other professionals – and it has been argued that the rules for truth-telling in the patient-physician relationship allow for

selective non-disclosure of information that in the eyes of the physician, is assumed to be too disturbing for patients. It is however questionable whether such a traditional ‘therapeutic privilege’ can be justified at all, and maintained in current developments towards participatory healthcare, in particular also in the context of DTC (genetic) testing services ⁴(Prainsack 2011).

The second case, revealing information about ancestry and the origin of populations, is far more complex. As argued, in the context of science and scientific research, there is no escape from the commitment to the truth, or at least to truthfulness about the factual conclusions that we draw, to the best of our knowledge, from the systematic analysis of empirical findings.

In some cases, empirical evidence of ancestry – geographical, tribal – is actively sought for by communities or community leaders (Parfitt 2003; Thomas et al. 2000). In the case of the Lemba, the “Black Jews of

⁴ See e.g.: Society for Participatory Medicine.
<http://www.participatorymedicine.org> (accessed 29 October 2013)

Southern Africa”, the search for genetic evidence has been tightly connected with the affirmation of religious identity with Judaism. While genetic studies are ongoing, a complex situation exists, as Jewish ancestry can be highly relevant for the correct diagnosis of – otherwise rare – hereditary disorders (Ostrer & Skorecki 2013). As noted by Goodman in his seminal text book “If one is afflicted with a hereditary disease characteristically observed in Jews, in most cases, that individual must be a Jew genetically. According to the Halacha (Jewish Law), however, one is a Jew if one’s mother is Jewish or if one converts to Judaism according to the requirements of the Law.” (Goodman 1979, p. 3)⁵

While the Lemba sought for genetic evidence of ancestry and identity, other people did not want this type of knowledge to be imposed upon them and conclusions from studies turned out to be detrimental to the group and to individuals. For example, in the case of the Maori of New

⁵ With thanks to Rabbi T.R. Bard, Boston/Newton, MA, for the text book reference and discussion.

Zealand, population-based studies into particular genetic traits that were by the researchers interpreted as confirming hypotheses concerning ancestry and migration as well as causally connected with present-day culture and behaviour, led to increased stigmatization and tension in society (Perbal 2013; Evans 2012).

In both cases, the Lemba and the Maori, the genome analysis and interpretation may have been correct according to the objective criteria for biological research.

However, considerable harm to the people involved and a loss of trust in science and scientists may result under certain circumstances from taking the objectivist approach (Boghossian 2007). We will describe the genomics research among the people of the Havasupai tribe who live in the Grand Canyon in Arizona, as an example of the major impact of a neglected clash of cultures.

Genomics research in human populations: the case of the Havasupai

The story of the Havasupai people about their participation in genetic research (which ended in April 2010 with return of the samples and a settlement for damages), has received much attention (Harmon 2010; Couzin-Frankel 2010; Editorial 2010; Vorhaus 2010; Callaway 2010). The principal investigator of the project, Therese Markow, responded in a Letter to the publication in the New York Times (Markow 2010, p.A24).⁶ The report of a formal investigation initiated by Arizona State University (ASU) was published in 2003 (Hart & Sobraske 2003).

The focus of the discussion has been almost entirely on the informed consent or rather, the alleged lack of consent. That allegation, however, seems hard to substantiate, as the Havasupai gave so-called broad consent, that was not limited to the study of one particular trait in this

⁶In August 2013 the results were published of a study among institutional review board (IRB) chairs and researchers at National Institutes of Health (NIH)-funded institutions. This small, qualitative study showed that the Havasupai case did not have a large impact on the practice of these respondents (Garrison and Cho 2013).

particular study. In the following, we will examine the case from a different view point, highlighting the complex interaction of agents, acts, obligations, rights, and the relationships of accountability.

A brief description of the case:

The people of the Native American tribe of the Havasupai live in a remote part of the Grand Canyon in Arizona, US. The tribe is numerically small, with (in 2010) about 650 members. In 1990, a request from the part of tribe members for help in finding the cause of the very high incidence of type 2 diabetes (55% of Havasupai women and 38% of Havasupai men were affected in 1991) (Dalton 2004), led to the initiation of a medical genetics research project. At that time, an extensive genealogical data set already existed that had been collected in the course of anthropological research over several decades, providing an ideal source of background data for the analysis of genetic variation. The researchers – John Martin, the anthropologist who had studied the Havasupai for many years, and Therese Markow, a

geneticist – obtained funding from Arizona State University (ASU) and the National Alliance for Research on Schizophrenia and Depression (NARSAD) for a study of genetic variants among the Havasupai. The study participants signed a broad consent, for the study of “... the causes of behavioural/medical disorders”, although the initial request from the tribe members was only about finding a cause of the high incidence of diabetes. The collected samples and data were used in a multitude of studies, by the initial researchers as well as by others with whom data were shared over the years (Hart & Sobraske 2003, p.63-137). One early publication reported on HLA polymorphism among the Havasupai - that in theory this could have shed a light on the diabetes incidence, as previously found among the Native American Pima tribe, but the results were inconclusive (Markow et al. 1993). The researchers reported on their efforts towards diabetes control in a brief contribution in the Lancet (Zuerlein et al. 1991). A further early publication by Markow and Martin focused on the effects of inbreeding on so-called developmental stability (Markow & Martin 1993). Only

many years later, in 2003, the Havasupai community became by accident aware of the ways in which their samples and data had been used over the years. Meanwhile there had been publications on, among other topics, inbreeding, and population migration. The latter research findings contradict the Havasupai's own beliefs about their origin and geographical ancestry. In 2004, a law suit was filed, claiming over \$50 million in damages for "severe harm, extreme distress, and emotional trauma" (Editorial 2010). In April 2010, Arizona State University agreed in a settlement to pay \$700,000 to 41 members of the Havasupai tribe. In August 2013, the chain of events from the original project in 1990 to the publicity surrounding the settlement in 2010, was recounted by Ricky Lewis in a blog post that elicited many comments, including several responses by Teresa Markow (Lewis 2013). A key issue was the clarification about the actual scope of the research and the lack of publications from the project, taking into account the frequent reference in the media to schizophrenia studies performed on the

Havasupai or their data. According to Markow, with the techniques available at the time of the study, no sufficient and appropriate variants could be found to perform any association studies at all, neither for diabetes nor for other disorders. In the end, only clinical and educational help to reduce the burden of diabetes could be provided to the Havasupai, as reported by the team (Zuerlein 1991). Yet, there is much contradictory information on the actual course of the research and many questions remain open in spite of recent in-depth analysis (Van Assche et al. 2013).

Beyond consent: moral matters for indigenous people

The case of the research among the Havasupai raises many questions. As already indicated, much attention has been paid to the apparent problems with the original informed consent from 1990. The broad scope of it, in spite of the fairly narrow and concrete medical question concerning the Havasupai, the failed communication about the consent

implications, and the fact that for data sharing as well as for later new studies by the ASU group no re-consent was sought, suggest lack of appropriate attention to detail in the conduct of research to say the least. Strategies for improving the consent process in this type of research have been proposed (Mellow & Wolf 2010; Jacobs et al. 2010; Boyer et al. 2011). In general, the question of whether or not re-consent for later and/or other research is necessary, is an important matter of ongoing debate. But the case raises other questions as well, showing some morally relevant matters that by their very nature are beyond consent. First, the use of specific terminology by the researchers in their publications – a seemingly minor issue, but with serious consequences. “Inbreeding” originates from the context of livestock breeding, as a means to promote desirable and to eliminate not-desired traits in animals, and was applied from the mid-19th century on by the eugenics movement propagating the “improvement” of humans (Galton 1865). As the title of the early article by Markow and Martin shows (Markow & Martin 1993), the authors unfortunately

chose the technical term “inbreeding” to describe the actual *consanguinity* among the Havasupai people. After mentioning developmental instability “... *in inbred and outbred invertebrates and vertebrates*”, the authors continue to describe the rationale of their research question: “... *reports on the influence of inbreeding ... in humans have not been consistent. We have identified a population, the Havasupai Indians of northern Arizona, which is uniquely suited to address this question.*” (Markow & Martin 1993, p.389) Arguably few populations would not feel offended.

Apart from that, referring to inbreeding, a Havasupai spokesperson is quoted as: “*We say, if you do that, a close relative of yours will die*” (Harmon 2010), which suggests that there may be additional confusion concerning *inbreeding* and *incest*.

Careful explanation and use of the scientifically correct term of “*consanguinity*” might have prevented at least part of the humiliation as perceived by the tribe members.

Second, the more fundamental issue concerns the acceptability for individuals and communities of empirical evidence that contradicts traditional beliefs and sacred knowledge. By its very nature, this is beyond what can be a matter of consent. The application of genomics very often touches upon descent, paternity, ancestry and related issues. This applies not only to classical hereditary disorders, but with the development of genomic medicine this is the case for an increasing spectrum of health and disease traits. As a consequence, certain traditional narratives and longheld beliefs may appear in a different light. For a community this may result in considerable so-called ‘dignitary’ harm that, however, is highly subjective and situation specific and may be an unavoidable effect of scientific inquiry.⁷

Further considerations are that communities and populations may not accept the Western world model of science at all - or that a research agenda may be perceived - rightly or wrongly – as part of a political

⁷ On dignitary harm and the example of the Havasupai, see the in-depth analysis by Van Assche, Gutwirth and Sterckx , 2013.

agenda. This may happen in the field of genomics research, as the history of the Human Genome Diversity Project (HGDP) has shown, but it can in principle occur in any area of science (<http://hagsc.org>; Cavalli-Sforza 2005). Current criticism from representatives of indigenous peoples' organizations is directed towards the Genographic Project. The Genographic Ethical Framework Documents states that: "Principal Investigators are required to be (and are) sensitive to the fact that knowledge generated by the project may give rise to narrative accounts that function as an alternative to some traditional accounts of the origin of the cosmos (including people). All project participants understand that scientific narratives do not have priority over other types of narrative – and that Indigenous communities will determine the extent (if any) to which such narratives might complement their existing world views." (The Genographic Project 2013).

While this seems to be a sufficient warning in mainstream research practice, it is deemed inadequate and inappropriate by representatives

of indigenous peoples groups (Harry & Kanehe 2005). We have not addressed these issues here in detail, but these concerns are substantial and, obviously, cannot be resolved through traditional mainstream models of consent. Through the joint efforts of global organizations of indigenous peoples new approaches have been developed, notably by the Free, Prior and Informed Consent Initiative (FPIC), with a broad scope encompassing rights to land and natural resources and preservation of cultural identity (<http://www.culturalsurvival.org/consent>).

Science, inconvenient truths and accountability, some conclusions

We set out to investigate the intricate relationship between science, ethics and accountability against the background of developments in the genomic sciences.

We looked at the various forms of accountability and the way in which they function in the scientific environment and arrived at the question

about accountability for scientific content – to whom are scientists accountable with respect to the content and outcomes of their work?

Highly inconvenient truths may result from meticulous empirical observation and rigorous theoretical analysis. What to do, if carefully derived, robust research findings clash with the deep convictions and key components of traditional knowledge of people – in particular if it concerns vulnerable populations. Can people be expected to consent to the confrontation with “enlightenment”? Respect for persons and populations requires respect for choosing to adhere to tradition and narrative.

Scientists should adhere to the values of science that, according to Ismail Serageldin, presuppose “*freedom to enquire, to challenge, to think, and to envision the unimagined*” and they may thereby reveal some inconvenient truth (Serageldin 2008).

References

- Boghossian, P. 2007. *Fear of knowledge. Against relativism and constructivism*. Oxford/New York: Oxford University Press
- Boogerd, F.C., Ma, H., Bruggeman, F.J., van Heeswijk, W.C., García-Contreras, R., Molenaar, D., Krab, K., and Westerhoff, H.V. 2011. 'AmtB-mediated NH₃ transport in prokaryotes must be active and as a consequence regulation of transport by GlnK is mandatory to limit futile cycling of NH₄⁺/NH₃', *FEBS Letters* 585(1):23-28
- Boyer, B.B., Dillard, D., Woodahl, E.L., Whitener, R., Thummel, K.E. and Burke, W. 2011. 'Ethical Issues in Developing Pharmacogenetic Research Partnerships With American Indigenous Communities', *Clinical Pharmacology & Therapeutics* 89(3):343-345
- Callaway, E. 2010. 'Native American settlement highlights DNA dilemma', *New Scientist* 2757, 27 April 2010
- Cavalli-Sforza, L.L. 2005. 'The Human Genome Diversity Project: past, present and future', *Nature Review Genetics* 6:333-340
- Chadwick R. 2005. 'Professional ethics and the 'good' of science', *Interdisciplinary Science Reviews* 30(3):247-256
- Chigwedere, P., Seage, III, G., R., Gruskin, S., Lee, T-H., and Essex, M. 2008. 'Estimating the Lost Benefits of Antiretroviral Drug Use in South Africa', *Journal of Acquired Immune Deficiency Syndrome* 49(4):410-415
- Church, G.M. and Regis, E. 2012. *Regenesis: how synthetic biology will reinvent nature and ourselves*. New York: Basic Books

Couzin-Frankel, J. 2010. 'DNA Returned to Tribe, Raising Questions About Consent', *Science* 328:558

Cultural Survival. Free, Prior and Informed Consent Initiative (FPIC) <http://www.culturalsurvival.org/consent> (accessed 21 October 2013)

Dalton, R. 2004. 'When two tribes go to war', *Nature* 430:500-502

Diamandis, E.P. 2010. 'Cancer Biomarkers: Can We Turn Recent Failures into Successes?', *Journal of the National Cancer Institute* 102:1462-1467

Duesberg, P., Koehnlein, C., and Rasnick, D. 2003. 'The chemical bases of the various AIDS epidemics: recreational drugs, anti-viral chemotherapy and malnutrition', *Journal of Biosciences* 28(4):383-412

Editorial. 2010. 'Culture clash on consent', *Nature Neuroscience* 13(7):777

Elliot C, and Brodwin P. 2002. 'Identity and genetic ancestry tracing', *BMJ* 325:1469-1471

Evans, D. 2012. 'Whakapapa, Genealogy and genetics', *Bioethics* 26(4):182-190

Fanelli, D. 2012. 'Negative results are disappearing from most disciplines and countries', *Scientometrics* 90:891-904

Galilei, G. 1632. *Dialogo sopra i due massimi sistemi del mondo*. [Galilei, G., Drake, S.(transl.), Einstein, A. (Foreword), Heilbron,

J.L.(Introduction) 2001. *Dialogue Concerning the Two Chief World Systems, Ptolemaic & Copernican*. New York: Modern Library]

Galton, F. 1865. 'Hereditary talent and character', *Macmillan's Magazine* 12: 157–166;318–327

Garrison, N.A., and Cho, M.K. 2013. 'Awareness and acceptable Practices: IRB and Researcher Reflections on the Havasupai Lawsuit', *AJOB Primary Research* 4(4):55-63

Goodman, R.M. 1979. *Genetic disorders among the Jewish people*. Baltimore: John Hopkins University Press

Harmon, A. 2010. 'Indian Tribe Wins Fight to Limit Research of Its DNA', *New York Times*, April 21, 2010

Harry, D., Kanehe, L.M. 2005. 'Genetic Research: Collecting Blood to Preserve Culture?', *Cultural Survival Quarterly* 29(4) available at: <http://www.culturalsurvival.org/publications/cultural-survival-quarterly/none/genetic-research-collecting-blood-preserve-culture> (accessed 21 October 2013)

Hart,S., Sobraske, K.A. 2003. 'Investigative report concerning the medical genetics project at Havasupai', available at: <http://www.cnhp.montana.edu/conference/HartReport.pdf> (accessed 29 October 2013)

Human Genome Diversity Project. <http://www.hagsc.org/hgdp/> (accessed 21 October 2013)

Institute of Medicine. 2012. *'Evolution of Translational OMICS. Lessons Learned and the Path Forward'*, Washinton D.C.:The National Academies Press

Investigation Committee Bell Labs. 2002. *'Report of the investigation committee on the possibility of scientific misconduct in the work of Hendrik Schön and co-authors'*, available at: <http://www3.alcatel-lucent.com/wps/portal/> (accessed 3 November 2013).

Ioannidis, J.P. 2005. 'Why most published research findings are false', *PLoS Medicine* August 2(8):e124

Jacobs, B., Roffenbender, J., Collmann, J., Cherry, K., Bitsói, LM.L., Bassett, K., and Evans Jr., C.H. 2010. 'Bridging the Divide between Genomic Science and Indigenous Peoples', *Journal of Law, Medicine & Ethics* 38(3):684-696

Lehrer, J. 2010. 'The Truth Wears Off – Is there something wrong with the scientific method?', *The New Yorker*, December 13, 2010

Levelt, Noort, Drenth Committees. 2012. *'Flawed science: The fraudulent research practices of social psychologist Diederik Stapel'*, available at: <https://www.commissielevelt.nl/> (accessed 3 November 2013).

Lewis, R. 2013. 'Is the Havasupai Indian Case a Fairy Tale?', *PLOS Blogs, DNA Science blog*, 15 August 2013.

<http://blogs.plos.org/dnascience/2013/08/15/is-the-havasupai-indian-case-a-fairy-tale/> (accessed 21 October 2013)

[Mali, P.](#), [Yang, L.](#), [Esvelt, K.M.](#), [Aach, J.](#), [Guell, M.](#), [DiCarlo, J.E.](#), [Norville, J.E.](#), and [Church, G.M.](#) 2013. 'RNA-guided human genome engineering via Cas9', *Science* 339:823-826

Markow, T.A., Martin, J.F. 1993. 'Inbreeding and developmental stability in a small human population', *Annals of Human Biology* 20(4):389-394

Markow, T., Hedrick, P.W., Zuerlein, K., Danilovs, J., Martin, J., Vyvial, T. and Armstrong, C. 1993. 'HLA Polymorphism in the Havasupai: Evidence for Balancing Selection', *American Journal of Human Genetics* 53:943-952

Markow, T.A. 2010. 'Dispute Over Use Of DNA'. Letter. *New York Times* (New York edition), 3 May 2010

.Mello, M.M., Wolf, L.E. 2010. 'The Havasupai Indian Tribe Case – Lessons for Research Involving Stored Biological Samples', *New England Journal of Medicine* 363(3):204-207

National Geographic. The Genographic Project.
<https://genographic.nationalgeographic.com/>(accessed 21 October 2013)

Nutt, D.E., King, L.A., Saulsbury, W., and Blakemore, C. 2007. 'Development of a rational scale to assess harm of drugs and potential misuse', *Lancet* 369:1047-1053

Nutt, D. 2009. 'Government vs science over drug and alcohol policy', *Lancet* 374:1731-1732

Nutt, D.J., King, L.A., and Phillips, L.D. 2010. 'Drug harm in the UK: a multicriteria decision analysis', *Lancet* 376:1558-1565

O'Neill, O. 2002. *Autonomy and Trust in Bioethics*. Cambridge, Cambridge University Press.

Ong, E.K., and Glantz, S.A. 2000. Tobacco's industry efforts subverting International Agency for Research on Cancer's second-hand smoke study. *Lancet* 355:1253-1259

Ostrer, H., Skorecki, K. 2013. 'The population genetics of the Jewish people', *Human Genetics* 132:119-127

Parfitt, T. 2003. 'Constructing black Jews: Genetic tests and the Lemba – the 'Black Jews' of South Africa', *Developing World Bioethics* 3(2):112-118

Perbal, L. 2013. 'The 'Warrior Gene' and the Maori people: The responsibility of the geneticists', *Bioethics* 27(7):382-387

Power, M. 1994. *The Audit Explosion*. London: Demos

.Prainsack, B. 2011. 'Voting with their mice: Personal genome testing and the "participatory turn" in disease research', *Accountability in Research* 18:132-147

Prainsack, B. 'DIY Genetics: The right to know your own genome', (This volume xxxx)

Qi, H., Ghodousi, M., Du, Y., Grun, C., Bae, H., Yin, P., and Khademhosseini, A. 'DNA-directed self-assembly of shape-controlled hydrogels', *Nature Communications* 4:2275 (doi: 10.1038/ncomms3275)

Scott, E.C., and Matzke, N., J. 2007. 'Biological design in science classrooms', *Proceedings of the National Academy of Sciences of the USA* 104; Suppl 1:8669-8676

Serageldin, I. 2008. 'Science in Muslim Countries', *Science* 321:745

The Genographic Project. 2013. 'The Genographic Ethical Framework Document'. https://genographic.nationalgeographic.com/wp-content/uploads/2012/07/Geno2.0_Ethical-Framework.pdf (accessed 21 October 2013)

Thomas, M.G., Parfitt, T., Weiss, D.A., Skorecki, K., Wilson, J.F., Le Roux, M., Bradman, N., and Goldstein, D.B. 2000. 'Y Chromosomes Traveling South: The Cohen Modal Haplotype and the Origins of the Lemba – the "Black Jews of Southern Africa', *American Journal of Human Genetics* 66:674-686

Van Assche, K., Gutwirth, S., and Sterckx, S. 2013. 'Protecting Dignitary Interests of Biobank Research Participants: Lessons from Havasupai Tribe v Arizona Board of Regents', *Law, Innovation and Technology* 5(1):54-84

Vorhaus, D. 2010. 'The Havasupai Indians and the Challenge of Informed Consent for Genomic Research', *Genomics Law Report*, April 21, 2010.
<http://www.genomicslawreport.com/index.php/2010/04/21/the-havasupai-indians-and-the-challenge-of-informed-consent-for-genomic-research/> (accessed 21 October 2013)

Wolinsky, H. 2006. 'Genetic genealogy goes global', *EMBO Reports* 7(11):1072-1074

Zuerlein, K., Martin, J.F., Vaughan, L., and Markow, T.A. 1991. 'NIDDM: basic research plus education', *Lancet* 338:1271

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