Author's Commentary on "A DNA Dilemma"

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A DNA Dilemma

The elements of the case, "A DNA Dilemma," are intended to foster discussion of the ethical conduct of human subject genetic research; additional complexity is introduced by the supplementary details. Linguistic, cultural and authoritarian distinctions are presented to contextually cloud the waters of the case and realistically portray the complications that often accompany such circumstances. In this commentary, the following points will be presented in order: 1) Mark's options/ responsibilities; 2) human subject research ethics and regulations, 3) secondary responsibility of Thomas, Fan Chen and the institution. Concluding remarks will provide suggestions for the presentation of this case and a summation of the overall ethical questions it addresses.

Mark's options

The first discussion question focuses on the action that Mark should take; however, a more thoughtful review will first address Mark's responsibility for taking action. Mark's responsibility to act depends upon the regulations overseeing this type of human subject genetic research and upon the local IRB's interpretations and policy on these issues. These points will be discussed in the section on human subject research regulations. It can be concluded, however, on the basis of Mark's unsettled reaction that he must do something if even just to find out what the regulations are. The responsibility to act may ultimately be in the participants' interest, but Mark's personal uneasiness should also be a consideration in his decision. A thorough review of Mark's options might include, but should not necessarily be limited to, the following possibilities.

1. *Mark could speak with Thomas directly*. This option might be the reader's first reaction; however, the implications of such a discussion should be fully explored. It is apparent from Thomas's handwritten note to Fan that Thomas supports this use of the DNA. Therefore, in speaking with Thomas, Mark will need to navigate the conversation carefully to avoid appearing accusatory, at least if Mark anticipates a positive outcome from his conversation with Thomas. Clearly it would be in Mark's best interest to play the role of the learner/clarifier and not the accuser. Mark could inquire about the process of consent in human subject research from the point of view of wanting to learn about the processes from his knowledgeable adviser. This approach would help defuse the situation and reduce Thomas's defensiveness. This approach does include some elements of uncertainty and jeopardy. If Thomas feels accused or threatened, his relationship with Mark could quickly sour. If Thomas ultimately concludes that the use of the DNA is permissible, then Mark is left with either accepting the idea or informing third-party administrators. Both options have distasteful elements. Therefore, it becomes critical for Mark to guide the conversation to a positive outcome. This necessity may be overwhelming for Mark to consider, and the resolution will largely depend on the previous relationship and trust enjoyed by Thomas and Mark.
2. *Mark could contact the IRB*. Mark may choose to contact the local Institutional Review Board (IRB). He has at least two options. Mark could contact the IRB anonymously and merely alert them about the secondary use of the DNA in Thomas's lab, or he could contact the IRB and seek clarification of the regulations overseeing this type of research in general. In the first option, Mark would play the role of the anonymous informant. Although this strategy attempts to remove Mark from direct confrontation with Thomas, it does present some difficulties that should be considered. The possibility remains that Mark's anonymity may be compromised. In these situations, the informant eventually becomes suspect and then must endure an intensely damaged relationship with the parties involved. This risk is inherent in the first option. The second option allows Mark to seek the generalized advice of the IRB. This approach may be the best way to get a definitive answer to Mark's dilemma; nevertheless, it also presents some risks. The IRB may ask Mark for the reason for his inquiry, and the IRB will certainly review Thomas's research. If Thomas faces IRB questions he will begin to suspect lab members as informants. Ultimately this risk is similar to the anonymous note. Another quandary is what

Mark will do with the information once he receives it. If the IRB approves this use of the DNA, there is no problem, but if the IRB objects to the unconsented use of the DNA, Mark finds himself back at his original dilemma with proof of unethical conduct.

3. *Mark could contact administrative officials*. If Mark decides to speak with an administrational official (i.e., department chair, dean, office of research), he will face the risks presented in Option 2. The difference is that Mark will have introduced the situation to those who could directly affect Thomas, and it is likely that the officials will contact the IRB for clarification. The implications for a negative outcome for Thomas are heightened, which makes this choice less desirable than Option 2. It may, however, provide a third party that Mark may feel more comfortable addressing.
4. *Mark could suggest that Fan use DNA from another source*. This option may be the most palatable, but may not be the first resolution considered. It does present some potential for harm to Mark. It is apparent that Thomas has authorized and suggested the use of the breast cancer DNA. If Mark suggests that Fan use a different source of DNA (i.e., a commercially available control), it may appear that Mark is excusing Thomas's role as principal investigator. If the experiments work well, the repercussions to Mark may be minimal and even positive; however, if the experiments fail, then Mark's intervention in the protocol outlined by Thomas may be blamed for the failure. In suggesting the change, Mark must also consider whether he will inform Thomas of his intervention. This may present some of the same concerns addressed in Option 1.

Human subjects regulations

The National Bioethics Advisory Commission, which generated the Belmont report in 1974, laid the foundation for the ethical considerations that should accompany the thoughtful review and approval of human subject research. The Belmont report focused on three meta-ethical principles: beneficence, respect for persons (autonomy) and distributive justice, which provided the underpinning for the federal regulation overseeing human subject research (45CFR46). This law, known as the Common Rule, has been adopted by all of the federal agencies sponsoring human subject research.

Genetic research has provided a unique spin on these basic principles and regulations, necessitating a review of the role of confidentiality, kinship, the autonomous and informed consent of a subject to donate DNA for specific purposes, and limitations on use of donated DNA in research that the donor finds morally repugnant. It is interesting that genetic research even affects the conception of distributive justice; however, this element of genetic research is beyond the scope of this case, which focuses on the confidentiality of the donor in genetic testing and the donor's rights in determining the use of donated DNA.

Clearly the elements of beneficence and autonomy are central in such a consideration. Beneficence is the principle of "first, do no harm." Some benefit must justify the risk. The element of beneficence has previously been the common endpoint of both utilitarian and Kantian thought; however, the element of kinship may alter the endpoint of these two modes of moral philosophy. The utilitarian would justify the use of genetic material of a few if it produces benefit (information, cures) for the larger society. Kantian thought, however, would disagree with the use of the genetic material as a means and not the end. The role of kinship and the fact that one's genetic information may affect one's relatives may alter the application of these principles. This type of discussion may be addressed as a tangential debate about of the morality of genetic research.

Kinship also plays a unique role in autonomy. If Relative A does not want to participate in a study but Relative B does, the information obtained by Relative B may affect the decision and confidentiality of Relative A. This element may play some role in the case depending upon the use of identifiers in labeling the DNA and whether the code can be broken. A more significant threat to autonomy may be a complication of the enduring nature of genetic material. Genetic material can be immortalized in cell lines that will persist long after the donor is deceased. Also, the genetic material may be used in a staggering array of research studies. Should donors have the ability to determine the use of their DNA? Unfortunately, this decision may depend upon the state in which the research is conducted. To date, Oregon has one of the most comprehensive statutes on the use of genetic material. Currently in Oregon, genetic material is considered to be the property of the donor, and the donor must be informed and must consent to the use of DNA in every study in which its use is proposed.

Local institutional review boards are at liberty to reach their own conclusions about the human genetic research context as it applies to federal regulations. The

continuum of opinions range from broad acceptance of DNA use as an exempt-status protocol (at least where the samples have been coded) to requiring that each novel or secondary use of the DNA be regarded as a modification of protocol that must gain IRB approval.

In the case presented, Mark appears to be unaware of the requirements and interpretations espoused by his local IRB. The case offers little information about the database and storage of the DNA for their intended use in the breast cancer study, which also may affect the possibility of secondary use of the DNA. Central in this evaluation is the informed consent process and the document signed by each participant. Mark notes that the consent form neither authorizes nor precludes the use of the DNA in secondary studies.

This lack is a common oversight. Due to the unique semi-permanence of genetic material, it is not uncommon for an IRB to fail to consider the secondary use of donated DNA. Many IRBs are requiring the inclusion of language in the consent document that allows the donor to indicate whether the DNA may be used only for the present study, whether they would like to be contacted in the future to give consent for later studies or whether they give a blanket consent to the use of the DNA for all future research studies.

This central consideration should be the primary message of the case and should underscore the importance of including appropriate language in the consent form for human genetic research. In the case as presented, the informed consent document does not specify whether the DNA will be used in secondary studies or not. Since the purpose of the research, as stated in the informed consent document, is to study cancer, it is the commentator's opinion that the participants should be asked to give consent for secondary use of the DNA -- even if it is used as a control -- because it is not known what generalizable knowledge or personal information may be discovered by the secondary use of the DNA, and such research or information may be distasteful to the donor.

Responsibilities of Thomas, Fan Chen and the Institution

During the discussion of the case, there will likely be an interchange over Thomas's role. The roles of Fan and the institution may not be immediately voiced; however, their roles should not be overlooked. Thomas's role seems apparent. He has condoned and even advocated the secondary use of the DNA. His part in creating the problem may be clear, but his level of accountability is not clear. Thomas may be unaware to the ethical problems associated with secondary use of the DNA. However, Thomas may be aware of the IRB's standing policy on such use of the DNA and be in compliance with those institutional regulations. He may already have contacted the IRB and gained approval for the secondary use, but may have failed to notify Mark.

Fan Chen's role is also uncertain because of the language barrier. It is difficult to determine Fan's level of responsibility, but the discussion about the language and cultural barriers provide depth to the considerations of Fan's responsibility. It should also be noted, however, that Fan may have some responsibility, and his role should not be minimized or overlooked when discussing the case.

Finally, the institution is responsible to provide adequate IRB review of the wording of the consent form. The institution should provide avenues for researchers to access its regulations and policies overseeing human subject research. A clearer communication of these regulations could be achieved via an Internet module, institutional forums educating researchers and more direct interaction between the IRB and the researchers. They should provide better oversight of human subject research or at least well-publicized mechanisms for inquiry. As a tangential idea, as the number of foreign student post-docs and graduate students continues to increase (particularly in the area of human subject research), the institution should offer supplementary educational opportunities in research conduct, U.S. regulations and, possibly, cultural and linguistic courses to assist foreign students in the process of assimilation.

In conclusion, this case is intended to provide a rich forum for the discussion of human genetic research and the regulations overseeing this branch of human subject study and an avenue for discussion of the federal regulations and how student researchers as well as the principal investigator need to be aware of these regulations. The contextual elements of the case may be altered to provide additional points of discussion. For example, the language barrier could be removed; Fan could be an undergraduate; the note from Thomas could be omitted. By altering

these contextual features the discussion may change or the central ethical dilemma may be more clearly delineated.

References

- Ferraro, F. Richard; Szigeti, Elvira; Dawes, Kenneth J.; Pan, Shihua. "A Survey Regarding the University of North Dakota Institutional Review Board: Data, Attitudes, and Perceptions," *Journal of Psychology*: 133 (3, May 1999): 272-280.
- National Bioethics Advisory Commission, *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance, Executive Summary, Volume I and II: Report and Recommendations of the National Bioethics Advisory Commission*. Rockville, Md.: National Bioethics Advisory Commission, August 1999.

Informative Websites

- http://bioethics.gov/pubs.html: Web address for the National Bioethics Advisory Commission.
- http://ohrp.osophs.dhhs.gov/: Web address for the Office of Human Research Protections (links provided to regulatory documents (i.e. 45 CFR 46) and other historical documents (e.g., The Belmont Report).