From Tissues to Genomes

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While it is always tempting to judge alleged scientific misconduct with the benefit of hindsight, it is not necessarily ethical or legal. Recently, much has been written on the multiple scientific and commercial uses of the cells of Henrietta Lacks, archived following her medical treatment in the 1950s. But today the publication of the whole genome sequence of one HeLa cell line raises novel issues regarding the use of patient tissue samples that merit discussion. Finding solutions to these issues may be as valuable for policy as the HeLa cells have been for science. Such discussion needs, however, to be informed by the ethical, legal, and social implications (ELSI) currently governing the use of tissues leftover from medical care.

At the beginning of the Human Genome Project (HGP), the ELSI community was quick to draw attention to the implications of using human tissues for genetic research (Knoppers and Laberge 1989, 1995). Generally, ethics guidance for biomedical research starting from the Nuremberg Code (1947), to the Helsinki Declaration (1964), and the Belmont Report (1978) had already informed the legal and ethical norms of each country when the HGP began. The scientific research community quickly developed its own self-regulatory ethical frameworks for genetic research (Knoppers et al. 1996).

In contrast to this recognition of the importance of consent for research on human tissues, tissues acquired during medical care in order to establish or confirm diagnoses were stored in pathology labs or incinerated as biological waste (Clayton et al. 1995). Consent for their use in research was generally not required. The first “official” policies for the secondary use of archived, residual tissues removed during medical care did not emerge until 1996 (The College of American Pathologists 1996).

The use in genetic research of tissues from vulnerable populations such as children and incompetent adults or deceased individuals also drew the attention of policymakers (UNESCO 1997). Their legal representatives were granted the same authority and duties whether the tissue was left over after medical care or specifically collected for research. Today, the best interests of the child or of other children of the same age or condition govern biomedical research involving children, while the wishes of adults expressed while still competent or alive (if known) govern research on material from incompetent or deceased adults.

Since the human genome sequence was determined in 2003 the range of approaches suggested for the use of residual medical care tissues from patients include: destruction; unlimited use; an ethics waiver; an explicit and specific consent for each research use; and patient notification with the choice to opt-out from research. While recognition of the need to respect the personal and cultural values of each patient (even concerning leftover tissues) is necessary and a laudable goal, there is danger in promoting the “sacralization” of residual tissues as equivalent to the “person” by requiring an explicit and specific consent for every research use. Likewise, emphasizing the considerable scientific and economic value of tissues also risks the “commodification” of the person. Indeed, the danger is that individuals would be awarded greater or lesser control over the disposition of their personal material depending on the potential for its commercialization and the economic value of its by-products. Even if tissues are treated neither as persons nor as potential marketable objects, that does not circumvent the requirement for transparency of governance of the “residual” participation of patients in genetic research. What is needed is an approach that is proportional to the risks and benefits specific to the context of the research use of residual medical care tissues.

The recently acquired ability to determine the genome sequence of a person using residual tissues resulting from medical care complicates any resolution on the use of the HeLa cells. Putting such information in the public domain essentially risks exposing not only that person but their families to (un?)desired identifiability. When individuals agree to donate their personal genome to research, such as in the Personal Genome Project (Church), their decision to place their genome in an open access database is fully informed. Individuals can even place their “personal” genome on the web (Watson).

There are also open access databases such as the HapMap (International HapMap Project) and the 1000 Genomes Project (The 1000 Genomes Project) that serve as population reference maps. In these international research projects, “anonymized” (i.e., irretrievably delinked) participants are warned that total privacy could not be forever guaranteed, but there was informed choice and an explicit, written consent to such risks.

In contrast, controlled access databases such as dbGap (The database of Genotypes and Phenotypes (dbGAP)) or that of the
International Cancer Genome Consortium (The International Cancer Genome Consortium (ICGC)) provide researchers and the world access to coded genomic data under strict conditions of ethics, data privacy, security and ongoing monitoring (Data Access Compliance Office (DACO) of the ICGC). The controlled access approach allows for research with privacy and data security protections in place. Researchers submit and use the genomic data and participants are aware of and have consented to international sharing of their coded data and samples under these conditions.

The same cannot be said for those who have died, or for children or incompetent adults who cannot or have not expressed an informed choice concerning the disposition of their leftover, medical care tissues. In such cases, as already mentioned, their legal representatives must be consulted for a decision. Would a controlled access approach to the research use of residual tissues from children, incompetent adults and the deceased be appropriate when their legal representatives agree? Is this a solution for HeLa cells?

Before answering that question, a strong argument could be made for the open, ethics-approved research use of anonymized residual material archived following medical care without explicit, informed consent as a systemic approach to improved health care. Such an approach however would require broad public awareness and acceptance, as well as the possibility to opt-out. The problem is that genome sequencing could make such anonymization moot as the possibility of re-identification remains (Gymrek et al. 2013).

Biomedical research seeks to improve patient health. Thus, it could also be argued that medical care would be better served if coded, residual samples (i.e., not anonymized) were used in research to allow the linking back of research results for the medical care of individual patients. Furthermore, patients may not want to be “privacy-protected” or anonymized. The advocacy of rare disease groups for more – rather than less – international, coded data and sample sharing is particularly telling in this regard (Mascalzoni et al. 2013).

I would go even further and argue that in countries with universal public health care systems, coded, residual tissues should at a minimum be used for ethics-approved research and for quality assurance programs if the public is properly notified. Patients should, however, be free to opt-out from research. Linkage with individual patient records and care would be ideal. There can be no sustainability of equitable health care if every tissue is either sacralized and rendered unusable, or commodified and rendered marketable, usable only by those who can pay. The use of residual medical care tissues from children, incompetent adults and the deceased should be strongly encouraged. They are necessarily important sub-populations in a health care system and have their own diseases that merit research, the consent of a legal representative should be required. The health care system of any country could however, could put in place the framework for ethics-approved research that could use residual tissues from these populations as a more systemic approach to the improvement of their medical care.

Henrietta Lacks was not a patient in a time or place when either opt-out or equitable and universal health care were available, nor are they available to most patients today. Before being research participants or patients, we are however first and foremost citizens who exercise political will and can change both ethical and legal norms. Today, her relatives can either continue her valuable legacy of contribution and symbolic value.

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