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Biospecimen policy: Family matters

Kathy L. Hudson & Francis S. Collins*Nature* **500**, 141–142 (08 August 2013) doi:10.1038/500141a

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Kathy L. Hudson and Francis S. Collins discuss how and why the US National Institutes of Health worked with the family of Henrietta Lacks, the unwitting source of the HeLa cell line, to craft an agreement for access to HeLa genome data.

Subject terms: Policy Genomics Cell biology Medical research

In March, two of the most deeply held values in the medical-research community — public data-sharing and respect for research participants — collided when the genome of the ubiquitous cell line HeLa was published¹ and posted in a public database. Controversy ensued. The full sequence data could potentially uncover unwanted information about people whose identity is widely known: the family of the woman from whom this immortal line was derived 62 years ago, Henrietta Lacks.





LACKS FAMILY/VIRGINIA DEPT HISTORIC RESOURCES

Henrietta Lacks' family gather around a historical marker dedicated to her in Virginia in 2011.

So, since March, the US National Institutes of Health (NIH) in Bethesda, Maryland, has worked closely with Lacks' family. Together, we have crafted a path that addresses the family's concerns, including consent and privacy, while making the HeLa genomic sequence data available to scientists to further the family's commitment to biomedical research.

The agreement that we reached goes into effect this week. We hope that it, and its genesis, will spur broader discussions regarding consent for future use of biospecimens, with a goal of fostering true partnerships between researchers and research participants.

Medical history

In 1951, physicians at Johns Hopkins Hospital in Baltimore, Maryland, took a biopsy from Henrietta Lacks, a 31-year-old African American woman who had an aggressive form of cervical cancer. This biospecimen was taken without her permission or knowledge; US regulations requiring consent were still decades away. The tissue sample gave rise to the first human cancer-cell line that could grow endlessly in culture, called HeLa. Henrietta died later that year, but her cells live on. Today, more than 60 years later, scientists around the world use HeLa cells for research on almost every disease. The story of Lacks' unwitting contribution to science, and the proud and poignant legacy it left for her descendants, is told in Rebecca Skloot's best-selling book, *The Immortal Life of Henrietta Lacks* (Crown, 2010), which is now being made into a film by Oprah Winfrey's production company.

The German research team that in March this year posted the HeLa genome on open-access databases available through the European Bioinformatics Institute and the NIH's National Center for Biotechnology Information did not violate any laws or rules. The action did, however, upset the Lacks family, and it drew criticism from many quarters². The genome of these cells is not identical to Lacks' original genome. The cells carry the genetic modifications that allowed them to form a tumour and grow prolifically; and their passage in cell culture for more than six decades has led to other structural anomalies. Nonetheless, the sequence can reveal certain heritable aspects of Lacks' germline DNA, and can thus be used to draw inferences, admittedly of uncertain

significance, about her descendants.

Within days, the European researchers removed the sequence from the public databases, to allow time for consideration of alternative approaches. Meanwhile, an NIH-funded research paper by Andrew Adey and colleagues on the genome sequence of a second HeLa line was in press at *Nature* (published in this issue; see page 207)³. *Nature* mandates that authors of research papers make their data publicly available online. Something needed to be done — and in partnership with the Lacks family.

Weighing the options

Over the past four months, with help from Skloot and academic leaders at Johns Hopkins, we met members of the Lacks family in Baltimore on three occasions. At their request, some family members also met separately with an NIH genetic counsellor and medical-genetics expert to learn more about what the data might say about family members, and the implications of having it in the public domain.

We talked at length with the family about the three options available for the full HeLa sequence data: first, making the sequence freely available, allowing anyone access at any time and for any use; second, placing the data in a controlled-access database, which would require researchers to apply to the NIH to use the data in a specific study and to agree to terms of use defined by a panel including members of the Lacks family; or third, withholding the sequence and not making it available at all for research — an option that the NIH would have had difficulty supporting or implementing, philosophically and legally.

After much discussion, family members unanimously favoured the controlled-access option. This will allow them to be aware of and have a crucial role in the science that uses the HeLa genome. The NIH will help to implement this, but respecting the family's preferences has required (and will continue to require) cooperation and patience by many — including scientists, publishers, funders and scientific societies. The authors and publishers of both genome papers^{1, 3} have agreed to submit their data for controlled access (in the same way as for many other non-HeLa genome sequences) through the NIH's database of genotypes and phenotypes (dbGaP; see go.nature.com/fduced). Likewise, NIH-funded researchers who sequence other HeLa lines will be expected to deposit their data in the dbGaP. We hope that scientists whose work is supported by other funders will do the same.

Applications for access to the sequence data will be rapidly reviewed by a newly formed HeLa Genome Data Access working group at the NIH, on which two members of the Lacks family will

serve. We believe that this plan reflects the true partnership between the Lacks family and the biomedical-research community. We also ask that all researchers who generate or use genomic data from HeLa cells include in their publications an acknowledgement of the contribution of Lacks and the continued generosity of her family, such as that in Adey and colleagues' paper³.

Of course, someone could still stitch together a reasonable representation of the HeLa genome from the estimated 1,300 gigabytes of data already in public databases, which have been accumulating over the past 25 years — and the family knows this. The family is also aware that any lab with the right equipment, and non-NIH funds, could derive the full sequence from scratch at any point and post it on a non-NIH website. However, we urge the research community to act responsibly and honour the family's wishes. Downloading the HeLa sequence through controlled access is the right and respectful thing to do.

It is important to note, however, that we are responding to an extraordinary situation here, not setting a precedent for research with previously stored, de-identified specimens. The approach we have developed through working with the Lacks family is unique because HeLa cells were taken and used without consent, and gave rise to the most widely used human cell line in the world, and because the family members are known by name to millions of people.

The furore around HeLa cells has brought the absence of consent requirements for some biospecimen research to public attention. Under current US federal guidelines, it is still possible to use specimens and to generate whole-genome sequencing data without the knowledge or permission of the person providing the sample, as long as the biospecimen meets the definition of 'de-identified' (see go.nature.com/2jrzvz). The administration of President Barack Obama is undertaking fundamental reforms for the protection of human subjects in research. Among the factors motivating these reforms is the recognition that non-identifiability is increasingly illusory, owing to technological advances, especially in genomics and computing^{4, 5, 6, 7}. In addition, the relationship between researchers and participants is evolving: seeking permission emphasizes that participants are partners, not just 'subjects'.

“Non-identifiability is increasingly illusory, owing to technological advances.”

In July 2011, the US Department of Health and Human Services issued a notice requesting public comment on how current regulations for protecting participants in research might be revised to be more effective (see go.nature.com/LL6es9). Among other questions, the notice sought comment on whether the department should require consent for future research using samples, identified or not. The notice also sought input on the use of broad consent for unspecified future research use of

specimens. The question assumed that specimens that were collected before a change in regulations would be governed by the old rules. On the basis of those public comments, the department is preparing a new proposal.

It is fitting, given the priceless contributions that Henrietta Lacks has made to science and medicine, that her story is catalysing enduring changes in policy. These should afford future generations of research participants the protections and respect that were not in place during Lacks' lifetime.

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