

1 Biospecimen policy: Family matters

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

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



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LACKS FAMILY/VIRGINIA DEPT HISTORIC RESOURCES

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

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

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

23 Medical history

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

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

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

49 Weighing the options

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

55 We talked at length with the family about the three options available for the full HeLa
56 sequence data: first, making the sequence freely available, allowing anyone access at any time
57 and for any use; second, placing the data in a controlled-access database, which would require
58 researchers to apply to the NIH to use the data in a specific study and to agree to terms of use
59 defined by a panel including members of the Lacks family; or third, withholding the sequence

60 and not making it available at all for research — an option that the NIH would have had
61 difficulty supporting or implementing, philosophically and legally.

62 After much discussion, family members unanimously favoured the controlled-access
63 option. This will allow them to be aware of and have a crucial role in the science that uses the
64 HeLa genome. The NIH will help to implement this, but respecting the family's preferences has
65 required (and will continue to require) cooperation and patience by many — including
66 scientists, publishers, funders and scientific societies. The authors and publishers of both
67 genome papers^{1,2} have agreed to submit their data for controlled access (in the same way as for
68 many other non-HeLa genome sequences) through the NIH's database of genotypes and
69 phenotypes (dbGaP; see go.nature.com/fduced). Likewise, NIH-funded researchers who
70 sequence other HeLa lines will be expected to deposit their data in the dbGaP. We hope that
71 scientists whose work is supported by other funders will do the same.

72 Applications for access to the sequence data will be rapidly reviewed by a newly formed
73 HeLa Genome Data Access working group at the NIH, on which two members of the Lacks
74 family will serve. We believe that this plan reflects the true partnership between the Lacks
75 family and the biomedical-research community. We also ask that all researchers who generate or
76 use genomic data from HeLa cells include in their publications an acknowledgement of the
77 contribution of Lacks and the continued generosity of her family, such as that in Adey and
78 colleagues' paper³.

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

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

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

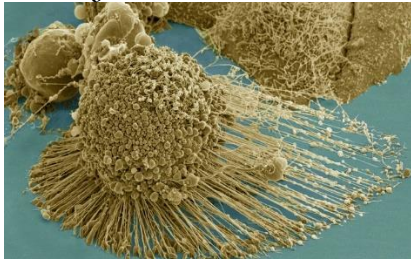
92 The furore around HeLa cells has brought the absence of consent requirements for some
93 biospecimen research to public attention. Under current US federal guidelines, it is still possible
94 to use specimens and to generate whole-genome sequencing data without the knowledge or
95 permission of the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

102 In July 2011, the US Department of Health and Human Services issued a notice
103 requesting public comment on how current regulations for protecting participants in research
104 might be revised to be more effective (see go.nature.com/LL6es9). Among other questions, the
105 notice sought comment on whether the department should require consent for future research
106 using samples, identified or not. The notice also sought input on the use of broad consent for
107 unspecified future research use of specimens. The question assumed that specimens that were
108 collected before a change in regulations would be governed by the old rules. On the basis of
109 those public comments, the department is preparing a new proposal.

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

1 Researchers Finally Ask Henrietta Lacks's Family If They Can Study Her Cells

2 ALLIE JONES



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4 It's taken 62 years, but researchers finally asked Henrietta Lacks's family for consent to use her
5 cancer cells, which have been employed in over 76,000 studies since her death in 1951. Lacks, a
6 poor, black mother of five, died of cervical cancer, but the so-called HeLa cells survived to
7 become a staple of medical science. Journalist Rebecca Skloot called attention to the ethical
8 issues surrounding Lacks's case in her 2010 bestseller *The Immortal Life of Henrietta Lacks*. Now the
9 Lacks family is finally seeing some justice.

10 Over the past four months, the National Institutes of Health has worked out an agreement with
11 the family so that privacy can be maintained while researchers study the cells.

12 When Lacks died, researchers at Johns Hopkins removed the cells from her body without her
13 family's knowledge or consent. Since then, the cells have led to major breakthroughs in various
14 fields of medical research — from the development of the polio vaccine, to treatment of AIDS, to
15 the discovery of how cervical cancer develops.

16 But Lacks's family did not even know about how extensively her cells were being studied until
17 1973. One of Lacks's grandchildren, Jeri Lacks Whye, told *The New York Times*:

18 The biggest concern was privacy — what information was actually going to be out there about
19 our grandmother, and what information they can obtain from her sequencing that will tell them
20 about her children and grandchildren and going down the line.

21 Francis Collins, head of the NIH, told *The Times*, "In my 20 years [here], I can't remember
22 something like this," referring presumably to scientists' tacit acknowledgment that the HeLa cell
23 line had essentially been disseminated (until now) with minimal concern for Lacks's
24 descendants. Were it not for Skloot's book, it is not clear that the present development would
25 have taken place.

26 Before the agreement was made, two separate studies were set to be published, making a
27 genome of a line of HeLa cells available to the public. Now, *The Times* reports that researchers will
28 have to go through a "HeLa Genome Data Access working group" at the NIH to gain access to
29 these studies. Reportedly, members of the Lacks family will have say over who studies the cell
30 line.

31 Though some have warned this solution doesn't address all the issues surrounding genome
32 research and family privacy, it is nevertheless a belated step in the right direction. Skloot, who
33 has been widely hailed for the research she conducted to write her book, thinks the current
34 compromise is a good one, telling CNN, "They get so much pride out of what HeLa cells have
35 done for society and the world. They want HeLa cells to continue to do good. They just want to
36 be part of the conversation.

1 Henrietta Lacks and Race

2 TA-NEHISI COATES

3 FEB 3, 2010

4 There's some talk below about what role race played in Henrietta Lacks' treatment. Here's the
5 author on Fresh Air:

6 GROSS: Was this a standard procedure then, or was this considered experimental?

7 Ms. SKLOOT: Absolutely standard. And this is one of the interesting things, it's sort of an
8 important point in the history of Henrietta Lacks. Her story has often been held up as one of,
9 you know, these sort of, you know, awful, white doctors who did these really kind of vicious
10 treatments to her and stole her cells without telling her because they knew they'd be valuable,
11 and that really wasn't the case at all.

12 They were taking cervical cancer tissues from any woman who walked into Hopkins with
13 cervical cancer, and this was absolutely the standard treatment. And, in fact, it was considered
14 the sort of top of the line.

15 But, you know, there are other questions about, you know, this was a colored ward. This was
16 the Jim Crow era. You know, the reason she was at Hopkins in the first place was because she
17 was black, and there were not really many other hospitals around where she could have gotten
18 treated. She also had no money, and Hopkins was a charity hospital. So she was in the public
19 wards. And, you know, there have been plenty of studies that have looked at how segregation
20 affected health care delivery.

21 So she did get the standard care of the day, but she was definitely sent home -many times after
22 her radiation treatment, she came back complaining of various pains and was sent home and
23 sent home and sent home until she eventually refused to go home and said no, put me in the
24 hospital. And at that point, her cancer had spread so much, and there probably wasn't anything
25 the doctors could have done either way. But, you know, the question of how race played into her
26 health care is a hard one to answer.

27 I just want to add that one thing I've tried to do is get us away from seeing racism/white
28 supremacy as the work of evil immoral hobgoblins, conspiring to do their worst to black people.
29 If it were ever that easy, there would be no racism, and there never would have been any white
30 supremacy. When I wrote:

31 On another point, I'm almost certain I'll never read this book. This has everything to do with me,
32 and nothing to do with the quality of the book, which I'm sure is top-notch. It's just that after
33 awhile, you come to some understanding about the broad truth of black people in this country.
34 Once I got that--once I understood that African-Americans have historically been this country's
35 great unwashed--stories like this are almost predictable.

36
37 Again, that's not a slight on the book, and it's a slight against stories like this. Part of how I've
38 come to that understanding is by reading books exactly like this one. (Bad Blood for instance.)

39 But for me personally, I think I've answered the question that this book would help me to
40 explore.

41 I did not so much mean to leave people with the impression that "clearly they targeted her
42 because she was black" so much as to point out that it's virtually impossible to seriously
43 consider any black person in 1951--a time when white supremacy was practiced in almost every
44 sphere--without thinking about race, about without thinking about black people as the
45 country's great unwashed.

46 It's certainly possible to say that her treatment at the hospital "was standard practice." But when
47 you understand the incredible web of racism which gripped this country in 1951, it becomes very
48 hard to look at any black person living in that time and say "this would have happened exactly
49 the same way to anyone." Racism altered everything.

50 It's never been clear to me that the Tuskegee experiments were performed strictly because the
51 farmers were black. Indeed, it would not shock me at all if at that very moment, some doctors,
52 somewhere in America, were doing something equally heinous to a group of whites. Moreover,
53 some of the black people who assisted thought they were actually helping. It's about more than
54 exclusive villainy. Being black isn't just about being singled out for a particular fate, it's about
55 a *disproportionate chance that you will suffer a particular fate*.

56 At the moment, cervical cancer is one of those fates. Maybe it wasn't back then.

1 Henrietta Lacks: Family win recognition for immortal cells
2 BBC News
3 8 August 2013

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5 The family of a US woman whose cells revolutionised medical research have been granted a say over
6 how they are used, six decades after her death.

7 Henrietta Lacks, a poor black woman from Maryland, had cells removed from her by doctors
8 when she was being treated for terminal cancer in 1951.

9 Researchers found they were the first human cells that could be grown indefinitely in a
10 laboratory.

11 The historic breakthrough paved the way for countless medical treatments.

12 The story of how an African-American tobacco farmer unwittingly transformed biomedicine
13 was made famous by a 2010 best-seller, *The Immortal Life of Henrietta Lacks*.

14 'Left in the dark'

15 She was 31 years old when she died of cervical cancer at Baltimore's Johns Hopkins Hospital.
16 Her tumour cells were removed without her consent, as was typical at the time.
17 Image caption Lacks' extracted cells did something never seen before - they could be kept alive
18 and grow

19 The genetic material later yielded key developments in such areas as vaccines, cancer and
20 fertility treatment, spawning nearly 75,000 studies.

21 But while the "HeLa" genome laid the foundations for the multi-billion dollar biotech industry,
22 Lacks' family have never shared in any of the riches generated by the so-called immortal cell line.

23 Her relatives only learned the cells had not only been extracted, but shipped to laboratories
24 around the world, when a scientist contacted them in 1973 to request a blood sample.
25 The family will still not be paid any money under the agreement reached on Wednesday with
26 the National Institutes of Health, the US government agency which oversees medical research.

27 But they will be granted some control over scientists' access to the cells' DNA code, and receive
28 acknowledgement in the resulting studies.

29 The agreement came about after the relatives raised privacy concerns when German researchers
30 published Lacks' DNA code in March.

31 Rebecca Skloot, author of the acclaimed book about Lacks, took part in the negotiations leading
32 to the agreement and said the family had never asked for money.

33 Jeri Lacks Whye, a granddaughter who lives in Baltimore, said the relatives had always been "left
34 in the dark" about research stemming from HeLa cells.

35 "We are excited to be part of the important HeLa science to come," she told the Associated Press
36 news agency.