A New Chapter for the Lacks Family

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Henrietta Lacks

- Henrietta was born in 1920
- At 31, she was being treated for aggressive cervical cancer at Johns Hopkins
- Researchers took cells from a biopsy for research without her knowledge
- She died that year
- Her cells have been growing for 62yrs
- Family has been dealing with this since

HeLa's History

1951. George Gey first to get human cells to continuously divide in culture

1971. *Obstetrics and Gynecology* identifies Henrietta Lacks as the source of HeLa cells, publishes a photo of Henrietta Lacks

1976. McKusick paper, genetic characteristics of the HeLa cell; includes Lacks pedigree

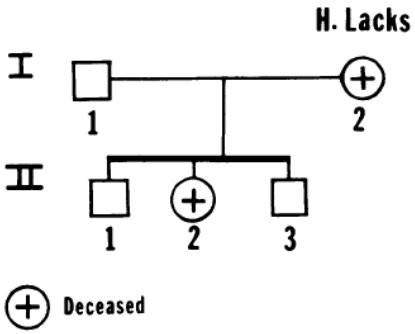
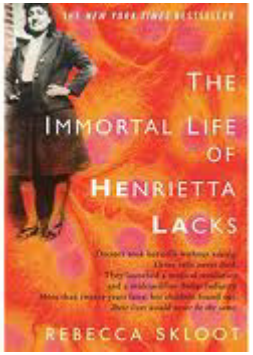


Fig. 1. The pedigree of the Lacks family.

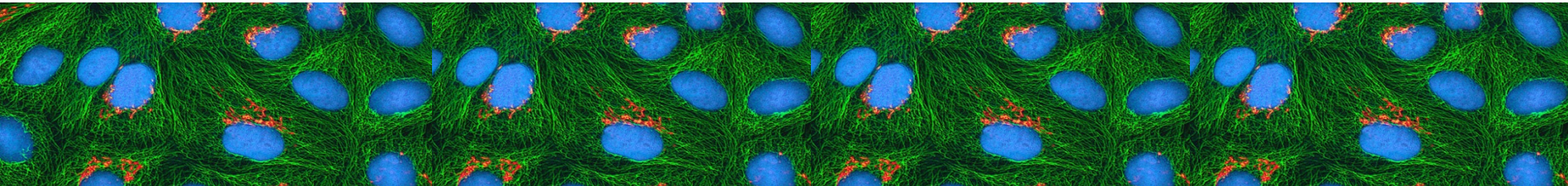
1997. BBC Documentary, *The Way of All Flesh*

2010. *The Immortal Life of Henrietta Lacks*, Skloot



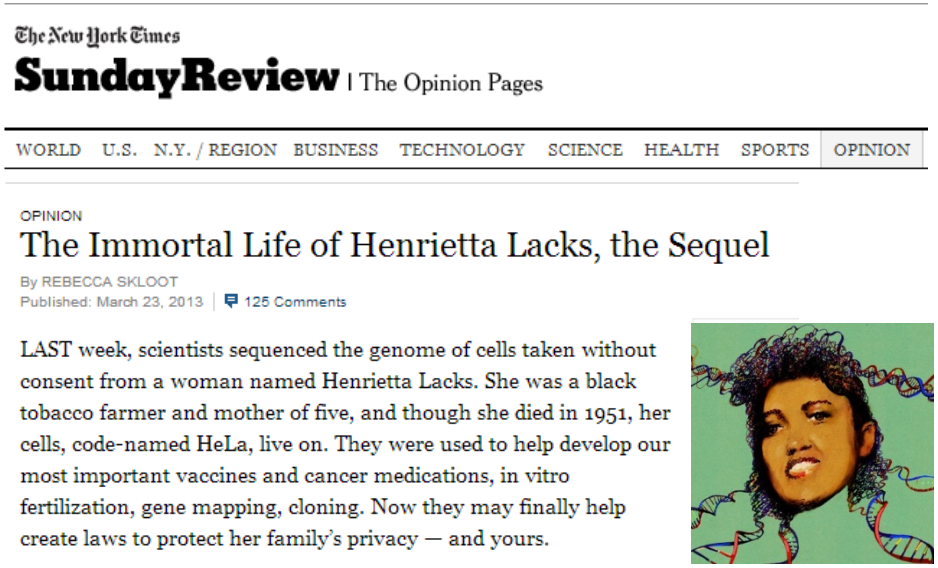
HeLa's Fame

- A Google search for "HeLa cell" generates **2.5 million results**
- **74,000 publications** citing HeLa cells
- In the last ten years, the majority of **Nobel Prizes** in medicine have used HeLa cells
- Accompanied the first man into **space** in 1961;
- And our **youngest scientists** are using HeLa too
  - HeLa cells and nanoscience to test new approaches to fight cancer *(2013 Semifinalist, Intel Science Talent Search)*
  - Screens for promising candidate compounds for a non-addictive painkiller *(2012 finalist, Siemens Competition in Math, Science, and Technology)*



Then…

- March 2013 – researchers in Germany posted the 1st HeLa whole genome sequence (EBI mirrored by NCBI)
- Lacks family asked that the sequence be removed – data taken down
- Another publication pending with Nature
- Twittersphere alive with suddenly hyperethical genomics researchers
- NIH reached out to the family



The New York Times
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OPINION

The Immortal Life of Henrietta Lacks, the Sequel

By REBECCA SKLOOT
Published: March 23, 2013 | 125 Comments

LAST week, scientists sequenced the genome of cells taken without consent from a woman named Henrietta Lacks. She was a black tobacco farmer and mother of five, and though she died in 1951, her cells, code-named HeLa, live on. They were used to help develop our most important vaccines and cancer medications, in vitro fertilization, gene mapping, cloning. Now they may finally help create laws to protect her family's privacy — and yours.

"I look at it as though these are my grandmother's medical records that are just out there for the world to see."

- Jeri Lacks-Whye, granddaughter

A Solution to Match the Problem

- HeLa cells have been invaluable; still used ubiquitously
- There are 1,300 gigabases of HeLa sequence in public data bases
- HeLa cells can be sequenced at any time
- The family has been through decades of unwanted intrusions and surprises
- Yet, no one had broken any laws
- Solution needed to advance science, respect family, and catalyze policy advances.

Working with the Lacks Family

LETTER

The haplotype-resolved genome an the aneuploid HeLa cancer cell line

Andrew Adey[1]*, Joshua N. Burton[1]*, Jacob O. Kitzman[1]*, Joseph B. Hiatt[1], Alexandra P
Choli Lee[1] & Jay Shendure[1]

The HeLa cell line was established in 1951 from cervical cancer cells taken from a patient, Henrietta Lacks. This was the first successful attempt to immortalize human-derived cells *in vitro*[1]. The robust growth and unrestricted distribution of HeLa cells resulted in its broad adoption—both intentionally and through widespread cross-contamination[2]—and for the past 60 years it has served a role analogous to that of a model organism[3]. The cumulative impact of the HeLa cell line on research is demonstrated by its occurrence in more than 74,000 PubMed abstracts (approximately 0.3%). The genomic architecture of HeLa remains largely unexplored beyond its karyotype[4], partly because like many cancers, its extensive aneuploidy renders such analyses challenging. We carried out haplotype-resolved whole-genome sequencing[5] of the HeLa CCL-2 strain, examined point- and indel-mutation variations, mapped copy-number variations and loss of heterozygosity regions, and phased variants across full chromosome arms. We also investigated variation and copy-number profiles for HeLa S3 and eight additional strains. We find that HeLa is relatively stable in terms of point variation, with few new mutations accumulating after early passaging. Haplotype resolution facilitated reconstruction of an amplified, highly rearranged region of chromosome 8q24.21 at which integration of the human papilloma virus type 18 (HPV-18) genome occurred and that is likely to be the event that initiated tumorigenesis. We combined these maps with RNA-seq[6] and ENCODE Project[7] data sets to phase the HeLa epigenome. This revealed strong, haplotype-specific activation of the proto-oncogene *MYC* by the integrated HPV-18 genome approximately 500 kilobases upstream, and enabled global analyses of the relationship between gene dosage and expression. These data provide an extensively phased, high-quality reference genome for past and future experiments relying on HeLa, and demonstrate the value of haplotype resolution for characterizing cancer genomes and epigenomes.

We generated a haplotype-resolved genome sequence of HeLa CCL-2 using a multifaceted approach that included shotgun, mate-pair and long-read sequencing, as well as sequencing of pools of fosmid clones[5] (Supplementary Table 1). To catalogue variants, we carried out conventional shotgun sequencing to 88× non-duplicate coverage and reanalysed 11 control germline genomes in parallel[8] (Supplementary Tables 2 and 3). Although normal tissue corresponding to HeLa is unavailable, the total number of single-nucleotide variants (SNVs) identified in HeLa CCL-2 ($n = 4.1 \times 10^6$) and the proportion overlapping with the 1000 Genomes Project[9] (90.2%) were similar to controls (mean $n = 4.2 \times 10^6$ and 87.7%, respectively), suggesting that HeLa has not accumulated appreciably large numbers of somatic SNVs relative to inherited variants. Indel variation was unremarkable after accounting for differences in coverage (Supplementary Fig. 1). Short tandem repeat profiles of HeLa also resembled controls, consistent with mismatch repair proficiency (Supplementary Fig. 2).

After removing protein-altering variants that overlapped with the 1000 Genomes Project or the Exome Sequencing Project[10], similar numbers of private protein-altering (PPA) SNVs were found in HeLa ($n = 269$) and cor
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(Supplementary Figs 5 a
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*These authors contributed equally to this work.

COMMENT

COURTESY OF LACKS FAMILY

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

Family matters

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.

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 published[1] 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.

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

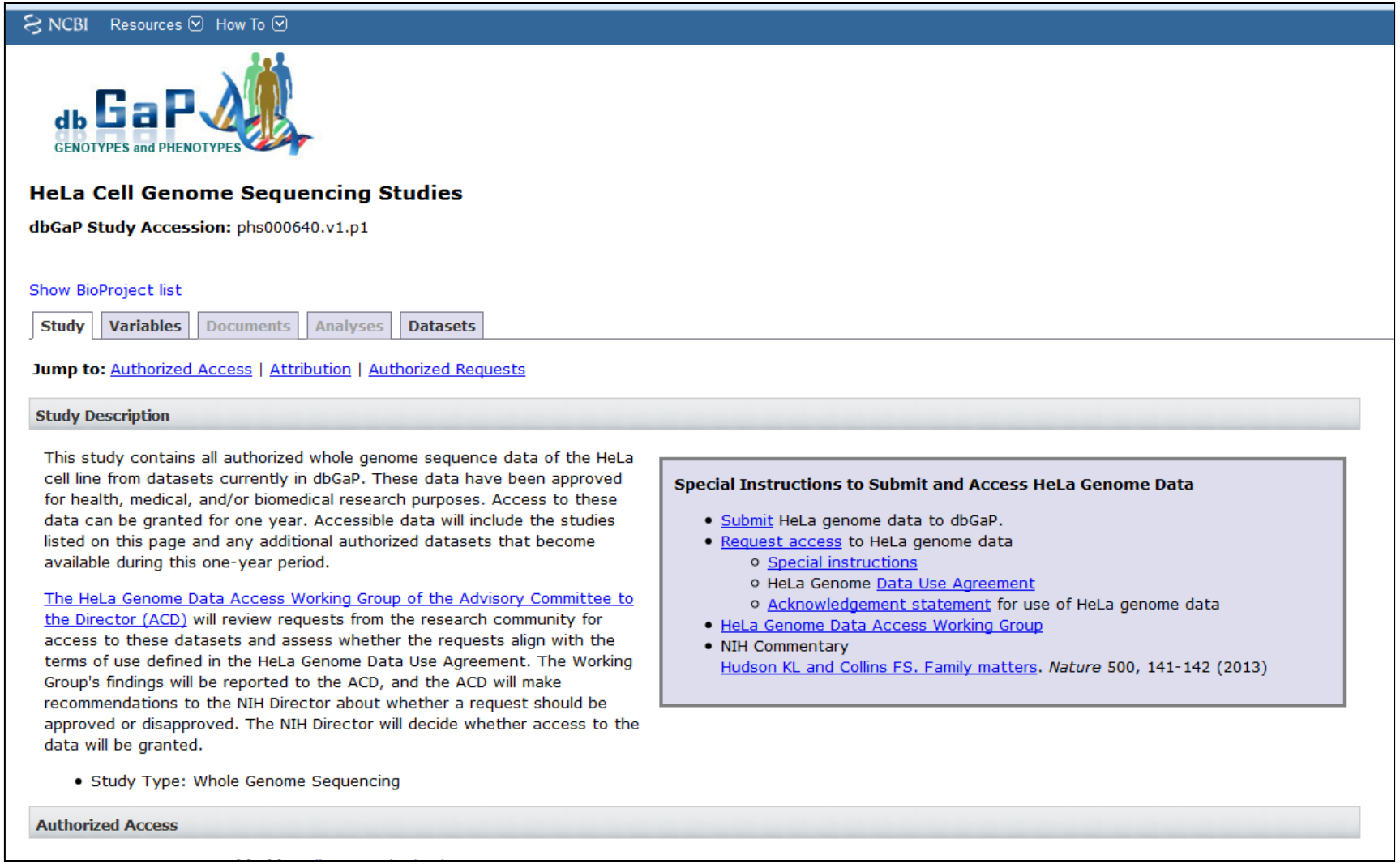
In 1951, physicians at Johns Hopkins Hospital in Baltimore, Maryland, took a biopsy from Henrietta Lacks, a 31-year-old African American woman who had an aggressive form of cervical cancer. This biospecimen was taken without her permission or knowledge; US regulations requiring consent ▶

Elements of the Agreement

NIH is requesting that **all researchers**:

- Apply for access to HeLa whole genome sequence
- Abide by terms defined by the Lacks family
  - Biomedical research only
  - No contact with family
  - Disclosure of commercial plans
  - Include acknowledgment in publications and presentations
- Deposit future whole genome sequence data into dbGaP
- New working group established to review requests

HeLa gets a dbGaP page



NCBI Resources How To

dbGaP GENOTYPES and PHENOTYPES

HeLa Cell Genome Sequencing Studies

dbGaP Study Accession: phs000640.v1.p1

Show BioProject list

Study | Variables | Documents | Analyses | Datasets

Jump to: Authorized Access | Attribution | Authorized Requests

Study Description

This study contains all authorized whole genome sequence data of the HeLa cell line from datasets currently in dbGaP. These data have been approved for health, medical, and/or biomedical research purposes. Access to these data can be granted for one year. Accessible data will include the studies listed on this page and any additional authorized datasets that become available during this one-year period.

The HeLa Genome Data Access Working Group of the Advisory Committee to the Director (ACD) will review requests from the research community for access to these datasets and assess whether the requests align with the terms of use defined in the HeLa Genome Data Use Agreement. The Working Group's findings will be reported to the ACD, and the ACD will make recommendations to the NIH Director about whether a request should be approved or disapproved. The NIH Director will decide whether access to the data will be granted.

- Study Type: Whole Genome Sequencing

Special Instructions to Submit and Access HeLa Genome Data

- Submit HeLa genome data to dbGaP.
- Request access to HeLa genome data
  - Special instructions
  - HeLa Genome Data Use Agreement
  - Acknowledgement statement for use of HeLa genome data
- HeLa Genome Data Access Working Group
- NIH Commentary
  Hudson KL and Collins FS. Family matters. *Nature* 500, 141-142 (2013)

Authorized Access

HeLa Genome Data Access Working Group
Advisory Committee to the Director

Renee Jenkins, M.D. (CHAIR)
Professor and Chair Emeritus
Department of Pediatrics and Child Health
Howard University

Russ B. Altman, M.D., Ph.D.
Professor, Bioengineering, Genetics, & Medicine
Director, Biomedical Informatics Training Program
Stanford University

Ruth Faden, Ph.D., M.P.H.
Philip Franklin Wagley Professor in Biomedical Ethics
Director, Johns Hopkins Berman Institute of Bioethics
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David Lacks Jr.
Representative, Henrietta Lacks Family
Baltimore, MD

Veronica Spencer
Representative, Henrietta Lacks Family
Baltimore, MD

Clyde W. Yancy, M.D.
Professor in Medicine-Cardiology and Medical Social Sciences
Chief, Division of Medicine-Cardiology
Northwestern University
Feinberg School of Medicine

"In the past, the Lacks family has been left in the dark…we are excited to be part of the important HeLa science to come."

- Jeri Lacks-Whye, granddaughter

nature

NATURE | NEWS

Deal done over HeLa cell line

Family of Henrietta Lacks agrees to release of genomic data.

Ewen Callaway

07 August 2013

Deborah Lacks wanted answers. In 1974, she asked a leading medical geneticist to tell her about HeLa cells, a tissue-culture cell line derived from the cancer that had killed her mother Henrietta in 1951. The researcher, who was collecting blood from the Lacks family to map HeLa genes, autographed a medical textbook he had

THE WALL STREET JOURNAL.

NIH in Pact to Protect Privacy of Family, Maintain Research

Agreement Affects Access to DNA Data From Cells of Henrietta Lacks

By RON WINSLOW August 7, 2013, 2:21 p.m. ET

The National Institutes of Health said Wednesday it reached an unprecedented agreement to protect the privacy of the family of a woman whose cancer cells have been used as a basis for thousands of medical studies in recent decades.

The pact, which affects researchers' access to DNA data from laboratory cells derived from the tumor tissue, addresses a thorny issue in medical research—how to balance the needs of researchers and the rights of patients when seeking access to scientifically important but potentially sensitive personal medical data.

AP

In 1951, long before federal regulations requiring patient consent were in place, Henrietta Lacks was diagnosed with an aggressive form of cervical cancer. Doctors at Johns Hopkins Hospital, Baltimore, took a biopsy of her tumor without her permission. It turned out that cells from the tissue had the rare ability to grow endlessly in laboratory cultures,

What now?

- Pending data requests
  - 1st data request to dbGaP: **August 19th**
  - We now have 4 data requests
  - Inaugural Working Group meeting: **September 12th**
  - Recommendations to ACD: **September 16th**

    entire process completed in under 1 month!

- Working Group to figure out other issues:
  - Scope of HeLa genomic data in dbGaP
  - Are the data use limitations the right ones?