

HeLa Genome Data Access Working Group

Report to the Advisory Committee to the Director

June 13, 2019

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Acting Chief of Staff
Associate Director for Science Policy
National Institutes of Health

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Director, Centers for American Indian and Alaska Native Health
The Colorado Trust Chair in American Indian Health
Associate Dean for Research at the Colorado School of Public
Health
University of Colorado

The HeLa Genome Data Use Agreement

Per the agreement between NIH and the Lacks family, NIH is requesting that ***all researchers***:

- Apply for access to HeLa whole genome sequence in the database of Genotype and Phenotype (dbGaP)
- Abide by terms outlined in the HeLa Genome Data Use Agreement, such as:
 - Data can only be used for biomedical research only; this does not include the study of population origins or ancestry
 - Requestors are not to make contact with the Lacks family
 - Requestors are to disclose any commercial plans
 - Requestors are to include an acknowledgment in publications and presentations
- Deposit future whole genome sequence data into dbGaP

Role of HeLa Genome Data Access Working Group

- Evaluate requests to access HeLa cell genome data in dbGaP for consistency with the terms of the HeLa Genome Data Use Agreement
 - Evaluation not based on scientific merit
- Report findings to the Advisory Committee to the Director
- Make recommendations to the ACD on changes to the terms specified in the HeLa Genome Data Use Agreement

HeLa Genome Data Access Working Group Roster

Spero M. Mason, Ph.D. (Co-Chair)

Distinguished Professor of Public Health and Psychiatry
Director, Centers for American Indian and Alaska Native Health
The Colorado Trust Chair in American Indian Health
Associate Dean for Research at the Colorado School of Public Health
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Carrie D. Wolinetz, Ph.D. (Co-Chair)

Acting Chief of Staff
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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
Bloomberg School of Public Health
Johns Hopkins University

David Lacks Jr.

Representative, Henrietta Lacks Family

Jeri Lacks-Whye

Representative, Henrietta Lacks Family

Richard M. Myers, Ph.D.

President, Director and Faculty Investigator
HudsonAlpha Institute for Biotechnology

Robert L. Nussbaum, M.D.

Chief Medical Officer
Invitae Corporation

Veronica Spencer

Representative, Henrietta Lacks Family

Working Group Evaluation Criteria

- Is the proposed research focused on health, medical, or biomedical research objectives?
 - Is the proposed research related to determining the ancestry or population origins of HeLa cells?
- Are there any plans to develop intellectual property?
Specifically:
 - Does the requestor anticipate or foresee IP or developing commercial products or services from the proposed research?
 - Has the requestor agreed to notify NIH if their plans for IP or commercial products change?
- Are there any plans to publish or present findings?

Types of Findings Reported by the Working Group

In evaluating a Data Access Request, the Working Group will report a finding as:

- **Consistent** with the Data Use Agreement
- **Inconsistent** with the Data Use Agreement
- **Conditional** (will be consistent with the Data Use Agreement if NIH staff find that additional information obtained from the Requestor is satisfactory)
- **Pending** (will require a re-evaluation from the Working group once additional information is obtained from the Requestor)

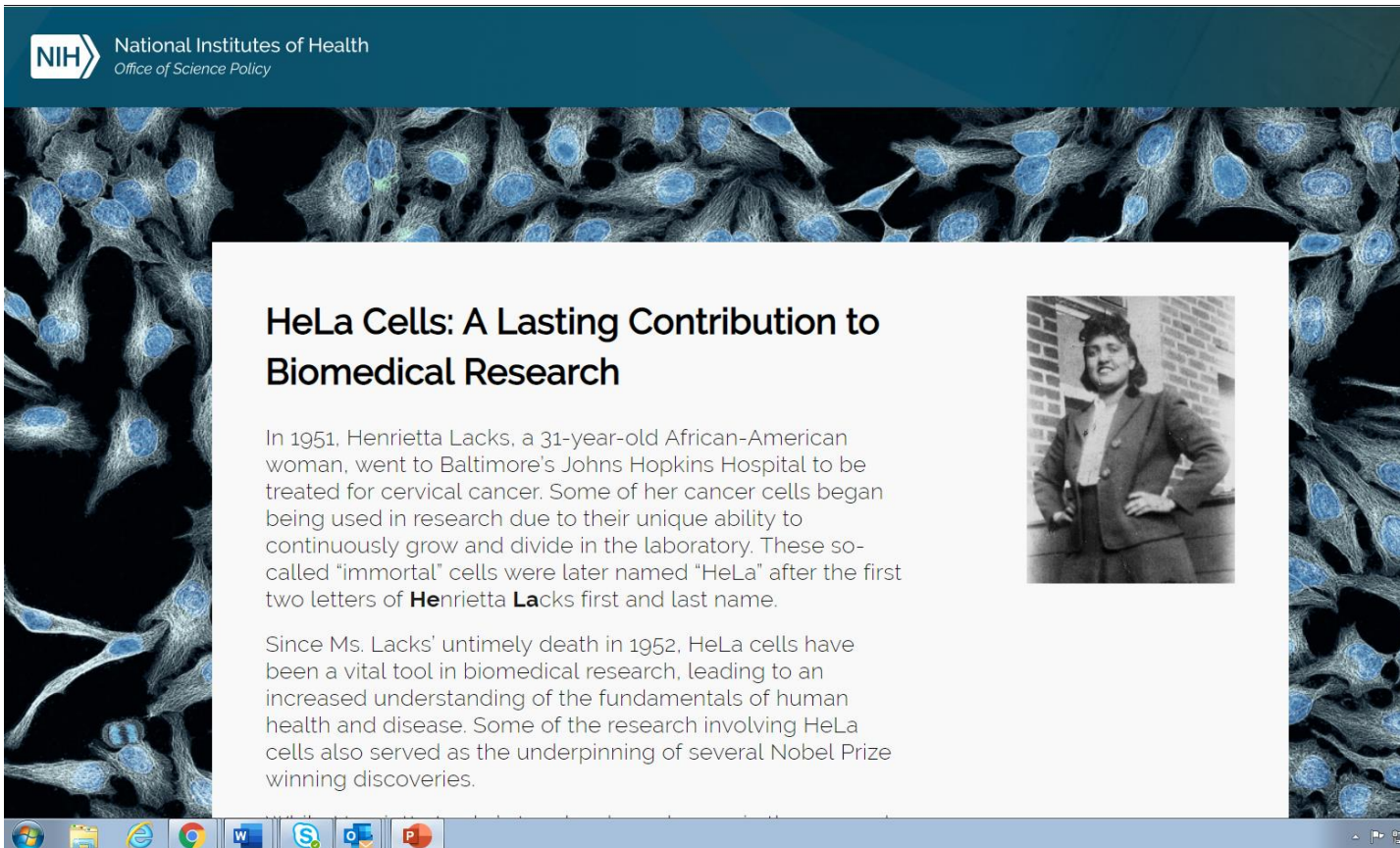
Status of Data Access Requests

Number of Requests	Status
84	Evaluated by the HeLa Genome Data Access Working Group
74	Approved by NIH Director
1	Disapproved by NIH Director
5	Disapproved by NIH staff (requestors did not respond to requests for clarifications regarding publication plans, IP, and/or the non-technical summary)
Number of New Requests	Status
4	Being reported to ACD today

HeLa Whole Genome Sequence Data in dbGaP

Principal Investigator	Institution	Project Title	Year
John Moran	University of Michigan	RNA Ligation Precedes U6 snRNA/LINE-1 Retrotransposition	2018
John Moran	University of Michigan	Examination of Engineered LINE-1 Integration Events in HeLa Cells	2018
David Gilbert	Florida State University	Bacterial Artificial Chromosomes Establish Replication Timing and Sub-nuclear Compartment de novo as Extra-chromosomal Vectors	2018
Wataru Yoshida	Tokyo University of Technology, Japan	Identification of G-quadruplex Clusters by High-throughput Sequencing of Whole Genome Amplified Products with G-quadruplex Ligand	2018
Andrew Adey	Oregon Health and Science University, USA	Construction of Thousands of Single Cell Genome Sequencing Libraries using Combinatorial Indexing	2017
Jay Shendure	University of Washington, USA	Massively Multiplex Single-cell Hi-C	2016
Xun Xu	BGI-Shenzhen, China	Full-length Single-cell RNA-seq Applied to a Viral Human Cancer: Applications to HPV Expression and Splicing Analysis in HeLa S3 Cells	2016
Erez Aiden	Baylor College of Medicine, USA	A 3D Map of the Human Genome at Kilobase Resolution Reveals Principles of Chromatin Looping	2016
Jay Shendure	University of Washington, USA	Chromosome-scale Scaffolding of de novo Genome Assemblies Based on Chromatin Interactions	2014
Jay Shendure	University of Washington, USA	The Haplotype-resolved Genome and Epigenome of the Aneuploid HeLa Cancer Cell Line	2013
Lars Steinmetz	European Molecular Biology Laboratory	The Genomic and Transcriptomic Landscape of a HeLa Cell Line	2013

A new interactive web resource!




The screenshot shows a web page from the National Institutes of Health Office of Science Policy. The page features a dark teal header with the NIH logo and text. The main content area is framed by a background image of HeLa cells. The central text is white on a dark background, with a small black and white photograph of Henrietta Lacks on the right. At the bottom, a Windows taskbar is visible with icons for various applications.

NIH National Institutes of Health
Office of Science Policy

HeLa Cells: A Lasting Contribution to Biomedical Research

In 1951, Henrietta Lacks, a 31-year-old African-American woman, went to Baltimore's Johns Hopkins Hospital to be treated for cervical cancer. Some of her cancer cells began being used in research due to their unique ability to continuously grow and divide in the laboratory. These so-called "immortal" cells were later named "HeLa" after the first two letters of **H**enrietta **L**acks first and last name.

Since Ms. Lacks' untimely death in 1952, HeLa cells have been a vital tool in biomedical research, leading to an increased understanding of the fundamentals of human health and disease. Some of the research involving HeLa cells also served as the underpinning of several Nobel Prize winning discoveries.

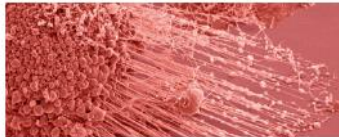


<https://osp.od.nih.gov/scientific-sharing/hela-cells-landing/>

Celebrating the contributions of HeLa

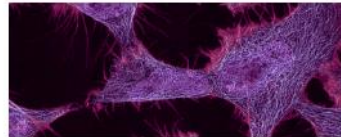
- Relational chord chart that shows the interconnectivity of HeLa cells in biomedical research
- An interactive world-map
- Links and information on highly cited papers, 1953-2017
- Timeline of significant research milestones

Explore HeLa's impact on research over the past six decades



Significant Research Advances Enabled by HeLa Cells

View a timeline of HeLa-related research achievements and events



HeLa Around the World

Navigate a map to see what countries have used HeLa cells for research



Science Topics Using HeLa Cells

Observe the vast spectrum of research areas that HeLa has supported



Publications Involving HeLa Cells

View the number of publications using HeLa cells over the years

Working Group Findings: Evaluation of Access Requests

Since the last ACD meeting, the Working Group found 2 requests to be consistent with the HeLa Genome Data Use Agreement

Project Title	Requestor's Affiliation	Project Overview	Working Group Findings
Allele-specific gene expression patterns in cancer	National Centre for Biological Sciences	<ul style="list-style-type: none"> • “Allele-specific” gene expression, or gene expression that varies because of a genetic change of the same gene, has been observed to have a role in the development of most cancers. The investigator proposes to study the role of allele-specific gene expression in cervical cancer. As a subset of cervical cancer arises as a result of infection and genomic integration by the human papillomavirus (HPV), the investigator also proposes to study the role of HPV in regulating allele-specific gene expression in cervical cancer. • Since the HeLa Cell Genome Sequencing Studies are derived from the HeLa cervical cancer cell line, the investigator requests to use the HeLa Cell Genome Sequencing Studies to identify cervical cancer-related genes whose expression may be changed by allele-specific gene expression and/or HPV. 	CONSISTENT WITH DATA USE AGREEMENT
Modified Capture-C approach	Mental Health Research Center	<ul style="list-style-type: none"> • Previous laboratory studies identified the importance of genome organization in the regulation of gene expression. To enhance the study of genome organization, chromosome conformation capture (i.e., a technique that quantifies the number of genomic interactions) followed by high-throughput sequencing utilizing a specific bioinformatics pipeline (i.e., Hi-C) was developed to identify specific regions of the genome that interact with one another to start and/or enhance gene expression. • The investigator proposes to use Hi-C data from the HeLa Cell Genome Sequencing studies to validate their Hi-C bioinformatics pipeline that looks to improve upon the ability to observe specific regions of the genome that start and/or enhance gene expression. 	CONSISTENT WITH DATA USE AGREEMENT

Working Group Findings: Evaluation of Access Requests

Project Title	Requestor's Affiliation	Project Overview	Working Group Findings
Spatial Interaction and Annotation of HPV Integrations	City University of Hong Kong	<ul style="list-style-type: none"> • Genome instability, such as chromosome addition, deletion, or duplication, occurs frequently in cancer. One cause of genome instability is when a virus embeds itself, or integrates, into a genome. Viral integration not only results in genome instability but can change chromosomal spatial organization, or the location of chromosomes, which can increase or decrease gene expression. Abnormal changes in gene expression are a common feature in cancer cells. • To investigate how viral integration can lead to genome instability, the investigator developed an algorithm that can identify viral integration sites on chromosomes. The investigator requests to use the HeLa Cell Genome Sequencing Studies, in particular the data that best describes the spatial organization of HeLa genomic data, to see if their algorithm can accurately detect viral integration sites and if so, then identify chromosomal regions that interact with the viral integration sites that increase or decrease gene expression. 	CONSISTENT WITH DATA USE AGREEMENT
Interplay of Chromatin Organization and Dynamics	European Molecular Biology Laboratory	<ul style="list-style-type: none"> • The DNA double helix in the cell nucleus is wound tightly and packaged by special proteins called histones. The protein/DNA complex is called chromatin. Chromatin organization, or the structural organization of the protein/DNA complex in a cell, is important to gene expression and function. • The investigator seeks to study the dramatic changes of chromatin structure using a live-cell time-lapse microscopy method, developed by the investigator, to identify and categorize chromatin movement and organization in HeLa cells. In order to conduct this study, the investigator requests the use of genomic data from the HeLa Cell Genome Sequencing Studies to inform the development of molecular probes that will label chromatin in HeLa cells to enable the use of the investigator's live-cell time-lapse microscopy method in HeLa cells. The investigator would also like to use the HeLa cell sequence genome as a reference to map HeLa cell chromatin changes. 	CONSISTENT WITH DATA USE AGREEMENT

ACD Discussion, Vote, and Recommendations

Working Group Findings: Evaluation of Access Requests

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Modified Capture-C approach	Mental Health Research Center	CONSISTENT WITH DATA USE AGREEMENT
Spatial Interaction and Annotation of HPV Integrations	City University of Hong Kong	CONSISTENT WITH DATA USE AGREEMENT
Interplay of Chromatin Organization and Dynamics	European Molecular Biology Laboratory	CONSISTENT WITH DATA USE AGREEMENT