HeLa Genome Data Access Working Group

Report to the Advisory Committee to the Director

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The Colorado Trust Chair in American Indian Health
Associate Dean for Research at the Colorado School of Public Health
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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)
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Russ B. Altman, M.D., Ph.D.
Professor, Bioengineering, Genetics, & Medicine
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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

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

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
88	Evaluated by the HeLa Genome Data Access Working Group
78	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

Working Group Findings: Evaluation of Access Requests

Since the last ACD meeting, the Working Group found 4 requests to be consistent with the HeLa Genome Data Use Agreement

Project Title	Requestor's Affiliation	Project Overview	Working Group Findings
Characterizing the role of immune gene polymorphisms in cancer predisposition	University of California	• Previous laboratory studies conducted by the Requestor demonstrated that genetic changes in key immune system genes play a role in how tumors develop and affect the ability of the immune system to attack tumors. • The investigator proposes to build upon this research by studying the genetic changes in more detail, how the changes are related the increased susceptibility that some individuals have to tumors, and how these individuals might respond to therapies that help the immune system attack tumors. • The Hela Genome Sequencing Studies data will be used to perform an analysis of HeLa cell surface protein "flags" that play an important role in the ability of immune system to identify and attack the cancer cell.	CONSISTENT WITH DATA USE AGREEMENT
High-risk HPV infection and development of cervical cancer	National Institutes of Health	• The investigator previously developed a method to detect the location of viruses that integrate, or cut-and-paste themselves, into other genomes. Viral integration into other genomes is random and, sometimes can promote cancer cell development. • The investigator proposes to use the HeLa Cell Genome Sequencing Studies, along with their new method, to verify viral integration and in some cases, better understand how viral integration at a particular location may have promoted cancer cell development.	CONSISTENT WITH DATA USE AGREEMENT

Working Group Findings: Evaluation of Access Requests

Project Title	Requestor's Affiliation	Project Overview	Working Group Findings
Spatial organization and disorganization in immortal cell genomes	Institut Pasteur	• The investigator's team has previously investigated the three-dimensional organization of genomes in various organisms such as bacteria and yeasts using special algorithms developed by the group. • The team would like to characterize loop structures in the HeLa genome with the goal of identifying the factors behind their formation and maintenance, and ultimately how the structures regulate gene expression and other vital functions.	CONSISTENT WITH DATA USE AGREEMENT
RNAseq analysis using HeLa genome sequence	Missouri State University	• Previous research with cancer cells treated with quantum dots (man-made nanocrystals that can emit light) or metal nanoparticles such as platinum and palladium, reported slower cancer cell growth and perhaps cancer cell targeting. • The investigator proposes to use the HeLa Cell Genome Sequencing Studies to study the impact quantum dots and platinum and pallidum-based nanoparticles have on cellular physiology by measuring changes in HeLa cell gene expression in treated and untreated cells.	CONSISTENT WITH DATA USE AGREEMENT

ACD Discussion, Vote, and Recommendations

Working Group Findings: Evaluation of Access Requests

Project Title	Requestor's Affiliation	Working Group Findings
Allele-specific Gene Expression Patterns in Cancer	National Centre for Biological Sciences	CONSISTENT WITH DATA USE AGREEMENT
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