HeLa Genome Data Access Working Group

Report to the Advisory Committee to the Director

June 8, 2017

Carrie D. Wolinetz, Ph.D.
Associate Director for Science Policy
National Institutes of Health

Lisa A. Cooper, M.D., M.P.H., FACP
Bloomberg Distinguished Professor
James F. Fries Professor of Medicine and Director, Johns Hopkins Center to Eliminate Cardiovascular Health Disparities
Johns Hopkins University School of Medicine

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

Lisa A. Cooper, M.D., M.P.H., FACP (Co-Chair)
Bloomberg Distinguished Professor,
James F. Fries Professor of Medicine and Director, Johns Hopkins Center to Eliminate Cardiovascular Health Disparities
Johns Hopkins University School of Medicine

Carrie D. Wolinetz, Ph.D. (Co-Chair)
Associate Director for Science Policy
National Institutes of Health

Russ 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

Richard Myers, Ph.D.
President, Director and Faculty Investigator
HudsonAlpha Institute

Robert 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	Submission Year
Andrew Adey	Oregon Health and Science University	Construction of thousands of single cell genome sequencing libraries using combinatorial indexing	2017
Jay Shendure	University of Washington	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	A 3D Map of the Human Genome at Kilobase Resolution Reveals Principles of Chromatin Looping	2016
Jay Shendure	University of Washington	Chromosome-scale scaffolding of de novo genome assemblies based on chromatin interactions	2014
Jay Shendure	University of Washington	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
67	Evaluated by the HeLa Genome Data Access Working Group
55	Approved by NIH Director
1	Disapproved by NIH Director
7	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 has found 4 requests to be consistent with the HeLa Genome Data Use Agreement:

Project Title	Requestor's Affiliation	Project Overview	Working Group Findings
HeLa Mitosis Chromatin Organization Study	**Stanford University**	• **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, which is highly dynamic, unwinding and rewinding to allow for numerous cellular events such as gene expression or DNA replication. Current evidence suggests that unregulated chromatin dynamics can lead to cell division errors, during a process called mitosis, and can lead to cancer.** • **The investigator proposes to study the changes in chromatin structure during cell division using a method, developed by the investigator, during the cell cycle in HeLa cells. The investigator requests to use the HeLa sequence genome data as a reference to accurately map chromatin changes in HeLa cells.**	**CONSISTENT WITH DATA USE AGREEMENT**
Study of Genome Stability in Humans	**University of Oxford**	• **Fanconi Anemia (FA) is a rare genetic disease that causes instability in the genome resulting from genetic mutations. Having the ability to use a cell line with well-characterized genetics to understand the molecular mechanisms of FA and genome instability could shed light on this disease.** • **The investigator requests to use the HeLa cell line and genome data to uncover the molecular mechanisms underlying the biological pathway responsible for FA using techniques that include biochemistry, molecular biology, cell biology, and genetics.**	**CONSISTENT WITH DATA USE AGREEMENT**

Working Group Findings: Evaluation of Access Requests

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

Project Title	Requestor's Affiliation	Project Overview	Working Group Findings
Genome Engineering in HeLa Cell Lines	**Shanghai Jiao Tong University School of Medicine**	• **As part of its life cycle, the human papillomavirus (HPV) inserts its DNA into the human genome, which may disrupt genes and lead to cervical cancer.** • **The number of HPV insertions into the human genome has been positively correlated with increased cervical cancer severity. Therefore, being able to identify where HPV preferentially inserts into the human genome could provide insight into how HPV drives cervical cancer.** • **The investigator proposes to precisely characterize the preferred insertion locations of HPV into the human genome to understand how HPV becomes a driver of cervical cancer, using the HeLa genome sequence data as a reference map.**	**CONSISTENT WITH DATA USE AGREEMENT**
HeLa CRISPR-Cas9 Editing	**Johns Hopkins University**	• **Cells can acquire mutations to their genomic sequence that can lead to cancer. These mutations do not appear in the human reference genome sequence. Therefore, the human reference genome may not provide enough information for investigators to accurately design molecular editing tools, such as the CRISPR-Cas9 editing technology.** • **The investigator proposes to study the effect of editing essential genes in cancer cells using the HeLa whole genome sequence data as a reference to develop CRISPR-Cas9 gene editing tools.**	**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
HeLa Mitosis Chromatin Organization Study	Stanford University	CONSISTENT WITH DATA USE AGREEMENT
Study of Genome Stability in Humans	University of Oxford	CONSISTENT WITH DATA USE AGREEMENT
Genome Engineering in HeLa Cell Lines	Shanghai Jiao Tong University School of Medicine	CONSISTENT WITH DATA USE AGREEMENT
HeLa CRISPR-Cas9 Editing	Johns Hopkins University	CONSISTENT WITH DATA USE AGREEMENT