TOPMed

Data overview and access

TOPMed Data Coordinating Center
University of Washington

October 26th, 2020
ASHG Ancillary Session

TOPMed Website - www.nhlbiwgs.org

About TOPMed

Updated 08/10/2020

Contents

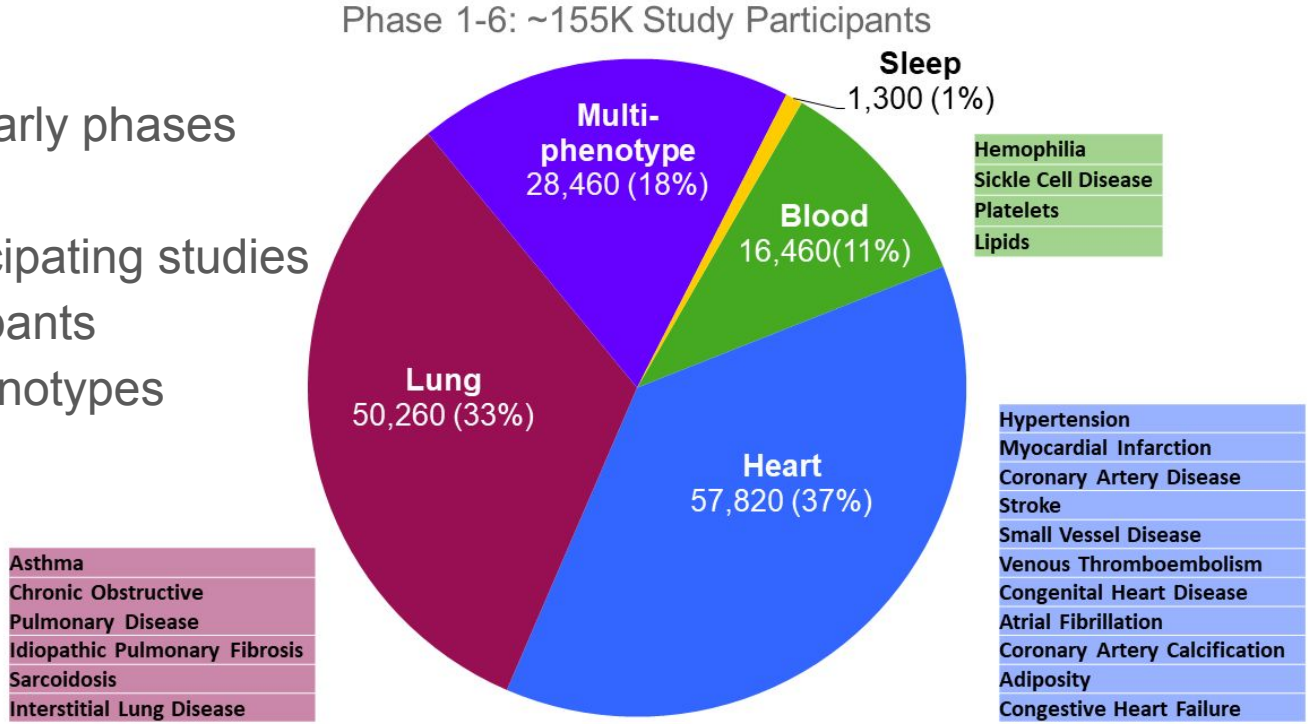
- Overview
- Study Characteristics
  - Study Designs
  - Participant Diversity
- Whole Genome Sequencing
- Resources for the Scientific Community

Central hub of information for the scientific community

- TOPMed Projects and Studies
- WGS and Omics methods documentation
- Data access instructions
- Publications and Abstracts

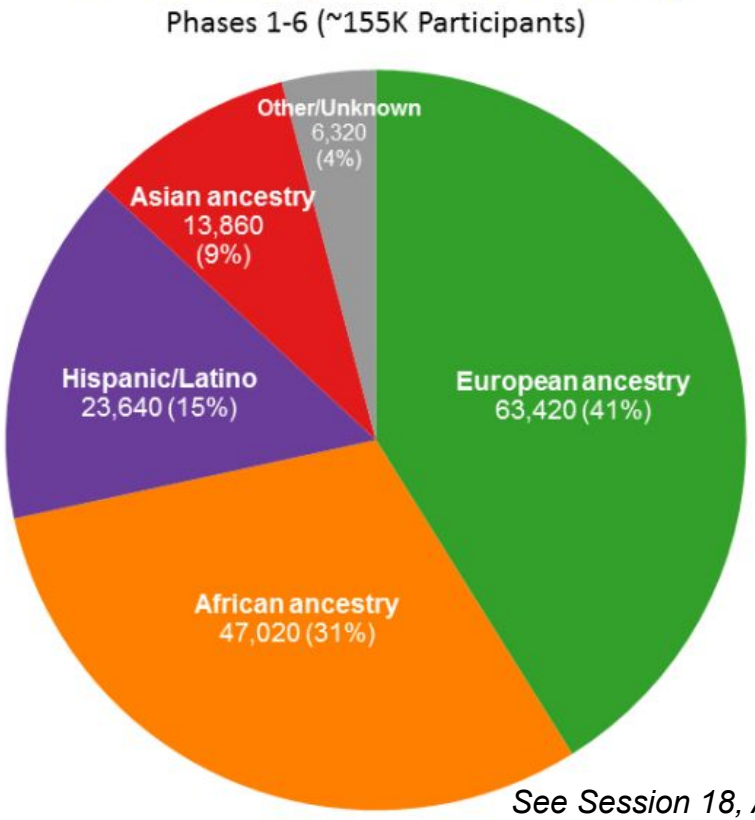
TOPMed: Participating Studies

- Studies added in yearly phases
- First phase in 2015
- Currently > 80 participating studies
- ~155K study participants
- Range of HLBS phenotypes

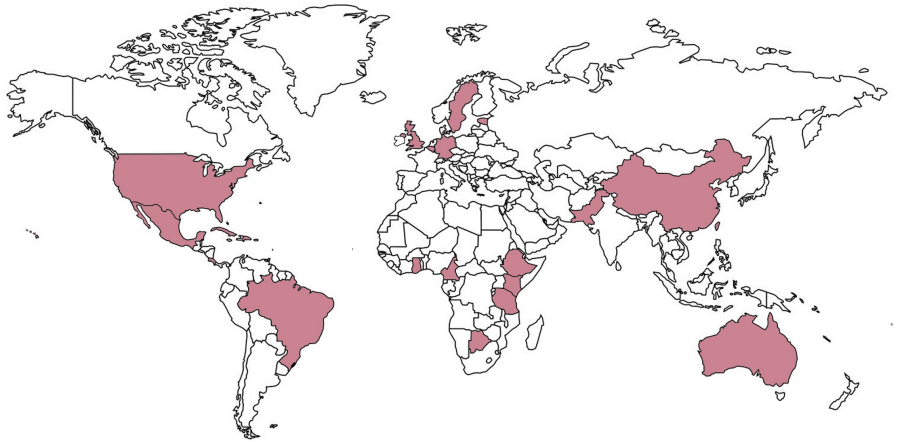


More info: www.nhlbiwgs.org/, “About TOPMed”; https://www.nhlbiwgs.org/group/project-studies

TOPMed: Participant Diversity

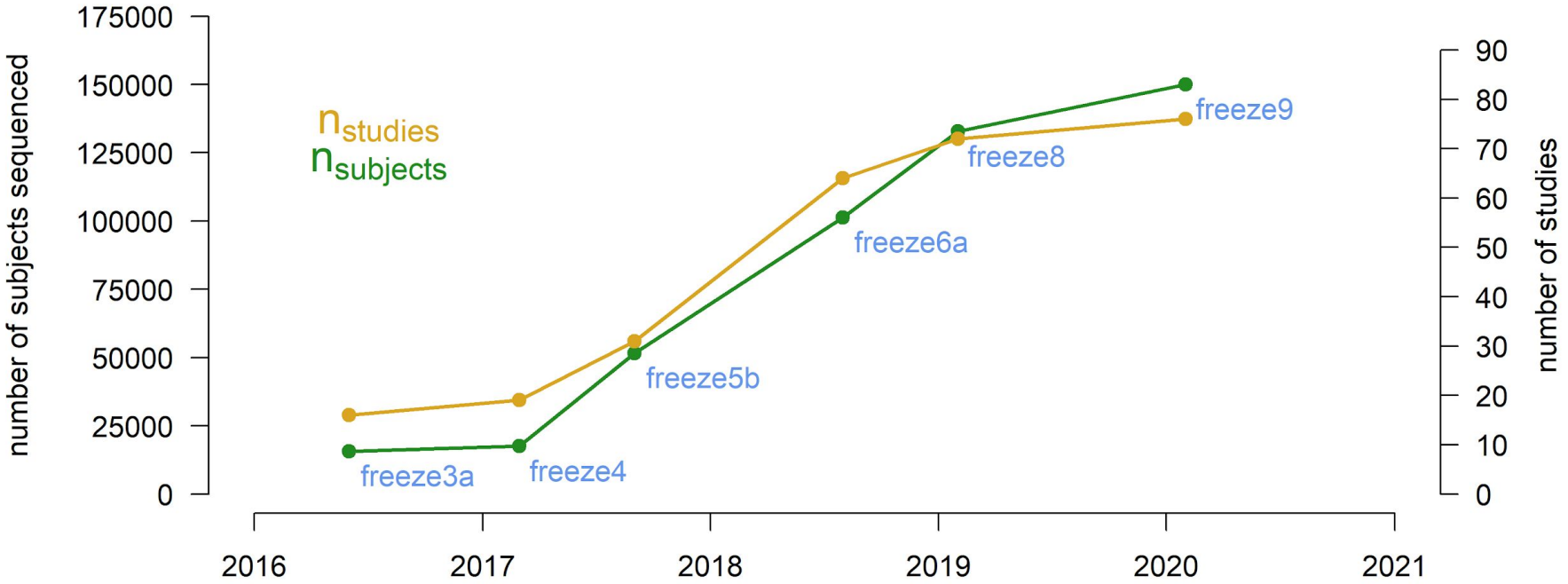


- Geographic, racial/ethnic, and genetic diversity
- ~60% non-European ancestry participants
- 18 countries represented

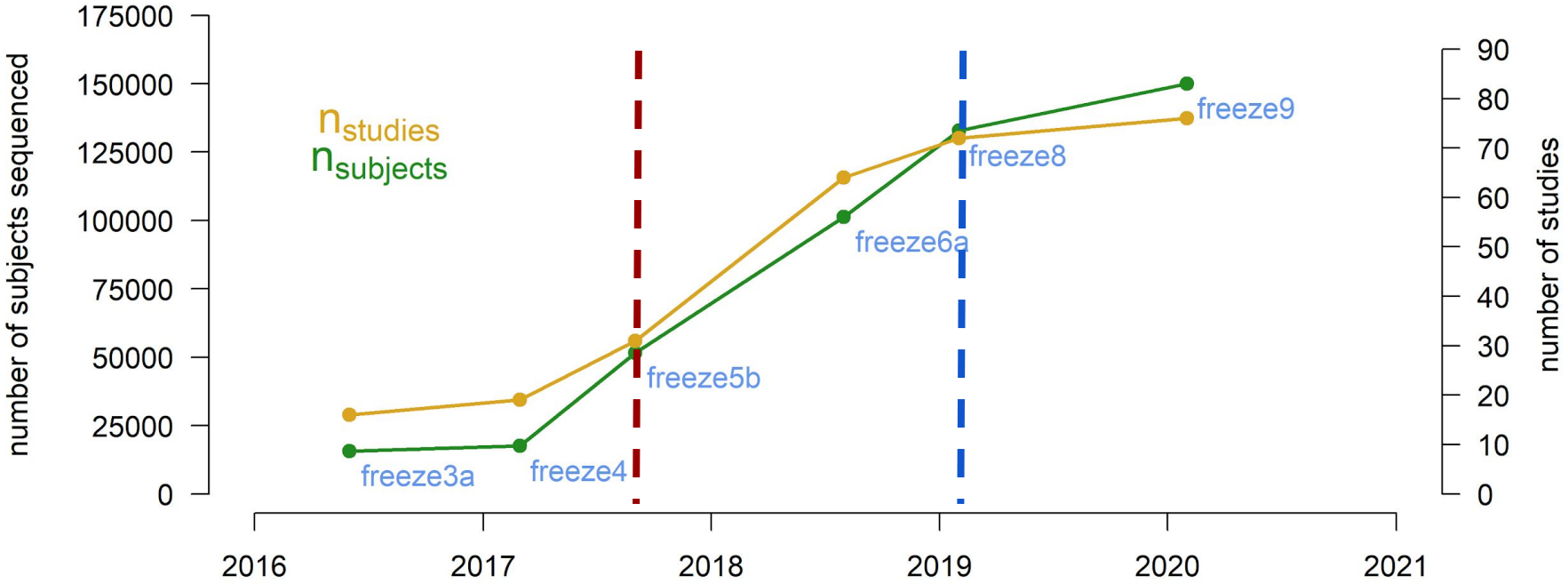


See Session 18, Alyna Khan presenting "Guidelines on the use and reporting of race, ethnicity, and ancestry in the NHLBI Trans-Omics for Precision Medicine (TOPMed) program"

TOPMed: WGS Data Production



TOPMed: WGS Data Production



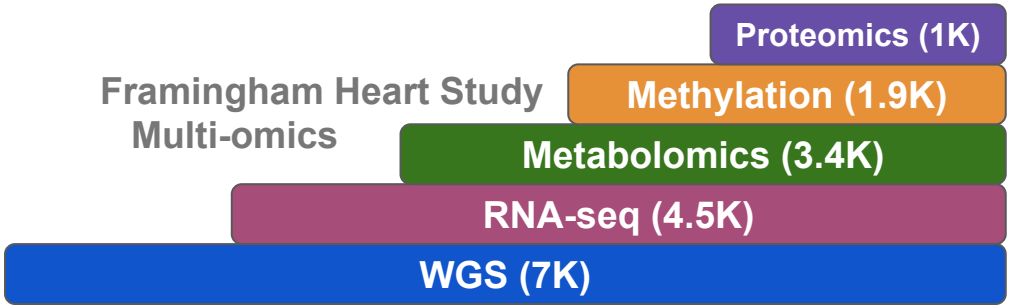
Freeze 5b: 32 studies, 56K participants
All studies released on dbGaP

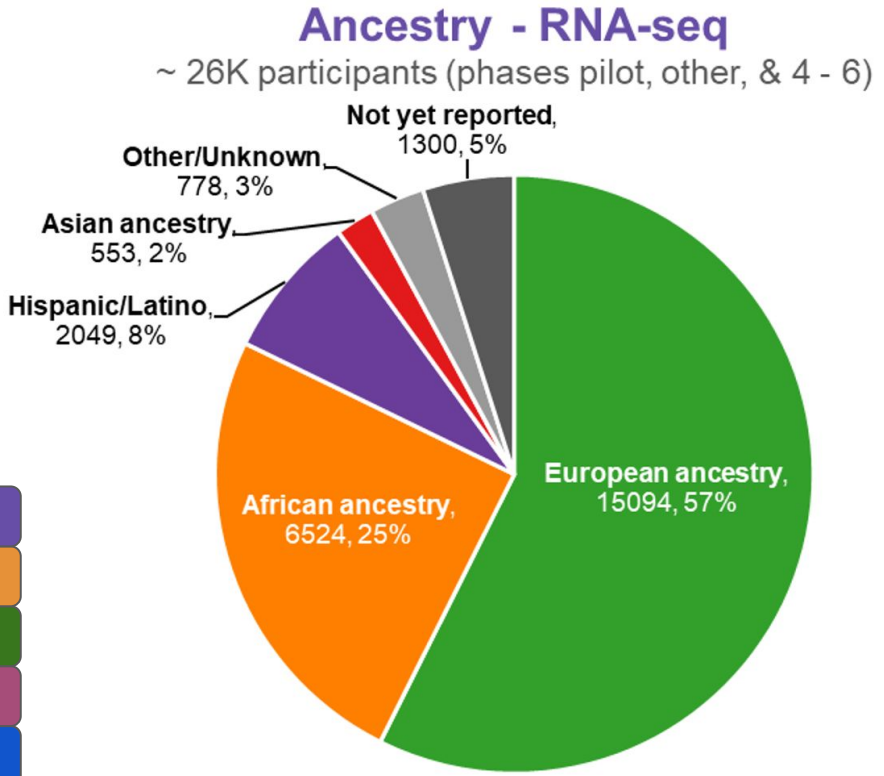
Freeze8: 72 studies, 138K participants
70/72 studies released on dbGaP

More info: https://www.nhlbiwgs.org/topmed-data-access-scientific-community

Multi-omics Integration

- A unique resource for integrative omics analysis and discovery in diverse participants
- Studies with multiple omics types on same participants (example: FHS)





TOPMed: Harmonized Phenotypes

- DCC harmonized >100 phenotype variables across dozens of TOPMed studies
  - Common covariates, demographics, inflammation, lipids, blood pressure, blood cell count, VTE, atherosclerosis
- Being made available through dbGaP and BioData Catalyst
- Publication describing robust, reproducible approach (currently in pre-print)

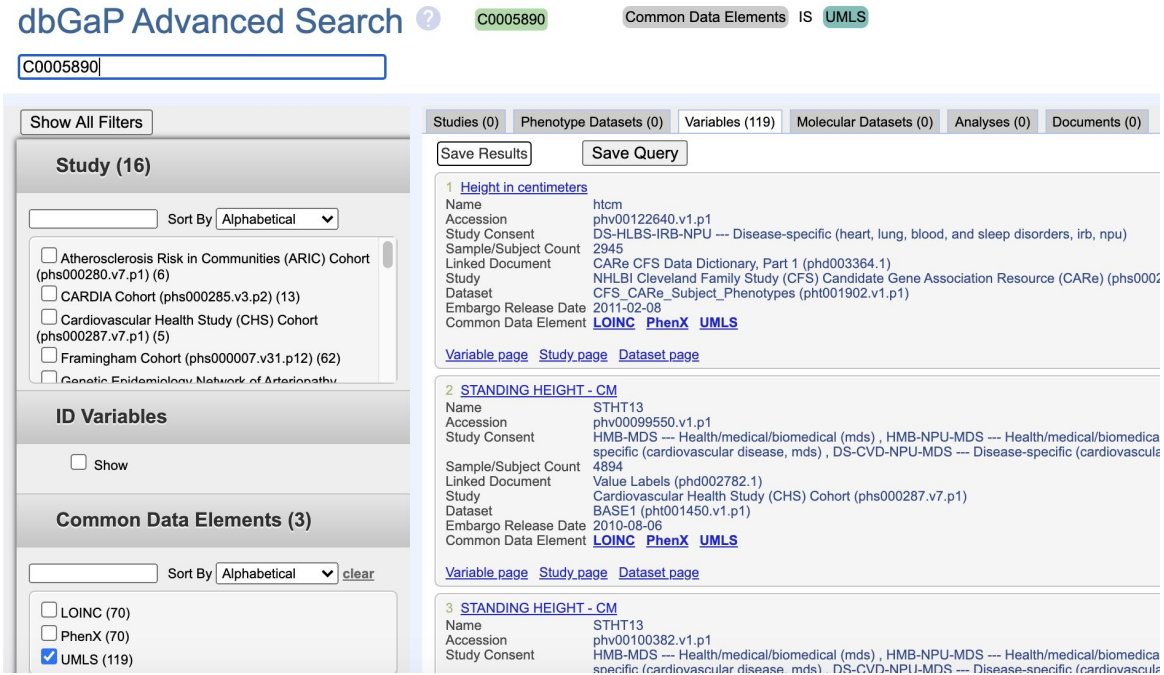
A system for phenotype harmonization in the NHLBI Trans-Omics for Precision Medicine (TOPMed) Program

Adrienne M. Stilp, Leslie S. Emery, Jai G. Broome, Erin J. Buth, Alyna T. Khan, Cecelia A. Laurie, Fei Fei Wang, Quenna Wong, Dongquan Chen, Catherine M. D'Augustine, Nancy L. Heard-Costa, Chancellor R. Hohensee, William Craig Johnson, Lucia D. Juarez, Jingmin Liu, Karen M. Mutalik, Laura M. Raffield, Kerri L. Wiggins, Paul S. de Vries, Tanika N. Kelly, Charles Kooperberg, Pradeep Natarajan, Gina M. Peloso, Patricia A. Peyser, Alex P. Reiner, Donna K. Arnett, Stella Aslibekyan, Kathleen C. Barnes, Lawrence F. Bielak, Joshua C. Bis, Brian E. Cade, Ming-Huei Chen, Adolfo Correa, L. Adrienne Cupples, Mariza de Andrade, Patrick T. Ellinor, Myriam Fornage, Nora Franceschini, Weiniu Gan, Santhi K. Ganesh, Jan Graffelman, Megan L. Grove, Xiuqing Guo, Nicola L. Hawley, Wan-Ling Hsu, Rebecca D. Jackson, Cashell E. Jaquish, Andrew D. Johnson, Sharon LR Kardia, Shannon Kelly, Jiwon Lee, Rasika A. Mathias, Stephen T. McGarvey, Braxton D. Mitchell, May E. Montasser, Alanna C. Morrison, Kari E. North, Seyed Mehdi Nouraie, Elizabeth C. Oelsner, Nathan Pankratz, Stephen S. Rich, Jerome I. Rotter, Jennifer A. Smith, Kent D. Taylor, Ramachandran S. Vasan, Daniel E. Weeks, Scott T. Weiss, Carla G. Wilson, Lisa R. Yanek, Bruce M. Psaty, Susan R. Heckbert, Cathy C. Laurie

doi: https://doi.org/10.1101/2020.06.18.146423

More info: www.nhlbiwgs.org/dcc-pheno

DCC Phenotype Tagging

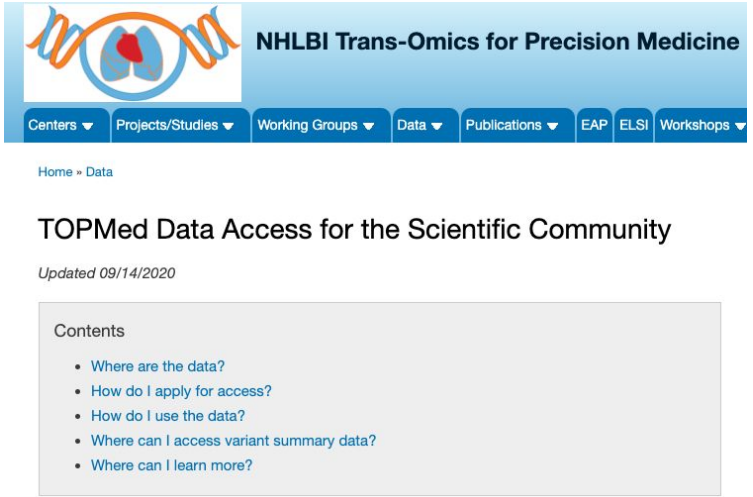


- DCC coordinated TOPMed effort to tag >16K dbGaP study variables
- Phenotype tags mapped to a standard ontology (UMLS)
- Results available through dbGaP searching tools

More info: www.nhlbiwgs.org/dcc-phenotype-tagging-details

How to access to TOPMed data

- Available through **study-specific accessions**
  - phsXXXXXX
  - All molecular data through TOPMed accession
  - Phenotype data may be in TOPMed or pre-existing accessions
- Submit **dbGaP application** for access
- **Data Use Limitations** (DULs) vary by study
- dbGaP applications reviewed by **NHLBI Data Access Committee** (DAC)



More info: https://www.nhlbiwgs.org/topmed-data-access-scientific-community

TOPMed Data Use Limitations

- Heterogeneity of DULs across TOPMed
- Compilation of diverse studies with unique histories, source populations, and informed consent processes
- Proposed research uses must align with DULs and participant consents
- Some studies further require
  - documentation of local IRB approval (-IRB)
  - letter of collaboration (-COL)
- Look for “Data Use Certification (DUC) Agreement” on dbGaP study pages

Image: NHGRI Media Gallery

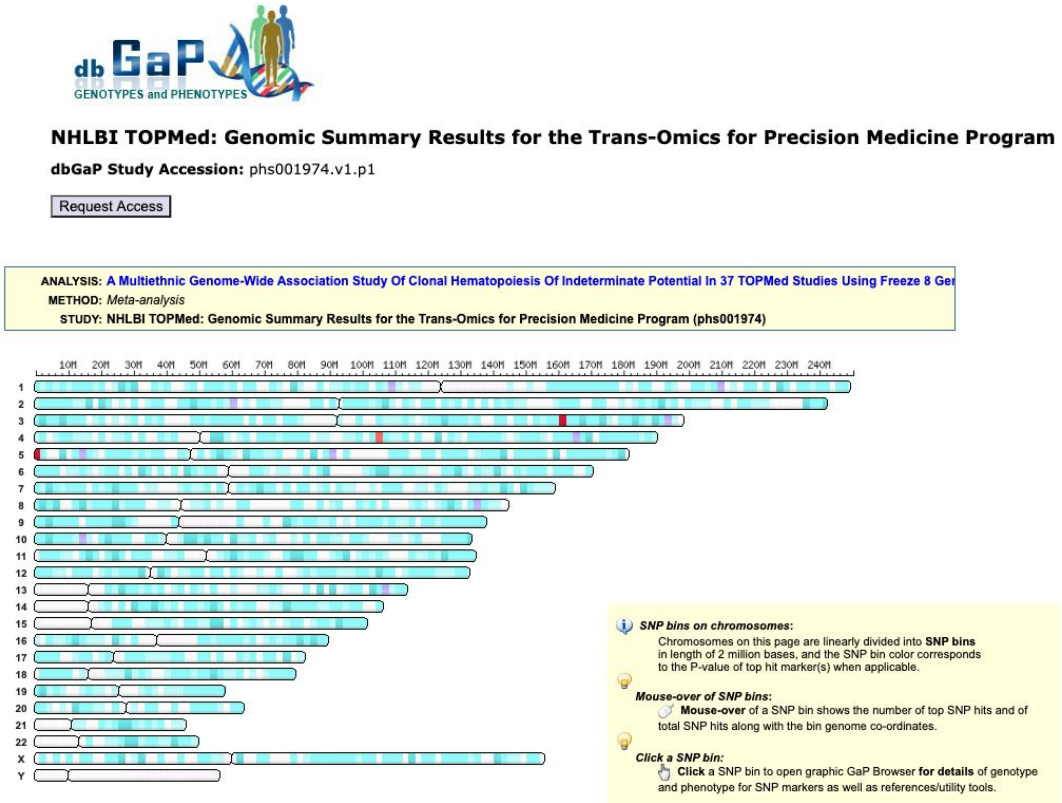
TOPMed Publications

- 48 publications and growing
  - Word cloud of abstracts
- 22 pre-prints in review

More info: www.nhlbiwgs.org/publications

TOPMed Genomic Summary Results (GSR)

- TOPMed GSR available through dbGaP phs0001974
  - e.g. association test results
- Controlled-access
  - numerous TOPMed studies are “sensitive” for GSR sharing under NIH Genomic Data Sharing policy
  - GRU consent
- Top hits publicly available on dbGaP Genome Browser



More info: www.nhlbiwgs.org/topmed-genomic-summary-results-public

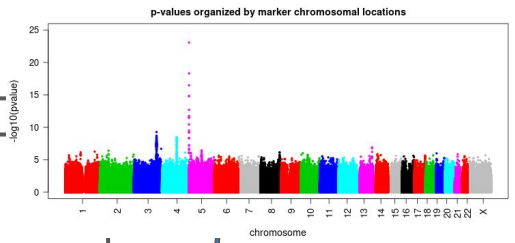
Article | Published: 14 October 2020

Inherited causes of clonal haematopoiesis in 97,691 whole genomes

Alexander G. Bick, Joshua S. Weinstock, [...] Pradeep Natarajan

Nature (2020) | Cite this article

4117 Accesses | **1** Citations | **186** Altmetric | Metrics



dbGaP Data Access Request to access full association results

View top hits in publicly available dbGaP Genome Browser

dbGaP GENOTYPES and PHENOTYPES

NHLBI TOPMed: Genomic Summary Results for the Trans-Omics for Precision Medicine Program

dbGaP Study Accession: phs001974.v1.p1

Request Access

Study version history

Study | Phenotype Datasets | Variables | Molecular Datasets | Analyses | Documents

- Browse all analyses within this study via Advanced Search
- List all analyses within this study

Analysis Name and Accession

Analysis Name: A Multiethnic Genome-Wide Association Study Of Clonal Hematopoiesis Of Indeterminate Potential In 37 TOPMed Studies Using Freeze 8 Genotypes
Analysis Accession: pha004972.1

View association results in Genome Browser

Acknowledgements

- TOPMed study investigators
- TOPMed study participants
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- Figures in this slide deck
  - Ken Rice
  - Caitlin McHugh
  - Catherine Tong
  - Alyna Khan

TOPMed DCC

- Faculty leadership: Susanne May (PI), Bruce Weir, Ken Rice, Bruce Psaty, Tim Thornton
- Project management: Matt Conomos, Sarah Nelson, Ben Heavner, Quenna Wong, Catherine Tong
- Analysts: Caitlin McHugh, Stephanie Gogarten, Deepti Jain, Adrienne Stilp, Jen Brody, Josh Bis, Dave Levine
- Administrative: Michael Bowers, Jenn Purnell, Kate Wehr, David Beame, Addison Keely
- ELSI leadership: Malia Fullerton

Former TOPMed DCC members

- Senior leadership and expertise: Cathy Laurie, Cecelia Laurie, Susan Heckbert
- Phenotype harmonization: Leslie Emery, Jai Broome, Erin Buth, Alyna Khan, Fei Fei Wang

TOPMed DCC including former members