Cross-Cohort Collaboration Consortium  
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Brief TOPMed Introduction  

TOPMed Data Coordinating Center  
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Trans-Omics for Precision Medicine (TOPMed)

• Part of the broader Precision Medicine Initiative
• Identify risk factors for heart, lung, blood and sleep disorders
  – Cross-study analyses to maximize power
  – Requires phenotype harmonization
• Develop targeted and personalized treatments
• Whole-genome sequencing – began Oct 2014, ~70k whole genomes at 30x completed, expect ~120k by end of year 3
• Additional ‘omics planned – RNAseq, metabolomics, Methylation, Proteomics
37 Different studies

Major Cohorts:
Framingham
Jackson
MESA
ARIC
HCHS/SOL
CARDIA
WHI

Phase 1 and 2: 72K subjects

- COPD: 13%
- Multi-phenotype cohorts: 28%
- Hypertension: 15%
- Stroke: 7%
- Haemophilia: 3%
- Platelets: 2%
- Lipids: 1%
- HF: 4%
- COPD: 1%
- Apnea: 1%
- Adiposity: 2%
Anthropometry – Adiposity
Asthma
Atherosclerosis
Blood Pressure
Bone Mineralization
COPD
Diabetes
EKG – Arrhythmia
Epigenetics
Family Studies
Heart Failure – Cardiac Function & Morphology
Hematology & Hemostasis
Inflammation Biomarkers
Kidney Function

Lipids
Lung Function
Metabolomics
Mitochondrial DNA
PFT
Population Genetics
Reproductive Health
Sarcoidosis
Sickle Cell Disease
Sleep
Smoking
Stroke
Structural Variation
VTE
Upcoming event of interest: Analysis Commons Hands-On Workshop in Houston, January 24-25, 2017. This is a hands-on workshop to help facilitate genotype-phenotype analysis and discovery using WGS data. Agenda

Whole Genome Sequencing in the NHLBI Trans-Omics for Precision Medicine

Trans-Omics for Precision Medicine (TOPMed), sponsored by the National Institutes of Health's National Heart, Lung and Blood Institute (NHLBI), is a program to generate scientific resources to enhance our understanding of fundamental biological processes that underlie heart, lung, blood and sleep disorders (HLBS). It is part of a broader Precision Medicine Initiative, which aims to provide disease treatments that are tailored to an individual's unique genes and environment. TOPMed will contribute to this initiative through the integration of whole-genome sequencing (WGS) and other -omics (e.g., metabolic profiles, protein and RNA expression patterns) data with molecular, behavioral, imaging, environmental, and clinical data. In doing so, this program seeks to uncover factors that increase or decrease the risk of disease, identify subtypes of disease, and develop more targeted and personalized treatments.

The Whole Genome Sequencing (WGS) project is part of NHLBI's TOPMed program and serves as an initial step for the larger initiative. In recent years, genetic research of complex disease using Genome-Wide Association Study (GWAS) and Exome-sequencing approaches has resulted in an unprecedented explosion of genetic discovery. However, a large portion of heritability in complex diseases remains elusive. Whole Genome Sequencing (WGS) will provide a comprehensive view of the genome, an opportunity to further understand the genetic architecture relevant to HLBS disorders, and an unprecedented resource to the scientific community.

The WGS project started in 2014 to generate deep WGS data for studies with diverse ancestries and extensive characterization of HLBS-related traits. The current TOPMed project studies have a variety of study designs including family, case-control, pharmacogenomic, cohort-based designs, founder populations and...