NCS Research Day Poster Abstract
Pacific Northwest Center for the National Children's Study (PNWNCS)

Building Capacity for Whole Genome Sequencing (WGS) in the National Children's Study (NCS): DNA Sequencing and the 100 Trios Project

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Introduction: Whole genome sequencing (WGS) is a potentially transformative new tool for discovery of genes influencing pediatric health-related traits. To develop a robust model for understanding natural human genetic variation and its impact on disease, sequencing genomes of a larger number of individuals is needed. We proposed to evaluate feasibility, acceptability, and cost of WGS in the National Children's Study (NCS) by using technological advances and low-cost protocols for DNA sequencing and analytic methods that assess genomic variation accurately.

Methods: We engaged a group of experts at the Northwest Genome Center and developed a plan for WSGS and analysis of 300 individuals (from 100 parent-proband trios). We obtained samples from the NCS Biorepository for a pilot study while waiting for OMB approval to implement the "100 Trios" study.

Results: We created additional capacity of 250 genomes/yr (current capacity of 4 Illumina HiSeq 2000 sequencers). For NCS Biorepository samples, we developed and validated DNA extraction from frozen mixed buffy coat and red blood cell samples. We sequenced at average 30-fold coverage across euchromatic genomic regions (~85% of the genome). We catalogued DNA variation in each sample and amongst parent-child trios to assess inheritance, concordance, and *de novo* mutation rates and to serve as test data for future assessments of genome-wide copy number variation.

Conclusions: Based on this experience, we can provide current empirical estimates and future projections of feasibility, acceptability, and cost of WGS in the NCS. This may provide valuable information for incorporating WGS into other large population-based cohort studies.