Evaluation of NHANES DNA Bank Specimens with High-Throughput Single Nucleotide Genotyping Arrays

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Background

The National Health and Nutrition Examination Surveys (NHANES) are a series of ongoing health examination surveys sponsored by the National Center for Health Statistics to assess the health and nutritional status of a multi-ethnic cross section of the United States population. DNA repositories have been collected from the NHANES III and NHANES 99-02 surveys to add a genetic component capability to studies of U.S. public health. Recent technological advances have produced DNA microarray assays that are capable of interrogating hundreds of thousands to over 1 million genetic markers in single individual. The latest generation microarray from Affymetrix, Genome-wide 6.0 Mapping Array, genotypes 906,000 individual single nucleotide markers (SNPs) and greater than 900,000 copy number variants and Illumina offers the Human1M which has over 1 million SNP assays and 50,000 CNV assays. We are evaluating the suitability of the NHANES III and 99-02 DNA bank specimens for use with these high-throughput genetic assays.

Methods

A set of NHANES III and NHANES 99-02 DNA bank specimens were selected for genotyping with the Genome-wide 5.0 (500K SNPs) and Genome-Wide 6.0 (900,000 SNPs) arrays. A total of 44 NHANES III samples were selected for genotyping with the Genome-wide 6.0 array, including 2 sets of blinded repeats, and 8 NHANES 99-02 samples, including one blind repeat, were selected for genotyping with the Genome-wide 5.0 and Genome-wide 6.0 arrays. The NHANES III DNA bank samples were whole-genome amplified by multiple displacement amplification while NHANES 99-02 samples were normalized to working concentrations. Genotype call rates for all samples and arrays were determined and genotype concordance of blinded sample repeats were calculated to assess genotype data quality.

Results

Genotype call rates for the Affymetrix Genome-wide 5.0 and Genome-wide 6.0 arrays were in excess of 99% for both the NHANES III and NHANES 99-02 samples. Genotype concordance measurements were likewise greater than 99% for both the NHANES III and NHANES 99-02 samples for both the Genome-wide 5.0 and 6.0 arrays.

Conclusion

This proof of principle evaluation indicates that the NHANES DNA banks are suitable for genotyping with the Affymetrix high-density DNA mapping microarrays. These results highlight the potential for using the NHANES DNA bank in whole genome association studies to confirm known and to identify novel genetic risk factors that impact health measures that are important to U.S. public health.