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New Genomic Technologies for Whole Genome Genotyping and Directed Re-Sequencing

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Despite many years of effort, the genes and variants responsible for complex genetic traits in humans, including susceptibility to common diseases and clinically important quantitative traits (such as blood pressure or measures of obesity) remain a mystery. For the first time, the resources and technologies required to systematically and most efficiently search for these causal genetic variations are becoming available. The ready availability of a complete genome sequence, abundant polymorphisms and a human haplotype map now permit the use of linkage disequilibrium (LD) to guide selection and of the most informative polymorphisms and downstream data analysis. Combined with dramatic improvements in genotyping technology, it is now practical to perform whole genome scans with about 500,000 SNPs and many such scans are underway. While newly available technologies create unprecedented opportunity, creating a resource for whole genome genotyping with appropriate scale, quality control and integration to advanced bioinformatics capability involves careful consideration of many factors. These include but are not limited to study design strategy, platform choice, effective capitol investment, ties to sophisticated analytic tools and the ability to rapidly follow up candidate association findings both for technologic validation and replication of the finding of association. In addition, several novel sequencing technologies have become or will soon become available, expanding the possibilities for following up association scans or completely cataloging variation deeply across focused regions in large sets of DNA samples. The presentation will discuss experiences with implementation, utilization and analysis of large datasets generated with new genomic technologies.