ImmunoChip Data on nPOD Samples

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Purpose: Genome Wide Association Studies (GWAS) have contributed substantially to identification of disease susceptibility loci. A recent meta-analysis of Type 1 Diabetes (T1D) identified more than 40 T1D risk loci. Despite this advance in knowledge, the identified loci contain a median of 4 genes with a range of 0 to 27. One of the tasks ahead is to fine-map each locus to better define the likely causative SNP(s) and genes. The ImmunoChip consortium was established to design a cost effective genotyping array to fine map well established GWAS reported risk loci in immunologically related human diseases including type 1 diabetes, ankylosing spondylitis, Crohn's disease, celiac disease, IgA deficiency, multiple sclerosis, primary biliary cirrhosis, psoriasis, rheumatoid arthritis, systemic lupus erythematosus, autoimmune thyroid disease and ulcerative colitis.

Methods: A total of 186 distinct loci were targeted in the genotyping array, with all loci having at least one GWAS reported index SNP that achieved genome wide significance criteria of $P<5x10\text{-}8$ in autoimmune related diseases. SNPs included in the ImmunoChip panel were chosen from the 1000Genomes Project pilot CEU population variants, investigator contributed variants identified through disease specific resequencing projects and additional “wild card” variants. A total of 196,524 SNPs passed Illumina design metrics and were included on the ImmunoChip. On average, 643 SNPs were included in each non-HLA T1D risk locus and over 6,000 SNPs saturated the HLA region.

Summary of Results: While 69% of SNPs genotyped were common (MAF>0.05), 31% of the SNPs were infrequent (14.7% 0.05>MAF>0.01 and 16.3% of the SNPs were rare (MAF<0.01)). We have genotyped 6,741 cases and 6,622 controls along with 2,835 affected sib pair (ASP) families and 494 T1D trio families (total of 12,983 samples) previously recruited by the Type 1 Diabetes Genetics consortium (T1DGC). We have also genotyped 149 nPOD samples using the ImmunoChip arrays in order to provide a unique pathological insight for any defined risk variants identified from the T1D ImmunoChip fine mapping efforts.

Conclusions: The nPOD samples will provide a unique resource to facilitate genotype-phenotype-tissue studies to help improve our understanding of disease development.