Genetic variations in the transcriptome and epigenome of human immune cells

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Abstract

Characterising the multi-facetted contributions of genetic factors to disease phenotypes is a major challenge in human genetics and medicine. At the molecular level, we seek to understand the complex hierarchical system of gene regulation that leads to disease risks. Here we explore high dimensional genomic maps to understand how DNA sequence variation in *cis* affects gene expression and chromatin states specifically in three major human immune cell types, CD14+ monocytes, CD16+ neutrophils and CD4+ naïve T cells.

From a cohort of up to 197 healthy individuals of European ancestry, we generated whole-genome sequencing data, 526 DNA methylation data (Illumina 450K arrays), 927 genome wide maps of active enhancers (H3K27ac and H3K4me1), and 557 total RNA sequencing.

We identified 204,725 independent QTLs affecting RNA expression, RNA splicing, DNA methylation levels and chromatin binding. We next describe properties and coordination of regulatory variants across multiple data layers and biological enrichment of cell-type specific genes. Finally, we dissect the contribution of molecular traits for hundreds of disease-associated variants in six autoimmune diseases.