Transcriptional and Epigenetic Variability Shapes Phenotypic Plasticity of Human Immune Cells

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Abstract

A healthy immune system requires immune cells that can adapt rapidly to environmental challenges. This phenotypic plasticity is mediated by transcriptional and epigenetic variability. We developed a novel analytical approach to measure such variability genome-wide in CD14+CD16– monocytes, CD66b+CD16+ neutrophils, and CD4+CD45RA+ naïve T cells, from the same 125 healthy individuals. We discovered substantially increased inter-individual variability in neutrophils, both in gene expression and DNA methylation patterns, compared to monocytes and T cells. In neutrophils, genes with hypervariable expression were found to be implicated in key immune pathways, and correlated with cellular properties and environmental exposure. Neutrophil-specific DNA methylation hypervariable sites were enriched at enhancer and dynamic chromatin states. Our data highlight the importance of transcriptional and epigenetic variability in the neutrophil's key role as the first responders to inflammatory stimuli, and provide a resource to enable further studies into the plasticity of immune cell functions.