Very rare genetic variants may result in uncommon primary immunodeficiency syndromes.

Genome-wide association studies (GWAS) similarly implicated common genetic variants to influence the immune system across several autoimmune and inflammatory diseases.

Understanding the functional impact of these common variants was limited.

Given their location in non-coding DNA, the majority of variants were thought to regulate the amount of a gene expressed. However in which cells and under which circumstances was unknown.

Common genetic variants unequivocally associated with severe infection (sepsis) were unknown.

We established functional evidence for how certain key regulatory genetic variants act across the whole genome.

We took these results and integrated them with GWAS disease associated variants, helping shed light on the cell types and activity of importance.

We explored how genetic variation makes individuals susceptible to sepsis.

WHAT THIS ADDS

Genetic variants modulating gene expression are common and frequently act in a specific cell type or context.

Many disease associated variants demonstrate this specific cell type and activity-dependent effect.

By understanding which genes are modulated by such variants we can gain new insights into biologically important pathways and gene networks, and inform drug target discovery and prioritisation.

Disease relevance of eQTL involving response to endotoxin includes sepsis, for which the first GWAS was completed.

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