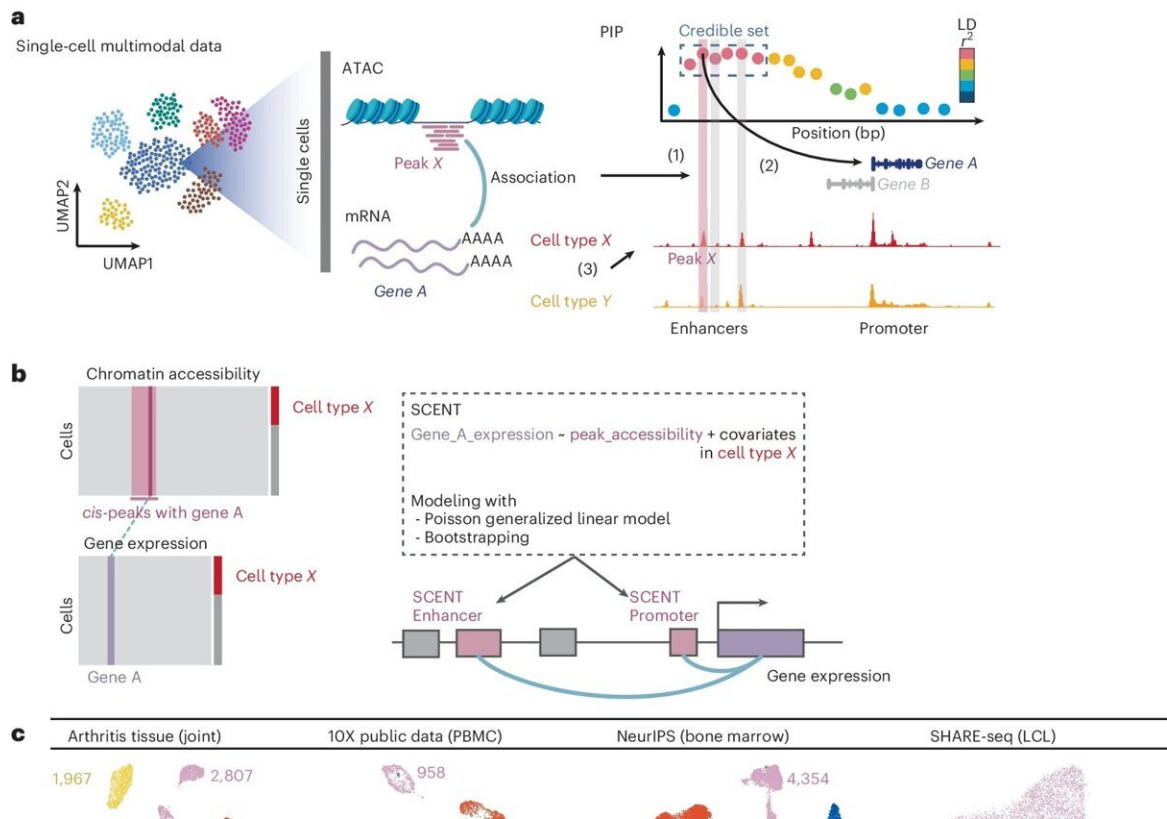


# Researchers develop statistical method for genetic mapping of autoimmune diseases

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Schematic overview of SCENT and SCENT enhancer–gene pairs across nine single-cell multimodal datasets. **a**, SCENT identifies (1) active *cis*-regulatory regions and (2) their target genes in (3) a specific cell type. Those SCENT results can be used to define likely causal variants, genes and cell types for GWAS loci. **b**, SCENT models association between chromatin accessibility from ATAC–seq and gene expression from RNA–seq across individual cells in a given cell type. **c**, Nine single-cell datasets on which we applied SCENT to create 23 cell-type-specific enhancer–gene maps. The cells in each dataset are described in UMAP

embeddings from RNA-seq, colored by cell types ( $n_{\text{cells}} > 500$ ) and annotated by cell numbers. Credit: *Nature Genetics* (2024). DOI: 10.1038/s41588-024-01682-1

Genetic studies of diseases map segments of the genome driving disease. But to understand how those changes contribute to disease progression, it is important to understand how they may alter gene regulation of disease genes in cell populations assumed to be driving disease.

"Enhancer-gene maps" link genomic regulatory regions to genes and are essential for understanding disease. But constructing them poses challenges due to limitations in current experimental methods, that make it difficult to apply the technique to rare [cell populations](#) and genes that only regulate specific cell types.

Researchers from Brigham and Women's Hospital, a founding member of the Mass General Brigham health care system, have developed a statistical method called SCENT (single-cell enhancer target gene mapping). This method uses multimodal single-cell data to establish links between regulatory elements and genes, allowing them to pinpoint probable causal gene loci for both common and rare diseases. These insights might assist the development of treatments for various conditions.

The research team applied SCENT to nine multimodal single-cell datasets representing various human tissues, including immune, neuronal, and pituitary cells, aiming to understand the intricacies of DNA regulation in each specific cell type.

With these data, they developed 23 distinct gene-enhancer maps to investigate genetic variants and expression patterns associated with 1,143

diseases and traits. Notably, they discovered that, for [immune diseases](#), crucial insights emerged not only from immune cells but also from cells within the affected tissues themselves.

"For most [autoimmune diseases](#), people assume that we need a general map of immune cells. But we find that the enhancer-gene maps of immune cells are different in affected disease tissues," said Soumya Raychaudhuri, MD, Ph.D., of Brigham's Division of Rheumatology, Immunology, and Inflammation. We demonstrate how such a map can be used to interpret [genetic data](#) from [rheumatoid arthritis](#) and other autoimmune diseases."

The study is [published](#) in the journal *Nature Genetics*.

**More information:** Saori Sakaue et al, Tissue-specific enhancer–gene maps from multimodal single-cell data identify causal disease alleles, *Nature Genetics* (2024). [DOI: 10.1038/s41588-024-01682-1](https://doi.org/10.1038/s41588-024-01682-1)

Provided by Brigham and Women's Hospital

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