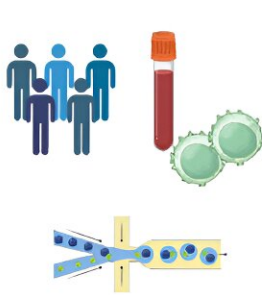


Small changes in specific immune cell populations linked to autoimmune disorders

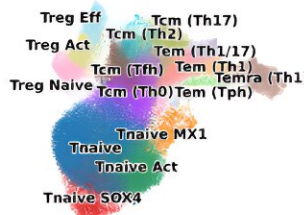
January 11 2024

Build human circulating CD4+ T cell Reference

Single-cell RNA+TCR-seq from healthy and autoimmune individuals

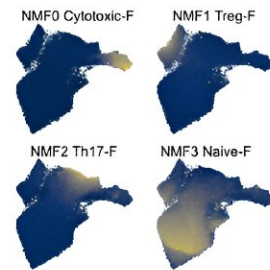


① Discrete clustering



18 clusters

② Continuous gene program extraction



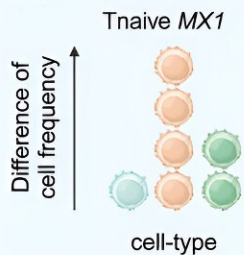
12 gene programs

Autoimmune disease profiling

Single-cell meta-analysis

20 diseases, 953 individuals, 1.8M cells

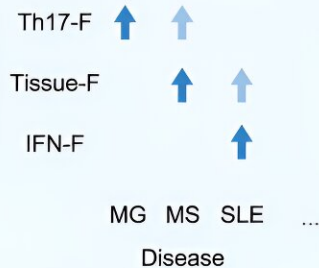
SLE



MG, MS ...

Quantitative change

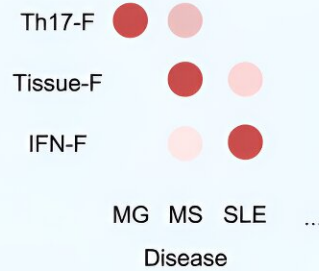
Gene program



Qualitative change

GWAS integration

13 autoimmune diseases



Partitioned heritability on gene programs

Credit: *Cell Genomics* (2024). DOI: 10.1016/j.xgen.2023.100473

Much like ripples on the water can betray powerful currents below the surface, small changes in our bodies can sometimes be an indicator of a serious condition. Now, researchers from Japan say that cells in the blood may provide telltale signs of important immune dysfunction.

In a study recently [published](#) in *Cell Genomics*, researchers from Osaka University have revealed that subtle changes in specific immune cell populations may signal the presence of an autoimmune disease.

In autoimmune conditions, which affect up to 5% of the population, the body's immune cells attack the body instead of disease-causing agents. A subset of immune cells known as CD4⁺ T cells are known to play a key role in the onset and progression of many autoimmune diseases.

"CD4⁺ T cells can exist in a naive or memory state, can exhibit polarization to a Th1, Th2, Th17, or Tfh phenotype, or can be regulatory T cells," says lead author of the study Yoshiaki Yasumizu. "However, there is still a lot of heterogeneity among the cells in these categories, and the effect that this has on autoimmune disease remains largely unclear."

To address this, the researchers used single-cell RNA sequencing and an [analytical approach](#) known as non-negative matrix factorization to analyze the gene expression profiles of CD4⁺ T cells in healthy individuals and patients with autoimmune diseases. This analysis identified 18 different types of CD4⁺ T cells and 12 distinct gene programs, which were then used as a reference to analyze almost 2 million CD4⁺ T cells from nearly 1,000 people with 20 different autoimmune diseases.

"The results were very exciting," explains Shimon Sakaguchi, senior author. "We found that characteristic changes in CD4⁺ T cells defined by the 18 categories and 12 gene programs were associated with specific autoimmune diseases, suggesting that these conditions have a detectable 'signature.'"

In addition, the researchers detected distinctive changes in CD4⁺ T cell categories and gene programs that were linked to aging and sex, two factors that are known to influence the risk of developing an autoimmune disorder. Furthermore, [genetic factors](#) that promote disease development accumulated in CD4⁺ T cells exhibiting specific gene programs.

"Our study presents a comprehensive catalog of the CD4⁺ T cell changes that are seen in 20 different [autoimmune diseases](#), providing an invaluable resource for researchers," says Yasumizu.

In the future, this catalog could potentially be used to detect autoimmune disease in patients by simply taking a [blood sample](#) and analyzing the CD4⁺ T cell features, thus paving the way for precision medicine.

More information: Yoshiaki Yasumizu et al, Single-cell transcriptome landscape of circulating CD4⁺ T cell populations in autoimmune diseases, *Cell Genomics* (2024). [DOI: 10.1016/j.xgen.2023.100473](https://doi.org/10.1016/j.xgen.2023.100473)

Provided by Osaka University

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