Autoimmune rheumatic diseases, Medical & healthcare, Disease prognosis prediction

Single-cell multi-omics analysis identifies two distinct phenotypes of newly-onset microscopic polyangiitis

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Abstract

The research group conducts single-cell transcriptome analyses on peripheral blood mononuclear cells (PBMCs) from newly-onset patients with microscopic polyangiitis (MPA). Increased proportions of activated CD14$^+$ monocytes and CD14$^+$ monocytes expressing interferon signature genes (ISGs) are distinctive features of MPA. Patient-specific analysis further classifies MPA into two groups. The MPA-MONO group is characterized by a high proportion of activated CD14$^+$ monocytes, which persist before and after immunosuppressive therapy. These patients are clinically defined by increased monocyte ratio in the total PBMC count and have a high relapse rate. The MPA-IFN group is characterized by a high proportion of ISG$^+$ CD14$^+$ monocytes. These patients are clinically defined by high serum interferon-alpha concentrations and show good response to immunosuppressive therapy. Our findings identify the immunological phenotypes of MPA and provide clinical insights for personalized treatment and accurate prognostic prediction.

Background & Results

The immune system's role in autoimmune vasculitis is not well understood. This study classified new-onset, treatment-naive microscopic polyangiitis (MPA) patients into two groups using single-cell multi-omics analysis of PBMCs. CITE-seq analyses of PBMCs from eight people with MPA and seven healthy individuals were conducted. The data show that MPA is characterized by increased proportions of CD14$^+$ monocytes expressing interferon genes and activated CD14$^+$ monocytes, and by decreased proportions of naive CD8$^+$ T cells. Two main types of MPA were identified based on the presence of specific genes or proteins. The MPA-MONO group had a high percentage of monocytes among PBMCs and did not respond well to immunosuppressive therapy. The MPA-IFN group had a high proportion of ISG$^+$ CD14$^+$ monocytes, high serum concentrations of IFNα and a good response to immunosuppressive therapy.

Significance of the research and Future perspective

The findings suggest that understanding the immune system in people with MPA could help develop new treatments and predict how they will respond to them. Further research is needed before the results can be translated to the clinic.

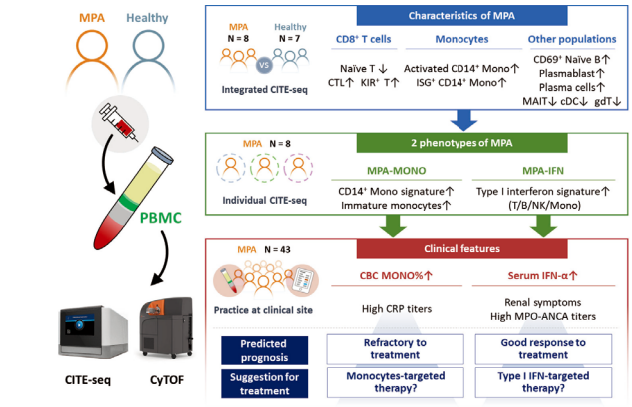

Figure1: Single-cell analysis identifies two distinct phenotypes of microscopic polyangiitis. MPA is subclassified into two groups based on the high expression of CD14+ monocytes signature genes (MPA-MONO) or high expression of ISGs (MPA-IFN). The percentage of monocytes and serum IFN-α levels are the clinical markers that clearly distinguished MPA-MONO and MPA-IFN groups, respectively. The findings of this study suggest clinical recommendations for estimating prognosis for each patient based on the immunological phenotypes of MPA.

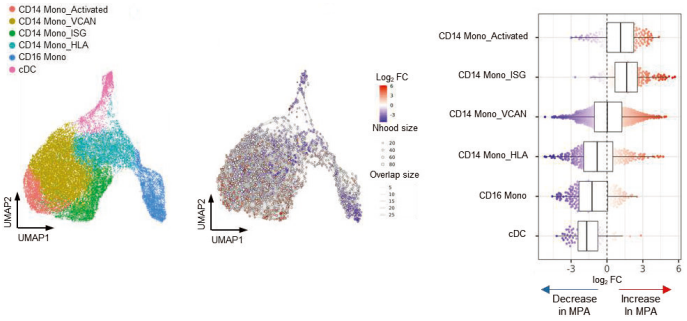

Figure2: Differential abundance analysis of monocyte populations.
In this study, we employed the Differential Abundance Analysis method 'Milo' to analyze cell groups showing differences in Reference mapping. Detailed clustering based on gene expression characterizes each monocyte cell group, independent of surface markers or existing references.

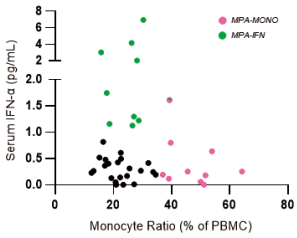

Figure3: Monocyte ratio/IFN-α concentration are markers for bedside classification.
From 43 patients with stored serum samples and clinical information, patients were distinctly separated into 9 cases each of MPA-MONO and MPA-IFN.

Patent

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Nishide, Masayuki; Shimagami, Hiroshi; Kumanogoh, Atsushi. Single-cell analysis in rheumatic and allergic diseases: insights for clinical practice. Nature Reviews Immunology. 2024, 24(1), 781-797. doi: 10.1038/s41577-024-01043-3

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Keyword single-cell RNA sequencing, multi omics, ANCA-associated vasculitis, microscopic polyangiitis, CD14$^+$ monocytes