



OPEN ACCESS

EDITED AND REVIEWED BY
Betty Diamond,
Feinstein Institute for Medical Research,
United States

*CORRESPONDENCE

Naoki Iwamoto
✉ naoki-iwa@nagasaki-u.ac.jp

RECEIVED 05 September 2025

ACCEPTED 09 September 2025

PUBLISHED 16 September 2025

CITATION

Iwamoto N, Kawakami A, Miyake S and Fujio K
(2025) Editorial: Community series in the role
of monocytes/macrophages in autoimmunity
and autoinflammation, volume II.
Front. Immunol. 16:1699650.
doi: 10.3389/fimmu.2025.1699650

COPYRIGHT

© 2025 Iwamoto, Kawakami, Miyake and Fujio.
This is an open-access article distributed under
the terms of the [Creative Commons Attribution
License \(CC BY\)](#). The use, distribution or
reproduction in other forums is permitted,
provided the original author(s) and the
copyright owner(s) are credited and that the
original publication in this journal is cited, in
accordance with accepted academic
practice. No use, distribution or reproduction
is permitted which does not comply with
these terms.

Editorial: Community series in the role of monocytes/ macrophages in autoimmunity and autoinflammation, volume II

Naoki Iwamoto^{1*}, Atsushi Kawakami¹, Sachiko Miyake²
and Keishi Fujio³

¹Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Department of Immunology, Juntendo University Faculty of Medicine, Tokyo, Japan, ³Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

KEYWORDS

monocyte, macrophage, autoimmune disease, M1 macrophage, M2 macrophage, interferon

Editorial on the Research Topic

Community series in the role of monocytes/macrophages in autoimmunity
and autoinflammation, volume II

Monocytes and macrophages are central innate immune cells that regulate inflammatory responses, tissue remodeling, and host defense (1). Their dysregulation contributes to a wide range of autoimmune and inflammatory diseases through overproduction of cytokines and chemokines, aberrant activation, and maladaptive repair (2, 3). In recent years, new investigative techniques such as single-cell technologies have highlighted the remarkable heterogeneity of these cells, moving the field beyond oversimplified classifications toward recognition of diverse and context-dependent states. For example, a recent single-cell study in systemic sclerosis (SSc) identified EGR1⁺ CD14⁺ monocytes associated with scleroderma renal crisis and tissue-damaging macrophages, underscoring how cellular diversity contributes to organ-specific pathology (4). This recognition has spurred renewed interest in their role as both drivers of pathology and potential therapeutic targets. While the previous editorial in 2022 (topic title: the role of monocytes/macrophages in autoimmunity and autoinflammation) focused broadly on macrophage polarization, trained immunity, and osteoclastogenesis across various autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE), and vasculitis (5), the present Research Topic serves as a continuation, featuring new original studies and reviews that specifically highlight the evolving relationship between monocytes, macrophages, and autoimmune diseases.

Hyperactivation and excessive infiltration of macrophages in tissue are hallmarks of hemophagocytic lymphohistiocytosis (HLH), Hu et al. investigated the treatment of HLH with chidamide, a histone deacetylase inhibitor, in combination with etoposide and glucocorticoids. They reported high response rates and favorable safety, indicating that epigenetic modulation can restrain macrophage overactivation and may offer new options for cytokine storm syndromes. Hovd et al. examined murine models of Sjögren's disease

(SjD) and identified a subset of podoplanin+CX3CR1+ macrophages enriched in inflamed salivary glands. These cells localized in the parenchyma during the acute inflammatory phase and near tertiary lymphoid structures (TLSs) in the later stages of inflammation, and appeared to promote lymphoid neogenesis, suggesting that macrophages play a dual role by contributing to both pro-inflammatory and anti-inflammatory processes. In complementary patient-based studies, Yan et al. conducted DNA microarray analysis followed by single-cell RNA sequencing of salivary gland tissue from SjD patients, and demonstrated that Toll-like receptor (TLR)8+ macrophages infiltrate the glands, express co-stimulatory molecules such as CD86, and activate T cells. Together, these findings emphasize that macrophages orchestrate both tissue architecture and adaptive immune responses in glandular autoimmunity.

In SSc-associated interstitial lung disease (ILD), Gotelli et al. described a distinct population of circulating (peripheral blood) and alveolar fluid hybrid TLR4+M2 marker (CD163, CD204 and CD206) positive cells. These cells simultaneously expressed fibrotic and inflammatory markers, suggesting dual pathogenic potential, and their presence in blood offers a potential biomarker for disease progression. Kuga et al. reviewed evidence that, although plasmacytoid dendritic cells have long been recognized as the canonical source of type I interferon (IFN) in SLE, monocytes—particularly those with senescence-like features—also produce substantial amounts of these cytokines, highlighting an intriguing additional pathway of IFN generation in the disease. They highlighted cGAS–STING and TLR pathways activated by self-nucleic acids and neutrophil extracellular traps, broadening the scope of IFN biology and suggesting that, in addition to existing therapies such as anifrolumab that target the IFN axis, strategies directed specifically at monocyte-driven IFN production may represent a promising future approach.

Izuka et al. provided a comprehensive overview of monocytes and macrophages in idiopathic inflammatory myopathies (IIMs), including dermatomyositis and immune-mediated necrotizing myopathy. They noted that macrophages infiltrate skeletal muscle and contribute to tissue injury through pro-inflammatory mediators and reactive oxygen species, but also participate in regeneration and repair through specialized subsets. In the muscle, these macrophages are involved in phagocytosis and tissue damage, whereas in the lung they are associated with ILD, often accompanied by elevated ferritin and type I IFN responses. Advances in single-cell transcriptomics have revealed heterogeneity that may serve as biomarkers of prognosis and guide reprogramming therapies, and potential therapeutic approaches include targeting chemokine receptors, cytokine pathways, oxidative stress responses, or IFN signaling. Finally, Wang et al. reviewed the role of macrophages in rosacea, a chronic inflammatory skin disease characterized by flushing and persistent erythema. They described how macrophages regulate angiogenesis, oxidative stress, and fibrosis, underscoring their plasticity and potential as therapeutic targets even in dermatological conditions not traditionally linked to systemic autoimmunity.

Collectively, these contributions reveal several unifying themes. Macrophages *in vivo* are highly plastic and exist in hybrid states shaped by tissue-specific cues, as exemplified by TLR4+M2 cells in SSc-ILD or podoplanin+ subsets in SjD. They serve as critical bridges between innate and adaptive immunity, both sensing nucleic acids via TLRs and cGAS–STING and delivering co-stimulatory signals to T cells. Their functions are profoundly organ-specific, acting as fibrosis drivers in lung, lymphoid architects in salivary glands, IFN producers in lupus, tissue repair facilitators in myositis, and vascular remodelers in rosacea. Importantly, translational relevance is increasingly evident: chidamide in HLH demonstrates therapeutic modulation of macrophages in hyperinflammation, anifrolumab exemplifies IFN pathway targeting in lupus, and emerging strategies aim at selective macrophage reprogramming in muscle and skin diseases.

In conclusion, monocytes and macrophages emerge from these studies not as static entities but as dynamic populations integrating signals from their microenvironment and determining the trajectory of immune-mediated tissue damage or repair. We are pleased that this issue dedicated to “*The role of monocytes/macrophages in autoimmunity and autoinflammation, volume II*” has gathered a range of innovative studies and reviews, advancing our understanding of the diverse functions of monocytes and macrophages and their relevance to autoimmune and autoinflammatory diseases.

Author contributions

NI: Writing – original draft, Writing – review & editing. AK: Writing – review & editing. SM: Writing – review & editing. KF: Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that Generative AI was used in the creation of this manuscript. Generative AI was used only for language polishing and formatting support. No original data, results, or interpretations were generated by AI, and all scientific content was written, verified, and approved by the authors.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated

organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Ginhoux F, Jung S. Monocytes and macrophages: developmental pathways and tissue homeostasis. *Nat Rev Immunol.* (2014) 14:392–404. doi: 10.1038/nri3671
2. Park MD, Silvin A, Ginhoux F, Merad M. Macrophages in health and disease. *Cell.* (2022) 185:4259–79. doi: 10.1016/j.cell.2022.10.007
3. Italiani P, Boraschi D. From monocytes to M1/M2 macrophages: phenotypical vs. Functional differentiation. *Front Immunol.* (2014) 5:514. doi: 10.3389/fimmu.2014.00514
4. Shimagami H, Nishimura K, Matsushita H, Metsugi S, Kato Y, Kawasaki T, et al. Single-cell analysis reveals immune cell abnormalities underlying the clinical heterogeneity of patients with systemic sclerosis. *Nat Commun.* (2025) 16:4949. doi: 10.1038/s41467-025-60034-7
5. Kawakami A, Iwamoto N, Fujio K. Editorial: The role of monocytes/macrophages in autoimmunity and autoinflammation. *Front Immunol.* (2022) 13:1093430. doi: 10.3389/fimmu.2022.1093430