Department of Pharmacology
Division of Pharmaceutical Sciences
School of Pharmaceutical Sciences

Outline

Understanding the mechanisms underlying diseases and the pharmacological actions of drugs is essential for the development of effective therapies. Our laboratory focuses on elucidating the pathophysiological mechanisms of immune-related diseases—including allergic disorders, autoimmune diseases, infections, and cancer—as well as investigating how drugs modulate the immune system. Through our research, we aim to contribute to the advancement of rational and innovative pharmacotherapy.

Faculty members

Professor; Yoshiki YANAGAWA, Ph.D.
Assosiate Professor; Natsumi MIZUNO, Ph.D.
Assistant Professor; Saki SHIGA, Ph.D.

Main research in progress

- Exploration of novel methods to induce M2-type (alternatively activated) macrophages
- Investigation of the balance between immune checkpoint molecules and costimulatory molecules
- Analysis of macrophage functional modulation by therapeutic agents for immune-related diseases

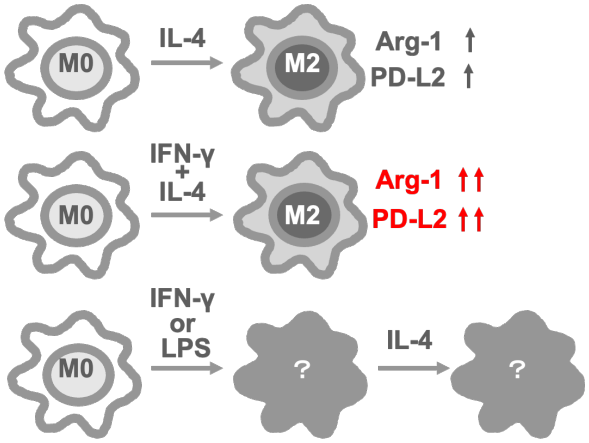

Fig. 1 Synergy of IL-4 and IFN-γ in arginase-1 production in macrophages.
IFN-γ and LPS induce M1-type macrophages that promote inflammation, whereas IL-4 from Th2 cells drives M2-type macrophages that suppress it. We found that IL-4 combined with IFN-γ synergistically increases arginase-1 expression and cell surface expression of PD-L2, an immune checkpoint molecule. Arg-1, arginase-1; PD-L2, programmed death-ligand 2. (Endo et al., 2023)
Our current research aims to clarify the molecular mechanisms behind this synergy and how M1 polarization affects subsequent IL-4–induced M2 macrophage functions.

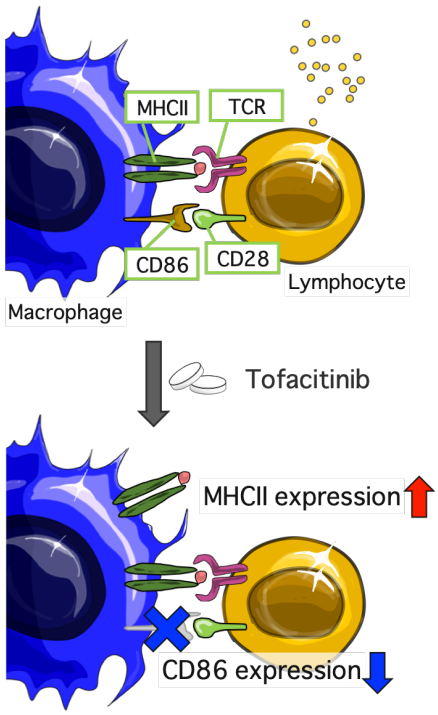

Fig. 2 Tofacitinib induced CD86$^-$ MHC II$^+$ macrophages in the presence of IFN-γ.
Tofacitinib is an approved treatment for rheumatoid arthritis. CD86, co-stimulatory molecules; MHCII, major histocompatibility complex II.
(Mizuno *et al.,* 2022)

Current publications

CDK8/19 inhibitor enhances arginase-1 expression in macrophages via STAT6 and p38 MAPK activation.
Mizuno N, Shiga S, Tanaka Y, Kimura T, Yanagawa Y.
Eur J Pharmacol. 2024 Sep 15;979:176852.

Synergy of interleukin-4 and interferon-γ in arginase-1 production in RAW264.7 macrophages.
Endo TH, Mizuno N, Matsuda S, Shiga S, Yanagawa Y.
Asian Pac J Allergy Immunol. 2023 Dec; 41(4):379-388.

Tofacitinib enhances interferon-γ-induced expression of major histocompatibility complex class II in macrophages.
Mizuno N, Yanagawa Y.
Eur J Pharmacol. 2022 Jan 15;915:174564.

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