Department of Pharmacology Division of Pharmaceutical Sciences School of Pharmaceutical Sciences

Outline

To elucidate pathological mechanisms and pharmacological effects is important for appropriate drug therapy and its development. We are studying the pathological mechanisms of diseases caused by immune abnormalities; allergic diseases, autoimmune diseases, infectious diseases, and cancer, as we ll as the mechanisms of drug action in the immune system.

Faculty members

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

Main research in progress

- 1) The effects of simultaneous treatment with IFN- γ and IL-4 on macrophage functions.
- 2) The regulation of the expression of immune checkpoint molecules and co-stimulatory molecules in macrophages.
- 3) The effects of therapeutic agents for immune diseases on the antigen presentation of macrophages.
- 4) The effects of therapeutic agents for immune diseases on macrophage polarization.



Fig. 1 Synergy of IL-4 and IFN- γ in arginase-1 production in macrophages. Macrophages can be divided into two groups; M1 macrophages (classical macrophages) and M2 macrophages (alternatively activated macrophages), based on their functions. IL-4 combined with IFN- γ synergistically increased arginase-1 protein production, and additionally, cell surface expression of PD-L2. PD-L2; programmed cell death 1 ligand 2 (an immune checkpoint molecule). (Endo *et al.*, 2021)



Fig. 2 Tofacitinib induced CD86⁻ MHC II⁺ macrophages in the presence of IFN-γ.

Tofacitinib is an approved treatment for rheumatoid rthritis. CD86; co-stimulatory molecules, MHCII; major histocompatibility complex II. (Mizuno *et al.*, 2022)

Current publications

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.

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.* 2021 Sep 5.

Tranilast inhibits interleukin-33 production by macrophages. Hiraide S, Yanagawa Y, Iizuka K. *Eur J Pharmacol.* 2018 Jan 5;818:235-240.

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