Immune Netw. 2024 Feb;24(1):e13
https://doi.org/10.4110/in.2024.24.e13
pISSN 1598-2629·eISSN 2092-6685

IMMUNE NETWORK

Editorial

Cytokines and Immune Disorders: Illuminating Cytokines as Hubs Within the *Immune Network*

Seung-Woo Lee, Deputy Editor of *Immune Network* [1,*], **Chong-Kil Lee, Editor-in-Chief of *Immune Network*** [2]

[1]Department of Life Sciences, Pohang University of Science and Technology, Pohang 37666, Korea
[2]Department of Pharmaceutics, College of Pharmacy, Chungbuk National University, Cheongju 28644, Korea

Received: Feb 14, 2024
Accepted: Feb 15, 2024
Published online: Feb 26, 2024

***Correspondence to**
Seung-Woo Lee
Department of Life Sciences, Pohang University of Science and Technology, 77 Cheongam-ro, Nam-gu, Pohang 37666, Korea.
Email: sw_lee@postech.ac.kr

ORCID iDs
Seung-Woo Lee
https://orcid.org/0000-0002-6714-2463
Chong-Kil Lee
https://orcid.org/0000-0001-9070-341X

Conflict of Interest
The authors declare no potential conflicts of interest.

Abbreviations
GC, germinal center; KAI, Korean Association of Immunologists; γc, gamma chain.

Author Contributions
Conceptualization: Lee SW, Lee CK; Writing - original draft: Lee SW; Writing - review & editing: Lee SW, Lee CK.

The *Immune Network* has organized a special review collection to celebrate the 50th anniversary of the Korean Association of Immunologists (KAI). This year is particularly notable as KAI, in collaboration with the International Cytokine and Interferon Society, will host Cytokines 2024. To commemorate this event, the special issue is themed "Cytokines and Immune Disorders" featuring contributions from researchers representing KAI as well as internationally acclaimed scientists.

In all situations where immune system is engaged, the regulation of immune or non-immune cells through cytokines plays a critical role at every stage of the immune response. Particularly, the modulation of innate immune cell functions through cytokines is crucial at the onset of inflammation. TNF is the most well-known among pro-inflammatory cytokines and plays various roles in immune and inflammatory responses. Eun-Kyeong Jo and Jae-Min Yuk (Chungnam National University, Korea), who have long studied the interaction between microbial infections and innate immunity, review the various role of TNF in *Mycobacterium tuberculosis* infection (1). They explore the nuanced role of TNF in the pathogenesis of tuberculosis, emphasizing the importance of investigating the functions of TNF and its receptors. Charles Dinarello (University of Colorado, USA), a distinguished scientist known for pioneering early research in cytokine immunobiology, including IL-1, along with Soo-Hyun Kim (Konkuk University, Korea), reflects on the journey from discovering IL-18BP, a natural antagonist of the cytokine IL-18 that regulates innate immunity, to its clinical application (2).

As KAI marks its 50th year, the society has witnessed remarkable advancements in research across various fields of immunology. Hyungseok Seo, Yeonseok Chung, and Chang-Yuil Kang (Seoul National University, Korea), who have studied various aspects of helper T cell biology, review the diverse roles of their favorite cytokines, IL-17 and IL-21, associated with Th 17 and T follicular helper (Tfh) cells, respectively. The article delves into the dual roles of these cytokines in pathogen defense and in fueling chronic inflammation and autoimmune diseases, while also highlighting recent breakthroughs in understanding their mechanisms for potential therapeutic applications in autoimmune disorders and cancer (3). Youn Soo Choi (Seoul National University, Korea) and Jinyong Choi (The Catholic University, Korea) with their guru Shane Crotty (La Jolla Institute for Immunology, USA), review the Tfh cytokines like IL-21 and IL-4, critical for regulating B cell activities in the germinal centers (GCs). They also investigate the impact of additional cytokines involved in Tfh

cell differentiation and functions on GC dynamics and their connections to autoimmune diseases, allergies, and cancer (4).

In the advancing era of single cell multi-omics, we are confronted with the reality that many immune cells, long defined as specific subsets, are being divided into heterogeneous sub-populations in terms of phenotype and function. Young scientists might be quite surprised to learn that just 3 decades ago, most immune responses could be adequately described by simply categorizing them into two types (type-1 vs. type-2) based on their distinct cytokine profiles. For over 2 decades, Do-Hyun Jung, Hye-Young Kim (Seoul National University, Korea), and Ji Hyung Kim (Korea University, Korea) have been researching type-2 immunity particularly in innate-like lymphocytes. They analyze the dual role of type-2 innate cytokines in immune responses, acting both as defenders and as factors in pathologies such as parasite infections, asthma, and fibrosis, while also exploring recent advances in therapies targeting type-2 cytokines like IL-4, IL-5, and IL-13 (5). Meanwhile, Wan-Uk Kim (The Catholic University, Korea), and Seung-Hyo Lee (Korea Advanced Institute of Science and Technology, Korea), who have primarily focused on type 17 autoimmunity, investigate the complex roles of cytokines in autoimmune diseases, with a special emphasis on rheumatoid arthritis and multiple sclerosis. Additionally, they provide an overview of the roles of vascular growth factors in autoimmunity, including VEGF, angiopoietin, and placental growth factor, which they describe as an angio-lymphokine (6).

Up to now, there are hundreds of substances identified as cytokines, yet the common gamma chain (γc) cytokine family likely includes the molecules most favored by T cell immunologists. The last three papers of this special issue focus on T cell-mediated immunity through specific cytokines within the γc family. Eui-Cheol Shin (Institute for Basic Science, Korea), and Su-Hyung Park (Korea Advanced Institute of Science and Technology, Korea), who have been studying viral immunology, summarize the role of IL-15 in TCR-independent bystander T cell activation in infections and chronic diseases. In particular, they explain how IL-15 regulates various CD8 T cell subsets, including conventional and virtual memory, senescent, and the recently identified NKR-positive cells, significantly impacting immunopathology of tissues (7). Jung-Hyun Park (NCI/NIH, USA), Donghoon Choi (NeoImmuneTech, USA), Seung-Woo Lee, and Young Chul Sung (Pohang University of Science and Technology, Korea), provide a comprehensive review on therapeutic approaches involving IL-7, a T cell homeostatic cytokine. They cover the immunobiology of IL-7, from preclinical and clinical trials to the use of IL-7 recombinant proteins or IL-7 genes in cancer and infectious diseases. Through these studies, they present the current state and future prospects of IL-7-mediated immunotherapeutics (8). Lastly, Jonathan Sprent (Garvan Institute, Australia), and Onur Boyman (University of Zurich, Switzerland), who have made significant contributions to the field of CD8 T-cell immunity over the past decades, discuss anticancer immunotherapy via their beloved cytokine, IL-2. They deliver a perceptive analysis of IL-2's function in maintaining normal homeostasis and its involvement in the immune response, extending to its utilization in cancer immunotherapy (9).

Since 2001, the official journal of KAI, *Immune Network*, has been named to signify that all immune responses must be understood through the vast network of interactions among tissues, cells, and molecules. In this context, addressing cytokines, which act as "*Hubs within the Immune Network*," in a special issue is a particularly appropriate theme. We hope that the reviews in this special issue offer readers a broad spectrum of information on various cytokines, along with insights for future research. Finally, we would like to express special

https://doi.org/10.4110/in.2024.24.e13

thanks to Jon Sprent, who graciously agreed to write a review article, which he mentioned might be his last contribution to the scientific literature.

ACKNOWLEDGEMENTS

Lee SW has been supported by the Korea Basic Science Institute (National Research Facilities and Equipment Center) grant funded by the Ministry of Education (2021R1A6C101A390) and the "Leaders in INdustry-university Cooperation 3.0" Project, supported by the Ministry of Education and National Research Foundation of Korea (1345370629/LINC3.0-2023-10).

REFERENCES

1. Yuk JM, Kim JK, Kim IS, Jo EK. TNF in human tuberculosis: a double-edged sword. *Immune Netw* 2024;24:e4. CROSSREF
2. Kim S, Yu H, Azam T, Dinarello CA. Interleukin-18 binding protein (IL-18BP): a long journey from discovery to clinical application. *Immune Netw* 2024;24:e1. CROSSREF
3. Koh CH, Kim BS, Kang CY, Chung Y, Seo H. IL-17 and IL-21: their immunobiology and therapeutic potentials. *Immune Netw* 2024;24:e2. CROSSREF
4. Choi J, Crotty S, Choi YS. Cytokines in follicular helper T cell biology in physiologic and pathologic conditions. *Immune Netw* 2024;24:e8. CROSSREF
5. Kim HY, Jeong D, Kim JH, Chung DH. Innate type-2 cytokines: from immune regulation to therapeutic targets. *Immune Netw* 2024;24:e6. CROSSREF
6. Lee YE, Lee SH, Kim WU. Cytokines, vascular endothelial growth factors, and PlGF in autoimmunity: insights from rheumatoid arthritis to multiple sclerosis. *Immune Netw* 2024;24:e10. CROSSREF
7. Lee H, Park SH, Shin EC. IL-15 in T-cell responses and immunopathogenesis. *Immune Netw* 2024;24:e11. CROSSREF
8. Park JH, Lee SW, Choi D, Lee C, Sung YC. Harnessing the power of IL-7 to boost T cell immunity in experimental and clinical immunotherapies. *Immune Netw* 2024;24:e9. CROSSREF
9. Sprent J, Boyman O. Optimising IL-2 for cancer immunotherapy. *Immune Netw* 2024;24:e5. CROSSREF