



Article scientifique

Editorial

2022

Accepted version

Open Access

This is an author manuscript post-peer-reviewing (accepted version) of the original publication. The layout of the published version may differ .

---

## Special Issue “IL-1 family cytokines in host defense, inflammation and cancer”

---

Palmer-Lourenco, Gaby; Gabay, Cem

### How to cite

PALMER-LOURENCO, Gaby, GABAY, Cem. Special Issue “IL-1 family cytokines in host defense, inflammation and cancer”. In: Cytokine, 2022, vol. 158, p. 156010. doi: 10.1016/j.cyto.2022.156010

This publication URL: <https://archive-ouverte.unige.ch/unige:162988>

Publication DOI: [10.1016/j.cyto.2022.156010](https://doi.org/10.1016/j.cyto.2022.156010)

## **Special Issue “IL-1 family cytokines in host defense, inflammation and cancer”**

### **Editorial**

Gaby Palmer<sup>1,2</sup>, Cem Gabay<sup>1,2</sup>

<sup>1</sup>Division of Rheumatology, Department of Medicine, Faculty of Medicine, University of Geneva, Geneva, Switzerland

<sup>2</sup>Department of Pathology and Immunology, Faculty of Medicine, University of Geneva, Geneva, Switzerland

### **Correspondence**

Gaby Palmer

Department of Pathology and Immunology

University of Geneva Faculty of Medicine

1 rue Michel-Servet

CH-1211 Geneva 4

Email: [gaby.palmer@unige.ch](mailto:gaby.palmer@unige.ch)

The interleukin (IL)-1 family of cytokines includes 11 members: IL-1 $\alpha$ , IL-1 $\beta$ , IL-1Ra, IL-18, IL-33, IL-36 $\alpha$ , IL-36 $\beta$ , IL-36 $\gamma$ , IL-36Ra, IL-37, and IL-38 that share a similar gene structure, C-terminal amino acid homology and a conserved tertiary protein conformation. The receptors for these cytokines possess intracellular domains homologous to those of Toll-like receptors (TLRs) and share common signaling with TLRs, thereby placing these cytokines at the apex of immune responses against a variety of exogenous and endogenous danger signals. Thus, IL-1 cytokines play important roles in host defense against pathogens, but dysregulation of their activity also contributes to the development of inflammatory diseases. The multifaceted functions of these molecules are well reflected by the variety of topics covered in the articles collected in this Special Issue.

IL-1 family cytokines are widely expressed in epithelial surfaces, where they contribute to the maintenance of barrier integrity and to host defense. Matarozzo et al, provide an in-depth discussion of the roles of IL-1 cytokines in lung, gut and skin barriers at homeostasis, and in inflammatory conditions [1]. Teufel et al. further address the role of IL-1 family members in the induction and regulation of innate immune memory [2], while Frisch reviews the role of IL-1 $\alpha$  in cell senescence, as well as in anti-viral responses [3]. Anti-viral immunity is also the focus of the contribution by Declercq et al., who discuss the role of inflammasomes and IL-1 family

cytokines in the immunopathogenesis of COVID-19 [4].

Members of the IL-1 family have a remarkable biology, including their release via unconventional secretion routes and their dependency on post-translational modifications for optimal extracellular bioactivity. Proteolytic activation of IL-1 family cytokines has emerged as an important regulatory mechanism involved in danger sensing, as highlighted by Martin et al., who revisit the role of IL-1 family members as sentinels for aberrant protease activity [5]. In a complementary contribution, Cayrol and Girard provide an in-depth discussion of the biology and regulation of IL-33, and of its role in airway inflammation [6].

Excessive activity of pro-inflammatory IL-1 family members is associated with immunopathology, in particular in the context of chronic inflammatory and autoimmune diseases. Hals et al. report that, in adults with latent autoimmune diabetes, high autoimmune activity was associated with a decrease of IL-1Ra and IL-1 $\beta$  levels in the circulation over time, suggesting that these cytokines could represent markers of beta cell directed autoimmunity [7]. Harel et al. discuss the role of excessive IL-18 activity in relation to autoinflammatory diseases, such as adult-onset Still's disease and macrophage activation syndrome [8], and Sachen et al. review the link between dysregulated IL-36 pathway activation and inflammatory skin diseases [9]. Finally, Diaz-Barreiro et al. summarize our current understanding of the roles of IL-38 in inflammation and in cancer [10].

Depending on the context, IL-1 family cytokines can exert both pro- or anti-tumorigenic effects.

In their contribution, Pretre et al. review evidence for tumor promoting effects of IL-1 and discuss the clinical utility of IL-1 $\beta$  inhibition in cancer patients [11], while Yeoh et al. extensively discuss the multifaceted role of IL-33 in different types of cancers, in relation to its biology and regulation [12].

Altogether, the articles included in this Special Issue provide a flavor of current topics in research on IL-1 family cytokines. They illustrate some key functions of these molecules, both beneficial and detrimental to the host, emphasize the importance of a carefully orchestrated regulation of their activity, and highlight the complexity of their biology, which remains to be fully elucidated.

### **Grant Support**

GP's work is supported by the Swiss National Science Foundation (grant 310030-188470), the Rheumasearch Foundation, and by a generous donor advised by Carigest SA. CG's work is supported by the Swiss National Science Foundation (grant 310030B-201269) and the Rheumasearch Foundation.

## References

- [1] L. Matarazzo, Y.E. Hernandez Santana, P.T. Walsh, P.G. Fallon, The IL-1 cytokine family as custodians of barrier immunity, *Cytokine* 154 (2022) 155890.
- [2] L.U. Teufel, R.J.W. Arts, M.G. Netea, C.A. Dinarello, L.A.B. Joosten, IL-1 family cytokines as drivers and inhibitors of trained immunity, *Cytokine* 150 (2022) 155773.
- [3] S.M. Frisch, Interleukin-1 $\alpha$ : Novel functions in cell senescence and antiviral response, *Cytokine* 154 (2022) 155875.
- [4] J. Declercq, E. De Leeuw, B.N. Lambrecht, Inflammasomes and IL-1 family cytokines in SARS-CoV-2 infection: from prognostic marker to therapeutic agent, *Cytokine* 157 (2022) 155934.
- [5] S.J. Martin, V. Frezza, P. Davidovich, Z. Najda, D.M. Clancy, IL-1 family cytokines serve as 'activity recognition receptors' for aberrant protease activity indicative of danger, *Cytokine* 157 (2022) 155935.
- [6] C. Cayrol, J.P. Girard, Interleukin-33 (IL-33): A critical review of its biology and the mechanisms involved in its release as a potent extracellular cytokine, *Cytokine* 156 (2022) 155891.
- [7] I.K. Hals, A. Björklund, H. Fiskvik Fleiner, V. Grill, Time-dependent effects on circulating cytokines in patients with LADA: A decrease in IL1-ra and IL-1 beta is associated with progressive disease, *Cytokine* 151 (2022) 155792.
- [8] M. Harel, S. Fauteux-Daniel, C. Girard-Guyonvarc'h, C. Gabay, Balance between Interleukin-18 and Interleukin-18 binding protein in auto-inflammatory diseases, *Cytokine* 150 (2022) 155781.
- [9] K.L. Sachen, C.N. Arnold Greving, J.E. Towne, Role of IL-36 cytokines in psoriasis and other inflammatory skin conditions, *Cytokine* 156 (2022) 155897.
- [10] A. Diaz-Barreiro, A. Huard, G. Palmer, Multifaceted roles of IL-38 in inflammation and cancer, *Cytokine* 151 (2022) 155808.
- [11] V. Pretre, D. Papadopoulos, J. Regard, M. Pelletier, J. Woo, Interleukin-1 (IL-1) and the inflammasome in cancer, *Cytokine* 153 (2022) 155850.
- [12] W.J. Yeoh, V.P. Vu, P. Krebs, IL-33 biology in cancer: An update and future perspectives, *Cytokine* 157 (2022) 155961.