

The role of IL-1 family cytokines in Sjögren's syndrome

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Abstract

Sjögren's syndrome (SS) is a prevalent autoimmune disorder primarily characterized by xerostomia and keratoconjunctivitis sicca. The interleukin-1 (IL-1) cytokine family is implicated in the pathogenesis of SS during its onset and progression. Members of this cytokine family contribute to various pathological pathways in SS by facilitating the aberrant activation of salivary gland epithelial cells, augmenting type 1 immune responses, and modulating Th17 cell differentiation and function. This paper offers a comprehensive review of the historical and recent research advances in research on the mechanisms of action of IL-1 family cytokines in SS, with the objective of providing a theoretical foundation for the clinical diagnosis and management of SS.

Key words: Sjögren's syndrome, interleukin-1 family, Th1, Th17, $\gamma\delta$ T cells.

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Introduction

Sjögren's syndrome (SS) is a chronic systemic autoimmune disorder characterized by the progressive lymphocytic infiltration of exocrine glands [1]. The pathological hallmark of SS is the focal infiltration of CD4+ T lymphocytes and B lymphocytes within exocrine glands, such as the salivary and lacrimal glands, resulting in structural destruction of the glands and a progressive decline in their secretory function [2]. Clinically, this manifests as symptoms such as xerostomia (dry mouth) and keratoconjunctivitis sicca (dry eyes) [3]. SS is classified into two categories based on the presence of concomitant autoimmune diseases: primary Sjögren's syndrome (pSS), when it occurs in isolation, and secondary Sjögren's syndrome (sSS), when it coexists with other autoimmune disorders [4].

Interleukins (IL), a class of cytokines secreted by immune cells, play a pivotal role in immune regulation, inflammatory responses, and cellular communication [5]. To date, over 40 distinct interleukins have been identified. These molecules are categorized based on their functional roles into pro-inflammatory (e.g., IL-1 β , IL-6, IL-17), anti-inflammatory (e.g., IL-10), and regulatory (e.g., IL-2, IL-4) types [6]. They modulate the activation, proliferation, and differentiation of immune cells through complex networks, participating in infection defense, tissue repair, and the development of autoimmune diseases [7-9].

In the pathogenesis of SS, various interleukins are involved and play pivotal roles. Specifically, IL-1 β and IL-6 are known to facilitate inflammatory responses, thereby exacerbating damage to glandular tissues [10]. IL-17 contrib-

utes to immune-mediated tissue destruction by promoting the release of additional pro-inflammatory cytokines [11]. Conversely, the anti-inflammatory cytokine IL-10 has the capacity to mitigate excessive immune responses, thereby exerting a protective effect [12]. Research indicates that the expression profiles of interleukins vary among patients with different SS subtypes, highlighting their potential utility in disease classification, diagnosis, and evaluation of treatment responses. This paper focuses on the role of the IL-1 cytokine family within the context of SS.

Biological characteristics of IL-1 family cytokines

The IL-1 family currently comprises 11 members, including seven pro-inflammatory cytokines (IL-1 α , IL-1 β , IL-18, IL-33, IL-36 α , IL-36 β , IL-36 γ) and four anti-inflammatory cytokines [(IL-1 receptor antagonist (IL-1Ra), IL-36Ra, IL-37, IL-38] [13, 14]. Based on structural and functional characteristics, the IL-1 family can be further categorized into four major subfamilies (IL-1, IL-18, IL-33, and IL-36) and two regulatory cytokines (IL-37 and IL-38) [15]. These cytokines exert their effects through specific receptor systems, with IL-1 receptor accessory protein (IL-1RAcP) acting as a common co-receptor for signaling within the IL-1, IL-33, and IL-36 subfamilies, whereas IL-18 employs the distinct IL-18R β as its co-receptor. Each subfamily assembles unique signaling complexes *via* different receptor combinations (IL-1R1/IL-1RAcP, ST2/IL-1RAcP, IL-36R/IL-1RAcP, and IL-18R α /

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Table 1. IL-1 family cytokine members

Cytokine		Type	Primary/co-receptor	Primary function	Ref.
IL-1 subfamily	IL-1 α	Agonist	IL-1R1/IL-1RAcP	Pro-inflammatory	[22]
	IL-1 β	Agonist	IL-1R1/IL-1RAcP	Pro-inflammatory	[21]
	IL-1Ra	Antagonist	IL-1R1 (Competitive binding)	IL-1 α , IL-1 β antagonists	[20]
IL-18 subfamily	IL-18	Agonist	IL-18R α /IL-18R β	Pro-inflammatory	[25]
IL-33 subfamily	IL-33	Agonist	ST2/IL-1RAcP	Pro-inflammatory	[19]
IL-36 subfamily	IL-36 α	Agonist	IL-36R/IL-1RAcP	Pro-inflammatory	[17]
	IL-36 β	Agonist	IL-36R/IL-1RAcP	Pro-inflammatory	[23]
	IL-36 γ	Agonist	IL-36R/IL-1RAcP	Pro-inflammatory	[18]
	IL-36Ra	Antagonist	IL-36R (Competitive binding)	IL-36 α , IL-36 β , IL-36 γ antagonists	[27]
Regulatory subfamily	IL-37	Antagonist	IL-18R α /SIGIRR	Anti-inflammatory	[24]
	IL-38	Antagonist	IL-1R1/IL-36R	Anti-inflammatory	[26]

IL-18R β), thereby executing diverse functions within distinct signaling pathways (Table 1) [16-27].

Receptors and signaling pathway of IL-1 family cytokines

Cytokines of the IL-1 family serve as fundamental regulatory molecules in inflammatory responses, exerting a crucial influence on immune processes through highly conserved signaling mechanisms [28]. Central to their signaling is the precise recognition of ligands by members of the IL-1 receptor (IL-1R) superfamily, followed by a series of signaling events. Upon ligand binding to their respective receptors, IL-1 family members (including IL-1 α/β , IL-33, IL-18, etc.) recruit co-receptors to form functional signaling complexes. This interaction triggers myeloid differentiation factor 88 (MyD88)-dependent signaling pathways, which ultimately activate the transcription factor nuclear factor kappa B (NF- κ B), thereby promoting the expression of inflammatory genes [29]. Concurrently, various endogenous regulatory mechanisms finely tune this activity through decoy receptors, antagonists, and inhibitory signaling pathways, thereby preventing excessive inflammatory responses (Fig. 1).

Role of IL-1 family cytokines in SS

IL-1 subfamily and SS

Relevant studies suggest that inflammatory responses and oxidative stress contribute to the progression of pSS. Benchabane *et al.* [10] reported significantly elevated levels of the proinflammatory cytokine IL-1 β in patients with pSS, which exhibited a strong positive correlation with concentrations of oxidative stress markers, such as malondialdehyde (MDA) and nitric oxide (NO). This finding indicates that inflammatory responses and oxi-

dative damage reinforce each other, collectively driving the progression of pSS, with IL-1 β serving as a sensitive biomarker for monitoring disease activity in pSS [10]. Although IL-33 levels also vary during disease progression, they showed no significant correlation with MDA or NO, suggesting that IL-33 may contribute to pSS pathogenesis through pathways independent of oxidative stress.

Subsequent research has demonstrated that IL-33 predominantly facilitates the activation of salivary gland epithelial cells and promotes type I immune responses *via* the IL-33/sST2 axis, thereby contributing to the pathogenesis of pSS. In patients with pSS, serum levels of IL-33 and its decoy receptor sST2 are significantly elevated [30-32], showing a positive correlation with disease activity indices (such as SSDAI and ESSDAI scores) and clinical parameters (including thrombocytopenia and disease duration) [31, 32]. This suggests a specific activation of the IL-33/sST2 pathway in pSS and highlights its potential utility as a biomarker for assessing disease activity [33]. Histological investigations by Jung *et al.* [31] and Dong *et al.* [33] have revealed increased expression of IL-33 and ST2 in the salivary glands of pSS patients, predominantly localized to glandular epithelial and endothelial cells. Further studies by Awada *et al.* [30] and Jung *et al.* [31] found that IL-33 expression levels were significantly elevated during the mid-stage of the disease (Chisholm score 2-3) but tended to stabilize or decrease in the late stage (Chisholm score 4), indicating that IL-33 activation may be an early event in the disease process. Mechanistically, both Awada *et al.* [30] and Dong *et al.* [33] have demonstrated that IL-33 does not directly induce proinflammatory cytokines. Instead, it synergistically enhances the production of interferon-gamma (IFN- γ) by NK and NKT cells in conjunction with IL-12 and IL-23, thereby facilitating localized inflammatory immune responses. Dong *et al.* [33] further elucidated that IL-33-stimulated salivary gland epithelial cells activate the NF- κ B pathway, leading to the upregulation of

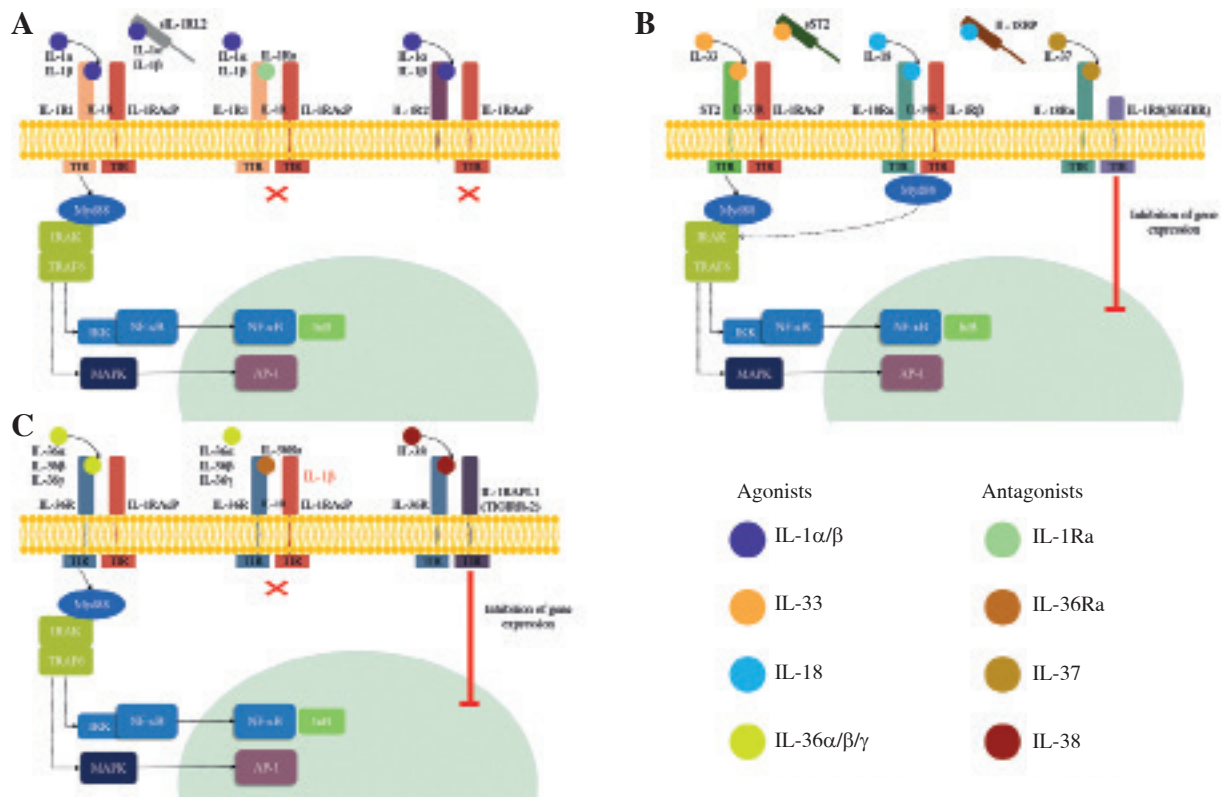


Fig. 1. Signaling pathways and regulatory mechanisms associated with the IL-1 family. **A)** The proinflammatory signaling initiated by IL-1 α and IL-1 β commences with their binding to the IL-1R1 receptor, followed by the recruitment of the co-receptor IL-1RAcP. This ligand-receptor complex formation leads to the recruitment of the intracellular TIR domain-containing receptor complex, which subsequently engages MyD88, thereby activating IRAKs and TRAF6. This cascade results in the activation of TAK1, which concurrently initiates two pivotal pathways: the NF- κ B pathway, through the degradation of I κ B mediated by phosphorylation of the IKK complex, and the MAPK pathway, through the phosphorylation of transcription factors via the p38/JNK/ERK cascade, thereby augmenting AP-1 activity. The activated NF- κ B and AP-1 transcription factors collaboratively regulate the expression of inflammatory mediators, including TNF- α and IL-6. This signaling process is tightly controlled by negative regulatory mechanisms involving the decoy receptor IL-1R2, which competitively binds ligands without initiating signaling, and the natural antagonist IL-1Ra, which binds to IL-1R1 but is unable to recruit co-receptors. **B)** IL-18 engages the classical MyD88-IRAK-TRAF6-NF- κ B signaling pathway through its specific receptor IL-18R α and the recruitment of the co-receptor IL-18R β , thereby promoting the production of proinflammatory cytokines such as IFN- γ . This signaling pathway is governed by two major regulatory mechanisms. The soluble high-affinity decoy protein IL-18BP sequesters free IL-18, thereby preventing its interaction with membrane receptors. Concurrently, the anti-inflammatory cytokine IL-37 associates with IL-18R α and recruits the inhibitory receptor SIGIRR (IL-1R8), thereby inhibiting TAK1 and NF- κ B activation to mitigate inflammatory responses. IL-33 engages the MyD88-IRAK-NF- κ B signaling cascade by binding to its membrane receptor ST2L and recruiting the co-receptor IL-1RAcP, which facilitates Th2-type immune responses and the production of cytokines such as IL-4, IL-5, and IL-13. This pathway is tightly regulated by the soluble decoy receptor sST2, generated through alternative splicing of the ST2 gene. sST2 binds free IL-33 with high affinity but lacks the transmembrane and intracellular domains necessary for signal transduction, thus competitively inhibiting IL-33 from binding to ST2L. **C)** The cytokine IL-36 activates the MyD88-IRAK-NF- κ B pathway by binding to its receptor IL-36R and recruiting the co-receptor IL-1RAcP, thereby promoting the production of pro-inflammatory mediators such as IL-8 and IL-6. This pro-inflammatory process is primarily subject to negative regulation by the endogenous antagonist IL-36Ra. As a structural analog, IL-36Ra competitively binds to IL-36R but does not initiate signal transduction due to its inability to effectively recruit IL-1RAcP. Furthermore, the anti-inflammatory protein IL-38 can interact with both IL-36R and the inhibitory receptor TIGIRR-2, thereby not only preventing signal initiation but also directly suppressing the pathway, resulting in a dual inhibitory effect.

immune molecules such as CD86 and CCL2, which in turn promote Th1 and B cell infiltration. In contrast, Liu *et al.* [34] identified that adipose-derived mesenchymal stromal cells (ADSCs), when stimulated with IL-1 β , produce IL-33 *via* the TAK1, ERK, and p38 pathways. This process fosters the proliferation of CD4+Foxp3+ST2+ regulatory T cells and mitigates experimental autoimmune dry syndrome, suggesting that IL-33 also has immunomodulatory capabilities. In conclusion, the IL-33/sST2 system plays a significant role in the onset and progression of pSS through interactions between epithelial and immune cells. Dong *et al.* [33] confirmed that IL-33 $^{-/-}$ and ST2 $^{-/-}$ mouse models exhibited reduced pathological damage and inflammatory responses in the later stages of the disease, further underscoring the critical role of the IL-33/sST2 axis in the pathogenesis of pSS. In summary, the IL-33/sST2 system contributes to the onset and progression of pSS through epithelial-immune cell interactions and synergistic effects with inflammatory cytokines.

Beyond the IL-33/sST2 axis, Hu *et al.* [35] further elucidated that respiratory viral infections exacerbate the pathogenesis of SS by inducing IL-33 expression. In their study, poly(I:C) was administered intratracheally to simulate viral infection, resulting in markedly elevated IL-33 expression in the submandibular glands and lung tissues of NOD mice. In the salivary glands, this upregulation of IL-33 was associated with increased interferon levels and specific activation of Th1 cells, while Th17 cell activity remained unchanged. This suggests that IL-33 predominantly drives Th1-mediated immune responses. Consequently, this process led to aggravated glandular tissue damage, increased infiltration of inflammatory cells, and diminished salivary secretion. Notably, the alterations in IL-33 expression and T cell proportions in the lungs following poly(I:C) stimulation paralleled the lesions observed in distal salivary glands. This highlights the crucial intermediary role of IL-33 in linking respiratory infections to autoimmune damage in the salivary glands, thereby exacerbating the immune and functional dysregulation characteristic of SS through the promotion of Th1 immune responses.

IL-18 subfamily and SS

Relevant research indicates that IL-18 plays a crucial role in the pathogenesis of pSS. Numerous studies consistently report significantly elevated levels of IL-18 in both the serum and local salivary gland tissues of patients with pSS compared to healthy controls [36, 37]. Moreover, IL-18 expression shows a positive correlation with rheumatoid factor and disease-specific autoantibodies, including anti-SSA/Ro and anti-SSB/La antibodies [36, 38], suggesting a strong association with the intensity of autoimmune responses. At the tissue level, Bombardieri *et al.* [36] demonstrated extensive IL-18 expression within the inflammatory infiltrates of salivary glands, particular-

ly within follicular-like structures. IL-18 is predominantly secreted by infiltrating macrophages (CD68+) and ductal epithelial cells in these regions [36, 39]. Eriksson *et al.* [38], exploring novel roles of IL-18 in pSS, observed that IL-18 not only enhances Th1 immune responses but also promotes the production of IgG1 antibodies. Additionally, Sakai *et al.* [40] demonstrated that IL-18 synergistically amplifies inflammatory responses through the IL-17 pathway, resulting in the substantial secretion of cytokines such as IL-6 and IL-8, thereby exacerbating tissue damage. Ciccina *et al.* [41] reported that IL-18 facilitates the onset and progression of lymphoma – a significant complication associated with pSS – by inducing aberrant expression of the IL-22 receptor 1 (IL-22R1) protein in myeloid cells.

Concurrently, various studies have demonstrated that the body attempts to mitigate excessive inflammation by upregulating anti-inflammatory mediators such as IL-37 and IL-18-binding protein (IL-18BP) [42, 43]. Although some studies have reported no significant alterations in serum IL-37 levels, Parisi *et al.* [44] observed its co-expression with IL-18, IL-18BP, and IL-18 receptor alpha (IL-18R α) in local tissues, thereby forming a potential immunoregulatory axis. Furthermore, Conti *et al.* [45] have confirmed the anti-inflammatory properties of IL-37 in SS (Fig. 2). Collectively, these findings support a role for IL-18 as a pro-inflammatory mediator in pSS, contributing to aberrant immune responses and tissue damage. Its interaction with associated inhibitory cytokines may reflect the overall intensity of immune activity in the disease, suggesting its potential as a biomarker and therapeutic target.

IL-36 subfamily and SS

Ciccina *et al.* [46] provided a systematic elucidation of the role of the IL-36 inflammatory axis in pSS by comparing patients with pSS to control subjects. Their research demonstrated a significant overexpression of the pro-inflammatory cytokine IL-36 α in both the serum and submandibular gland tissue of pSS patients, with the primary sources being $\alpha\beta$ T cells and CD68+ macrophages infiltrating the salivary glands. Importantly, IL-36 α expression levels were found to significantly correlate with IL-17, IL-22, and IL-23p19, suggesting that the IL-36 axis may interact with the IL-23/IL-17 inflammatory pathway. Research conducted by Nguyen *et al.* [47] and Ciccina *et al.* [48] has identified the activation of the IL-23/IL-17/IL-22 axis as an important factor in the pathogenesis of pSS. Despite the compensatory upregulation of the natural inhibitor IL-38, it remains inadequate to suppress the overall inflammatory response. Notably, the study demonstrated that $\gamma\delta$ T cells in the salivary glands of pSS patients, although not increased in number, exhibit heightened functional activation. These cells show a significantly enhanced capacity for IL-17 production, which positively correlates with tissue lesion scores, and they express high levels of

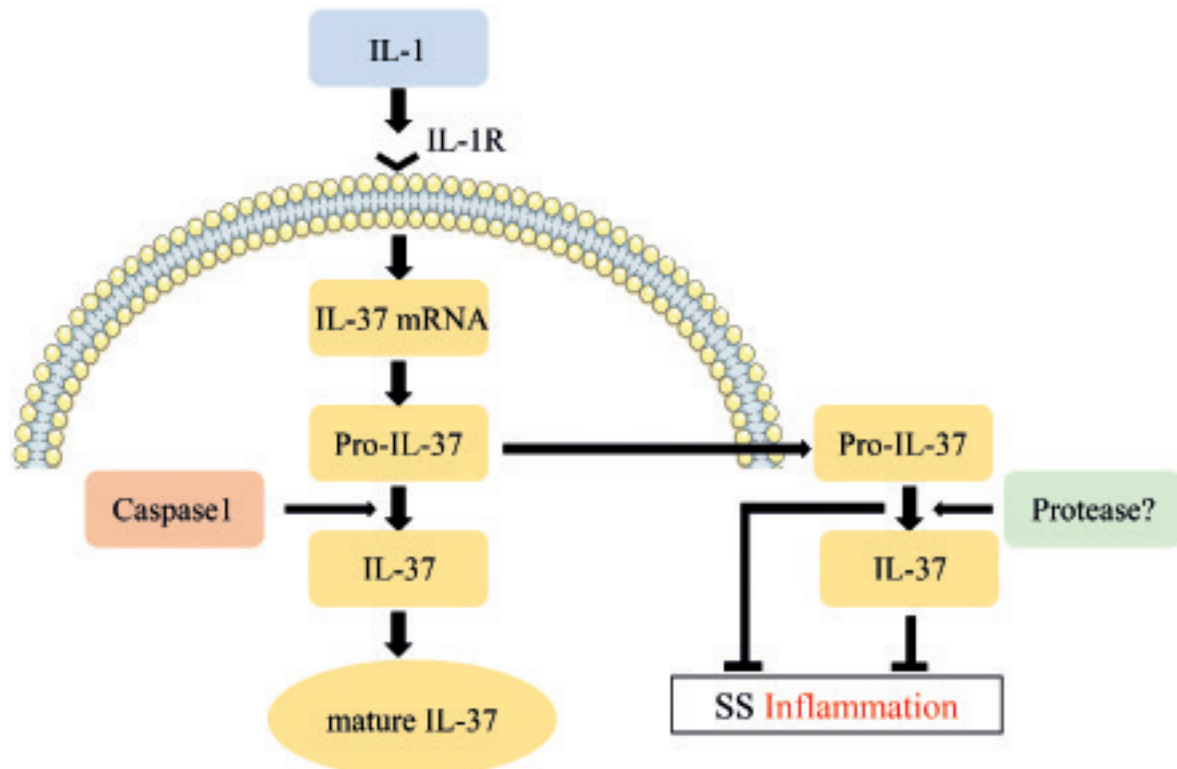


Fig. 2. Schematic representation of the anti-inflammatory mechanism of IL-37 in SS. Throughout the pathological progression of SS, IL-1 functions as an external signaling molecule that binds to IL-1 receptors on the cell membrane, initiating intracellular signal transduction. This interaction may increase the transcriptional levels of IL-37 mRNA within the cell, thereby enhancing the synthesis of the IL-37 precursor. A fraction of the synthesized IL-37 precursor is further processed intracellularly to form mature IL-37, which is subsequently released or stored; another fraction is secreted extracellularly, where it may be converted by proteases into its biologically active form. This active IL-37 may contribute to the regulation of inflammatory processes in SS

IL-36 α and its receptor IL-36R. This suggests that $\gamma\delta$ T cells function not only as effector cells but also as potentially important components that connect and amplify the IL-36 and IL-17 inflammatory network [45].

Luo *et al.* [49] focused on the regulatory role of IL-38 in pathogenic Th17 responses within pSS. Their findings demonstrated a significant reduction in IL-38 expression in pSS patients compared to healthy controls, accompanied by elevated levels of Th17-associated cytokines, such as IL-17 and IL-23. Subsequent in vitro cellular assays and in vivo mouse model experiments showed that exogenous administration of IL-38 effectively inhibited Th17 cell differentiation and activity. Consequently, IL-38 acts as a critical negative regulator of Th17-mediated immune responses in pSS, highlighting its potential as a novel therapeutic target for the disease.

Conclusions and perspectives

This paper presents a systematic review of the research advancements concerning the mechanisms of

action of the IL-1 family in SS. Despite these advancements, numerous aspects of the specific functions of this cytokine family in SS remain inadequately understood. Furthermore, the limitations inherent in current cytokine detection technologies may compromise the accuracy and reliability of research outcomes. Future research should aim to both deepen and broaden the exploration of the IL-1 family's mechanisms in SS, with a particular emphasis on the comprehensive regulation of cytokine networks. This includes elucidating the synergistic or antagonistic interactions among cytokines and their regulatory pathways to clarify their functional roles in the pathogenesis of SS. Such investigations may provide a theoretical basis for improving the diagnosis and treatment of SS, support translational research on cytokines as potential therapeutic targets, and potentially improve clinical management of SS.

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Disclosures

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References

- Negrini S, Emmi G, Greco M, et al. (2022): Sjögren's syndrome: a systemic autoimmune disease. *Clin Exp Med* 22: 9-25.
- Chen B, Zhang C, Zhou M, et al. (2025): CD4+ T-cell metabolism in the pathogenesis of Sjögren's syndrome. *Int Immunopharmacol* 150: 114320.
- Zhu Y, Zhang K, Luo Z, et al. (2025): Gut microbiota on anxiety and depression in primary Sjögren's syndrome: A novel insight. *Heliyon* 11: e42045.
- Hernández-Molina G, Avila-Casado C, Cárdenas-Velázquez F, et al. (2010): Similarities and differences between primary and secondary Sjögren's syndrome. *J Rheumatol* 37: 800-808.
- Mantovani A, Dinarello CA, Molgora M, et al. (2019): Interleukin-1 and Related Cytokines in the Regulation of Inflammation and Immunity. *Immunity* 50: 778-795.
- Cavaillon JM (2001): Pro- versus anti-inflammatory cytokines: myth or reality. *Cell Mol Biol (Noisy-le-grand)* 47: 695-702.
- Rahman NAA, Balasubramaniam VRMT, Yap WB (2023): Potential of interleukin (IL)-12 group as antivirals: severe viral disease prevention and management. *Int J Mol Sci* 24: 7350.
- Short WD, Rae M, Lu T, et al. (2023): Endogenous interleukin-10 contributes to wound healing and regulates tissue repair. *J Surg Res* 285: 26-34.
- Yao X, Huang J, Zhong H, et al. (2014): Targeting interleukin-6 in inflammatory autoimmune diseases and cancers. *Pharmacol Ther* 141: 125-139.
- Benchabane S, Sour S, Zidi S, et al. (2024): Exploring the relationship between oxidative stress status and inflammatory markers during primary Sjögren's syndrome: A new approach for patient monitoring. *Int J Immunopathol Pharmacol* 38: 3946320241263034.
- Zhan Q, Zhang J, Lin Y, et al. (2023): Pathogenesis and treatment of Sjögren's syndrome: Review and update. *Front Immunol* 14: 1127417.
- Roescher ., Tak PP, Illei GG (2009): Cytokines in Sjögren's syndrome. *Oral Dis* 15: 519-526.
- Palomo J, Dietrich D, Martin P, et al. (2015): The interleukin (IL)-1 cytokine family – balance between agonists and antagonists in inflammatory diseases. *Cytokine* 76: 25-37.
- Wu Q, Zeng Y, Geng K, et al. (2025): The role of IL-1 family cytokines in diabetic cardiomyopathy. *Metabolism* 163: 156083.
- Teufel LU, Arts RJW, Netea MG, et al. (2022): IL-1 family cytokines as drivers and inhibitors of trained immunity. *Cytokine* 150: 155773.
- Griffiths JS, Camilli G, Kotowicz NK, et al. (2021): Role for IL-1 family cytokines in fungal infections. *Front Microbiol* 12: 633047.
- Andoh A, Nishida A (2023): Pro- and anti-inflammatory roles of interleukin (IL)-33, IL-36, and IL-38 in inflammatory bowel disease. *J Gastroenterol* 58: 69-78.
- Bridgewood C, Stacey M, Alase A, et al. (2017): IL-36γ has proinflammatory effects on human endothelial cells. *Exp Dermatol* 26: 402-408.
- Cayrol C, Girard JP (2018): Interleukin-33 (IL-33): A nuclear cytokine from the IL-1 family. *Immunol Rev* 281: 154-168.
- Eisenberg SP, Evans RJ, Arend WP, et al. (1990): Primary structure and functional expression from complementary DNA of a human interleukin-1 receptor antagonist. *Nature* 343: 341-346.
- Gaidt MM, Ebert TS, Chauhan D, et al. (2016): Human monocytes engage an alternative inflammasome pathway. *Immunity* 44: 833-846.
- Gubler U, Chua AO, Stern AS, et al. (1986): Recombinant human interleukin 1 alpha: purification and biological characterization. *J Immunol* 136: 2492-2497.
- Hayran Y, Allı N, Yücel Ç, et al. (2020): Serum IL-36α, IL-36β, and IL-36γ levels in patients with hidradenitis suppurativa: association with disease characteristics, smoking, obesity, and metabolic syndrome. *Arch Dermatol Res* 312: 187-196.
- Wu Q, Zhou J, Yuan ZC, et al. (2022): Association between IL-37 and systemic lupus erythematosus risk. *Immunol Invest* 51: 727-738.
- Yadavalli CS, Upparahalli Venkateshaiah S, Kumar S, et al. (2023): Allergen-induced NLRP3/caspase1/IL-18 signaling initiate eosinophilic esophagitis and respective inhibitors protect disease pathogenesis. *Commun Biol* 6: 763.
- Zhang XH, Li Y, Zhou L, et al. (2022): Interleukin-38 in atherosclerosis. *Clin Chim Acta* 536: 86-93.
- Zhao Z, Zhang R, Gao X, et al. (2020): Altered serum levels of IL-36 cytokines (IL-36α, IL-36β, IL-36γ, and IL-36Ra) and their potential roles in Guillain-Barré syndrome. *Medicine (Baltimore)* 99: e23832.
- Dinarello CA (2011): Interleukin-1 in the pathogenesis and treatment of inflammatory diseases. *Blood* 117: 3720-3732.
- Janssens S, Burns K, Tschopp J, et al. (2002): Regulation of interleukin-1- and lipopolysaccharide-induced NF-κappaB activation by alternative splicing of MyD88. *Curr Biol* 12: 467-471.
- Awada A, Nicaise C, Ena S, et al. (2014): Potential involvement of the IL-33-ST2 axis in the pathogenesis of primary Sjögren's syndrome. *Ann Rheum Dis* 73: 1259-1263.
- Jung SM, Lee J, Baek SY, et al. (2015): The interleukin 33/ST2 axis in patients with primary Sjögren syndrome: expression in serum and salivary glands, and the clinical association. *J Rheumatol* 42: 264-271.
- Margiotta DP, Navarini L, Vadacca M, et al. (2016): The IL33/ST2 axis in Sjögren syndrome in relation to disease activity. *Eur Rev Med Pharmacol Sci* 20: 1295-1299.
- Dong Y, Ming B, Gao R, et al. (2022): The IL-33/ST2 axis promotes primary Sjögren's syndrome by enhancing salivary epithelial cell activation and type 1 immune response. *J Immunol* 208: 2652-2662.
- Liu O, Xu J, Wang F, et al. (2021): Adipose-mesenchymal stromal cells suppress experimental Sjögren syndrome by IL-33-driven expansion of ST2(+) regulatory T cells. *iScience* 24: 102446.
- Hu P, Ming B, Wu X, et al. (2021): Intratracheal poly(I:C) exposure accelerates the immunological disorder of salivary glands in Sjögren's-like NOD/ShiLtJ mice. *Front Med (Lausanne)* 8: 645816.
- Bombardieri M, Barone F, Pittoni V, et al. (2004): Increased circulating levels and salivary gland expression of interleukin-18 in patients with Sjögren's syndrome: relationship with autoantibody production and lymphoid organization of the periductal inflammatory infiltrate. *Arthritis Res Ther* 6: R447-456.

37. Deng Y, Wang Y, Cheng Y, et al. (2025): Expression of interleukin-18 in primary Sjögren syndrome and its potential mechanisms with disease: A systematic review and meta-analysis. *Medicine (Baltimore)* 104: e41919
38. Eriksson P, Andersson C, Ekerfelt C, et al. (2004): Relationship between serum levels of IL-18 and IgG1 in patients with primary Sjögren's syndrome, rheumatoid arthritis and healthy controls. *Clin Exp Immunol* 137: 617-620.
39. Manoussakis MN, Boiu S, Korkolopoulou P, et al. (2007): Rates of infiltration by macrophages and dendritic cells and expression of interleukin-18 and interleukin-12 in the chronic inflammatory lesions of Sjögren's syndrome: correlation with certain features of immune hyperactivity and factors associated with high risk of lymphoma development. *Arthritis Rheum* 56: 3977-3988.
40. Sakai A, Sugawara Y, Kuroishi T, et al. (2008): Identification of IL-18 and Th17 cells in salivary glands of patients with Sjögren's syndrome, and amplification of IL-17-mediated secretion of inflammatory cytokines from salivary gland cells by IL-18. *J Immunol* 181: 2898-2906.
41. Ciccia F, Guggino G, Rizzo A, et al. (2015): Interleukin (IL)-22 receptor 1 is over-expressed in primary Sjögren's syndrome and Sjögren-associated non-Hodgkin lymphomas and is regulated by IL-18. *Clin Exp Immunol* 181: 219-229.
42. Chen Y, Deng F, Zheng J, et al. (2016): High circulating level of interleukin-18 in patients with primary Sjögren's syndrome is associated with disease activity. *Mod Rheumatol* 26: 156-158.
43. Liuqing W, Liping X, Hui S, et al. (2017): Elevated IL-37, IL-18 and IL-18BP serum concentrations in patients with primary Sjögren's syndrome. *J Investig Med* 65: 717-721.
44. Parisi D, Sarraud J, Soyfoo M (2025): The potential contribution of the IL-37/IL-18/IL-18BP/IL-18R axis in the pathogenesis of Sjögren's syndrome. *Int J Mol Sci* 26: 4877.
45. Conti P, Stellin L, Caraffa A, et al. (2020): Advances in mast cell activation by IL-1 and IL-33 in Sjögren's syndrome: promising inhibitory effect of IL-37. *Int J Mol Sci* 21: 4297.
46. Ciccia F, Accardo-Palumbo A, Alessandro R, et al. (2015): Interleukin-36 α axis is modulated in patients with primary Sjögren's syndrome. *Clin Exp Immunol* 181: 230-238.
47. Nguyen CQ, Hu MH, Li Y, et al. (2008): Salivary gland tissue expression of interleukin-23 and interleukin-17 in Sjögren's syndrome: findings in humans and mice. *Arthritis Rheum* 58: 734-743.
48. Ciccia F, Guggino G, Rizzo A, et al. (2012): Potential involvement of IL-22 and IL-22-producing cells in the inflamed salivary glands of patients with Sjögren's syndrome. *Ann Rheum Dis* 71: 295-301.
49. Luo D, Chen Y, Zhou N, et al. (2020): Blockade of Th17 response by IL-38 in primary Sjögren's syndrome. *Mol Immunol* 127: 107-111.