Press release

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To Members of the Press

Keio University School of Medicine
Sysmex Corporation

Identification of Serum IL-22 and IL-18 as Cytokines Reflecting Disease Activity in Atopic Dermatitis During Dupilumab Therapy

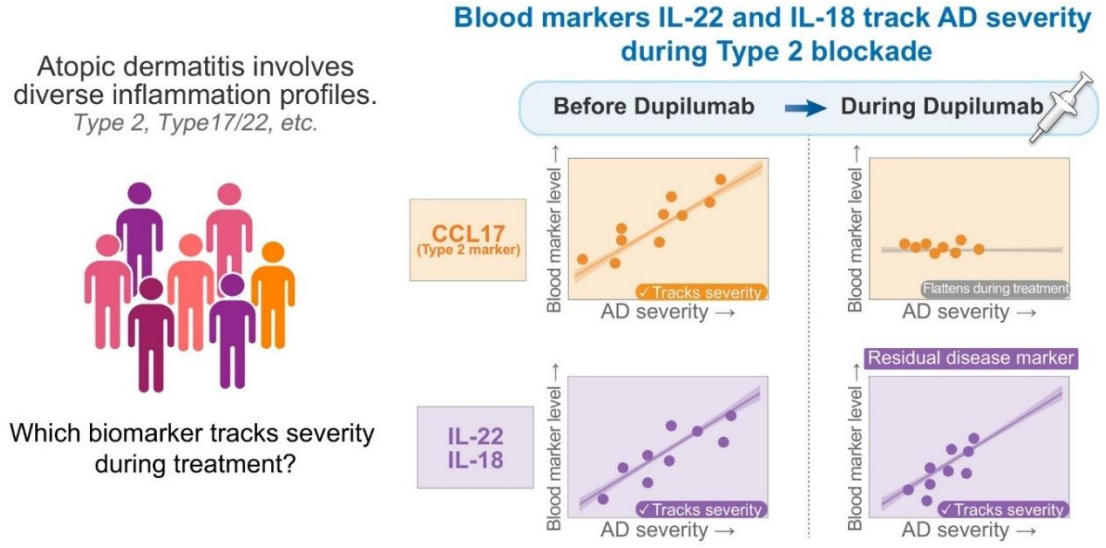
— Potential for New Monitoring Indicators Accounting for Diverse Inflammatory Patterns —

A collaborative research group led by Dr. Ayano Fukushima-Nomura (Assistant Professor), Dr. Hiroshi Kawasaki (Senior Lecturer), and Prof. Masayuki Amagai of the Department of Dermatology, Keio University School of Medicine; Dr. Akihiko Koseki (Team Director, Laboratory for Developmental Genetics), RIKEN Center for Integrative Medical Sciences; and Takehiro Hasegawa and colleagues at Sysmex Corporation has revealed plasma IL-22 and IL-18 levels as potential biomarkers that reflect disease activity over the course of dupilumab treatment in patients with atopic dermatitis.

The levels of serum CCL17 (TARC), a representative type 2 inflammation–related biomarker, are widely utilized in clinical practice in Japan and are useful for assessing disease severity prior to treatment. In this study, the team analyzed plasma cytokine levels from 170 patients with atopic dermatitis and conducted a 6-month longitudinal evaluation of 24 patients undergoing dupilumab therapy. The results showed that CCL17 levels declined rapidly after treatment initiation, reflecting early treatment response; however, their association with disease activity during treatment tended to be limited. In contrast, IL-22 and IL-18 levels demonstrated sustained variability during dupilumab therapy and consistently reflected the severity of cutaneous symptoms throughout the treatment period.

These findings contribute to a reappraisal of monitoring indicators for atopic dermatitis that take into account disease heterogeneity and the phase of treatment. Looking ahead, combining conventional markers such as CCL17 with novel indicators like IL-22 may enable more precise assessment of disease activity in patients receiving biologic therapies.

This study was published online in the international journal *Allergy* on February 18, 2026.



1. Background and Overview

Atopic dermatitis (AD) is a highly heterogeneous inflammatory disease; although it is predominantly mediated by type 2 inflammation, its pathogenesis also involves multiple immune pathways, notably Th17- and Th22-related responses (Note 1). Previous studies, including our report (Ayano Fukushima-Nomura et al, *Nature Communications*, 2025), have shown that activation patterns of cutaneous inflammatory pathways differ among patients with AD. Based on these findings, in the present study, we analyzed blood from patients with AD with a focus on multiple inflammatory pathways.

Serum CCL17 (TARC) is widely used as a representative biomarker that reflects type 2 inflammation (Note 2) and is covered by Japan's national health insurance. However, in the era of type 2-targeted biologics such as dupilumab, the biomarkers to assess residual disease activity during treatment have not been fully established.

In this study, a collaborative team from the Department of Dermatology, Keio University School of Medicine, the RIKEN Center for Integrative Medical Sciences (IMS), and Sysmex Corporation conducted a cross-sectional analysis of blood cytokines (Note 3) in 170 patients with AD and performed a 6-month longitudinal study following 24 of these patients who received dupilumab. In addition to the established marker CCL17, we examined the relationships between multiple inflammation-related cytokines—including IL-22 and IL-18—and the severity of skin symptoms as measured by the Eczema Area and Severity Index (EASI).

2. Findings, Significance, and Future Directions

2.1 Cross-sectional analysis of correlations between patient severity and the levels of blood cytokines (Figure 1)

In the cross-sectional analysis (n = 170), several blood cytokines correlated with disease severity as measured by the EASI. In particular, CCL17, IL-22, and IL-18 levels were associated with EASI, suggesting that, in patients not receiving systemic therapies such as biologics, these blood cytokines serve as biomarkers of disease severity.

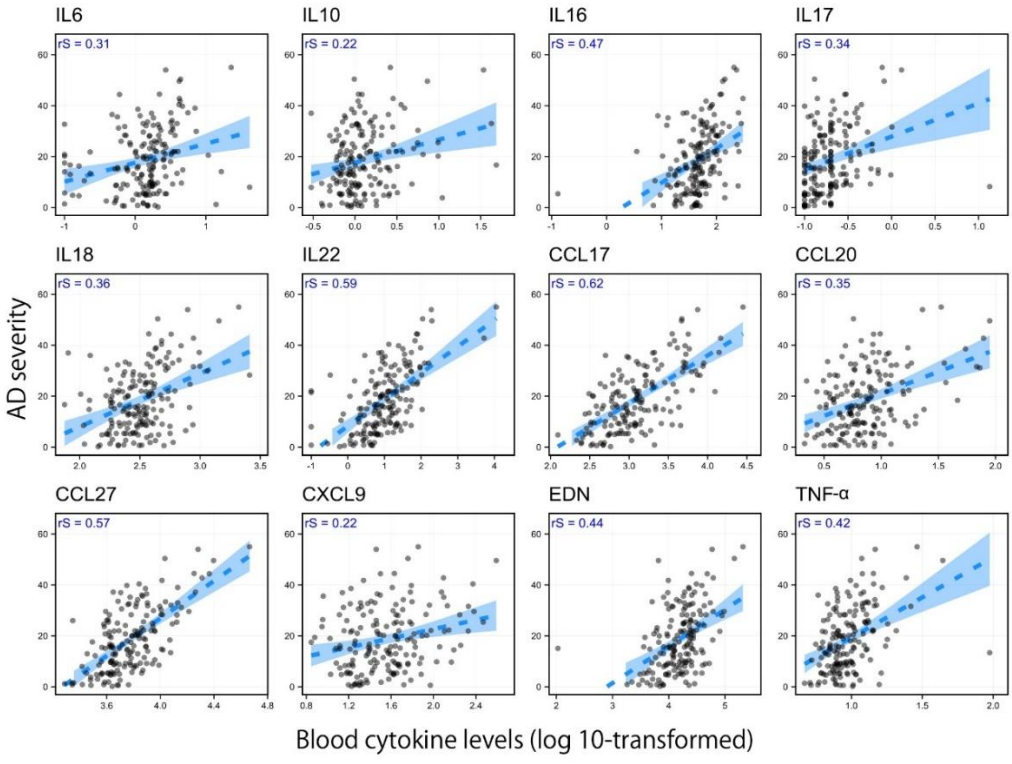


Figure1 Association between blood cytokines and disease severity (EASI) in patients with atopic dermatitis: cross-sectional analysis

In a cross-sectional cohort of 170 patients with AD, associations between log10-transformed blood cytokine levels and disease severity (EASI) were examined. The levels of multiple cytokines—including CCL17, IL-22, and IL-18—were associated with EASI, supporting the potential of blood testing for assessing disease activity. Spearman's rank correlation coefficients (rS) are shown in the figure.

2.2 Changes during dupilumab treatment (Figure 2, Figure 3)

In the longitudinal analysis (n = 24; 6-month follow-up), blood CCL17 levels declined rapidly after treatment initiation and subsequently remained low. Consequently, while CCL17 levels correlated with EASI in the early phase of treatment, their association with disease severity tended to weaken during ongoing therapy.

By contrast, IL-22 and IL-18 levels also decreased after treatment initiation but continued to show a range of values and remained associated with EASI throughout the treatment period. These results suggest that, during dupilumab treatment, IL-22 and IL-18 may serve as complementary biomarkers for assessing residual disease activity.

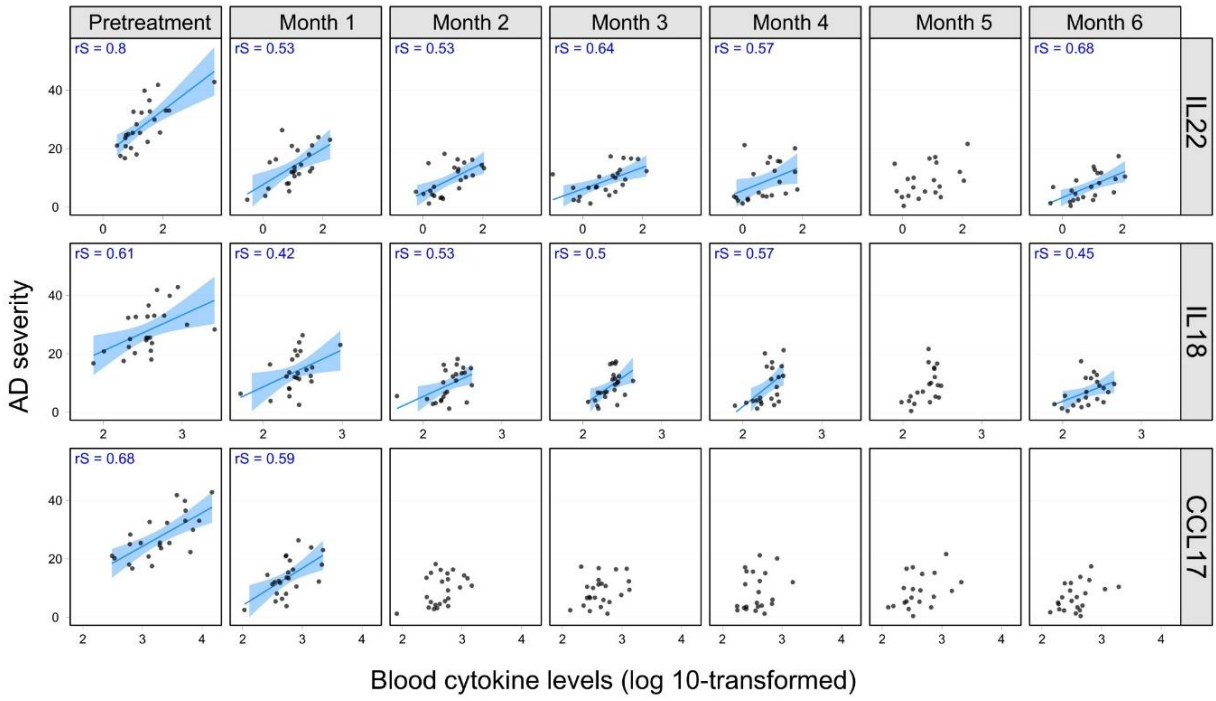


Figure 2 Association between blood cytokines and disease severity (EASI) during dupilumab treatment (longitudinal analysis)

In 24 patients with AD receiving dupilumab, associations between blood IL-22, IL-18, and CCL17 levels and disease severity (EASI) were evaluated at each time point from pretreatment (month 0) through month 6. While CCL17 levels showed associations with severity primarily in the early phase after treatment initiation, IL-22 and IL-18 levels tended to remain associated with EASI throughout the treatment period. Spearman's rank correlation coefficients (rS) at each time point are shown in the figure.

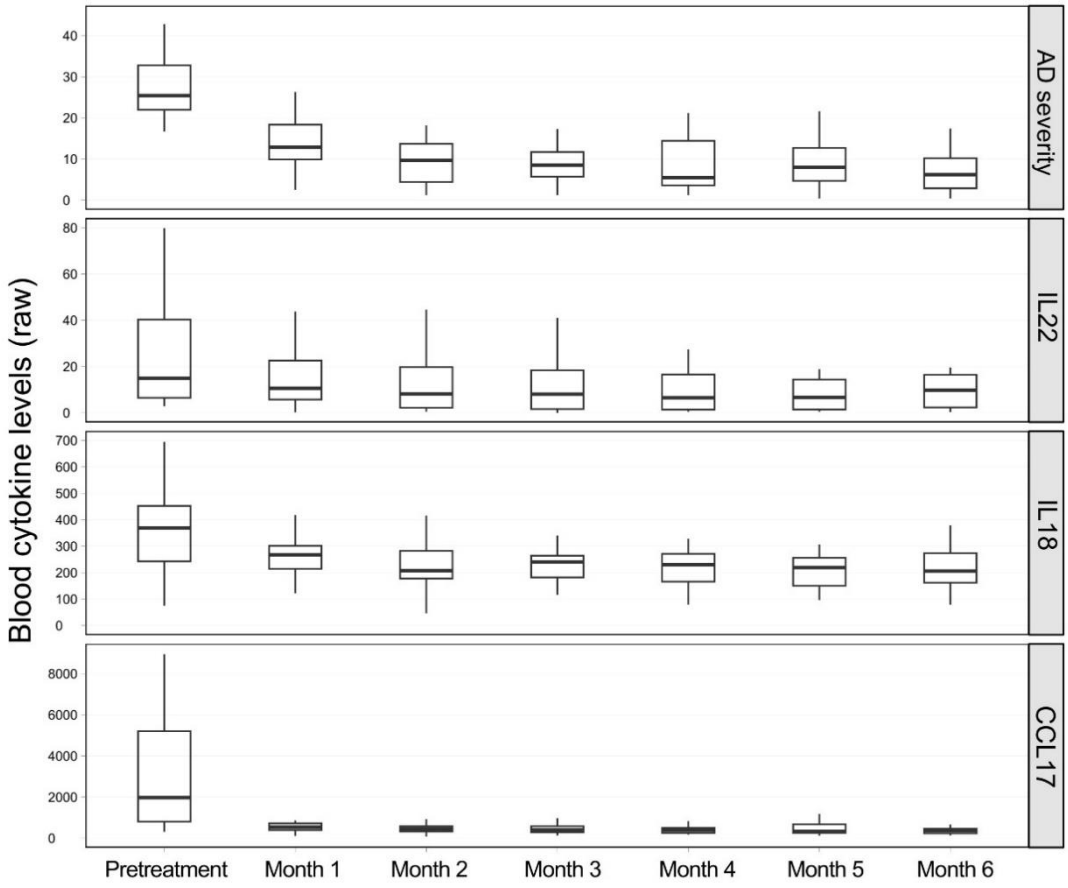


Figure 3 Longitudinal changes in disease severity (EASI) and blood biomarkers during dupilumab treatment

Time courses of disease severity (EASI) and blood CCL17, IL-22, and IL-18 levels over the 6 months following initiation of dupilumab treatment. CCL17 levels decreased rapidly after treatment initiation and then remained at low levels, whereas IL-22 and IL-18 levels although they decreased after treatment initiation, continued to show a range of values over time.

2.3 Future Prospects

While acknowledging the established role of CCL17 under topical treatment, this study indicates that, during dupilumab therapy, IL-22 and IL-18 may serve as complementary on-treatment biomarkers that capture residual disease activity in AD. These findings provide a new perspective for more objective evaluation of disease dynamics during biologic therapy in the context of the immunological heterogeneity of AD. With further validation, they are expected to facilitate the development of an assessment framework that leverages blood-based indicators reflecting multiple inflammatory pathways.

3. Remarks

This study was supported by the Japan Agency for Medical Research and Development (AMED) under the Practical Research Project for Allergic Diseases and Immunology, including the following programs: “Development of novel therapies for atopic dermatitis based on bidirectional understanding of skin microbiota and the host,” “Development of novel therapies for atopic dermatitis using anti-inflammatory skin bacterial communities,” “Skin transcriptome analysis toward personalized and predictive medicine for atopic dermatitis,” “Integrated analysis of clinical and omics data to elucidate the pathogenesis of atopic dermatitis and associated multi-organ allergic diseases,” and “Interdisciplinary research on atopic dermatitis aimed at elucidating the diversity of allergic pathophysiology and establishing sustainable data-driven precision medicine.” This work was also supported by the Program for Creating Innovation

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4. Article

Title：Interleukin-22 and interleukin-18 as potential blood biomarkers in dupilumab-treated atopic dermatitis

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[Glossary]

(Note 1) Type 2, Type 17, and Type 1 inflammation

Immune responses encompass several types. In patients with atopic dermatitis, type 2 inflammation—commonly associated with allergic responses—predominates. In the skin of a subset of patients, activation of pathways linked to type 17 inflammation (responses to bacteria and fungi) and type 1 inflammation (responses to viruses) has also been reported.

(Note 2) Biomarker

A biological indicator used to evaluate the presence of a disease, the degree of its progression, and responses to treatment. Typical examples include proteins and gene-expression measures detected in specimens such as blood, urine, or tissue.

(Note 3) Cytokines

A family of small signaling proteins produced by immune, epithelial, endothelial, and fibroblast cells, which participate in the activation and suppression of various inflammatory responses and contribute to host defense against pathogens and to the pathogenesis of inflammatory conditions (e.g., allergy).