When Immune Tolerance Fails: From Mechanisms to Clinical Phenotypes

Dear Colleagues,

Immune tolerance preserves the balance between an effective immune response and the protection of healthy tissues. Its failure can lead to autoreactive responses and a wide range of autoimmune and immune-mediated diseases. Despite their diverse clinical presentations, these disorders often share common features, including impaired regulatory mechanisms, altered immune checkpoints, environmental influences, and autoantibody production.

In the second issue of the *Turkish Journal of Immunology* in 2026, one review and five original articles examine different aspects of immune dysregulation, ranging from basic mechanisms to potential clinical biomarkers.

The review, *Immune Dysregulation: Mechanisms of Tolerance Failure, Clinical Spectrum, and Emerging Therapeutic Strategies*, provides an overview of the mechanisms responsible for defective immune tolerance and discusses new therapeutic approaches aimed at restoring immune homeostasis.

The experimental study, *Maternal Gut Dysbiosis Exacerbates Offspring Susceptibility to Collagen-Induced Arthritis in Mice*, draws attention to the influence of the maternal gut microbiota on immune development and autoimmune susceptibility in offspring. It also raises important questions about how early-life and intergenerational factors may contribute to the later development of immune-mediated disease.

In the article *Association Between Vitamin D Status, Regulatory T Cells, and Disease Severity in Pediatric Systemic Lupus Erythematosus,* the relationship between vitamin D levels, regulatory T cells, and clinical severity is evaluated in children with systemic lupus erythematosus. The study brings together metabolic, immunological, and clinical parameters in the assessment of systemic autoimmunity.

The article *Immune-Biochemical Stratification Identifies the Pure Primary Biliary Cholangitis Phenotype in AMA-Positive Individuals* examines whether combined immunological and biochemical assessment can improve the characterization of individuals positive for anti-mitochondrial antibodies (AMA). This integrated evaluation may contribute to more accurate patient classification and follow-up.

The final two studies address different aspects of psoriasis. *Association of CTLA-4 Gene Polymorphisms and Serum Soluble CTLA-4 Levels with Psoriasis Vulgaris* investigates the relationship between psoriasis and both genetic and soluble components of the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) pathway. *Anti-ADAMTSL5 and Anti-K17 Autoantibodies in Psoriasis: Diagnostic Performance and Associations with*

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Systemic Inflammation focuses on autoreactivity against ADAMTSL5 and keratin 17. Together, these studies offer complementary perspectives on the roles of immune regulation and autoantigen recognition in psoriasis.

The articles presented in this issue remind us that immune dysregulation rarely results from a single defect. It more often reflects the interaction of genetic susceptibility, regulatory immune cells, checkpoint pathways, microbiota, metabolic factors, and tissue-specific responses. A better understanding of these relationships will support the development of more informative biomarkers and more precisely targeted treatments.

We thank the authors, reviewers, and editorial team for their contributions, and we hope our readers will find this issue both informative and stimulating.

With warm regards,

Prof. Günnur Deniz
On behalf of the Editorial Board
Turkish Journal of Immunology