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2025 Nobel Prize: Tregs Unlock Immune Tolerance

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ABSTRACT

The 2025 Nobel Prize in Physiology or Medicine has been awarded to the researchers who identified regulatory T cells, abbreviated as Tregs, a groundbreaking discovery concerning peripheral immune tolerance. These cells protect our body from autoimmune diseases. The fields of immunology and clinical medicine have been influenced by their discoveries. With the increased knowledge of immunology, novel therapeutic strategies for the treatment of allergies, lethal autoimmune diseases, and organ transplant rejection are being introduced. While, targeted therapies to restore immune balance are expected.

Keywords: autoimmunity, immunoregulation, Nobel Prize 2025, peripheral immune tolerance, regulatory T Cells

Highlights

- Nobel Prize winning discovery on Regulatory T cells (Tregs) and the FOXP3 gene explains how the immune system cross-talks with peripheral tolerance and autoimmunity.
- Defects in Tregs or FOXP3 imbalance immune homeostasis are, therefore, central to serious autoimmune diseases, such as rheumatoid arthritis, multiple sclerosis, and type 1 diabetes.
- Treg-based precision therapies are emerging as promising strategies, not only to treat autoimmune, inflammatory, and allergic diseases but also transplant and cancer treatment outcomes.

1. INTRODUCTION

Regulatory T cells are a specialized subset of $CD4^+$ T cells, which are abbreviated as Tregs. These cells maintain immune balance by suppressing unnecessary immune responses and preventing autoimmunity. So, they are also known as the security guards of the immune system [1]. They were discovered by Mary E. Brunkow, Fred Ramsdell, and Shimon Sakaguchi. This discovery has earned them the prestigious 2025 Nobel Prize in

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Physiology or Medicine, as announced by the Nobel Prize Assembly at Karolinska Institutet on October 6, 2025 [2]. Their formative discoveries have enhanced our knowledge of how the self and non-self are distinguished by the immune system. As a result, we are protected from infections while simultaneously preventing destructive autoimmune reactions [1].

This letter aims to highlight the scientific significance and medical relevance of their findings. It focuses on how their discoveries have redefined immunological research and clinical practice around the world.

2. DISCOVERY AND IMPACT

Sakaguchi laid the basis of this discovery during the 1990s when he identified a subset of CD4+ T cells expressing CD25 which is capable of suppressing immune activation, thus plays a role in maintaining self-tolerance. CD4+ T cells, also known as T-helper cells, coordinate immune responses by activating other immune cells. CD25 is a protein that forms part of the Interleukin-2 receptor which plays an important role in regulating T cell growth and survival [3]. His pioneering research demonstrated that the removal of these cells leads to autoimmunity, firmly establishing their suppressive role. Simultaneously, two other researchers Brunkow and Ramsdell discovered that mutations in the *FOXP3* gene are linked to scurfy phenotype in mice, a fatal autoimmune disorder. This discovery established that *FOXP3* is the master regulatory gene for the development of Tregs [4]. Their discovery was later confirmed in human studies as well. It was shown that *FOXP3* expression defects account for lethal autoimmune diseases, thereby strengthening the evidence of their role in peripheral tolerance. Their combined work established *FOXP3* as the master regulator of Tregs development, providing the molecular basis of immune tolerance.

These researchers confirmed the Tregs as a major factor in maintaining homeostasis in the immune system. The molecular and cellular mechanism for immune regulation was defined by these discoveries, since they demonstrated how the immune system prevents pathological inflammation by suppressing the self-reactive T cells of the immune system [5]. The fields of basic immunology and clinical medicine have both been profoundly influenced by the discovery of Tregs. Rheumatoid arthritis, multiple sclerosis, and Type 1 diabetes are a few well-known autoimmune diseases[5]. Mutations in Tregs and the associated dysregulation of Treg activity are recognized as hallmarks of these autoimmune diseases. Researchers are

now developing therapeutic techniques to utilize Treg functions both ways. On the one hand, they are striving to enhance Treg function in inflammatory and autoimmune diseases. On the other hand, they are attempting to reduce its activity in the immunotherapy of cancers. This is because reduced immune tolerance is more effective in anti-tumor actions. Precision immune modulation is also being focused by the engineering of Tregs, which is made possible by recent developments in gene editing and cellular therapies. Organ transplantation and allergy treatment are the potential applications of this approach [3,4]. Further research should aim to find the different adaptations of Tregs in varying tissue environments. Their functional stability that allows the researchers to manipulate them safely in patients and during therapeutic processes will be answered in the future [6]. This would be helpful for patient care in South Asia, where the rising burden of autoimmune and inflammatory disorders demands the requirement of precise Treg-based therapeutic strategies.

3. CONCLUSION

The groundbreaking discoveries of the *FOXP3* gene and Tregs have enhanced our understanding of immune tolerance. These have helped combine basic research with therapeutic implications. The findings have influenced modern immunology and shown the way forward to treat disorders related to the immune system by restoring immune tolerance and balance. These Nobel Laureates have, in fact, resolved one of immunology's deepest mysteries of how the immune system prevents self-destruction.

Author Contribution

Muhammad Shoaib Khan: sole author

Conflict of Interest

The author of the manuscript has no financial or non-financial conflict of interest in the subject matter or materials discussed in this manuscript.

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This study discusses the potential of regulatory T cells as a therapeutic strategy for inflammatory bowel disease, highlighting emerging approaches to enhance Treg stability and function in gut inflammation.