

*Perspective*

# Immunotherapy for autoimmune diseases: Balancing immune suppression and tolerance induction

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## DESCRIPTION

Autoimmune diseases occur when the immune system mistakenly attacks healthy cells and tissues in the body. These diseases surround a wide range of conditions, including rheumatoid arthritis, lupus, multiple sclerosis, and type 1 diabetes, among others. Traditional treatments for autoimmune diseases often involve suppressing the immune system to reduce inflammation and alleviate symptoms. However, this approach can lead to increased susceptibility to infections and other adverse effects. Immunotherapy offers a potential alternative by aiming to restore immune balance through various mechanisms, including immune suppression and tolerance induction. Autoimmune diseases arise from a complex exchange of genetic, environmental, and immunological factors. In individuals predisposed to autoimmune conditions, the immune system becomes dysregulated, leading to the production of autoantibodies and inflammatory mediators that target healthy tissues. The specific triggers for autoimmune responses vary depending on the disease but may include infections, hormonal changes, or exposure to certain drugs or environmental factors.

### Immune suppression in autoimmune therapy

One approach to treating autoimmune diseases involves suppressing the immune system to reduce inflammation and prevent further tissue damage. This can be achieved through the use of corticosteroids, immunosuppressive drugs, or biologic agents that target specific components of the immune response. While immune suppression can effectively control symptoms in many patients, it also carries significant risks, including increased susceptibility to infections, metabolic disturbances, and long-term organ damage.

### Challenges of immune suppression

Despite its efficacy in managing autoimmune diseases, immune suppression is not without its limitations. Prolonged use of immunosuppressive agents can compromise the body's ability to fight off infections, leading to serious complications. Moreover, some patients may experience relapses or develop resistance to

treatment over time, necessitating alternative therapeutic approaches.

### Tolerance induction as a therapeutic strategy

In recent years, there has been growing interest in tolerance induction as a strategy for treating autoimmune diseases. Unlike immune suppression, which aims to dampen immune activity, tolerance induction seeks to retrain the immune system to recognize and tolerate self-antigens, thereby preventing autoimmune attacks. This approach holds the potential for long-term remission without the need for continuous immunosuppressive therapy.

### Mechanisms of tolerance induction

Tolerance induction can be achieved through various mechanisms, including antigen-specific therapies, regulatory T cell (Treg) modulation, and the use of tolerogenic dendritic cells. Antigen-specific therapies involve exposing the immune system to specific autoantigens in a controlled manner, either through oral, subcutaneous, or intravenous administration. This process helps to educate immune cells to recognize self-antigens as harmless, thereby reducing autoimmune responses.

### Harnessing regulatory t cells

Regulatory T cells play a important role in maintaining immune tolerance by suppressing the activity of autoreactive T cells. Therapeutic strategies aimed at expanding or enhancing the function of Tregs hold potential for treating autoimmune diseases. This can be achieved through the administration of low-dose interleukin-2 (*IL-2*) to promote Treg expansion or the adoptive transfer of *ex vivo* expanded Treg populations.

### Tolerogenic dendritic cells

Dendritic cells are key regulators of immune responses and play a central role in initiating and modulating autoimmune reactions. Tolerogenic dendritic cells are a specialized subset of dendritic cells that promote immune tolerance by inducing antigen-specific T cell hyporesponsiveness or regulatory T cell differentiation.

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Emerging research suggests that harnessing the tolerogenic properties of dendritic cells could offer new avenues for the development of targeted immunotherapies for autoimmune diseases. Immunotherapy holds great promise for the treatment of autoimmune diseases by restoring immune balance and preventing the harmful immune responses that underlie these conditions. While immune suppression remains a cornerstone of

autoimmune therapy, tolerance induction represents a paradigm shift towards more targeted and sustainable treatment approaches. By harnessing the mechanisms of immune tolerance, researchers are working towards developing safer and more effective therapies that offer long-term remission and improved quality of life for patients with autoimmune diseases.