2025 Nobel Prize in Medicine: Immune tolerance as the key to balancing the immune system

The 2025 Nobel Prize in Physiology or Medicine goes to *Shimon Sakaguchi*, *Mary E. Brunkow*, and *Fred Ramsdell*. The three researchers have deciphered a fundamental mechanism of the immune system that is essential for maintaining immunological balance. Their discoveries on the function of regulatory T cells, known as Tregs, form the scientific basis for a better understanding of immune system malfunctions and thus provide valuable starting points for aging research.

Stockholm/Jena. Regulatory T cells are specialized immune cells that prevent the immune system from attacking the body's own structures. They ensure what is known as immune tolerance—the body's ability to distinguish between “self” and “non-self.” This balance is essential for preventing autoimmune reactions and chronic inflammation and for keeping organs and tissues functioning properly in the long term.

"The 2025 Nobel Prize discoveries illuminate a fundamental process that also governs aging: the maintenance of immune tolerance. With age, the regulatory systems that keep immune responses in check falter, leading to inflammation, tissue damage, and reduced regenerative capacity. Understanding and preserving Treg function may thus be key to extending healthy lifespan."

– Prof. Dr. Dario Riccardo Valenzano, Scientific Director of the Leibniz Institute on Aging (FLI)

Aging, inflammation, and immune regulation

With increasing age, the immune system gets out of balance. It reacts more sensitively to stimuli and shows permanent, low-grade inflammatory activity – even without infection or external triggers. This chronic activation is called inflammaging, a process that is closely linked to aging and many age-related diseases.

The discoveries made by Sakaguchi, Brunkow, and Ramsdell provide a deeper understanding of how regulatory T cells prevent such malfunctions. They illustrate that the immune system's ability to self-regulate is crucial for limiting inflammation and maintaining tissue homeostasis.

These findings are highly relevant for the FLI – the Leibniz Institute on Aging in Jena. They open up new perspectives on how immune imbalance and healthy tissue aging are linked.

The award winners

Shimon Sakaguchi (Japan)

In the 1990s, the immunologist discovered a special group of T cells ($CD4^+$ $CD25^+$) that are now known as regulatory T cells. These cells prevent autoimmune reactions and ensure the balance of the immune system. Sakaguchi is a professor at the Immunology Frontier Research Center at Osaka University.

Mary E. Brunkow (USA)

The molecular biologist identified the Foxp3 gene, which is necessary for the development of functional Tregs. Her research on the so-called scurfy mouse, a model for misdirected immune responses, provided crucial insights into the genetic basis of immune tolerance. Brunkow is now Senior Program Manager at the Institute for Systems Biology in Seattle.

Fred Ramsdell (USA)

Together with Brunkow, the immunologist researched the genetic causes of autoimmune diseases and contributed significantly to the discovery of the central role of Foxp3. Today, he works as a scientific advisor at Sonoma Biotherapeutics, a company that develops new immunotherapies.

A boost for aging research

Even though this year's Nobel Prize-laureates' work primarily relates to immunology, it has far-reaching significance for aging research. A better understanding of the mechanisms that keep the immune system in balance can help us understand age-related inflammation and develop long-term strategies for healthy aging.

At the FLI, researchers are investigating how immune regulation and cell communication contribute to maintaining tissue homeostasis and regenerative capacity—with the aim of deciphering the molecular basis of healthy aging and making it therapeutically useful.

Further information:

https://www.nobelprize.org/prizes/medicine/2025/summary/

Nobel Prize in Physiology or Medicine 2025

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Graphic

Illustration of Treg cells (© The Nobel Committee for Physiology or Medicine. Ill. Mattias Karlén)

Background

The Leibniz Institute on Aging - Fritz Lipmann Institute (FLI) in Jena is a federal and state government-funded research institute and member of the Leibniz Association (Leibniz-Gemeinschaft). FLI conducts internationally recognized, high-impact research on the biology of aging at the molecular, cellular, and systems levels. Scientists from around 40 countries investigate the mechanisms of aging to uncover its root causes and pave the way for strategies that promote healthy aging. Further information: www.leibniz-fli.de.

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