NEWS

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE 2025

Mary E. Brunkow
Born: 1961, Portland, Oregon, United States
Affiliation at the time of the award: Institute for Systems Biology, Seattle, WA, USA

Frederick J. Ramsdell
Born: 4 December 1960, Elmhurst, IL, USA
Affiliation at the time of the award: Sonoma Biotherapeutics, San Francisco, CA, USA

Shimon Sakaguchi
Born: 19 January 1951, Nagahama, Shiga, Japan
Affiliation at the time of the award: Osaka University, Osaka, Japan

The Nobel Assembly at Karolinska Institutet has decided to award the 2025 Nobel Prize in Physiology or Medicine to **Mary E. Brunkow**, **Fred Ramsdell** and **Shimon Sakaguchi** "*for their discoveries concerning peripheral immune tolerance*".

They discovered how the immune system is kept in check.

The body's powerful immune system must be regulated, or it may attack our own organs. **Mary E. Brunkow**, **Fred Ramsdell** and **Shimon Sakaguchi** are awarded the Nobel Prize in Physiology or Medicine 2025 for their groundbreaking discoveries concerning peripheral immune tolerance that prevents the immune system from harming the body.

Every day, our immune system protects us from thousands of different microbes trying to invade our bodies. These all have different appearances, and many have developed similarities with human cells as a form of camouflage. So how does the immune system determine what it should attack and what it should defend?

Mary Brunkow, Fred Ramsdell and Shimon Sakaguchi are awarded the Nobel Prize in Physiology or Medicine 2025 for their fundamental discoveries relating to peripheral immune tolerance. The laureates identified the immune system's security guards, regulatory T cells, which prevent immune cells from attacking our own body.

"Their discoveries have been decisive for our understanding of how the immune system functions and why we do not all develop serious autoimmune diseases," says Olle Kämpe, chair of the Nobel Committee.

Shimon Sakaguchi was swimming against the tide in 1995, when he made the first key discovery. At the time, many researchers were convinced that immune tolerance only developed due to potentially harmful immune cells being eliminated in the thymus, through a process called central tolerance. Sakaguchi showed that the immune system is more complex and discovered a previously unknown class of immune cells, which protect the body from autoimmune diseases.

Mary Brunkow and Fred Ramsdell made the other key discovery in 2001, when they presented the explanation for why a specific mouse strain was particularly vulnerable to autoimmune diseases. They

had discovered that the mice have a mutation in a gene that they named Foxp3. They also showed that mutations in the human equivalent of this gene cause a serious autoimmune disease, IPEX.

Two years after this, Shimon Sakaguchi was able to link these discoveries. He proved that the Foxp3 gene governs the development of the cells he identified in 1995. These cells, now known as regulatory T cells, monitor other immune cells and ensure that our immune system tolerates our own tissues.

The laureates' discoveries launched the field of peripheral tolerance, spurring the development of medical treatments for cancer and autoimmune diseases. This may also lead to more successful transplantations. Several of these treatments are now undergoing clinical trials.

https://www.nobelprize.org/prizes/medicine/2025/press-release/