How pollution and the microbiome interact with Tregs, the immune system regulators whose discovery was honored with the Nobel Prize

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Published: October 10, 2025 8:36am EDT

Treg cells have been thrust into the limelight thanks to the Nobel Prize-winning work of a team of researchers from the U.S. and Japan.

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A special group of immune cells known as regulatory T cells, or Tregs for short, became an overnight sensation when a trio of U.S. and Japanese scientists won the Nobel Prize in physiology or medicine on Oct. 6, 2025, for their discovery and elucidation of these cells.

Treg cells act as the “master regulators” of the immune system – much like conductors leading an orchestra – ensuring that all other immune cells work in harmony. People with too few or defective Treg cells often develop autoimmune diseases, where unchecked immune cells mistakenly attack the body’s own tissues or organs. Yet when Treg cells become too numerous, people can become more susceptible to cancer and infections.

For this reason, Treg cells are often described as a double-edged sword. Treg cells also control internal revolt in the form of an overactive immune response by other immune cells that can trigger allergies and autoimmune diseases such as arthritis, lupus and multiple sclerosis – diseases that develop when Treg cells are defective in either number, function or both.

The well-established functions of Treg cells in autoimmune diseases, cancer and infections have recently been complemented by research unraveling how environmental factors influence these cells and modulate the immune response.

We are a husband-wife team of immunologists who study how environmental factors such as chemicals, diet and gut bacteria affect Treg cells and the overall functioning of the immune system.

While our study dating back to 1984 found that certain environmental contaminants induce T cells that suppress the immune system, further study on such cells was hampered by an inability in the field at large to isolate and characterize these cells. The discoveries honored by this year’s Nobel Prize transformed how researchers understand the immune system.

One of the three Nobel Prize-winning researchers, Mary E. Brunkow, responds emotionally as she receives the news of the prize.

AP Photo/Lindsey Wasson

The interplay of environmental factors

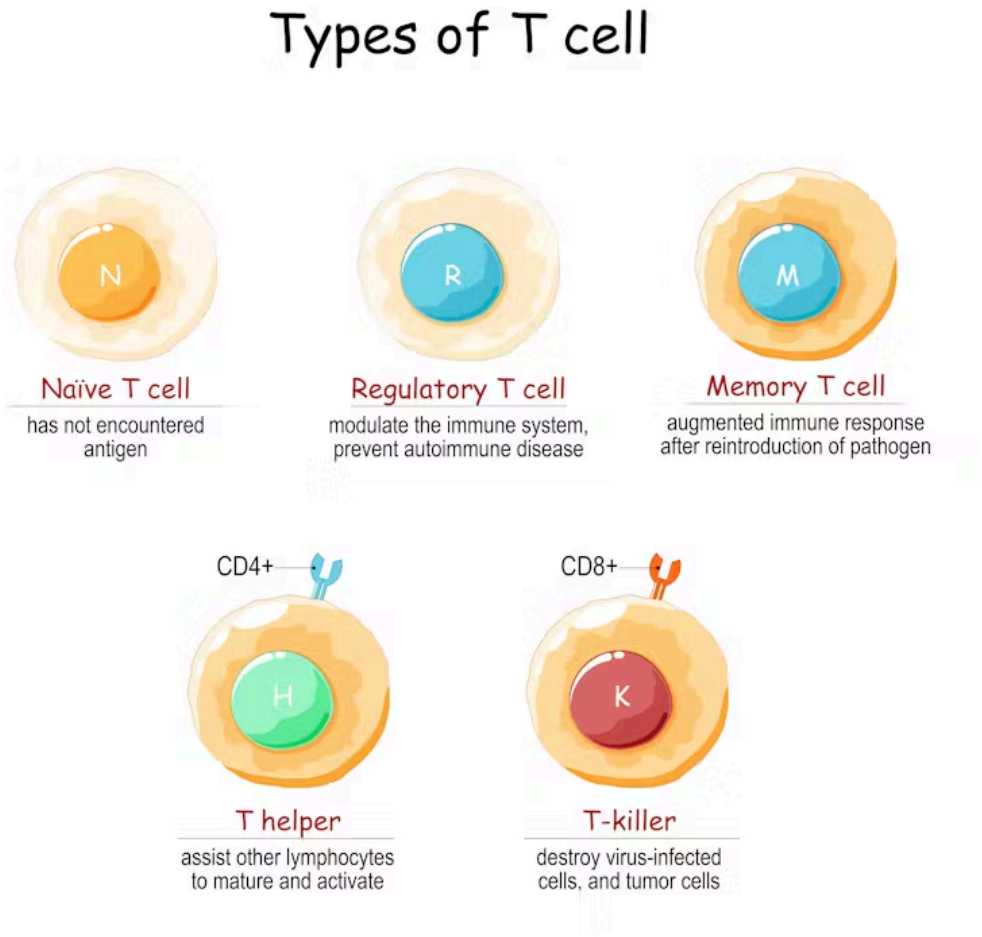
The environment plays a profound role in regulating the development, maintenance and functions of Treg cells. Some examples of environmental factors include chemical pollutants found in the air and water, microbes, sunlight, diet and medications.

Rather than being a single, static population, Treg cells are highly adaptable. They integrate a variety of environmental cues to either suppress or manage immune responses. They accomplish this by producing key molecules such as FoxP3 that send a signal to other immune cells to stop mounting an aggressive immune response.

Certain toxic chemicals can increase the number or activity of Treg cells. One of the best-known examples is a group of long-lasting pollutants called dioxins that accumulate in fatty tissues through consumption of contaminated meat, dairy and fish. They are produced from burning waste as well as chemical manufacturing and forest fires.

The most toxic dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin, or TCDD, is a known human carcinogen. Researchers have linked exposure to this chemical to various health problems, including cancer and reproductive and developmental issues. Research shows that dioxins activate Treg cells through a sensor known as the aryl hydrocarbon receptor. This constitutes one of the mechanisms through which certain environmental chemicals promote cancer by enhancing Treg activity and suppressing the anti-cancer immune response.

Air pollution, such as diesel exhaust, can have the opposite effect, impairing Treg cell function and contributing to inflammatory diseases such as asthma. This may occur through damage to the FoxP3 gene.



Regulatory T cells, or Treg cells, are one of at least five major types of T cells.

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How diet interacts with Treg cells

Diet also plays a powerful role in regulating Treg cells. Compounds known as indoles, found in vegetables from the cabbage family such as broccoli, cabbage and cauliflower, can activate Treg cells and help prevent gut inflammation. These compounds also work by stimulating the aryl hydrocarbon receptor, which boosts Treg numbers and activity.

Another way diet can influence Treg cells is through the regulation of the microbes that live in the gut.

The gut has trillions of microbial residents, both benefical and harmful. Previous research found that Treg cells in the gut play a crucial role in maintaining gut homeostasis – the dynamic balance between microbiota and immune cells found in the gut. Any disturbance leading to loss of Treg cell function can lead to hyperactivation of other immune cells in the gut. This can trigger inflammation in which the immune cells destroy the lining of the intestine, leading to conditions such as inflammatory bowel disease.

Other naturally occurring substances – such as naringenin, a chemical abundant in citrus fruits, and epigallocatechin-3-gallate, a compound found in green tea – also activate the aryl hydrocarbon receptor and promote Treg development.

A fiber-rich diet supports the growth of beneficial gut bacteria. This bacteria ferments fiber into short-chain fatty acids that enhance Treg cell function and help maintain gut health. Probiotic bacteria also increases Treg cell populations, thereby reducing inflammation.

In addition, dietary tryptophan – an amino acid found in foods such as poultry, eggs, tofu and seeds – is metabolized into compounds that activate the aryl hydrocarbon receptor, further boosting Treg cell activity and protecting against gut inflammation.

By contrast, a Western diet high in fat, sugar and processed foods disrupts the balance of gut bacteria. This, in turn, reduces the population of microbes that support Treg cells and promotes a more inflammatory environment in the gut.

Keeping Treg cells in harmony

Scientists like us and many others are working to understand the processes involved in maintaining the delicate balance of Treg cells that are influenced by all of these outside factors. The goal is to learn how Treg cells and other immune cells can be kept in equilibrium – strong enough to defend against infections and cancer yet restrained enough to prevent autoimmune and inflammatory diseases.

The profound environmental influence on Treg cell development and function makes understanding these interactions crucial for defining the fine line between health and disease.

Prakash Nagarkatti receives funding from the National Institutes of Health.

Mitzi Nagarkatti receives funding from the National Institutes of Health.