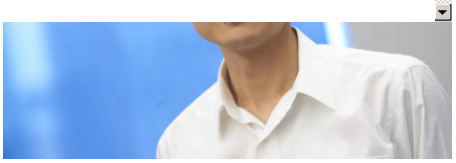
cell called a regulatory T cell controls immune responses. Their findings from research in mice, published in the journal *Nature* in November, might eventually pave the way for new strategies to control a range of diseases, including autoimmune disorders and cancer.



Immunologist Ming Li

Immunologist Ming Li, the study's senior author and a researcher in the Sloan Kettering Institute's Immunology Program, commented on the study in an interview.

What are regulatory T cells?

Our immune system has evolved highly sophisticated ways of fighting infections that hinge on its capability to distinguish between foreign intruders — such as virally infected cells — and healthy cells. This system provides powerful protection against pathogens, but it comes at a price. Unless the different cell types of the immune system are controlled very precisely, they may inflict severe damage on the body's own cells and tissues.

Regulatory T cells — which are actually a subtype of white blood cells known as T lymphocytes — play an important role in controlling how and when the immune system reacts to foreign cells. For example, regulatory T cells are able to shut down the activity of certain other T lymphocytes at the end of an immune response, preventing accidental damage to healthy tissues. In addition, we know that regulatory T cells prevent autoimmune reactions, which occur when the immune system mistakenly recognizes the body's own tissues as foreign and attacks them.

Without regulatory T cells, the immune system typically runs rampant. For instance, people suffering from a rare genetic disease called IPEX do not form regulatory T cells, and this causes extensive autoimmune reactions that can be fatal.

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Can you tell us about some of the key findings of your study?

My colleagues and I discovered that a gene called *Foxo1* controls regulatory T cell function and is essential for the cells' immune-suppressing activities.

We engineered mice in which this gene can be specifically shut off in regulatory T cells while functioning normally in other cell types. Our experiments revealed that without *Foxo1*, regulatory T cells lose their ability to curb immune responses. As a result, the mice developed severe autoimmune symptoms similar to those seen in patients with IPEX.

In addition, we identified a large number of genes that are regulated by *Foxo1*, some of which might be promising to investigate further as potential

therapeutic targets.

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How might these findings be of value for patients in the future?

Understanding how regulatory T cells function — what genes and biological pathways underlie the cells' ability to keep the immune system under control — has many potential applications in the clinic. The knowledge might one day enable us to develop new types of drugs that act by either enhancing or inhibiting the function of regulatory T cells.

Therapies that boost regulatory T cells could potentially be used to treat conditions characterized by an overactive immune system — including autoimmune disorders such as rheumatoid arthritis, psoriasis, and some types of diabetes, to mention a few.

In contrast, drugs that act by repressing regulatory T cell function might offer new and effective ways to control cancer. Studies have shown that tumors can use regulatory T cells to suppress immune reactions that otherwise would fight cancer. Many scientists in the field are now looking for ways in which the activity of regulatory T cells could be temporarily reduced in tumors to allow the immune system to more effectively recognize and attack cancer cells.

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How are you and your colleagues continuing this research?

One of our immediate goals is to figure out the functioning of *Foxo1* and *Foxo1*-regulated genes that influence regulatory T cells, and how these genes and pathways are rewired in autoimmune diseases and cancer. Hopefully, these investigations will not only add to our understanding of how the immune system works, but also lead to the development of new drugs that potentially could make a real difference for patients.

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