T cells found to require rest and maintenance

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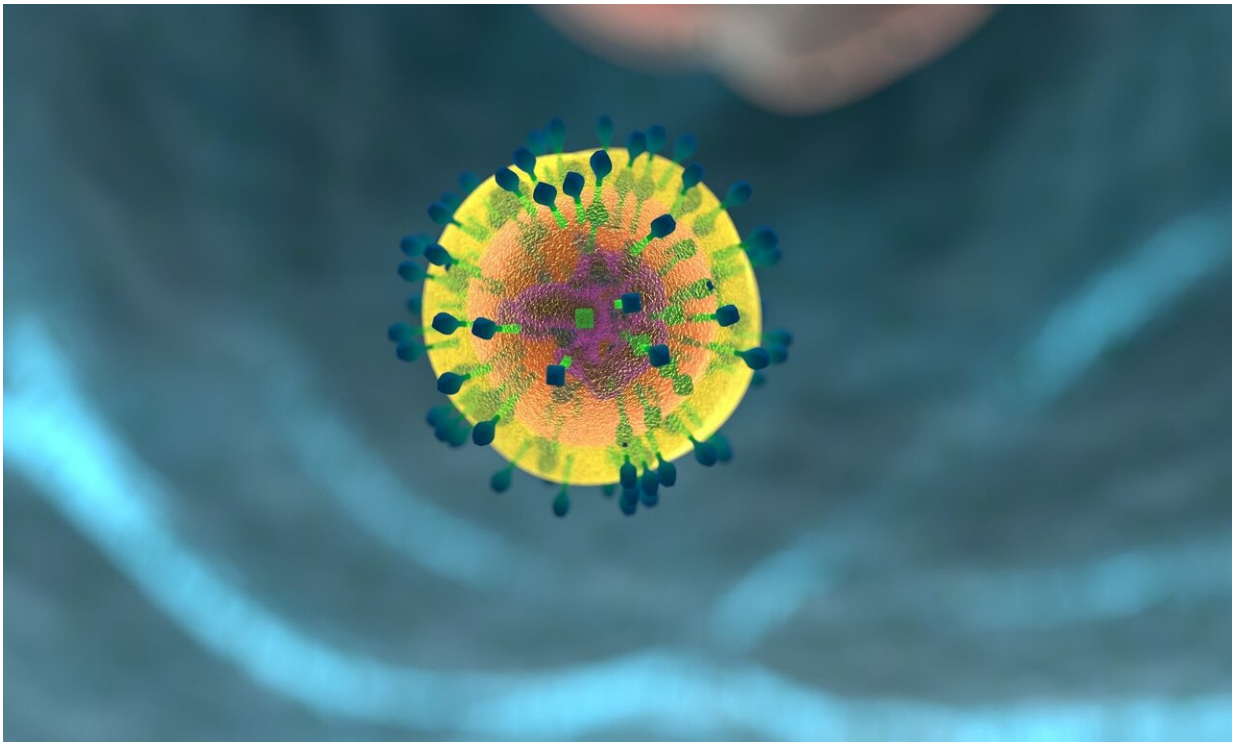

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T cells, biology textbooks teach us, are the soldiers of the immune system, constantly on the ready to respond to a variety of threats, from viruses to tumors. However, without rest and maintenance T cells can die and leave their hosts more susceptible to pathogens, Yale scientists report May 27 in the journal *Science*.

"We may have to change how we teach T cell biology," said Lieping Chen, the United Technologies Corporation Professor in Cancer Research at Yale, professor of immunobiology, of dermatology, and of medicine and senior author of the study.

Until pathogens are detected, T cells remain in a quiescent state. However, the molecular mechanisms that keep T cells inactive were previously unknown.

In the new study, Yale researchers show that a protein known as CD8a—which is found in a subset of T cells called CD8 cells—is crucial to keeping the cells in this dormant state. When scientists deleted this protein in mice, the protective CD8 cells were unable to enter a quiescent state and died, leaving the host vulnerable to infections.

Further, they identified another protein, PILRa, that provides a biochemical signal to CD8a. By disrupting this protein pair, both "memory" CD8 cells—cells that previously had been exposed to pathogens—and naïve cells died because they lacked the ability to stay in a quiescent state.

The researchers hope that understanding why this resting state is crucial to maintenance and survival of T cells can lead to improved immune system function.

Chen noted that as people age they tend to lose both naïve and memory T cells, making older individuals more susceptible to infections. It is possible that the inability of T cells to remain in a quiescent state could lead to people becoming more susceptible to infections and cancer, the authors suggest.

More information: Linghua Zheng et al, The CD8α–PILRα interaction maintains CD8 + T cell quiescence, *Science* (2022). DOI:

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