How T cells make sure they have quiet time

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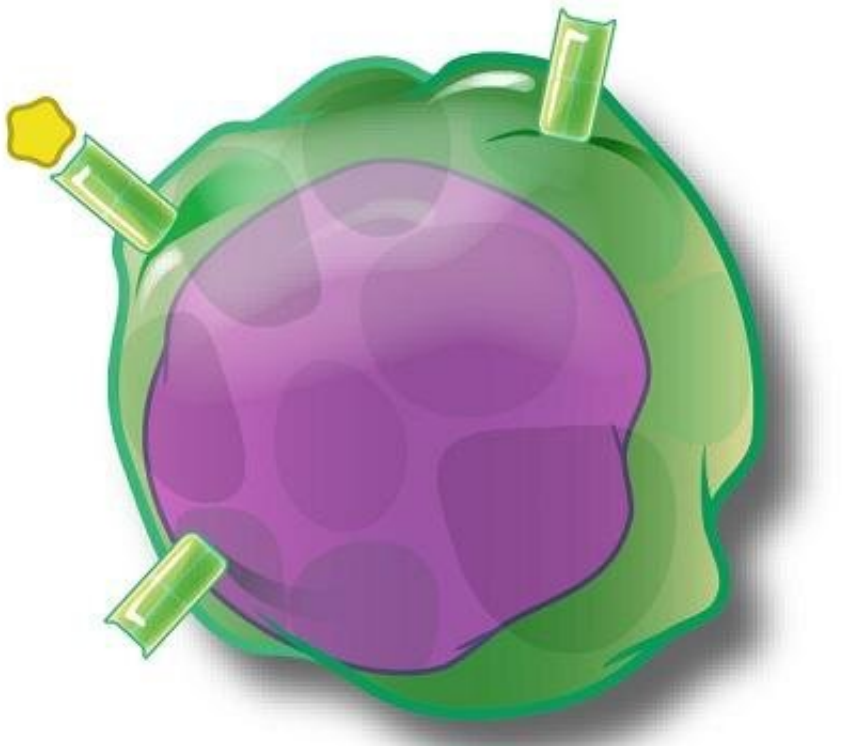

An artist's depiction of a T cell. Credit: NIAID

All cells, like all people, need "quiet" time to function properly, and this is particularly true of T cells, one of the immune system's main weapons. They must be ready for activation at all times, and primed to divide more rapidly than almost any cell in the body.

When T cells are overworked, people can be more susceptible to diseases of an overactive immune response, such as lymphomas,

leukemia, and autoimmune disorders.

Now, Yale researchers have discovered a pair of key factors for maintaining the quiet phase of T cell cycling, or the stages the cell goes through as it divides. The finding suggests a potential new drug target for diseases involving an overactive immune system response. They report their work March 12 in the journal *Science*.

"Each T cell has a gas pedal and brakes that operate simultaneously," said senior author Richard Flavell, Sterling Professor of Immunobiology and a Howard Hughes Medical Institute investigator. "Once these brakes go away, the car takes off at high speed."

Flavell and co-first author Soo Seok Hwang wanted to explore what keeps T cell "brakes" in order. Rapid activation by immune cells is crucial for a timely response to pathogens, but like all cells, T cells must enter the quiet phase of its cycle in order to divide and replicate.

The lab found that two specific factors, BTG1 and BTG2, act as cellular brakes by lessening the amount of messenger RNA (mRNA) within them. Messenger RNA contains instructions for making, in this case, T cells. Mice lacking the two factors showed excessive mRNA and the proteins they code for, as well as high levels of T cell activation.

The researchers speculate that enhancing these factors might help prevent hyper-activation of T cells, a state characteristic of some cancers and autoimmune diseases. Conversely, targeting BTG1 and BGT2 might help jump-start a response from a sluggish immune system, they said.

More information: Soo Seok Hwang et al. mRNA destabilization by BTG1 and BTG2 maintains T cell quiescence, *Science* (2020). DOI: 10.1126/science.aax0194

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