Scientists uncover proteins essential for memory B cell survival

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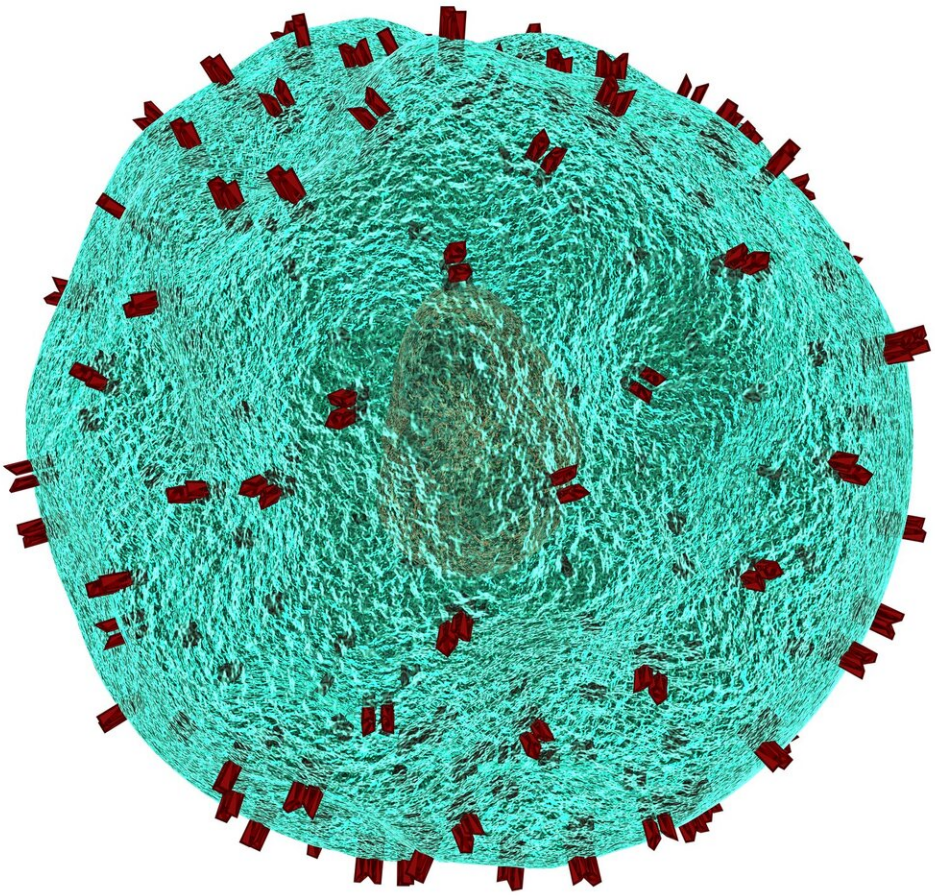

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Signals from two key proteins are essential for the survival of our 'immunological memory', according to new research from scientists at the Francis Crick Institute, published in the *Journal of Experimental Medicine*.

Memory B cells are long-lived cells that confer immunological memory by providing rapid and robust antibody responses to infections our body has seen before. Their longevity is key to protecting us from infection for a long time, sometimes for a lifetime. However very little is known about how these cells are kept alive.

The Crick team studied the survival of these immune cells from mice in great detail. Using a technique called inducible genetic ablation, they were able to generate populations of memory B cells and then delete specific proteins of interest in order to understand their role in keeping the cells alive.

They found that two cell surface proteins called BCR and BAFFR, and signals from these proteins, are critical for the survival of memory B cells.

When these proteins were experimentally deleted or blocked, there was an impaired secondary immune response to a model antigen or viral infection. Without signals from these key proteins, the immunological memory was impaired, with the immune system unable to recall and mount a response to infections it had previously been exposed to.

"The survival requirements we've identified for memory B cells are very similar to those needed for naïve B cells that haven't yet been exposed to

an antigen," says Jennifer Müller-Winkler, first author and visiting scientist in the Immune Cell Biology Laboratory at the Crick.

"This means the two types of immune cells may compete for the same survival signals and could explain why we've also uncovered critical survival niches for memory B cells in both the spleen and bone marrow."

This insight into immune cell survival could help with the development of future vaccines and also treatments for disorders of the immune system, such as autoimmunity.

"At a time when the whole world is waiting to understand how long immunity to SARS-CoV-2 will last and how effective a vaccine might be, it's clear that there's still much more to understand about what determines the longevity of immunological memory," says Victor Tybulewicz, lead author and group leader of the Crick's Immune Cell Biology Laboratory.

"Our study focuses on just a couple of key proteins and there could be many additional factors that affect the duration of our immunological memory. As our understanding grows, we could better inform the design and production of vaccines and treatments for a range of different infections."

More information: Jennifer Müller-Winkler et al. Critical requirement for BCR, BAFF, and BAFFR in memory B cell survival, *Journal of Experimental Medicine* (2020). DOI: 10.1084/jem.20191393

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