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New regulator of immune reaction discovered

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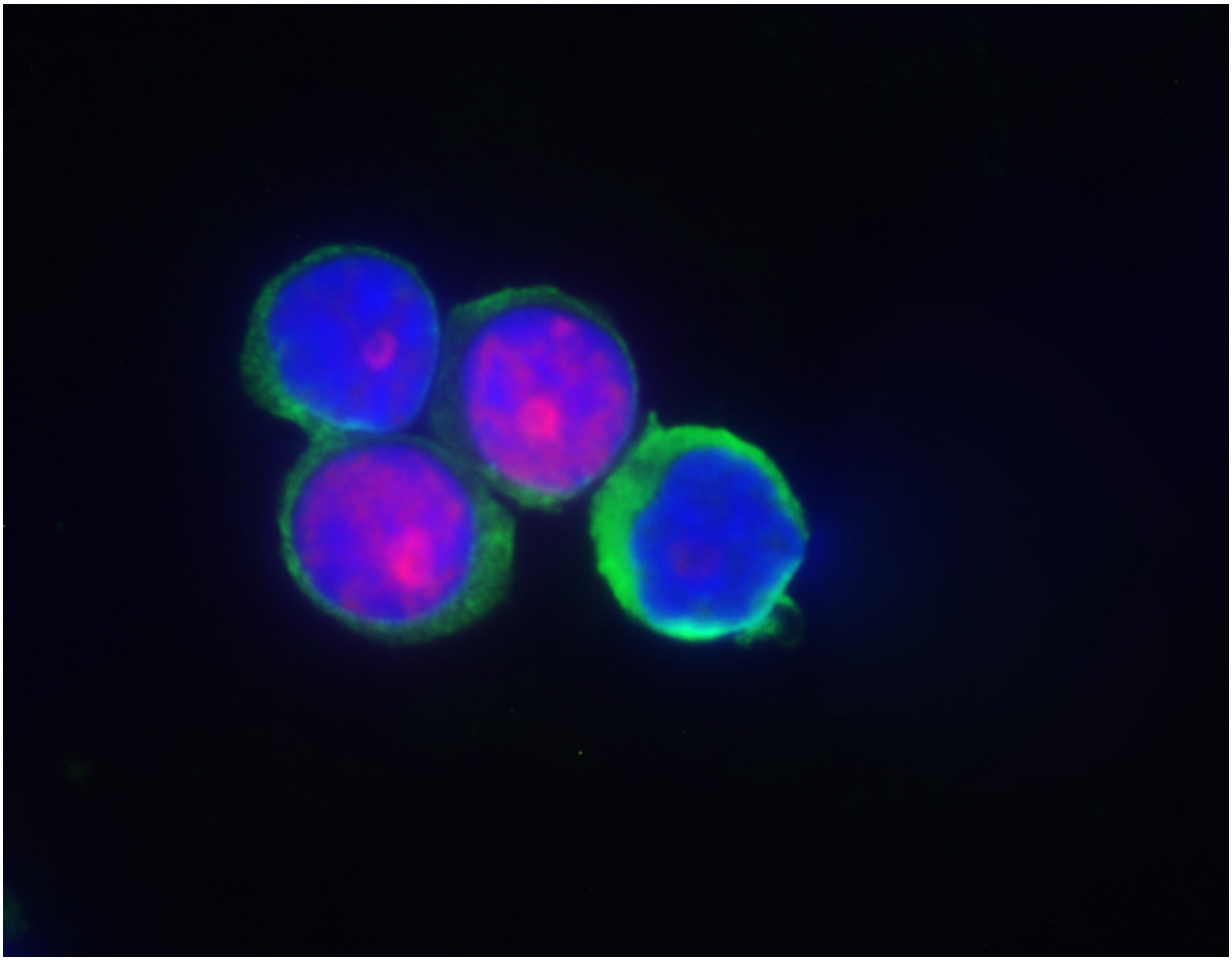

Immunostained human T lymphocytes. Credit: Sara Monaco (neurobiology)

Cells of the immune system can distinguish between protein molecules that are "self" and "non-self". For example, if we are exposed to

pathogens such as bacteria or viruses that carry foreign molecules on their surface, the body reacts with an immune response. In contrast, cells are "tolerant" of the body's own molecules. This state of unresponsiveness, or anergy, is regulated by a cellular signal, a calcium-controlled switch that was known to control also many brain functions. Neuroscientists from Heidelberg University and immunologists of Heidelberg University Hospital identified this signal. The research results were published in the *Journal of Cell Biology*.

The research work was led by Prof. Dr Hilmar Bading from the Interdisciplinary Center for Neurosciences working together with the research group of Prof. Dr Yvonne Samstag, Director of the Molecular Immunology Section. The Heidelberg research team identified a calcium signal in the cell nucleus of human T lymphocytes as a decision-maker in the immune system. They showed that a nuclear calcium signal is required for the immune reaction that T-cells trigger after contact with molecules foreign to the body.

This study was inspired by previous work of Prof. Bading on the function of calcium in the cell nucleus. The neuroscientist demonstrated that the messenger calcium, after invading the cell nucleus, acts as a master switch in the nervous system. The nuclear calcium signal triggers genetic programmes that control virtually all of the brain's adaptive capabilities, including memory, chronic pain and neuroprotection – a process that prevents damaged nerve cells from dying.

"When we started our study, we thought that nuclear calcium may play a similar role in the immune system as in the brain by activating a specific immune reaction gene programme," says Prof. Bading. "But we were surprised to see that human T lymphocytes became tolerant, i.e. shifted towards an anergic state, as soon as we switched off the nuclear calcium signal." According to Hilmar Bading, this discovery has important implications for the development of novel types of immunosuppressive

therapies.

After organ transplants, for example, it is common to use drugs that completely block the immune reaction. On the basis of this new research, it may be possible to redirect the immune reaction towards tolerance – described by the Heidelberg research team as "pro-tolerance immunosuppression." Prof. Bading indicates this may be possible to achieve by blocking nuclear calcium in activated immune cells.

More information: Sara Monaco et al. Nuclear calcium is required for human T cell activation, *The Journal of Cell Biology* (2016). DOI: 10.1083/jcb.201602001

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