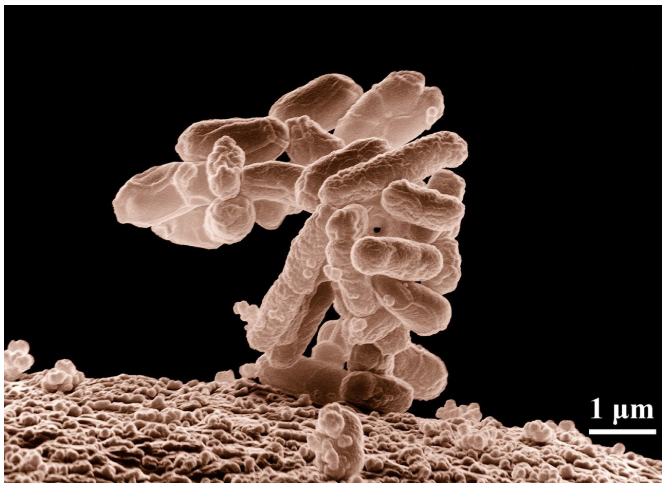
# How an immune system regulator shifts the balance of immune cells

4 February 2020




Credit: CC0 Public Domain

Researchers have provided new insight on the role of cyclic AMP (cAMP) in regulating the immune response.

Their study, published today in *eLife*, reveals that cAMP shifts the type of immune system t-helper (Th) cells created in response to a threat by repressing gene transcription by key proteins. The findings may help scientists develop new ways of manipulating the immune system to treat diseases.

Th cells help the immune system identify infections and flag infected cells for destruction by killer T-cells. Previous studies had shown that low cAMP levels cause the immune system to produce more Th2-type cells, while high cAMP levels boost the production of Th17 cells. "In the current study, we dissected the molecular mechanisms by which cAMP levels regulate these Th responses," says lead author Jihyung Lee, Assistant Project Scientist in Medicine at the University of California San Diego School of Medicine (UC San Diego), US.

Lee and the team showed that treating cells with cAMP reprograms Th2 cells to Th17 cells. It does this by suppressing IRF4 and KLF4, two transcription factors that turn on the genes needed to produce Th2 cells. The team then verified this by showing that mice genetically engineered to lack IRF4 have more Th17 cells. Treating these mice with IRF4 restored their Th2 cell levels.

"Our findings identify a new role for cAMP in immune system flexibility and may suggest new therapeutic approaches to control immune responses," says senior author Eyal Raz, Director of the Center for Immunology, Inflammation, and Immune-mediated Disease at Guangzhou Medical University, China, and Emeritus Professor of Medicine at UC San Diego School of Medicine. "For example, drugs that boost cAMP levels may help people recover from bacterial infections by boosting the number of Th17 cells. Drugs that decrease cAMP levels may be helpful in treating parasitic infections, which require a more robust Th2 response."

The results also suggest that drugs repressing IRF4 or KLF4 might be useful in, for example, treating blood cancers that emerge from immune cells called B-cells in the bone marrow.

**More information:** Jihyung Lee et al, Inhibition of IRF4 in dendritic cells by PRR-independent and -dependent signals inhibit Th2 and promote Th17 responses, *eLife* (2020). DOI: 10.7554/eLife.49416

Provided by eLife