T follicular helper cells research makes new immune system discoveries

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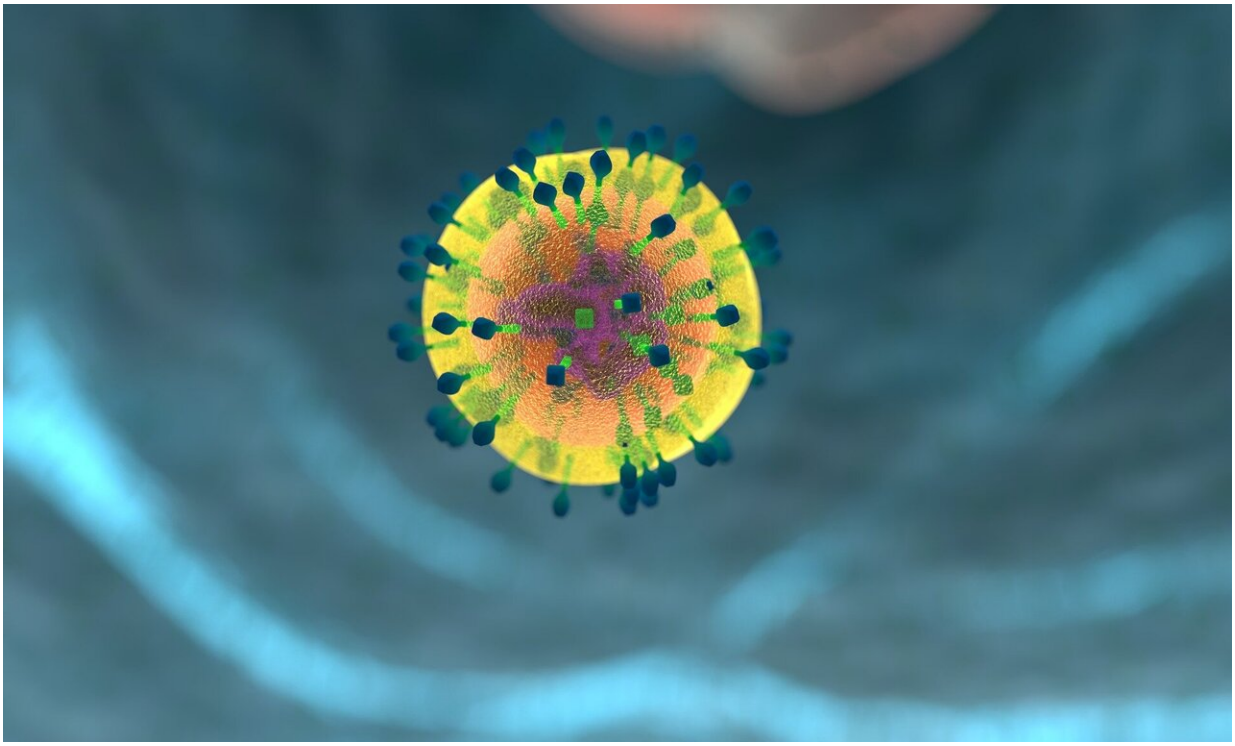

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T follicular helper cells (Tfh) are essential for strong antibody-mediated reactions of our immune system during infections and vaccinations. However, if they get out of control, this can cause diseases such as autoimmunity, allergies or cancer.

Researchers from the University Hospital Bonn (UKB) and the Cluster of Excellence ImmunoSensation^2 at the University of Bonn investigated the underlying mechanisms of Tfh cell development in a mouse model and thus decoded their internal networking. They hope that this will lead to new strategies for the development of highly effective vaccines and new therapies to combat various diseases. The results have been published in *Science Immunology*.

T follicular helper cells (Tfh cells) are a specialized subgroup within the so-called $CD4^+$ T helper cells in the immune system. Their main task is to assist the B cells in the immune defense. They are essential for the generation of highly effective antibodies. Tfh cells therefore play a decisive role in protecting against and fighting infections.

"Although Tfh cells were first described over 20 years ago, there is still no reliable protocol for their generation in cell culture," says co-first author Dr. Yinshui Chang, former postdoctoral researcher at the University of Bonn at the UKB, describing the motivation to take a closer look at the process in the mouse model.

The transforming growth factor TGF-β is a cytokine. This is a group of proteins that initiates and regulates the growth and differentiation of cells.

The Bonn team led by Prof. Dr. Dirk Baumjohann has now discovered that this signaling molecule induces strong protein expression of both the transcription factor Bcl6 and the chemokine receptor CXCR5, which are characteristic of Tfh cells. The latter plays an important role in the targeted migration of Tfh cells into the vicinity of B cells.

"We were able to show that the Tfh cells induced by TGF-β in cell culture are quite similar to the Tfh cells generated in a living organism. They provide crucial help for B cells," says co-first author Luisa Bach,

doctoral student at the University of Bonn at the UKB.

Transcription factor c-Maf controls the fate of T helper cells

Using a new method based on CRISPR gene scissors, the international team led by the Bonn researchers discovered that the production of CXCR5 induced by TGF-β is independent of the transcription factor Bcl6, but requires the transcription factor c-Maf.

Remarkably, although Tfh and Th17 cells partially undergo common developmental stages, c-Maf acts as a switching factor for Tfh versus Th17 cell fates. Th17 cells are another special type of $CD4^+$ T helper cells and play an important role in bacterial infections and autoimmune diseases.

"Overall, our data clarify important aspects of the long-unclear prerequisites and molecular pathways for the development of Tfh cells. They also highlight the diverse functions of the transforming growth factor TGF-β. Furthermore, these data indicate that Tfh cell development in mice and humans may not be as different as we previously assumed," says Prof. Baumjohann from the Medical Clinic III for Hematology, Oncology, Immuno-Oncology and Rheumatology at the UKB, who is a member of the Cluster of Excellence ImmunoSensation[2] and the Transdisciplinary Research Area (TRA) "Life & Health" at the University of Bonn.

"Importantly, our findings may have implications for the development of new therapeutic strategies that enhance Tfh cells during vaccinations and infections or inhibit them in autoimmune and allergic diseases."

More information: Yinshui Chang et al, TGF-β specifies T_{FH} versus

T_H17 cell fates of murine $CD4^+$ T cells through c-Maf, *Science Immunology* (2024). DOI: 10.1126/sciimmunol.add4818.
www.science.org/doi/10.1126/sciimmunol.add4818