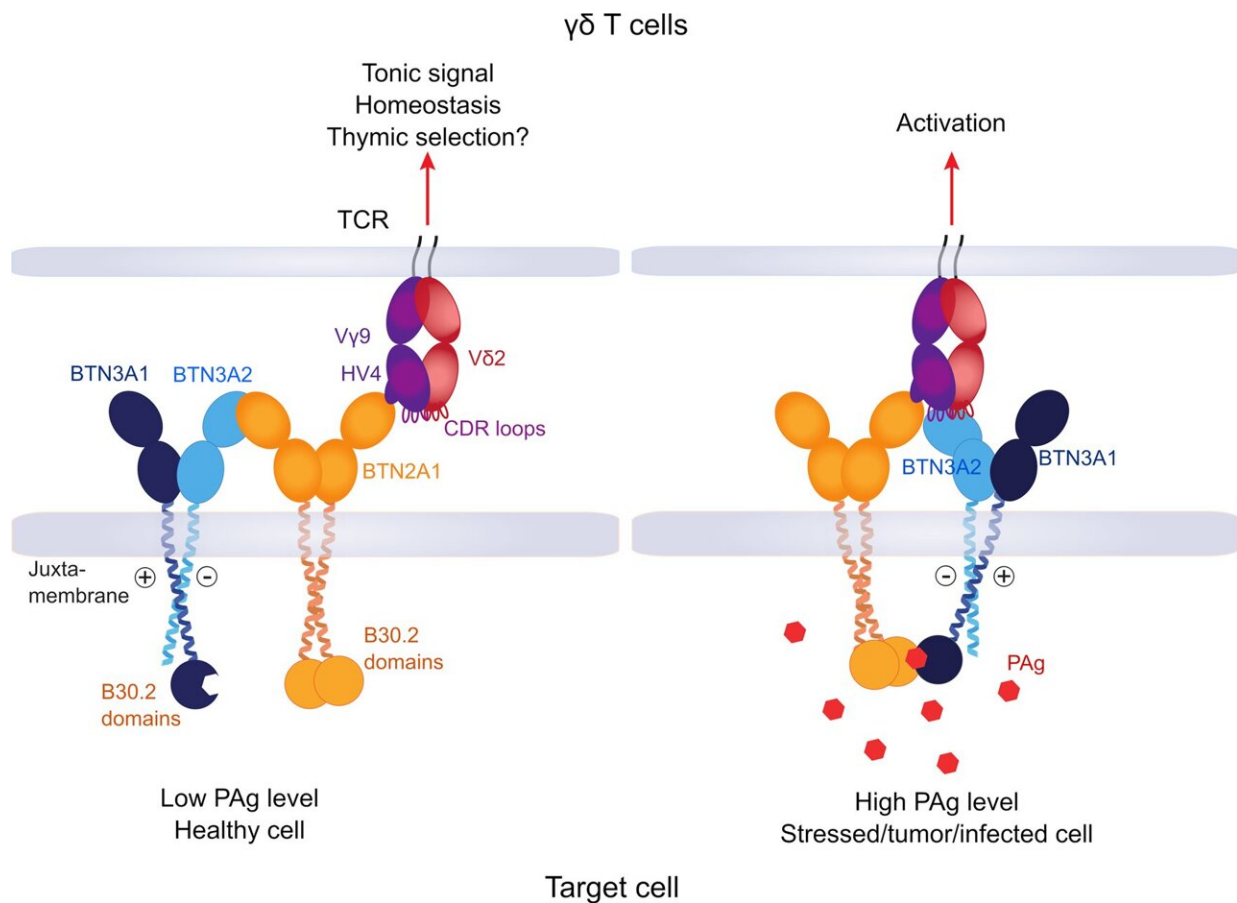


Study offers new insights into how immune cells recognize their enemies

December 8 2023, by Gunnar Bartsch



PAg induced V γ 9V δ 2 T cell activation by BTN3A-BTN2A1 composite ligand.
Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-41938-8

In order for immune cells to do their job, they need to know against

whom they should direct their attack. Research teams at the University of Würzburg have identified new details in this process.

As complicated as their name is, they are important for the human organism in the fight against pathogens and cancer: V γ 9V δ 2 T cells are part of the immune system and, as a subgroup of white blood cells, fight [tumor](#) cells and cells infected with pathogens. They recognize their potential victims by their altered cell metabolism.

Research teams from the University of Würzburg and the University Hospital of Würzburg, together with groups in Hamburg, Freiburg, Great Britain and the U.S., have now gained new insights into how these cells manage to look inside the cell. Thomas Herrmann, Professor of Immunogenetics at the Institute of Virology and Immunobiology and his colleague Dr. Mohindar Karunakaran at Julius-Maximilians-Universität Würzburg (JMU), were responsible for the study published in the journal [Nature Communications](#).

"Around one to five percent of lymphocytes, a subgroup of white blood cells in the [human body](#), are so-called V γ 9V δ 2 T cells. However, these multiply massively under certain circumstances," says Thomas Herrmann, explaining the background to the research project.

"Certain circumstances" in this case means that the T cells encounter so-called phosphoantigens, metabolic products of pathogens, which can also accumulate spontaneously in [tumor cells](#) or after drug-based cancer therapy. "V γ 9V δ 2 T cells are therefore crucial for the control of infections and tumors," explains Herrmann.

Receptors give the signal to kill

As the scientists discovered, phosphoantigens bind to a special group of [molecules](#) inside the cell, the so-called BTN3A1 molecules, with which

they then form [molecular complexes](#). "These complexes are recognized by receptors on the surface of the V γ 9V δ 2 T cells, which gives the cell the signal to kill," says the immunogeneticist. However, it turned out that relatives of the BTN3A1 molecules that do not bind phosphoantigens are also required to trigger these signals.

Which areas of the molecules involved react with each other and which areas are not necessary for this: The research groups have now identified further details on this.

"These findings can improve the clinical use of V γ 9V δ 2 T cells in the fight against tumors," explains Herrmann. On this basis, it is conceivable, for example, to develop drugs that strengthen this interaction. However, further analyses of the interaction between the BTN molecules and the receptors of the V γ 9V δ 2 T cells are still required.

Some BTN molecules prevent infections

However, the BTN molecules are also interesting from another point of view. "Some forms of the BTN3 molecules prevent human cells from becoming infected with the bird flu virus, for example," says Herrmann. And the BTN3A1 molecule suppresses the fight against tumors by so-called conventional T lymphocytes.

In future studies, the scientists therefore now want to investigate whether these different functions are mediated by the same areas of the BTN molecules and whether certain properties of these molecules can be specifically enhanced or suppressed.

More information: Mohindar M. Karunakaran et al, A distinct topology of BTN3A IgV and B30.2 domains controlled by juxtamembrane regions favors optimal human $\gamma\delta$ T cell phosphoantigen

sensing, *Nature Communications* (2023). DOI: [10.1038/s41467-023-41938-8](https://doi.org/10.1038/s41467-023-41938-8)

Provided by Julius-Maximilians-Universität Würzburg

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