Medical Xpress

Maturation instead of cell death: Defective signaling pathways disrupt immune cell development

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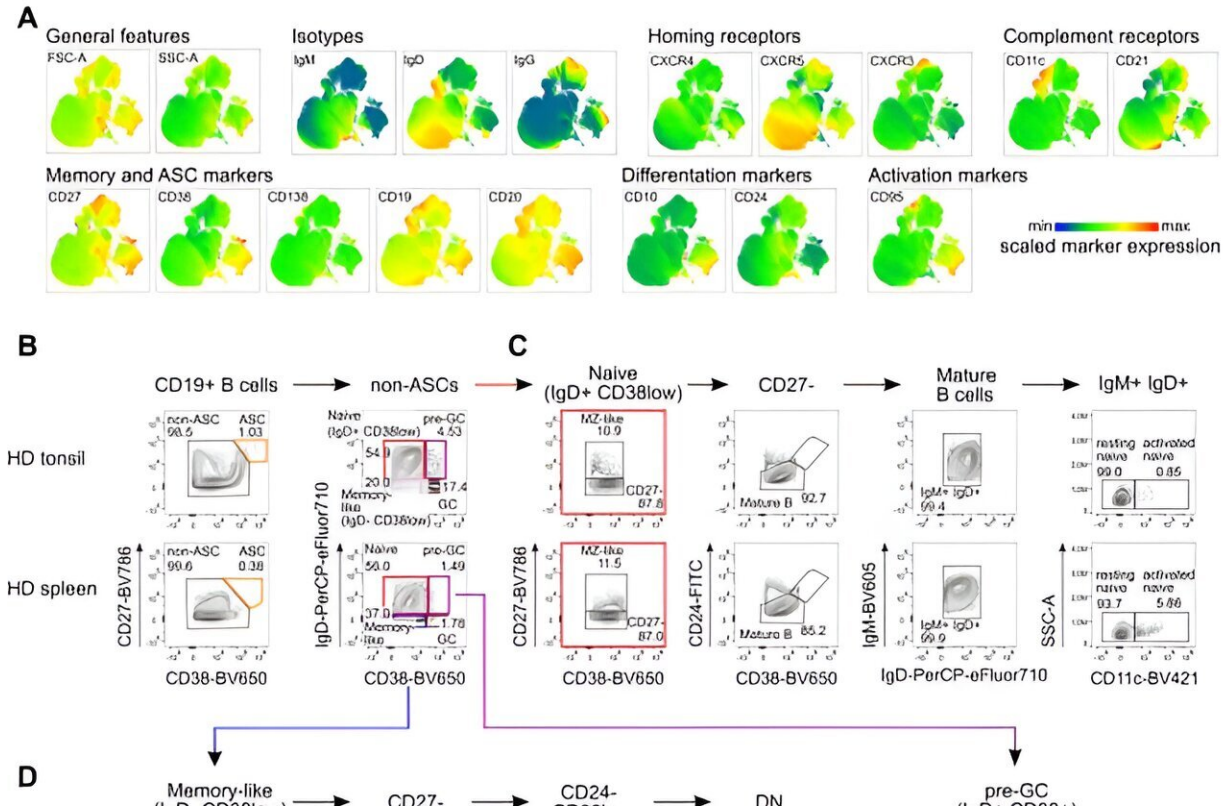

(A) UMAP projection of composite healthy donor (HD) samples from CD19+ cells of tonsil (n=7) and spleen (n=7) analyzed by spectral flow cytometry. (B) Identification of primary populations in one representative HD spleen and tonsil. (C) Identification of populations in the naïve B cell gate ($IgD^{+}CD38^{low}$). (D) Identification of populations within the memory-like gate ($IgD^{-}CD38^{low}$) and the pre-GC gate ($IgD^{+}CD38^{+}$). (E) CD95 expression (median fluorescent intensity,

MFI) in rN and aN cells (left panel) and DN1 and DN2 cells (right panel) in comparison to $CD27^+$ conventional memory B cells. (F) Frequency of $CD27^+IgD^+CD38^{low}$ MZ-like B cells within indicated parent gate in HD tonsils and spleens. Credit: *Science Immunology* (2024). DOI: 10.1126/sciimmunol.adj5948

In the case of an autoimmune disease, the immune system not only attacks pathogens, but also the body's own cells. Researchers at the University of Freiburg—Medical Center have now been able to show that defective signaling pathways in the body play a decisive role in the development of immune cells, a discovery that opens up new therapeutic approaches for autoimmune diseases such as autoimmune lymphoproliferative syndrome (ALPS).

The study was published on 12 January 2024 in the journal *Science Immunology*.

"The findings show how profound the effects that signaling pathway disorders have on the way our immune system functions, which helps us to better understand the mechanisms of immune cell development and function," says Prof. Dr. Marta Rizzi, Research Group Leader at the Department of Rheumatology and Clinical Immunology at the University of Freiburg–Medical Center and the Medical University of Vienna.

Important insights into immune cell development

The FAS signaling pathway plays an important role in the regulation of programmed cell death, also known as apoptosis. However, activation of the signaling pathway also influences non-lethal processes such as the maturation of B cells in the human immune system.

The study indicates that disruptions in this signaling pathway can lead to problems in the development and function of B cells. "The next step for us will be to look for ways in which these findings can help us treat patients," says Rizzi, who is also a member of the Cluster of Excellence CIBSS–Center for Integrative Biological Signaling Studies at the University of Freiburg.

More information: Julian Staniek et al, Non-apoptotic FAS signaling controls mTOR activation and extrafollicular maturation in human B cells, *Science Immunology* (2024). DOI: 10.1126/sciimmunol.adj5948

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