

Single-cell analysis reveals how immune cells are related and which ones accumulate in the tonsils during childhood

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T follicular helper (T_{FH}) cells are a heterogeneous group of immune cells, commonly found in the tonsils, but also detectable in blood. A*STAR scientists have developed a method to distinguish the different types of T_{FH} cells and analyze how they are interrelated. This knowledge may be useful in the future to treat autoimmune diseases and to increase the effectiveness of vaccination.

Scientists from the A*STAR Singapore Immunology Network, led by Evan Newell, identified 15 subtypes of T_{FH} cells, which can be clustered into three major categories: cells that are found only in <u>blood</u>, only in the tonsils or in both. "We used a single-cell technology based on mass cytometry to analyze the cells according to more than 40 parameters, and then we simplified the interpretation and visualization of the data with statistical methods. Overall, this process allowed us to appreciate the broad diversity of T_{FH} subtypes," explains Newell.

Beyond detecting distinctive cell subtypes, the team also studied how these different T_{FH} cells contribute to the immune response and the immunological memory. After infection, most immune cells that help to eliminate the pathogen are cleared from the body, while others, called memory cells, are preserved to create a long-term immunity against that pathogen and defend the organism more rapidly in case of reinfection. "The comparison of T_{FH} cells from blood and tonsils allowed us to find that those type of cells present in both tonsils and blood are memory T_{FH}



cells," remarks Newell. "They probably represent the cells that circulate in the blood and then migrate from the blood to lymphoid tissues, like tonsils."

While the function of T_{FH} cells in the blood is still unknown, tonsillar T_{FH} cells boost the immune response by helping the maturation of antibody-generating cells (B cells). The researchers also analyzed how tonsillar T_{FH} cells change over time before adulthood. Analysis of children's tonsils revealed that a heterogeneous population of memory T_{FH} cells, containing several T_{FH} subtypes, accumulates over childhood years. When they re-encounter the same pathogen, these memory T_{FH} cells are likely to support a quicker immune response; one that is diversified according to the specific T_{FH} subtype.

"We mapped a possible pathway by which \underline{memory} T_{FH} cells traffic from the blood to the $\underline{tonsils}$," explained Newell. "Future studies should address the functional relevance of the numerous subtypes of T_{FH} cells, as well as determine their association with age and response to vaccinations."

More information: Michael T. Wong et al. Mapping the Diversity of Follicular Helper T Cells in Human Blood and Tonsils Using High-Dimensional Mass Cytometry Analysis, *Cell Reports* (2015). <u>DOI:</u> 10.1016/j.celrep.2015.05.022

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