Medicine / Healthcare

Mechanism for the establishment of immunological memory

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Abstract

Understanding the mechanism how our bodies respond to re-infection of pathogens, such as Influenza virus and SARS-CoV-2 virus, is now one of the most important and urgent global issues to be tackled. Successful vaccination, our best weapon against these infectious diseases, relies on the induction of immunological memory, but a still unanswered question is what drives the small fraction of activated B cells to become quiescent memory B cells. We found that a small population of germinal center (GC) B cells with low metabolic activity and high expression of B cell receptors serves as memory-prone precursor cells. Our achievement provides the underlying mechanism for the establishment of immunological memory, which will help to develop new vaccine design strategies.

Background & Results

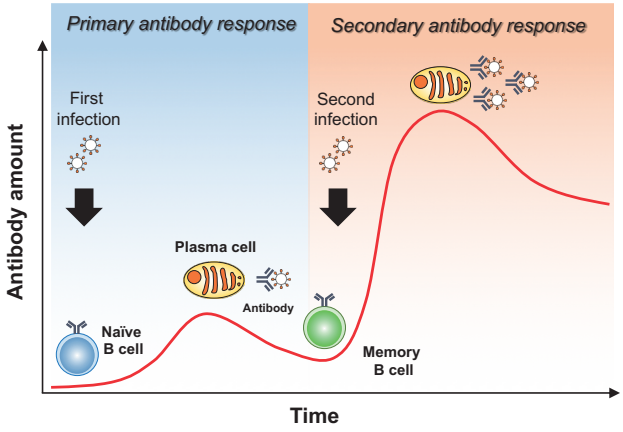
Lymphocytes, such as B cells and T cells, are essential for immune responses against bacterial and viral infections. Especially, memory B cells, which are generated during the first infection, quickly differentiate into plasma cells (antibody-secreting cells) and block or eliminate antigens efficiently upon second infection (Fig. 1). Vaccination is a strategy to artificially induce the immunological memory using this mechanism.

When exposed to antigens, such as viruses or bacteria, GC is generated in the secondary lymphoid organs including spleens and lymph nodes. B cell fate decision occurs during GC reaction, but it is still unclear how they are selected to differentiate into plasma cells, memory B cells, or to remain in the GC. In this study, we have identified and characterized a small GC population of precursors for memory B cells, which express both a GC marker transcription factor Bcl6 and a memory B cell marker surface molecule CD38. Through the analysis of these memory precursor B cells, we found that the GC B cells with lower mTORC1 activity favor a memory B cell fate. In fact, a B cell-specific inhibition of mTORC1 activity during GC response resulted in increased memory B cell differentiation. We also observed that memory precursor B cells express higher surface B cell receptors (BCR) and a survival factor Bcl2 compared with other GC B cells. Our results suggested a model in which weak T cell help from T cells together with provision of an increased survival signal from BCR are the key for GC B cells to adopt a memory B cell fate (Fig. 2).

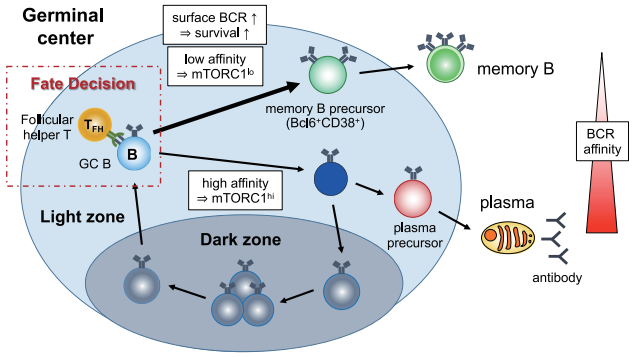
Significance of the research and Future perspective

It is well known that upon HIV or influenza virus infection, we acquire the protective immunity against mutated viruses through the ability of GC B cells to accumulate the somatic hypermutations in immunoglobulin genes and to differentiate into long-lived memory B cells. Our research on the mechanism of memory B cell generation may help to understand the reason for our requirements of annual influenza vaccination, and will provide basic data underlying a novel universal vaccine design strategy.

Immunological memory:
quick and robust secondary response upon re-infection



B cell fate decision during germinal center reaction



low metabolism and high survival signal favor memory fate

Patent

Treatise Inoue, Takeshi; Shinnakasu, Ryo; Kawai, Chie et al. Exit from germinal center to become quiescent memory B cells depends on metabolic reprograming and provision of a survival signal. J Exp Med, 2021; 218(1):e2020866. doi: 10.1084/jem.20200866.

URL http://lymph.ifrec.osaka-u.ac.jp/index.html
https://resou.osaka-u.ac.jp/ja/story/2019/icfbo5

Keyword B cell, antibody, vaccine, immunological memory