Following the Fate of a Naïve B Cell

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After antigen recognition by its receptor, the naïve B cell migrates to the border of the T cell zone where it receives signals to proliferate and originates several types of effector cells, such as antibody secreting plasma cells, germinal center (GC) cells and GC-independent memory cells. The question of whether a single naïve B cell has the potential to give rise to all three of these effector cells or is already committed to a specific path is central for vaccine development.

In an article published on *Science*, Dr. Justin Taylor from the Vaccine and Infectious Disease Division (VIDD) at Fred Hutch follows the fascinating path of a single naïve B cell after antigen recognition. The results showed immense heterogeneity in the progeny of different B cells. In 44% of cases, a single cell originated a single effector cell subset (plasma cells, GC cells, GC-independent memory cells or activated precursor cells). Only 4 out of 74 clonal population contained all the subsets and the rest 2-3 subsets. Not surprisingly, large clonal populations were more likely to give rise to multiple subsets. Surprisingly however, no relationship was observed between the size of the clonal population and the capacity to proliferate. Dr. Taylor and his colleagues hypothesized that the size of the responding population was related to the ability of a clonal population to resist apoptosis. Indeed, single B cells resistant to apoptosis by genetic knockout of the pro-apoptotic mediator Bim carried the potential to generate a bigger population of effector cells and were more likely to generate multiple subsets.

Previous research had suggested that another factor influencing the fate of a naïve B cell is the affinity of the receptor for the antigen. To test this hypothesis, the response of transgenic B cells to high or medium affinity antigen were compared. Stimulation with high affinity antigen resulted in the preferential production of plasma cells and GC cells, and fewer GC-independent memory cells as compared to the medium affinity stimulated clones. This role that receptor affinity for antigen plays in effector cell differentiation is similar to recent findings with T cells.

This study represents a milestone in B cell and vaccine research. As Dr. Taylor puts it, "The implication of our work is that not every B cell stimulated by a vaccine is going to respond the way that we want it to. What we need to do is figure out how to ensure that the most useful B cells resist apoptosis and differentiate down the pathway that will yield a long-lived protective response."

Taylor JJ, Pape KA, Steach HR, Jenkins MK. 2015. Humoral immunity. Apoptosis and antigen affinity limit effector cell differentiation of a single naive B cell. *Science*, 347(6223), 784-787.

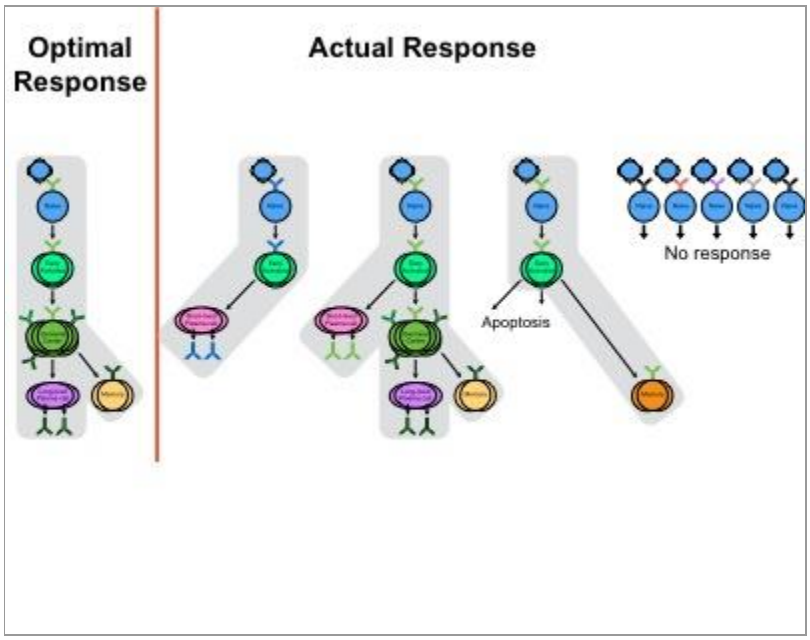

Image provided by Dr. Justin Taylor

Schematic representation of the optimal B cell response to vaccination, on the left, and actual response, on the right.