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B CELLS

Whatever will B cell be?

Following activation, naive B cells can differentiate into short-lived plasma cells, germinal centre (GC) B cells or GC-independent memory B cells — but can an individual naive B cell give rise to each of these effector cell types?

To address this, Taylor *et al.* used a limiting dilution approach to track the response of individual antigen-reactive naive B cells during immunization with the protein allophycocyanin. Based on calculations from preliminary experiments, the authors transferred a certain number of polyclonal naive B cells into recipient mice that were subsequently immunized with allophycocyanin in complete Freund's adjuvant, with the expectation that less than one donor-derived allophycocyanin-responsive naive B cell would survive in each recipient. At 7 days following immunization, donor-derived allophycocyanin-responsive B cells could be detected in 19% of the recipient mice and, based on the Poisson distribution, more than 91% of these populations arose from a single naive B cell.

The populations that differentiated from individual naive B cells were highly heterogeneous in terms of overall size and composition. Single naive B cells produced between four and 957 progeny (with a mean of 16) and although 44% of the clonal populations comprised only one effector cell type (namely, plasma cells, GC B cells, memory B cells or undifferentiated activated precursors), many populations contained two or three effector cell types, and a few populations contained all four subsets. Larger clonal populations were more likely to contain multiple effector cell types but surprisingly, population size did not correlate with an increased rate of cell division. Furthermore, populations containing all four effector cell subsets exceeded their expected size, whereas the populations with only one effector cell type had a lower than expected median size.

This suggested that resistance to cell death may be linked to the multipotentiality of the progeny of a single naive B cell.

Experiments using B cells deficient in the pro-apoptotic mediator BCL-2-interacting mediator of cell death (BIM) seemed to confirm this idea, as individual BIM-deficient B cells were more likely to produce multiple types of effector cells in response to allophycocyanin immunization. Further analyses in both transgenic B cell receptor (BCR) and polyclonal systems showed that BCR affinity for antigen also influenced the fate of the progeny of an individual cell; clones with higher affinity BCRs showed a tendency to differentiate into plasma cells.

These data indicate that individual naive B cells show great diversity in terms of their response to antigen-mediated activation, with the ability to resist apoptosis being linked to increased potentiality. Importantly, this is likely to ensure that a diverse set of effector cell types will be generated during a primary B cell response.

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> "individual naive B cells show great diversity in terms of their response to antigen-mediated activation"

ORIGINAL RESEARCH PAPER Taylor, J. J. *et al.* Apoptosis and antigen affinity limit effector cell differentiation of a single naive B cell. *Science* http://dx.doi.org/10.1126/science.aaa1342 (2015)
FURTHER READING Nutt, S. L. *et al.* The generation of antibody-secreting plasma cells. *Nature Rev. Immunol.* **15**, 160–171 (2015)