Nature Reviews Immunology | Published online 11 Jul 2016; doi:10.1038/nri.2016.82

Journal club

B CELL–T CELL INTERACTION: ANTIGEN BRIDGE TO ANTIGEN PRESENTATION

The start of my postdoc in late 1983 began a career-long interest in how B cells and T cells interact. A landmark study by Antonio Lanzavecchia in 1985 reinforced my passion for this subject, as it led to an important change in our understanding of cognate B cell–T cell communication.

The major paradigm of the early 1980s argued that T cells, previously activated by myeloid antigen-presenting cells (APCs), deliver lymphokines to B cells that are both necessary and sufficient for B cell activation. My own early experiments and others found instead that activated B cells both stimulated and were activated by T cells independently of lymphokines. To account for such MHC-restricted, antigen-specific B cell activation, additional models proposed that B cells and T cells interact through MHC–MHC contact, as well as by the T cell receptor (TCR) recognizing antigen bound to membrane immunoglobulin of the B cell. In this 'antigen bridge' model, B cells did not function as effective APCs.

> “he could separately block antigen uptake and presentation”

The elegant paper by Antonio Lanzavecchia (*Nature*, 1985) made several fundamental advances that changed our understanding of B cell–T cell interactions. It was the culmination of multiple preceding studies from several laboratories that hinted at a new model. Lanzavecchia used antigen-specific B cell and T cell clones from single human donors. By briefly pulsing the B cells with antigen, washing them, then allowing antigen presentation to T cells, he could separately block antigen uptake and presentation, and so demonstrate that the two events are independent. His experiments showed that antigen uptake by B cells requires membrane immunoglobulin and concentrates soluble antigen; antigen presentation by B cells requires lysosomal processing and loading onto MHC molecules. The resulting B cell–T cell interactions result in both T cell activation, through MHC-restricted antigen presentation, and contact-mediated B cell activation. The study showed that B cells process and present MHC-bound antigen acquired through membrane immunoglobulin to the TCR, thereby functioning as classical APCs in cognate B cell–T cell communication rather than simply as an antigen bridge.

This study also raised important new questions about the role of membrane immunoglobulin as a B cell signalling receptor, and how antigen presentation by B cells regulates T cell activation and T cell-mediated B cell activation (see Further reading), processes that continue to occupy and fascinate immunologists today.

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The author declares no competing interests.

ORIGINAL ARTICLE Lanzavecchia, A. Antigen-specific interaction between T and B cells. *Nature* **314**, 537–539 (1985)
FURTHER READING Swain, S. L & Dutton, R. W. Consequences of the direct interaction of helper T cells with B cells presenting antigen. *Immunol. Rev.* **99**, 263–280 (1987) | Bishop, G. A. & Hostager, B. S. B lymphocyte activation by contact-mediated interactions with T lymphocytes. *Curr. Opin. Immunol.* **13**, 278 –85 (2001)