

## **Programmed Tolerance of CD8<sup>+</sup> T cells by B cell APC**

Xiaoting Z. Wang, Keith S. Bahjat, Kiley R. Prilliman#,  
Marc K. Jenkins†, Amnon Altman¶ & Stephen P. Schoenberger

The Laboratory of Cellular Immunology and ¶Division of Cell Biology, La Jolla Institute for Allergy and Immunology, 9420 Athena Circle, La Jolla CA 92037, †Center for Immunology and Dept. of Microbiology, University of Minnesota Medical School, 20 Delaware St. SE Minneapolis, MN 55455, #Department of Pathology, University of New Mexico Health Sciences Center, 915 Camino de Salud, Albuquerque, NM 87131

The generation and maintenance of an effective peripheral CD8<sup>+</sup> T cell repertoire requires the continuous reinforcement of tolerance to self-antigens by immature antigen-presenting cells (APC). Relatively little is known about resting B cells in this process, despite their comprising an abundant cell type in the blood and secondary lymphoid organs. Using a novel *in vivo* experimental system that allows the fate of both endogenous and transgenic CD8<sup>+</sup> T cells to be evaluated in the absence of cross-presentation by host antigen-presenting cells (APC), we now report that direct presentation by resting B cells results in a unique form of tolerance in CD8<sup>+</sup> T cells in which clonal precursors become programmed to undergo a normal primary expansion, but develop a profound state of unresponsiveness in their clonal progeny that involves the uncoupling of TCR proximal activation pathways from downstream signaling events. This tolerizing function of B cell APC can be converted to full effector priming by treatment with LPS through a mechanism that requires the upregulation of CD80/CD86 molecules on the B cells. Our results demonstrate that resting B cells can function as efficient APCs able to directly program a state of durable tolerance in CD8<sup>+</sup> T cells *in vivo*, or, under conditions of immune activation, promote their development into competent effectors.

### References:

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