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Programmed Tolerance of CD8$^+$ T cells by B cell APC

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The generation and maintenance of an effective peripheral CD8$^+$ 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$^+$ 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$^+$ 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+ T cells *in vivo*, or, under conditions of immune activation, promote their development into competent effectors.

References:

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