B CELLS

The B boyz of sepsis

Activation of innate immune cells is the first step of the inflammatory response to invading pathogens, with adaptive immune cells classically considered as bystanders during this acute phase. However, recent studies have shown that T cells provide important feedback signals to the innate immune system during acute inflammatory responses to viral infection. Now, Moldawer and colleagues show that type I interferon (IFN)-activated B cells can also contribute to acute inflammation during caecal ligation and puncture (CLP)-induced sepsis.

Mice lacking adaptive immune cells (*Rag1*$^{-/-}$ mice) succumbed more readily to CLP-induced sepsis, and the authors found that the levels of innate inflammatory cytokines and chemokines were lower in these mice at early time points than in wild-type mice. B cell-deficient mice ($\mu mt^{-/-}$ mice), but not T cell-deficient mice, were similarly susceptible to sepsis and also had reduced early inflammatory responses, suggesting that B cells have an important role early in the response to sepsis.

Further analysis showed that $\mu mt^{-/-}$ mice had impaired bacterial clearance, which was probably due to the reduced levels of innate inflammatory cytokines and chemokines.

But how does sepsis affect B cells? The percentage of activated CD69^{hi} B cells was increased in the spleen and bone marrow as early as 24 hours following CLP-induced sepsis. This early activation of B cells required signalling through the type I IFN receptor (IFNAR1) but was independent of Toll-like receptor (TLR) signalling in B cells.

Previous studies by this group showed that loss of type I IFN-inducible production of CXC-chemokine ligand 10 (CXCL10) increased sepsis-induced lethality owing to impaired recruitment of and phagocytosis by neutrophils. Here, they found that the loss of B cells resulted in decreased production of CXCL10 and other type I IFN-inducible chemokines, and that CXCL10 administration 2 hours after CLP improved survival.

So, this study shows that B cells are activated by type I IFNs during the acute immune response to CLP-induced sepsis and help to promote survival by producing factors that contribute to the clearance of bacteria.

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ORIGINAL RESEARCH PAPER Kelly-Scumpia, K. M. *et al.* B cells enhance early innate immune responses during bacterial sepsis. *J. Exp. Med.* 11 Jul 2011 (doi:10.1084/jem.20101715)