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B cell-intrinsic MyD88 signaling controls IFN-γ-mediated early IgG2c class switching in mice in response to a particulate adjuvant

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Abstract

Adjuvants improve the potency of vaccines, but the modes of action (MOAs) of most adjuvants are largely unknown. TLR-dependent and -independent innate immune signaling through the adaptor molecule MyD88 has been shown to be pivotal to the effects of most adjuvants; however, MyD88's involvement in the TLR-independent MOAs of adjuvants is poorly understood. Here, using the T-dependent antigen NIPOVA and a unique particulate adjuvant called synthetic hemozoin (sHZ), we show that MyD88 is required for early GC formation and enhanced antibody class-switch recombination (CSR) in mice. Using cell-type-specific MyD88 KO mice, we found that IgG2c class switching, but not IgG1 class switching, was controlled by B cell-intrinsic MyD88 signaling. Notably, IFN-γ produced by various cells including T cells, NK cells, and dendritic cells was the primary cytokine for IgG2c CSR and B-cell intrinsic MyD88 is required for IFN-γ production. Moreover, IFN-γ receptor (IFNγR) deficiency abolished sHZ-induced IgG2c production, while recombinant IFN-γ administration successfully rescued IgG2c CSR impairment in mice lacking B-cell intrinsic MyD88. Together, our results show that B cell-intrinsic MyD88 signaling is involved in the MOA of certain particulate adjuvants and this may enhance our specific understanding of how adjuvants and vaccines work.

Keywords: B cells; IFN-γ; adjuvant; class switching; intrinsic MyD88.

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