IN BRIEF

B CELLS

The adjuvant action of bisphosphonates

Bisphosphonates are clinically used inhibitors of bone resorption. Previous studies have noted an increase in humoral immune responses in bisphosphonate-treated mice. Investigating this phenomenon in vesicular stomatitis virus-infected mice, the authors found that bisphosphonates increased neutralizing antibody levels (both IgM and IgG) by 100-fold compared with controls. Similarly, bisphosphonates increased antibody responses to proteins, haptens and existing commercial vaccine formulations. Bisphosphonates were shown to directly target B cells, and although the mechanism of this adjuvanticity remains to be determined it was independent of the Toll-like receptor and inflammasome pathways. Of note, patients with skeletal disease had a transient but significant increase in total IgG levels following a single intravenous infusion of bisphosphonates. Thus, bisphosphonates are B cell-targeting adjuvants that could be readily combined with vaccines, given that bisphosphonates are already widely used in the clinic.

ORIGINAL RESEARCH PAPER Tonti, E. *et al.* Bisphosphonates target B cells to enhance humoral immune responses. *Cell Rep.* **5**, 323–330 (2013)

ANTIBODIES

Kupffer cells mediate B cell depletion

CD20-specific antibodies are a common therapy for B cell malignancies and autoimmune disorders, but the mechanism of the resulting B cell depletion has been unclear. This study shows that the liver has a central role. Using intravital two-photon imaging in mice and a fluorescence-tagged reporter to mark Kupffer cells, the authors showed that B cells circulating in the liver sinusoids arrested on Kupffer cells and were engulfed by these cells after injection with a CD20-specific monoclonal antibody. This process was impaired in mice lacking FcRγ, which shows that engagement of Fc receptors on Kupffer cells is required for antibody-dependent cellular phagocytosis of B cells. Kupffer cells were also shown to engulf spontaneously developing lymphoma cells in mice receiving CD20-specific antibody therapy. The authors predict that depletion of malignant lymphoid cells in humans will be more efficient for recirculating tumour cells than those in secondary lymphoid organs.

ORIGINAL RESEARCH PAPER Montalvao, F. *et al.* The mechanism of anti-CD20-mediated B cell depletion revealed by intravital imaging. *J. Clin. Invest.* http://dx.doi.org/10.1172/JCI70972 (2013)

MACROPHAGES

BACH2 normal

This study identifies a new role for the transcription regulator BACH2 in alveolar macrophage (AM) function and lung homeostasis. *Bach2*$^{-/-}$ mice were shown to develop pulmonary alveolar proteinosis-like disease, which comprised an accumulation of surfactants and infiltration of granulocytes and AMs in the lungs. Compared with wild-type AMs, *Bach2*$^{-/-}$ AMs showed increased uptake of surfactant lipids and impaired cholesterol metabolism, which contributed to a foamy appearance. Moreover, they had an altered expression of genes involved in chemotaxis (which probably contributed to the granulocyte infiltration) and showed a bias towards alternative M2 macrophage activation, which suggests that BACH2 normally limits M2 polarization. Importantly, the disease could be relieved by wild-type bone marrow transfer, which supports the key role for AMs in lung homeostasis.

ORIGINAL RESEARCH PAPER Nakamura, A. *et al.* Transcription repressor Bach2 is required for pulmonary surfactant homeostasis and alveolar macrophage function. *J. Exp. Med.* **210**, 2191–2204 (2013)