

## 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 FcR $\gamma$ , 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*<sup>-/-</sup> 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*<sup>-/-</sup> 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)