IN BRIEF

DENDRITIC CELLS

Side-effects of DC depletion

Much of what we know about the *in vivo* function of dendritic cells (DCs) has been derived from *Cd11c*.DTR mice, in which DCs are conditionally depleted by injection of diphtheria toxin (DT). This study shows that, in addition to causing DC depletion, DT administration unexpectedly results in an early increase (within 24 hours) in blood neutrophils in *Cd11c*.DTR mice and was associated with improved bacterial clearance in a model of pyelonephritis compared with non-depleted mice. Similarly, early neutrophilia and enhanced bacterial clearance were observed following DT administration in a related mouse line termed *Cd11c*.DOG mice. Finally, the authors describe another mouse line, termed *Cd11c*.LuciDTR mice, that was not associated with early neutrophilia (but did develop late neutrophilia) following DT administration. Bacterial clearance was delayed in these mice compared with non-depleted *Cd11c*.LuciDTR mice. So, the choice of transgenic mouse model for DC depletion may influence experimental results under conditions in which neutrophils may be involved.

ORIGINAL RESEARCH PAPER Tittel, A. P. *et al.* Functionally relevant neutrophilia in CD11c diphtheria toxin receptor transgenic mice. *Nature Methods* 26 Feb 2012 (doi:10.1038/nmeth.1905)

AUTOIMMUNITY

Restoring natural order

Although self-reactive natural antibodies are diagnostic of systemic lupus erythematosus, it has been controversial whether they have protective or pathological roles in the disease. Mannoor *et al.* used a transgenic system to expand a natural antibody-producing B cell population in lupus-prone MRL–*lpr* mice. Notably, MRL–*lpr* mice with increased numbers of natural antibody-producing B cells developed less kidney pathology and had increased survival rates compared with control MRL–*lpr* mice. Natural antibody-producing B cells produced interleukin-10 (IL-10) following stimulation with Toll-like receptor ligands, and the presence of these B cells in MRL–*lpr* mice was associated with increased numbers of IL-10-producing $CD4^+$ T cells and the skewing of serum IgG antibodies from the IgG2a and IgG3 subclasses (which are associated with pathology in lupus) to the less-pathogenic IgG1 subclass. These findings suggest that natural antibody-producing B cells have protective roles in lupus nephritis.

ORIGINAL RESEARCH PAPER Mannoor, K. *et al.* Expression of natural autoantibodies in MRL-lpr mice protects from lupus nephritis and improves survival. *J. Immunol.* 9 Mar 2012 (doi:10.4049/jimmunol.1102859)

CELL MIGRATION

HMGB1-mediated inflammatory cell recruitment

HMGB1 (high mobility group box 1) is released at sites of inflammation and/or tissue damage and promotes cytokine production and cell migration. However, the underlying mechanism for this cell migration is unknown. Now, Schiraldi *et al.* show that the migration of mouse fibroblasts and human monocytes in response to HMGB1 *in vitro* depends on CXCL12 and CXCR4. Further analyses showed that HMGB1 forms a heterocomplex with CXCL12 and that this complex triggers different conformational changes in CXCR4 dimers compared with CXCL12 alone. The HMGB1–CXCL12 complex induces the early migration of mononuclear cells into air pouches and to sites of cardiotoxin-induced muscle injury *in vivo* independently of the HMGB1 receptor RAGE. So, HMGB1 promotes the recruitment of inflammatory cells by forming a complex with CXCL12 that signals through CXCR4.

ORIGINAL RESEARCH PAPER Schiraldi, M. *et al.* HMGB1 promotes recruitment of inflammatory cells to damaged tissues by forming a complex with CXCL12 and signaling via CXCR4. *J. Exp. Med.* 27 Feb 2012 (doi:10.1084/jem.20111739)