IN BRIEF

REPRODUCTIVE IMMUNOLOGY

Autoantibodies bring out the son

This paper shows how maternal antibodies can affect fetus viability in a gender-specific manner. Patients with systemic lupus erythematosus (SLE) produce antibodies specific for double-stranded DNA, and a subset of these can cross-react with and activate the *N*-methyl-D-aspartate receptor (NMDAR). Using a mouse model in which pregnant mice produce antibodies that cross-react with NMDAR, the authors found that these antibodies crossed the placenta and induced apoptosis in fetal neurons via the NR2A subunit of NMDAR. Female fetuses were more susceptible to autoantibody-induced neuronal cell death than males; this was linked to gender-specific differences in fetal brain development and expression of NR2A. Patients with SLE give birth to more males than females; this study offers a possible explanation for this observation.

ORIGINAL RESEARCH PAPER Wang, L. *et al.* Female mouse fetal loss mediated by maternal autoantibody. *J. Exp. Med.* 7 May 2012 (doi: 10.1084/jem.20111986)

ASTHMA AND ALLERGY

IL-25-responsive myeloid cells promote type 2 lung pathology

Interleukin-25 (IL-25) signals through the IL-17RA–IL-17RB receptor and has a key role in the pathogenesis of asthma. This study describes a unique population of type 2 cytokine-producing IL-17RB^{+}CD11b^{+}GR1^{mid} myeloid cells (termed T2M cells) in mice with chronic allergic lung inflammation. Intratracheal administration of recombinant IL-25 induced the expression of the type 2 cytokines IL-4 and IL-13 specifically in T2M cells. Adoptive transfer of IL-25-treated T2M cells from wild-type mice to *Il17rb*$^{-/-}$ mice (which are IL-25 insensitive), together with the administration of recombinant IL-25, resulted in the induction of airway pathology. T2M cells were shown to be steroid resistant, as IL-25-induced pathology and type 2 cytokine expression were not reduced after treatment with dexamethasone. The authors identified a similar population of T2M cells in patients with asthma, suggesting that T2M cells may represent a new therapeutic target for this disease.

ORIGINAL RESEARCH PAPER Petersen, B. C. *et al.* Interleukin-25 induces type 2 cytokine production in a steroid-resistant interleukin-17RB^{+} myeloid population that exacerbates asthmatic pathology. *Nature Med.* **18**, 751–758 (2012)

B CELLS

A metabolic checkpoint for B cell development

Using a chemical mutagenesis strategy, the authors identified a pedigree of mice (LPAB.1 mice) that completely lack peripheral B cells. Absence of B cells in LPAB.1 mice resulted from a deletion in the *Fnip1* gene. Absence of folliculin-interacting protein 1 (FNIP1) blocked B cell maturation in a cell-autonomous manner at the large pre-B cell to small pre-B cell transition, which is mediated by the formation of the pre-B cell receptor (pre-BCR). However, *Fnip*$^{-/-}$ pre-B cells responded in a similar manner to wild-type B cells to proliferative signals through the pre-BCR and interleukin-7 receptor. The block in B cell development could not be rescued by the provision of rearranged immunoglobulin chains. Instead, the authors found that *Fnip*$^{-/-}$ pre-B cells had both increased expression of AMPK-regulated catabolic genes and increased mTOR-mediated anabolic growth. The results showed that FNIP1 is normally required for the inhibition of mTOR pathways through AMPK triggering under conditions of nutrient stress and that, in its absence, excessive mTOR-mediated metabolite consumption triggers B cell apoptosis. Thus, FNIP1 is required as a metabolic checkpoint for B cell maturation.

ORIGINAL RESEARCH PAPER Park, H. *et al.* Disruption of *Fnip1* reveals a metabolic checkpoint controlling B lymphocyte development. *Immunity* 17 May 2012 (doi:10.1016/j.immuni.2012.02.019)