Jellyfish Pictures / Photo Researchers, Inc.

to nonself antigens, such as allergens, commensal microbiota and food, whereas thymically generated regulatory T (tT_{reg}) cells are thought to be responsible for tolerance to self antigens during development. Interestingly, pT_{reg} cells are known to harbor an enhancer element, conserved noncoding sequence 1 (CNS1), in the promoter of *Foxp3* (encoding a transcription factor required for T_{reg} cell function) that allows for the development of pT_{reg} cells but is dispensable for the generation of tT_{reg} cells. Samstein *et al.* show that CNS1 is unique to placental mammals and that it is required for the generation of pT_{reg} cells specific for fetal alloantigens during pregnancy in mice. They also show that the absence of CNS1 results in more fetal absorption by pregnant dams when mated to allogenic males but has no effect when mutant females are mated to syngenic males.

These results suggest that pT_{reg} cells are a crucial component of maternal-fetal tolerance and that the system arose during mammalian evolution.—*RL*

■ IMMUNITY

Gut bugs alter antiviral immunity

At mucosal surfaces, commensal microbes can promote the development of pathogenic and regulatory adaptive immune cells that help contain pathogens and prevent infection. Whether commensal bacteria can regulate systemic immunity to viruses, however, remains unclear.

Two research groups now report that depletion of the gut microflora impairs the clearance of a viral infection. Andreas Diefenbach and his colleagues (*Immunity* doi:10.1016/j.immuni.2012.05.020) found that natural killer cell activity was impaired in germ-free mice. These splenic natural killer cells failed to receive priming signals from dendritic cells, which in response to viral infection, normally produce type I interferons (IFN-I). The serum concentrations of IFN-I were reduced in virally infected germ-free mice, and IFN-I injection normalized natural killer cell responses.

David Artis (*Immunity* doi:10.1016/j.immuni.2012.04.011) and his colleagues report that virus-specific adaptive immune responses are impaired in antibiotic-treated mice. The expression of genes that regulate antiviral immunity was decreased in macrophages isolated from the gut of antibiotic-treated mice. These macrophages responded weakly to IFN stimulation and were impaired in their ability to control viral infection.

Taken together, these studies reveal distinct ways in which commensal bacteria can influence innate immune activation and antiviral immunity. —*KDS*

■ CARDIOVASCULAR DISEASES

STAMPing down inflammation

Macrophage activation, which contributes to vascular inflammation, is a central feature of atherosclerotic plaque initiation and development. Gökhan Hotamisligil and his colleagues now identify a new anti-inflammatory mechanism in macrophages that protects against atherosclerosis in mice (*Cell Metab.* **16**, 81–89).

These authors previously showed that the transmembrane protein Stamp2 is needed for normal metabolic homeostasis in mice, including in adipose tissue and liver. In their new work, they show that Stamp2, which was previously characterized as having reductase activity, lowers the amounts of NADPH in macrophages. The increased amounts of NADPH in Stamp2-deficient macrophages led to a proinflammatory phenotype with an increased expression of a host of inflammatory cytokines. Stamp2 deficiency also decreased cholesterol efflux and enhanced foam cell formation. To connect these findings to atherosclerosis, the researchers showed that Stamp2 is expressed in macrophages of atherosclerotic plaques in both humans and mice and that Stamp2 deficiency in mice promoted vascular inflammation and increased the size of atherosclerotic lesions. Stamp2 deficiency only in bone marrow cells also resulted in increased atherosclerotic lesion size, consistent with the idea that Stamp2 acts in macrophages to restrain inflammation and atherosclerosis.—*MB*

Written by Victoria Aranda, Michael Basson, Kevin Da Silva, Randy Levinson, Juan Carlos López and Meera Swami

New from NPG

Non-invasive prenatal measurement of the fetal genome

Fan, H.C. *et al. Nature* doi:10.1038/nature11251 (4 July).

The authors describe the complete sequencing of the fetal genome using a non-invasive method. This involves a molecular counting method to analyze the parental haplotypes in maternal plasma, allowing the fetal genome to be determined from this information.

NLRP6 negatively regulates innate immunity and host defence against bacterial pathogens

Anand, P.K. *et al. Nature* doi:10.1038/nature11250 (1 July).

Mice lacking the NOD-like receptor Nlrp6, which is involved in inflammasome signaling, are resistant to several bacterial pathogens. Infected Nlrp6-deficient cells produced more inflammatory cytokines, suggesting that NLRP6 downregulates inflammatory signaling and impede the systemic clearance of bacterial pathogens.

***De novo* germline and postzygotic mutations in *AKT3*, *PIK3R2* and *PIK3CA* cause a spectrum of related megalencephaly syndromes**

Rivière, J.-B. *et al. Nat. Genet.* doi:10.1038/ng2327 (24 June).

***De novo* somatic mutations in components of the PI3K-AKT3-mTOR pathway cause hemimegalencephaly**

Lee, J.H. *et al. Nat. Genet.* doi:10.1038/ng.2329 (24 June).

Two recent exome sequencing studies provide insights into the genetic basis of megalencephaly syndromes, sporadic overgrowth disorders associated with an enlarged brain size. Both studies identify *de novo* mutations in genes encoding components of the PI3K-AKT3-mTOR pathway, suggesting this pathway is important in driving tissue overgrowth in these conditions.

Rescue of aging-associated decline in Dnmt3a2 expression restores cognitive abilities

Oliveira, A.M. *et al. Nat. Neurosci.* doi:10.1038/nn.3151 (1 July).

The authors now provide a link between aging-related cognitive decline and hypomethylation by showing that aging in mice is associated with decreased expression of the DNA methyltransferase Dnmt3a2 in the hippocampus. Restoration of Dnmt3a expression rescued the aging-associated cognitive function.