be seen whether these factors directly influence immune cell development. Two new studies now reveal that increased dietary salt intake can promote autoimmune inflammation and the development of pathogenic T helper 17 (T_H17) cells (*Nature* http://dx.doi.org/10.1038/nature11868 and http://dx.doi.org/10.1038/nature11984).

Kleinewietfeld *et al.* and Wu *et al.* reported that a mouse model of multiple sclerosis develops more severe disease when fed a high-salt diet. *In vitro*, an increased concentration of NaCl promotes the differentiation of both mouse and human T_H17 cells. Mechanistically, NaCl induces the expression of serum glucocorticoid kinase 1 (SGK1). This kinase increases the expression of the IL-23 receptor, thereby stabilizing T_H17 cells and promoting IL-17 secretion. Mice deficient in SGK1 develop attenuated disease, have fewer T_H17 cells and are relatively resistant to the effects of high-salt diet on autoimmune inflammation. —*KDS*

■ METABOLISM

A role for MHCII in immunometabolism

Although the adipocyte's main function is to store fat, it is becoming clearer that it also contributes to sterile inflammation. A new study by Willa A. Hsueh and her colleagues (*Cell Metab.* **17**, 411–422) adds further insight into this role. The authors found that, compared with adipocytes from lean humans, adipocytes from obese individuals had higher expression of many genes involved in antigen presentation, including the class II major histocompatibility complex (MHCII). Similar findings were found in mice after 2 weeks of a high-fat diet. The team also uncovered a signaling pathway in mice by which adipocyte-derived leptin acts on adipose tissue–resident T cells to promote interferon-γ release. This cytokine then acts back on the adipocytes, and other antigen-presenting cells in the organ, to upregulate MHCII expression, resulting in T cell activation. This, in turn, promotes macrophage recruitment and polarization to a proinflammatory profile.

The team validated the pathological role of this signaling pathway by showing that mice deficient in either leptin or MHCII have less adipose tissue inflammation upon high-fat feeding, and in the case of the latter strain they also saw improved insulin sensitivity. One drawback to this study is that they used a strain with whole-body knockout of MHCII, so it is unclear if expression of this complex in adipocytes and/or in resident adipose tissue macrophages is necessary to cause metabolic dysfunction. Even so, the results are intriguing, especially given data from other labs showing alterations in the adipose tissue T cell receptor repertoire in obesity, suggesting that this condition is associated with antigen presentation and altered immune cell function. —*RL*

■ T CELLS

Cross-reactive memory

Analyzing the human T cell repertoire is possible thanks to sensitive techniques for its detection and characterization. Using such approaches, Mark Davis and his colleagues now find that $CD4^+$ T cells in humans can recognize pathogens without prior exposure, owing to antigen cross-reactivity (*Immunity* **38**, 373–383).

The researchers made peptide-MHC tetramer complexes incorporating peptides from self proteins, from various viruses or from tetanus toxin to determine the frequency of antigen-specific T cells in humans. They found $CD4^+$ T cells capable of recognizing antigens that they had never previously encountered, and prior exposure to an antigen did not increase the frequency of T cells recognizing that antigen. Moreover, many of these pathogen-specific $CD4^+$ T cells from unexposed individuals were phenotypically and functionally memory cells. Although the authors found similar frequencies of self peptide– or pathogen-specific $CD4^+$ T cells in cord blood from unexposed infants compared with adults, the antigen-specific T cells in cord blood were naive, and not memory cells, which might contribute to the lesser ability of newborns to respond to infections.

The researchers next looked at influenza-specific T cells from two individuals who received the seasonal influenza vaccine and showed that T cells specific for an epitope in the viral hemagglutinin also recognized peptides from other microbes, and that the vaccine expanded cross-reactive memory T cells. These findings suggest that infection or immunization with a particular microbe can elicit cross-reactive $CD4^+$ T cells that may help protect against pathogens to which an individual has had no prior exposure, and support the idea that environmental exposure to infectious agents can boost immune responses. —*AF*

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New from NPG

Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC

Raj, V.S. *et al. Nature* http://dx.doi.org/10.1038/nature12005 (14 March).

The authors identify dipeptidyl peptidase 4 (DPP4) as a functional receptor for the recently identified human coronavirus. They show that antibodies blocking DPP4 prevent infection of susceptible human cells and that expression of DPP4 in nonsusceptible cells can enable infection.

ATP-competitive inhibitors block protein kinase recruitment to the Hsp90-Cdc37 system

Polier, S. *et al. Nat. Chem. Biol.* http://dx.doi.org/10.1038/nchembio.1212 (17 March).

ATP-competitive kinase inhibitors, such as the cancer drugs vemurafenib and lapatinib, can block the access of kinases to HSP90, thus promoting their degradation. This mechanism might be important for the clinical efficacy of these drugs.

Seven new loci associated with age-related macular degeneration

Fritsche, L.G. *et al. Nat. Genet.* http://dx.doi.org/10.1038/ng.2578 (3 March).

A genome-wide association study, including >17,000 people with advanced age-related macular degeneration (AMD), identifies 19 susceptiblility loci associated with AMD, of which seven were new associations.

Intracellular antibody-bound pathogens stimulate immune signaling via the Fc receptor TRIM21

McEvan, W.A. *et al. Nat. Immunol.* http://dx.doi.org/10.1038/ni.2548 (3 March).

The authors show that antibodies entering the cytoplasm by binding pathogens are recognized by the cytosolic receptor TRIM21, which can then activate downstream innate immune signaling pathways and elicit an antiviral state.

Interplay of LRRK2 with chaperone-mediated autophagy

Orenstein, S.J. *et al. Nat. Neurosci.* http://dx.doi.org/10.1038/nn.3350 (3 March).

Mutations in the gene encoding leucine-rich repeat kinase 2 (LRRK2) are the most common cause of familial Parkinson's disease. These authors now show that wild-type LRRK2 can be degraded by chaperone-mediated autophagy (CMA) in lysosomes, but degradation of mutant forms is impaired, as the mutants block the formation of the CMA translocation complex at the lysosomal membrane.