Sins of the mother

Dietary fat consumption has well-established associations with inflammatory disease, in part through its effects on the host microbiota. In the *Journal of Immunology*, Datta and colleagues investigate the influence of the dietary fat of parents on the immune responsiveness of their offspring. They feed female mice a high-fat diet (HFD) during pregnancy and nursing, but switch their offspring to standard chow after weaning. Adult mice raised by female mice fed a HFD have enhanced responses in a broad variety of inflammatory, autoimmune and allergic models. However, the offspring of female mice fed a HFD show no obvious increase in signatures associated with obesity or glucose intolerance. Instead, these mice show alterations in the gut microbiome, including diminished overall diversity and a relative shift toward Firmicutes. Exposure of parents to a HFD may therefore have lasting effects on the immune system of their offspring through the influence of the HFD on microbial diversity. ***ZF***

***J. Immunol.* (9 August 2013) doi:10.4049/jimmunol.1301057**

Plaques keep it local

The pathological progression of atherosclerotic plaques depends on the presence and activity of macrophages. In *Nature Medicine*, Swirski and colleagues study mice deficient in apolipoprotein E to investigate the relative contributions of monocyte influx and *in situ* proliferation to the accumulation of macrophages in atherosclerotic plaques. Through the use of a parabiosis approach, they find that although the recruitment of monocytes is ultimately required for plaque seeding, the bulk of macrophages in the plaque can be accounted for by localized proliferation. Depletion of monocytes has minimal effect on macrophage numbers in established plaques, but inhibiting proliferation with the chemotherapeutic agent 5-fluorouracil diminishes lesion size. The contribution of localized macrophage proliferation to human atherosclerotic plaques remains to be determined; however, inhibiting proliferation with cytostatic drugs may be a useful therapeutic approach. *ZF*

Nat. Med. (11 August 2013) doi:10.1038/nm.3258

From lung to gut

Intestinal CD103$^+$ dendritic cells (DCs) that can metabolize vitamin A into retinoic acid induce expression of the gut-homing receptors integrin $\alpha_4\beta_7$ and CCR9 on T cells after being activated. In the *Journal of Experimental Medicine*, Ruane *et al.* show that lung DCs can also 'imprint' the expression of gut-homing receptors in T cells and 'license' them to migrate to the gut. Both CD103$^+$CD11b$^-$ and CD11b$^+$CD103$^-$ lung DCs express aldehyde dehydrogenase and induce the expression of CCR9 and $\alpha_4\beta_7$ on proliferating T cells in a manner dependent on signaling via the retinoic acid receptor, with lung CD11b$^+$ DCs being more effective than lung CD103$^+$ DCs. Intranasal delivery of antigen induces $\alpha_4\beta_7$ expression in T cells activated in the mediastinal lymph nodes, whereas subcutaneous immunization does not confer gut-homing tropism to T cells. In *in vivo* models of infection with pathogenic *Salmonella*, intranasal immunization extends survival and averts systemic pathology. ***IV***

***J. Exp. Med.* (19 August 1023) doi:101084/jem.20122762**

Written by Laurie A. Dempsey, Zoltan Fehervari & Ioana Visan

Becoming adaptive

In jawless vertebrates, variable lymphocyte receptors of two types, VLRA and VLRB, are reciprocally expressed by lymphocytes that resemble the T cells and B cells of jawed vertebrates. In *Nature*, Hirano *et al.* define another lineage of T cell–like lymphocytes that express the related VLRC receptors. Assembly of VLRC and VLRA occurs in the 'thymoid' organ. VLRA$^+$ and VLRC$^+$ cells have overlapping but distinct gene-expression profiles, with VLRA$^+$ cells expressing the transcription factor TCF-1 and VLRC$^+$ cells expressing the transcription factor SOX13. Both VLRA$^+$ and VLRC$^+$ cells proliferate after antigen stimulation and 'preferentially' populate the intestinal epithelium but do not differentiate into VLR-secreting cells. VLRC$^+$ cells are the main lymphocyte population in the lamprey epithelium, where they express a repertoire more restricted than that of other tissues. This suggests that having two distinct T cell lineages is a basic principle for a lymphocyte-based adaptive immune system. *IV*

Nature (11 August 2013) doi:10.1038/nature12467

lncRNAs in immune cells

Long noncoding RNAs (lncRNAs) can regulate gene expression. In *Science*, Fitzgerald and colleagues identify lincRNA-Cox2 as a regulatory lncRNA expressed in macrophages. This lincRNA, named for the proximity of its gene with *Cox2*, is upregulated by activation of the pathway consisting of Toll-like receptors, the adaptor MyD88 and the transcription factor NF-κB. Expression of lincRNA-Cox2 affects hundreds of genes, but notably those involved in immune responses. lincRNA-Cox2 downregulates *Ccl5* and various interferon-stimulated genes and upregulates *Tlr1*, *Il6* and *Il23a*. It associates with the heterogeneous nuclear ribonucleoproteins hnRNP-A/B and hnRNP-A2/B1. Knockdown of those or LincRNA-Cox2 relieves the repression of *Ccl5* and interferon-stimulated genes, although the spectrum of genes regulated by lincRNA-Cox2 and hnRNPs does not completely overlap. These findings introduce another layer of transcriptional regulation on inducible genes that control immunological function. ***LAD***

***Science* 341, 789–792 (2013)**

Blocking transcription

Glucocorticoids are anti-inflammatory factors that repress inducible gene expression dependent on the transcription factors NF-κB and AP-1. In the *Proceedings of the National Academy of Science*, Gupte *et al.* show that binding of ligand by the nuclear glucocorticoid receptor (GR) represses two classes of inflammatory signal–dependent gene transcription. GR and its corepressor GRIP1, which is recruited after ligand binding, inhibit the chromatin remodeling required by initiation-controlled genes, such as *Il1a* and *Il1b*. That action prevents recruitment of RNA polymerase II to unoccupied promoters. Additionally, GR-GRIP1 complexes block signal-dependent release by RNA polymerase II of stalled promoter-proximal complexes, including those at the *Tnf* and *Ccl3* promoters. GR-GRIP1 prevents release of the pausing factor complex NELP and inhibits recruitment of the kinase complex P-TEFb that is required for the conversion of RNA polymerase II into elongation complexes. Thus, glucocorticoid actions target the rate-limiting steps for inflammatory gene expression. *LAD*

Proc. Natl. Acad. Sci. USA (15 August 2013) doi:10.1073/pnas.1309898110