MUCOSAL IMMUNOLOGY

T_H17 cell flavors

Immunity https://doi.org/10.1016/j.immuni.2019.05.004 (2019)

The T_H17 subset of helper T cells is pathogenic in a variety of inflammatory disorders but also has tissue-resident homeostatic roles in the intestine. In *Immunity*, Omenetti et al. compare the characteristics of T_H17 cells induced by commensal microbiota, notably segmented filamentous bacteria (SFB), and those elicited by a pathogen (*Citrobacter rodentium*). Secretion of the cytokine IL-17A is higher in SFB-induced T_H17 cells, the cytokine IFN-γ is more abundant in *C. rodentium*–elicited T_H17 cells, and both groups of cells produce IL-22. SFB-induced T_H17 cells do not expand in response to infection with *C. rodentium*. RNA-sequencing analysis indicates enrichment for transcripts encoding molecules involved in anti-inflammatory pathways and oxidative phosphorylation in SFB-induced T_H17 cells and enrichment for markers of glycolysis, biosynthesis and pro-inflammatory pathways in *C. rodentium*–elicited T_H17 cells. These results indicate that two functionally distinct populations of T_H17 cells can reside in the gut simultaneously during pathogen-induced inflammation. *IV*

https://doi.org/10.1038/s41590-019-0459-1

IMMUNOMETABOLISM

Biochemical uncouple

Nature https://doi.org/10.1038/s41586-019-1311-3 (2019)

T cells require mitochondrial metabolism for their exit from the naive state and to become activated. In *Nature*, Flavell and colleagues show that the differentiation and terminal effector functions of helper T cells are biochemically uncoupled. Through the use of genetic interference with genes encoding subunits of complex II (*Sdha* and *Shac*) or enzymes involved in the malate–aspartate shuttle (*Mdh1* and *Mdh2*) or mitochondrial citrate export (*Slc25a1* and *Acly*), transport systems that fuel complex I, or the pharmacological inhibition of these processes, the authors show that complex I generates the substrates needed for epigenetic remodeling, such as histone acetylation, and proliferation during differentiation of the T_H1 subset of helper T cells, while complex II restricts this processes by moving carbon forward in the tricarboxylic acid cycle and thus promotes the terminal effector state in T_H1 cells. These observations describe a biochemical network that acts in parallel with the transcriptional programming to enforce cell state. *IV*

https://doi.org/10.1038/s41590-019-0458-2

MATERNAL ANTIBODIES

Protecting baby

Cell **178**, 202–215.e14 & **178**, 190–201.e11 (2019)

Passive transfer of maternal antibodies provides early immunological protection to neonates. In *Cell*, Jennewein et al. report the preferential transfer of human natural killer cell–activating antibodies from mothers to neonates. This property is due to digalactosylation of immunoglobulin G constant-fragment (Fc) domains, which enhance placental transfer via the neonatal Fc receptors FcRn and FcγRIIIA that are co-expressed on trophoblasts. Also in *Cell*, Martinez et al. report that mothers infected with human immunodeficiency virus (HIV) exhibit inefficient placental transfer of antibodies, which increases the susceptibility of HIV-exposed, uninfected neonates to post-partum infection. Curiously, maternal hypergammaglobulinemia is associated with poor placental transfer in HIV-infected mothers. Similarly, differences in Fc glycosylation affect the interactions of immunoglobulins with Fc receptors that mediate placental transfer. Those last findings suggest that maternal infection alters the glycosylation patterns during antibody production that can then affect the efficiency with which maternal passive antibody protection is provided to the offspring. *LAD*

https://doi.org/10.1038/s41590-019-0460-8

TISSUE-RESIDENT MACROPHAGES

Body-cavity niches

Immunity https://doi.org/10.1016/j.immuni.2019.05.010 (2019)

Resident macrophage populations contribute to tissue-specific 'identity' programs and maintain tissue homeostasis. In *Immunity*, Buechler et al. describe the stromal-cell interactions required for macrophage residency in visceral body cavities that include the peritoneal, pleural and pericardial spaces. Large cavity-resident macrophages require expression of the transcription factor GATA-6. A subset of podoplanin-positive stromal cells that express the transcription factor Wt1, which include mesothelial cells and fibroblasts, also express RALDH enzymes that metabolize vitamin A and provide the retinoic acid cofactors required for GATA-6 expression for the large cavity macrophages. Depletion of $Wt1^+$ stromal cells results in fewer peritoneal macrophages and disturbs peritoneal homeostasis. Thus, $Wt1^+$ stromal cells are needed to provide retinol metabolites in *trans* to maintain cavity-resident macrophages. *LAD*

https://doi.org/10.1038/s41590-019-0461-7

ASTHMA SUSCEPTIBILITY

Growing up on the farm

Nat. Med. https://doi.org/10.1038/s41591-019-0469-4 (2019)

In the midst of a rising tide of asthma, growing up on a rural farm is known to offer a strong protective effect, due in large part to the distinctive environmental microbiota there that alters lung immunity. In *Nature Medicine*, Kirjavainen et al. undertake a prospective non-interventional study to determine whether a 'farm-like' microbiota in an urban environment can also be protective. They develop an index, FaRMI, that describes how 'farm-like' the indoor environmental microbiota is during an early childhood window. In two urban cohorts from Finland and Germany, a 'farm-like' microbiota in an indoor setting also significantly protects children from developing asthma. The protective effect is independent of absolute bacterial richness or load, and 'farm-like' fungi do not seem to offer protection. Instead, alterations in select, potentially modifiable bacterial species are probably responsible for the protective effect. *ZF*

https://doi.org/10.1038/s41590-019-0462-6

Laurie A. Dempsey, Zoltan Fehervari and Ioana Visan