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Monocyte and DC atlas

There are a variety of specialized subsets of human dendritic cells (DCs) and monocytes, but full understanding of their diversity and ontogenic relationships has been hampered by the technologies used to assess them. In *Science*, Villani *et al.* use single-cell RNA sequencing combined with dimensionality reduction and functional analysis to produce a comprehensive mRNA-expression 'atlas' of DCs and monocytes from human peripheral blood. Through analysis of approximately 2,400 individual cells, six distinct subsets of DCs emerge, five of which correspond to established populations, with a sixth previously unknown population characterized by expression of the receptor tyrosine kinase AXL and particular SIGLEC receptors. That sixth subset is called 'AS-DC' and has a continuum of features including, to varying extents, those of plasmacytoid DCs (pDCs) and conventional DCs. For example, some AS-DCs are able to efficiently stimulate T cells but also express pDC markers, which suggests that they might be a confounding contaminant of procedures used to sort conventional pDCs. ***ZF***

Science **(21 April 2017) doi:10.1126/science.aah4573**

Superinduction!

Bacteria induce global inhibition of mRNA translation, which raises the question of how infected cells can launch an effective immune response. In *eLife*, Vance and colleagues provide support for one possible solution to this conundrum in a model of *Legionella* infection of macrophages. Through simultaneous measurement of transcriptional activity and translational activity, the authors find that *Legionella* blocks mainly translation elongation but also, to a lesser extent, translation initiation. In response, the host macrophage undergoes superinduction of mRNA encoding inflammatory mediators such as cytokines, without any obvious evidence for selective gene translation. Certain mRNAs encoding inflammatory molecules can be induced more than 1,000-fold. Collectively, this massive induction of mRNAs has the effect of 'saturating the system' and potentially provides an effective countermeasure to the interference, by bacteria, of host translation. *ZF*

eLife (6 April 2017) doi:10.7554/eLife.22707

Zika-neutralizing antibodies

Infection with Zika virus is asymptomatic in most people; however, devastating disease can occur in fetuses developing in infected mothers. In *Cell*, Robbiani *et al.* identify various neutralizing antibodies to Zika obtained from two independent cohorts in Brazil and Mexico. A large proportion of those antibodies are derived from somatically mutated B cell clones bearing V_H3-23–V_κ1-5 immunoglobulin chains. Structural analysis reveals interaction between both immunoglobulin chains and two adjacent amino acid residues, Glu393 and Lys394, found in domain III of the Zika envelope protein. Similar antibody recognition occurs with envelope protein of dengue virus serotype 1 but not with envelope proteins of other related flaviviruses. The authors show that neutralizing cross-reactivity occurs in people exposed to dengue virus serotype 1 before infection with Zika virus, which might explain the higher frequency of neutralizing antibodies identified in their cohorts. ***LAD***

Cell **(4 May 2017) doi:10.1016/j.cell.2017.04.024**

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

Fertilization and nucleic acid sensing

During fertilization, sperm-cell-derived DNA can be found in the oocyte cytoplasm. In *Immunity*, Abe *et al.* identify NLRP14 as a negative regulator of the cytosolic nucleic-acid-sensing pathway expressed specifically in germline cells. Deletion of NLRP14 enhances induction of the cGAS–STING and RIG-I–MAVS pathways in response to various DNA and RNA in 293T human embryonic kidney cells with ectopic expression of the components of these pathways, while overexpression of NLRP14 has the opposite effect. Overexpressed NLRC14 interacts with the kinase TBK1 and induces its polyubiquitination and a decrease in TBK1 protein. A previously described mutant NLRP14 with a stop codon at amino acid 108 that is associated with spermatogenic failure does not interact with TBK1 and fails to inhibit the TBK1-dependent activation of the transcription factors IRF3 and NF-κB. NLRP14 is downregulated immediately after fertilization, which indicates that modulation of the nucleic-acid-sensing pathways is required for normal fertilization. *IV*

Immunity **46**, 621–634 (2017)

Exploitation by Mtb

Elaboration of nitric oxide (NO) is necessary for control of *Mycobacterium tuberculosis* infection, yet it remains unclear how NO mediates protection. Bacterial counts are higher in hosts deficient in NO production, and severe disease ensues. In *Nature Microbiology*, Mishra *et al.* show that NO prevents exuberant neutrophilic responses to mycobacterial infection by suppressing the production of interleukin 1 (IL-1) and 12/15-lipoxygenase. Loss of NO production does not alter the control of intracellular bacteria in *Nos2*$^{-/-}$ macrophages, which suggests that the defective control is not cell autonomous. Instead, sustained influx of neutrophils leads to enhanced host-cell death and the release of iron and lipid nutrients that favor bacterial growth. Inhibition or deletion of inflammasome NLRP3, the IL-1 receptor or 12/15-lipoxygenase (ALOX12 in humans) diminishes the influx of neutrophils into infected lungs and lessens disease severity in mice, whereas increased ALOX12 activity in humans is correlated with more-severe disease. Thus, targeting this regulatory pathway might be beneficial in treating infection with *M. tuberculosis*. ***LAD***

Nat. Micro. **2, 17072 (2017)**

Enchained growth

Because classical agglutination mediated by immunoglobulin A (IgA) is inefficient at pathogen densities typically achieved during infection in the gut lumen, it remains unclear how IgA protects against bacterial pathogens *in vivo*. In *Nature*, Moor *et al.* show that high-affinity IgA-mediated cross-linking prevents daughter-cell separation after division and that such 'enchained growth' accelerates pathogen clearance. Oral vaccination in a mouse model of salmonellosis induces high-avidity, lipopolysaccharide-binding IgA antibodies that act protectively by inducing bacterial clumping in chain structures driven by bacterial growth rather than by collision. Enchained growth is density independent and drives clump formation at densities characteristic of natural infection with *Salmonella typhimurium*. IgA-induced enchainment into clonal clumps prevents horizontal gene transfer between plasmid-positive clones and plasmid-negative clones and thus diminishes pathogen evolution. Enchained growth is also observed for *Escherichia coli* strains, which indicates that this might represent an important mechanism of the control for pathogens and commensals. *IV*

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