Apoptosis footprint

Apoptotic cells are rapidly cleared by tissue-resident phagocytic cells. In *Nature*, Cummings *et al.* show that apoptotic mouse intestinal epithelial cells in the lamina propria of the small intestine are sampled by CD11b$^-$CD103$^+$ dendritic cells (DCs) and two subsets of macrophages, CD11b$^+$CD103$^+$ and CD11b$^+$, a process that induces subset-specific anti-inflammatory signatures in the sampling cells. The authors use a transgene encoding the diphtheria toxin receptor fused to enhanced green fluorescent protein (eGFP) driven by the villin promoter to induce apoptosis in conditions that do not trigger inflammation. Following phagocytosis of apoptotic cells, tracked via the acquisition of GFP, both DCs and macrophages downregulate genes encoding pro-inflammatory products and upregulate genes encoding negative regulators of inflammation, in a pattern unique to each subset. The CD103$^+$ DCs are the only subset to upregulate genes encoding products required for instruction of a regulatory T cell program and to travel to the mesenteric lymph nodes to induce the differentiation of regulatory T cells. ***IV***

***Nature* (9 November 2016) http://dx.doi.org/10.1038/nature20138**

Motile recognition

NETosis by neutrophils is characterized by the extrusion of genomic DNA embedded with antimicrobial factors in response to bacterial or fungal infection. In *PLoS Pathogens*, Rada and colleagues investigate the mechanisms by which the opportunistic pathogen *Pseudomonas aeruginosa* triggers NETosis. Flagellated *P. aeruginosa* can elicit NETosis, but non-flagellated *P. aeruginosa* cannot. However, NETosis is not dependent on the known flagellin receptors TLR5 or NLRC4, nor is the monomeric purified form of flagellin able to trigger NETosis. Instead, what seems to be critical is the motility of flagella, because non-motile mutant bacteria that have otherwise normal flagella cannot trigger NETosis. Flagellar motility is therefore an additional parameter sensed by the immune system and used to 'tune' the extent of the neutrophil response. *ZF*

PLoS Pathog. (17 November 2016) http://dx.doi.org/10.1371/journal.ppat.1005987

CD148 function in B-1 cells

Innate-like B-1 cells are developmentally and functionally distinct from B-2 cells. In *Immunity*, Weiss and colleagues demonstrate a unique role for the receptor-like tyrosine phosphatase CD148 in regulating the B cell antigen receptor (BCR) signaling cascade in B-1 cells. Mice lacking CD148 have defective antibody responses to polysaccharide antigens (T cell independent) commonly found in bacterial capsular coats. CD148-deficient B-1 cells have diminished activation of proximal BCR signaling components. In particular, the Src-family kinase Lyn is activated by CD148 after ligation of the BCR in B-1 cells and positively regulates their production of anti-polysaccharide immunoglobulin M, whereas Lyn negatively inhibits this response in follicular B-2 cells. These findings indicate that the CD148–Lyn axis is required specifically for the antibody responses of B-1 cells and that proximal BCR signaling differs in these two B cell subsets. ***LAD***

***Immunity* (15 November 2016) http://dx.doi.org/10.1016/j.immuni.2016.10.013**

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

Counting HSCs

The enforced proliferation of hematopoietic stem cells (HSCs) replicates features of their aging. In *Cell*, Bernitz *et al.* investigate how proliferative history correlates with lineage-reconstitution potential. The authors use a H2B-GFP label-retaining system in which all the long-term (LT) hematopoietic activity is contained in a population of rarely dividing GFP^{hi} HSCs. Through the use of GFP dilution to quantify cell division *in vivo* and mathematical modeling of the effect of division history on the progression of HSCs through the cell cycle, the authors define a model in which HSCs undergo four symmetric self-renewal divisions, followed by a state of dormancy. Once they have lost the GFP label due to cell division, HSCs acquire the expression of CD41, a marker that in HSCs correlates with diminished quiescence, higher cycling rates and myeloid bias. According to this model, the fifth division results in the loss of LT-HSC potential and generates HSCs with limited self-renewal ability and a myeloid-differentiation bias. LT-HSCs are thought to divide five times during the lifespan of a mouse. *IV*

Cell **167**, 1296–1309 (2016)

Clearing liver metastases

The liver is a common end organ for metastases, but the nature of the liver-intrinsic mechanisms that control the presence of metastatic lesions in this organ is unclear. In the *Proceedings of the National Academy of Sciences USA*, Taniguchi and colleagues use a mouse model of metastasis to investigate whether liver-resident populations of immune cells regulate metastatic disease. They find that within the liver, only Kupffer cells, which are liver-resident macrophages, express the C-type lectin receptor dectin-2 to any appreciable extent. Dectin-2-deficient mice show a much greater burden of liver-metastatic disease. Kupffer cells are able to engulf metastatic cancer cells in a dectin-2-dependent manner, although the ligand on the cancer cells remains unknown. This ability to clear metastatic cancer cells might be unique to Kupffer cells, because it is not exhibited by either alveolar macrophages or bone-marrow-derived macrophages. Kupffer cells, therefore, are important in clearing metastases from the liver. ***ZF***

***Proc. Natl. Acad. Sci. USA* (21 November 2016) http://dx.doi.org/10.1073/pnas.1617903113**

TSLP in bacterial skin infection

The complement system is an ancient antimicrobial defense system, whereas the cytokine TSLP is associated with influencing lymphocyte development and contributing to type 2 immune responses and is particularly abundant in skin. In *Science Immunology*, West *et al.* report that TSLP serves a role in antibacterial responses by boosting neutrophil production of reactive oxygen species. Both mouse neutrophils and human neutrophils express the receptor for TSLP, and its expression increases after exposure to *Staphylococcus aureus*. Mice deficient in this receptor show defective neutrophil-mediated killing of bacteria and are more sensitive to skin infection. TLSP-augmented neutrophil responses require the complement protein C5. Signaling via the TSLP receptor upregulates expression of the receptor for C5a, and C5 signaling acts in synergy with TSLP to enhance reactive-oxygen-species-mediated killing of *S. aureus* and *Streptococcus pyogenes*. Hence, TSLP and complement activation provide enhanced antibacterial responses during skin infection. *LAD*

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