'Short-term' residency

The contribution of circulating lymphocytes to the small intestine epithelium is thought to be limited at steady-state, because the niches are occupied by long-lived resident γδ T cells and unconventional αβ T cells. In *The Journal of Experimental Medicine*, Guy-Grand *et al.* show that circulating cells continuously colonize the small intestine and contribute to the dynamics of resident intraepithelial lymphocytes (IELs). Whereas conventional recent thymic emigrants (RTE) circulate preferentially to lymphoid organs, unconventional RTEs express high amounts of both $\alpha_4\beta_7$ and CD62L, which makes them equally tropic for the secondary lymphoid organs or the small intestine. Circulation through the gut associated lymphoid tissue (GALT) induces high proliferative and cytotoxic potential in unconventional RTEs, whereas those directly entering the small intestine do not proliferate *in situ*. The calculated average lifespan for γδ T cells in the small intestine epithelium is 40 days, indicating continuous thymic input of unconventional T cells to this site. ***IV***

***J. Exp. Med.* (5 August 2013) doi:10.1084/jem.20122588**

ILCs in liver pathology

Hepatic fibrosis develops as a consequence of persistent inflammation in chronic liver infections or metabolic disease. In *Immunity*, Wirtz and colleagues show that interleukin 33 (IL-33) released from liver cells in the context of stress is a key mediator of hepatic fibrosis. Type 2 innate lymphoid cells (ILC2) are present in the liver of naive mice and are activated by IL-33 to produce IL-13, which in turn stimulates hepatic stellate cells to produce extracellular matrix proteins and leads to pathologic remodeling of the tissue. Other IL-33–reponsive, IL-13–producing cells, such as basophils and mast cells, were not essential for IL-33–mediated pathology, suggesting that the IL-33–ILC2 axis is the key mediator of hepatic fibrosis in several *in vivo* models of liver injury or infection. *IV*

Immunity **39**, 357–371 (2013)

Fate-mapping DCs

Determining the ontogenetic origin of tissue dendritic cells (DCs) from macrophages is difficult. In *Cell*, Reis e Sousa and colleagues describe the generation of mice bearing *Clec9a*–yellow fluorescent protein (*YFP*) alleles and use these mice to fate-map the progeny of YFP$^+$ bone marrow cells. *Clec9a* encodes a C-type lectin receptor, also known as DNGR-1, which is highly expressed in bone marrow lineage-negative CD115$^+$ pre-DCs. Adoptive transfer of these cells yields exclusively CD11c$^+$ conventional DC cells, including CD11b$^+$, CD103$^+$ and CD8α$^+$ subsets. Importantly, monocytes, neutrophils and alveolar macrophages and Langerhans cells lack YFP labeling in the *Clec9a-YFP* mice. These data support the notion that Langerhans cells are a macrophage subset rather than DC subset. These mice thus provide a useful model to study the functional roles of distinct DC populations as compared to macrophages. ***LAD***

***Cell* 154, 843–858 (2013)**

mTOR in T_{reg} cells

The metabolic regulator mTOR senses nutrient availability and influences cell functionality. In *Nature*, Chi and colleagues show that mTORC1 directs regulatory T (T_{reg}) cell function *in vivo*. Targeted deletion of raptor, a component of mTORC1, leads to loss of ICOS and CTLA-4 expression, although CD25 and Foxp3 expression is not altered. Mice whose T_{reg} cells lack raptor develop a 'scurfy-like' autoimmune disease, consistent with a loss of effective suppressor cells. Conversely, targeted loss of rictor, which forms mTORC2 complexes, does not alter T_{reg} cell function. Interestingly, loss of mTORC1 also decreases cholesterol biosynthesis and lipid metabolism. Pharmacologic inhibition of cholesterol biosynthesis in wild-type T_{reg} cells likewise decreases T_{reg} cell suppressive ability, whereas addition of mevalonate, a key intermediate in this pathway, restores suppressive activity. Thus, mTORC1 regulates T_{reg} cell function by influencing cholesterol biosynthesis and inhibitory costimulation molecules. *LAD*

Nature **499**, 485–490 (2013)

Location is only part of the story

Gut-associated lymphoid tissue is particularly efficient at generating induced regulatory T cells (iT$_{reg}$ cells). In *Mucosal Immunology*, Pabst and colleagues use reciprocal lymph node (LN) transplantation to determine the roles of node-intrinsic and node-extrinsic factors in the generation of iT$_{reg}$ cells. Gut-draining LNs (mesenteric and celiac) maintain efficient iT$_{reg}$ cell–generating capacity even when transplanted to the popliteal fossa. Popliteal LNs transplanted to the mesenteries acquire iT$_{reg}$ cell–generating capacity, suggesting an influence of gut-draining antigens, but they are not as efficient as mesenteric LNs, so node-intrinsic factors must also be important. Depletion studies indicate that cooperation between stromal cells and dendritic cells are critical for the efficient iT$_{reg}$ cell-generating capacity of gut-draining LNs. Therefore both the position of the LN in the body as well as the inherent properties of the cells in the LN determine its function. ***ZF***

***Mucosal Immunol.* (14 August 2013) doi:10.1038/mi.2013.54**

Holding a latent virus at bay

Herpes simplex virus 1 (HSV-1) infection results in life-long latency of the virus in the trigeminal ganglia. In *PLoS Pathogens*, Verjans and colleagues use human cadavers to investigate the CD4$^+$ and CD8$^+$ T cell response to latently infected neurons in the trigeminal ganglia. Both CD4$^+$ and CD8$^+$ T cells are found juxtaposed to latently infected neurons. Both types of T cell show evidence of recent activation in the ganglion itself. Moreover, CD8$^+$ T cells upregulate granzyme B and perforin and the expression of these cytolytic molecules correlates with HSV-1 load. Clones generated from the T cells infiltrating the ganglia of the various donors responded to a range of known HSV-1 antigens. The identification of seemingly productive immune responses in the ganglia itself suggests it might be possible to design subunit vaccines capable of preventing the reactivation of latent virus. *ZF*

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