In vivo role for Vpr

Of the four accessory proteins expressed by human immunodeficiency virus type 1 (HIV-1), Vpr is the least well understood. In *PLoS Pathogens*, Koyanagi and colleagues use a humanized mouse model to demonstrate the important role of Vpr in accelerating HIV-1 replication. Regulatory T cells (T_{reg} cells) show 'preferential' infection with CCR5-tropic HIV-1, but not with CXCR4-tropic HIV-1, by virtue of their inherently high turnover rate and high expression of the entry coreceptor CCR5. Infection of T_{reg} cells by HIV-1 results in their apoptosis and concomitant generalized activation of the immune system. Similarly, pharmacological depletion of T_{reg} cells leads to the activation and proliferation of conventional T cells and a higher viral burden. Mutants with defective Vpr, however, show less infection and loss of T_{reg} cells as well as a lower viral burden. The decrease in T_{reg} cell numbers through the action of Vpr thus leads to impaired homeostatic regulation of conventional T cells and thereby increases the pool of activated cell targets and optimal HIV-1 replication. ***ZF***

***PLoS Pathog.* (5 December 2013) doi:10.1371/journal.ppat.1003812**

Mucus specificity

The mucus on mucosal barriers traps particles and pathogens and eliminates them through mucociliary clearance. In *Nature*, Evans and colleagues show that in mice, the mucin MUC5B is required for mucociliary clearance, homeostasis of the immune system and control of infection in the airways. MUC5A-deficient mice have upper airway obstruction with defective breathing and develop spontaneous and fatal infection with *Staphylococcus aureus*. Macrophages showing phagocytic exhaustion and signs of apoptosis accumulate in the lungs of MUC5A-deficient mice. However, activation of macrophages and elimination of *S. aureus* are enhanced in mice with transgenic expression of *Muc5b*. MUC6 is known to inhibit *Helicobacter pylori*, whereas MUC5AC inhibits *Trichuris muris*, but neither inhibits *S. aureus* growth, which suggests specificity in mucin-mediated defenses. Human *MUC5B* is highly polymorphic and promoter variants with higher expression are also known, which suggests that MUC5B variants may regulate airway homeostasis in humans. *IV*

Nature (8 December 2013) doi:10.1038/nature12807

Muscle T_{reg} cells

T_{reg} cells are important regulators of immune responses. In *Cell*, Mathis and colleagues show that phenotypically and functionally distinct T_{reg} cells accumulate in injured skeletal muscle and contribute to repair processes. T_{reg} cells in injured muscle have a 'regulatory T cell' profile but distinctly express amphiregulin, which functions as a muscle-repair factor by enhancing the differentiation of precursors of muscle cells and dampens the expression of proteins associated with fibrosis. T_{reg} cells in muscle tissue undergo clonal expansion and have a T cell receptor repertoire distinct from that of splenic T_{reg} cells or conventional T cells. Intramuscular depletion of T_{reg} cells results in enhanced inflammatory responses in the injured muscle with impaired regeneration of muscle fibers. Along with data describing a role for T_{reg} cells in visceral fat, these observations support the idea that T_{reg} cells have homeostatic functions beyond the immune system. ***IV***

***Cell* 155, 1282–1295 (2013)**

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

Virus-induced autophagy

Upregulation of the kinase GCN2 correlates with protective immune responses induced by YF-17D, a live attenuated vaccine against yellow fever virus. In *Science*, Ravindran *et al.* investigate how activation of GCN2 enhances the immune response elicited by YF-17D. GCN2 is a sensor of the intracellular abundance of amino acids and induces an autophagic stress response in antigen-presenting dendritic cells (DCs) after infection with live-virus vaccines but not after vaccination with killed viruses. Mice deficient in GCN2 have fewer virus-specific $CD4^+$ and $CD8^+$ T cells, which suggests a defect in the priming of T cell responses. GCN2-deficient DCs have defective induction of autophagy and diminished cross-presentation of antigen. Similarly, DCs that lack expression of the autophagy proteins beclin-1, Atg5 or Atg7 are defective in cross-presentation. Curiously, priming of cells of the immune system is enhanced when both DCs and the dying YF-17D-infected cells express GCN2. Hence, infection with live virus depletes amino acid stores, which activates GCN2-dependent autophagy and enhances cross-presentation and the induction of protective adaptive immunity. *LAD*

Science (5 December 2013) doi:10.1126/science.1246829

Aging B cell repertoires

Elderly humans respond less robustly to vaccination than do younger people; however, there are discrepancies in the literature on the characteristics of the elderly B cell repertoire. In the *Journal of Immunology*, Wang *et al.* examine the repertoire of genes encoding the immunoglobulin heavy chain (*IGH*) in young and elderly adults to determine what effects aging or chronic viral infection have on B cell populations. Age does not affect the use of variable, diversity or joining segments; however, older people lose the selection against longer complementarity-determining region 3 segments, which suggests a difference in tolerance mechanisms. People who are positive for Epstein-Barr virus have large, persistent expanded B cell clones, whereas those positive for cytomegalovirus have a higher frequency of highly mutated *IGH* in their IgM^+ and IgG^+ B cell repertoire. These findings suggest that earlier reports may have missed the influence of chronic infection and may have instead attributed such effects to the aging process. ***LAD***

***J. Immunol.* (11 December 2013) doi:10.4049/jimmunol.1301384**

A cold wake-up call for immunity

The ambient temperature at which mice are housed is generally an overlooked parameter, yet it can have a substantial influence on a wide range of experimental results. In the *Proceedings of the National Academy of Sciences*, Repasky and colleagues demonstrate how antitumor responses can vary according to whether mice are maintained at conventional housing temperatures (22–23 °C) or mouse 'thermoneutral' temperatures (30–31 °C). Mice kept under thermoneutral conditions have less tumor growth and metastasis in various standard models. The use of either immunodeficient hosts or depletion of cytotoxic T cells abolishes any temperature-dependent differences in tumor growth. Furthermore, under thermoneutral conditions, mice have a greater abundance of cytotoxic T cells, with more activation and interferon-γ production, as well as fewer T_{reg} cells in the tumor mass. Ambient temperature, therefore, has a considerable effect on antitumor functionality in mice, and the standard housing conditions in which mice are maintained triggers cold stress and may impair such responses. *ZF*

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