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 Tree 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

Treg 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 Treg cells have homeostatic IV functions beyond the immune system. Cell 155, 1282-1295 (2013)

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-y 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

Proc. Natl. Acad. Sci. USA 110, 20176-20181 (2013)

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