IN BRIEF

INFECTIOUS DISEASE

Fungal restriction of renal T cell migration

Although $CD4^+$ T cells, particularly T helper 17 (T_H17) cells, have a crucial role in antifungal immunity, it has been thought that T cells are redundant for the control of renal *Candida albicans* infection. Drummond *et al.* characterized the T cell response during systemic candidiasis and found that the antigen-specific $CD4^+$ T cell response in the renal lymph nodes was increased at day 3 post infection with the *C. albicans* strain Calb-Ag. However, this response became blunted at day 6. Furthermore, antigen-specific $CD4^+$ T cells did not migrate to the infected kidneys, although $CD8^+$ T cell recruitment was not affected. Enforced $CD4^+$ T cell migration using antigen-loaded immunoliposomes resulted in the accumulation of antigen-specific T_H17 cells and decreased fungal burdens in the kidneys. Although the reason for the defective migration of $CD4^+$ T cells to the kidneys remains to be determined, restoring tissue $CD4^+$ T cell responses helps to control fungal growth in the kidneys.

ORIGINAL RESEARCH PAPER Drummond, R. A. *et al.* Failure of antigen-specific $CD4^+$ T cell recruitment to the kidney during systemic candidiasis. *J. Immunol.* http://dx.doi.org/ 10.4049/jimmunol.1401675 (2014)

INNATE IMMUNITY

IFNs lead TLR4 responses down the TRIF path

Toll-like receptor 4 (TLR4) signals via two distinct pathways — one engages the adaptor protein MYD88 and the other is driven by TRIF. The MYD88 pathway is associated with the induction of pro-inflammatory gene expression, whereas the TRIF pathway is considered to be less inflammatory and more efficient at supporting adaptive immune responses. As such, there is interest in using TRIF-biased TLR4 agonists for vaccine purposes, as they are likely to be less toxic. Previous studies suggested that structural differences in TLR4 ligands may lead to the preferential activation of the TRIF pathway. However, Kolb *et al.* found that all of the TLR4 agonists that they tested were biased towards TRIF signalling, with these agonists activating the TRIF pathway at lower concentrations than were necessary for MYD88 activation. Notably, this TRIF bias was driven by type I interferons (IFNs), as equivalent concentrations of TLR4 agonists were necessary to recruit MYD88 and TRIF when IFN-mediated signalling was blocked.

ORIGINAL RESEARCH PAPER Kolb, J. P. *et al.* Cutting edge: type I interferon signaling contributes to the bias that Toll-like receptor 4 exhibits for signaling mediated by the adaptor protein TRIF. *Sci. Signal.* **7**, ra108 (2014)

ANTIVIRAL IMMUNITY

Linking lncRNA to IFN regulation

In this study, the authors identified a host long non-coding RNA named NRAV (negative regulator of antiviral response) that affects host control of influenza A virus replication in human alveolar epithelial cells. The expression of NRAV is downregulated during influenza virus infection and overexpression of NRAV was found to promote viral replication by suppressing the expression of several key interferon-stimulated genes (ISGs). The authors speculate that NRAV controls the expression of these ISGs in uninfected cells, and when a virus infection is sensed, a reduction in the levels of NRAV increases ISG expression, which promotes control of the viral infection.

ORIGINAL RESEARCH PAPER Ouyang, J. *et al.* NRAV, a long noncoding RNA, modulates antiviral responses through suppression of interferon-stimulated gene transcription. *Cell Host Microbe* **16**, 616–626 (2014)