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SPOTLIGHT

Articles of Significant Interest Selected from This Issue by the Editors

Novel PYRIN-Only Protein as a Regulator of Inflammasome-Mediated Interleukin-1β Generation

Activation of inflammasomes is required for the processing of the caspase-1 substrates pro-interleukin-1β (pro-IL-1β) and pro-IL-18 in response to pathogen infection and is mediated by PYRIN domain (PYD)-containing proteins via PYD-PYD interactions. Dorfleutner et al. (p. 1484–1492) identified a novel protein, cPOP2, composed of only a PYD, which prevents processing and secretion of IL-1β. This protein interacts with specific PYD-containing pathogen recognition receptors of the NLR family and the adaptor protein ASC and thereby prevents the recruitment of essential PYD-containing proteins into inflammasomes. These data suggest a novel regulatory mechanism for modulating inflammation during host response.

Small-Molecule Inhibitor of Type III Secretion Effector ExoU

The goal of identifying virulence factors of bacterial pathogens is to provide targets for the development of vaccines and therapeutics. Lee et al. (p. 1089–1098) utilized a chemical genetics approach to identify a number of compounds that can specifically inhibit ExoU, a *Pseudomonas aeruginosa* virulence factor delivered by a type III secretion system (TTSS). The whole-cell assay approach suggests the possibility of identifying inhibitors that act at a number of steps in the TTSS delivery pathway. These small-molecule inhibitors can be used to dissect the function of individual effectors and act as leads to potential antivirulence-based therapeutics.

Protective Role of Interleukin-12 in Host Defense against Pneumococcal Infection

Current vaccines against *Streptococcus pneumoniae* provide only limited protection to selected serotypes, and procedures to induce effective innate immunity are hampered by the lack of information regarding the cells required for defense against this pathogen. Sun et al. (p. 1196–1202) now demonstrate that intranasal interleukin-12 (IL-12) treatment of mice can significantly improve protection against pneumococcal respiratory infection. Their findings show that IL-12 induces gamma interferon production in the lung, which in turn promotes recruitment of neutrophils and, ultimately, bacterial clearance. These results indicate that protection against extracellular bacterial pathogens in the lung represents another important function for IL-12.

Antigenic Variation Comes at a Cost

Anaplasma marginale is a prototypical vector-borne pathogen that establishes persistent infection in reservoir mammalian hosts by antigenic variation. The repertoire of antigenic variants is initially generated by gene conversion using intact chromosomal donor sequences but later depends on mosaics assembled using gene segments from multiple different donors. Palmer et al. (p. 1502–1506) report that these mosaics, required for long-term persistence, exact a fitness cost to the pathogen that is tolerated only under immune pressure. This illustrates the balance between variation to evade immune clearance and the need to maintain growth fitness, with the genome reflecting both selective pressures.

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