The Journal of Immunology

IN BRIEF | DECEMBER 01 2022

Top Reads FREE

Online Issn: 1550-6606
Print Issn: 0022-1767

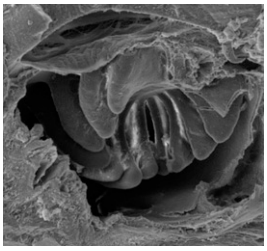
2022

Copyright © 2022 by The American Association of Immunologists, Inc.

J Immunol (2022) 209 (11): 2071.
https://doi.org/10.4049/jimmunol.2290023

The Journal of Immunology

Novel Lymphoid Structure in Trout

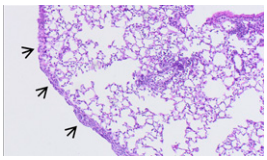


In this Top Read, Garcia et al. (p. 2215) reported a novel organized nasopharynx-associated lymphoid tissue (O-NALT), which resides within the nasal cavity of young trout and responds to vaccination in a way similar to mammalian germinal centers. This tissue contained organized aggregates of mostly CD4-2b$^+$ T cells and IgM$^+$ B cells, as well as a minor population of CD8a$^+$ T cells and IgT$^+$ B cells, though there was no evidence of distinct B and T cell zones. Intranasal vaccination with live attenuated infectious hematopoietic necrosis virus increased the number of all four cell types within the O-NALT, including proliferating and apoptotic IgM$^+$ B cells, but not in surrounding tissue. Finally, vaccine-dependent changes in expression of *aicda*, *cxcr4*, and *cxcr5*, cellular markers for B cell selection and maturation in mammalian germinal centers, were evident in the O-NALT, and were markedly different compared with those observed in the surrounding tissue. The discovery of the O-NALT, and its function in trout as a site of immune cell responses, confirms the existence of mucosa-associated lymphoid tissues in nonmammalian vertebrates, providing improved understanding of the evolution of adaptive immune responses in vertebrates.

MPYS Modulates Adipose Immune Tolerance

In this Top Read, Mansouri et al. (p. 2114) explored how the MPYS allele impacts immune tolerance. MPYS, or stimulator of IFN genes (STING), is a potent type I IFN stimulator, mediating responses to intracellular dsDNA. There are two dominant variants of the MPYS allele: R71H-G230A-R293Q (*HAQ*) and G230A-R293Q (*AQ*). Using AQ and HAQ knock-in mice, the authors showed that AQ mice have less fat storage and less inflammation in their epididymal white adipose tissue than HAQ and control mice. Furthermore, epididymal white adipose tissue in AQ mice contained more M2 macrophages as well as regulatory T cells (Tregs) and showed enhanced fatty acid metabolism compared with HAQ and control mice. Using conditional knockout mice and adoptive cell transfer, the authors showed that MPYS functions intrinsically in both macrophages and Tregs. In AQ mice, the MYPS effects are independent of type I IFNs. Mechanistically, the N-terminal region of MPYS interacts with activated fatty acid, fatty acyl–CoA, and AQ and HAQ MPYS have different conformations. Collectively, these data show that MPYS is important in controlling immune cell fatty acid metabolism.

Pneumonia Inflamm-aging



In this Top Read, Hollwedel et al. (p. 2172) compared the immune response of young and aged mice to infection with *Klebsiella pneumoniae*. Aged mice showed increased bacterial burden, proinflammatory cytokine responses, and mortality compared with young mice, and only the aged mice developed neutrophilic pleuritis. Inflammation following *K. pneumoniae* infection of aged mice was mitigated by caspase-1 inhibition, which decreased Nlrp3 inflammasome activation and IL-1β release. After transplantation of young bone marrow, the aged mice did not exhibit increased inflammation or bacterial burden compared with controls, demonstrating that aged mice have bone marrow–intrinsic defects in responding to *K. pneumoniae* infection. This work suggests that the bone marrow environment may be responsible for the inflamm-aging phenotypes seen in the elderly.

Poor Antitumor Vaccine Response in Dirty Mice

In this Top Read, Sjaastad et al. (p. 2149) characterized the T cell response of specific pathogen-free (SPF) mice compared with microbially experienced "dirty mice" to understand how microbial exposure of the immune system relates to efficacy of antitumor vaccination. First, SPF mice and SPF mice cohoused (CoH) with pet store mice were immunized with an adjuvanted cancer subunit vaccine (TriVax) to stimulate Ag-specific CD4$^+$ and CD8$^+$ T cells, and then challenged with tumor cells. TriVax-immunized CoH mice, like unvaccinated mice, failed to control tumor growth, whereas tumors in vaccinated SPF mice were significantly smaller. Reciprocal adoptive transfer of TCR-transgenic T cells between SPF and CoH mice showed that Ag-specific CD8$^+$ T cells failed to expand after vaccination only in the CoH mice, suggesting that the impact within CoH mice is extrinsic to T cells. The authors found a significant increase in IL-27p28 production by XCR1$^+$ type 1 conventional dendritic cells only in SPF mice after vaccination. Accordingly, administration of recombinant IL-27:EBI3 complex to CoH mice after vaccination enhanced CD4$^+$ and CD8$^+$ T cell expansion. Altogether, the data suggest that differences in the dendritic cell compartment, specifically in IL-27p28 production, may account for discrepancies in T cell responses observed in preclinical studies, which often use SPF mice, versus clinical studies of vaccine-mediated antitumor immunity.

www.jimmunol.org/cgi/doi/10.4049/jimmunol.2290023