Mast Cells and More

Mast cells were described and named by Paul Ehrlich in 1879. The observation was based on their unique dye-staining properties. The key roles of mast cells in allergic reactions through IgE-dependent release of histamine are well established [1]. However, mast cells also have a characteristic content of proteases, to which important roles in emerging states of disease, such as neoplastic disorders, mastocytosis, and hereditary α -tryptasemia, are attributed [2]. In this issue, Aida Paivandy and Gunnar Pejler [3] review current and future strategies to dampen harmful mast cell activities. This includes targeting of released mediators and corresponding receptors, inhibition of cellular activation, limiting mast cell proliferation and induction of apoptosis. This will become important in a broad set of diseases. Not least in developing countries, helminthic infestation and tuberculosis commonly occur in parallel. In a highly interesting study, Togarsimalimath et al. [4] show that helminths increase the killing of *Mycobacterium tuberculosis* owing to direct stimulatory effects of helminth antigens on phagocytic cells. In addition to macrophages, neutrophils play important roles in host defense against tuberculosis [5]. Interestingly, tapeworms release proteoglycans impairing the neutrophils' chemotaxis through inhibition of p38 MAP kinase activation [6]. Thus, the interactions of helminths with host defense are complex.

The complement system is an important arm of innate immunity [7, 8]. In their study, Mommert et al. [9] show that epidermal keratinocytes upregulate the C3a/anaphylatoxin–C3a receptor axis after stimulation with different TLR ligands. Their findings demonstrate that local generation and activation of complement is likely to be important at epithelium-covered barriers.

SARS-CoV-2 overshadows other important RNA viruses during the ongoing pandemic. However, one should not forget that the Zika virus quite recently emerged as an important pathogen. Our understanding of how RNA viruses interact with host defense, including the importance of long noncoding RNA, increases rapidly [10, 11]. In their article, Wang et al. [12] show that a long noncoding RNA (OASL-IT1) is important for increasing the levels of interferons and the subsequent activation of innate immune signaling pathways that are triggered by Zika virus infection. This mechanism may provide a template for the development of future therapeutic strategies.

We hope that this issue of *Journal of Innate Immunity* contains articles that the readership will enjoy reading.

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References

- 1 Valent P, Akin C, Hartmann K, Nilsson G, Reiter A, Hermine O, et al. Mast cells as a unique hematopoietic lineage and cell system: from Paul Ehrlich's visions to precision medicine concepts. *Theranostics*. 2020 Aug; 10(23):10743–68.
- 2 Pejler G. Novel Insight into the in vivo Function of Mast Cell Chymase: Lessons from Knockouts and Inhibitors. *J Innate Immun*. 2020;12(5):357–72.
- 3 Paivandy A, Pejler G. Novel Strategies to Target Mast Cells in Disease. *J Innate Immun*. 2021 Feb;1–17. doi: 10.1159/000513582.
- 4 Togarsimalimath SK, Pushpamithran G, Schön T, Stendahl O, Blomgran R. Helminth Antigen Exposure Enhances Early Immune Control of Mycobacterium tuberculosis in Monocytes and Macrophages. *J Innate Immun*. 2020 Dec;1–16. doi: 10.1159/000512279.
- 5 Andersson AM, Larsson M, Stendahl O, Blomgran R. Efferocytosis of Apoptotic Neutrophils Enhances Control of Mycobacterium tuberculosis in HIV-Coinfected Macrophages in a Myeloperoxidase-Dependent Manner. *J Innate Immun*. 2020;12(3):235–47.
- 6 Graves N, Venu VP, Yipp BG, Petri B, Hirota S, Gilleard J, et al. A Trypsin-Sensitive Proteoglycan from the Tapeworm Hymenolepis diminuta Inhibits Murine Neutrophil Chemotaxis in vitro by Suppressing p38 MAP Kinase Activation. *J Innate Immun*. 2019;11(2): 136–49.
- 7 van den Broek B, van der Flier M, de Groot R, de Jonge MI, Langereis JD. Common Genetic Variants in the Complement System and their Potential Link with Disease Susceptibility and Outcome of Invasive Bacterial Infection. *J Innate Immun*. 2020;12(2):131–41.
- 8 Laabei M, Ermert D. Catch Me if You Can: Streptococcus pyogenes Complement Evasion Strategies. *J Innate Immun*. 2019;11(1):3–12.
- 9 Mommert S, Doenni L, Szudybill P, Zoeller C, Beyer FH, Werfel T. C3a and Its Receptor C3aR Are Detectable in Normal Human Epidermal Keratinocytes and Are Differentially Regulated via TLR3 and LL37. *J Innate Immun*. 2021 Jan;1–15. doi: 10.1159/000512547.
- 10 Kikkert M. Innate Immune Evasion by Human Respiratory RNA Viruses. *J Innate Immun*. 2020;12(1):4–20.
- 11 Yue L, Yin X, Hao F, Dong J, Ren X, Xu O, et al. Long Noncoding RNA Linc00632 Inhibits Interleukin-13-Induced Inflammatory Cytokine and Mucus Production in Nasal Epithelial Cells. *J Innate Immun*. 2020;12(1):116–28.
- 12 Wang Y, Huo Z, Lin Q, Lin Y, Chen C, Huang Y, et al. Positive Feedback Loop of Long Noncoding RNA OASL-IT1 and Innate Immune Response Restricts the Replication of Zika Virus in Epithelial A549 Cells. *J Innate Immun*. 2021 Feb;1–15. doi: 10.1159/000513606.