Some Like It Hot

This year, the Nobel Prize in Physiology or Medicine has been awarded to David Julius and Ardem Patapoutian for their work on exploring the molecular basis for sensing heat, cold, and mechanical force. Though the research by the two Nobel Laureates is not at all dealing with the innate immune system, there are a number of common aspects involved. For instance, using receptors for sensing heat, cold, and touch will allow an organism to interact with its environment and alert if there is a dangerous situation. While the research of David Julius and Ardem Patapoutian addresses the exterior environment, the innate immune system is serving the same purpose inside an organism. Also, here, sensing heat is an essential parameter as already discovered by the Roman encyclopedist Aulus Cornelius Celsus more than 2,000 years ago. He identified an increase in the body temperature as one of the four cardinal signs of inflammation, which are, apart from *calor* (warmth), also *dolor* (pain), *tumor* (swelling), and *rubor* (redness) [1].

This issue of *Journal of Innate Immunity* is yet another example underlining that changes in temperature are of great importance in our fight against infectious diseases. For instance, the review article by Gabarin et al. [2] is addressing the role of intracellular and extracellular lipopolysaccharide signaling in sepsis. Notably, sepsis, a life-threatening condition, is characterized by an increased body temperature [3], which is often a sign of systemic inflammatory reactions that can be caused, for instance, by a cytokine storm [4–6].

In addition to sepsis, also allergic reactions can influence the body temperature. In particular, eosinophils have been described in these processes [7]. In this issue, Luo et al. [8] illustrate that flagellin can alleviate airway allergic response by stabilizing eosinophils by modulating oxidative stress. Eosinophils have recently attracted considerable attention as, among many other functions, they can be used as biomarkers in chronic obstructive pulmonary disease [9] and are involved in adipose tissue inflammation [10].

Likewise, also viral infections can trigger many pathological immune responses, including fever. Odoardi et al. [11] report in their article, published in this issue, that IL-27 has an important immunomodulatory role in Toll-like receptor 7 (TLR7) and TLR8 responses in viral infection. Though many other studies have shown that interleukins and TLRs are critical in evoking systemic inflammation in infectious diseases [12–14], the authors describe for the first time a prominent role for TLR8 in responding to ssRNA viruses and, therefore, they provide insight into how myeloid cell TLR-mediated responses are regulated during virus infection [11].

Another example is BAM15, a mitochondrial protonophore uncoupler, that was studied by Dang et al. [15]. Notably, mitochondrial uncouplers are involved in the thermoregulation and proton flux across membranes. Dang et al. [15] found in their study that Bam15 can attenuate inflammatory reaction in mice treated with the lipopolysaccharide.

However, not all immune regulatory mechanisms are modulated by heat and, for instance, the two remaining articles published in this issue do not deal with the role of temperature changes in the innate immune system. Instead, Khalili et al. [16] show in their article that the expression of a dominant-active form of the Ras oncogene in *Drosophila* salivary glands can lead to redistribution of components of the basement membrane and fibrotic lesions, and Lum et al. [17] report that hypoxia-inducible

factor 1 α is dispensable for clearing Group B streptococcal infections. In both articles, temperature changes do not affect the experimental models.

As always, we hope that the articles published in this issue will attract the attention of the readership of *Journal of Innate Immunity*.

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References

- 1 Talamonti G, D'Aliberti G, Cenzato M. Aulus Cornelius Celsus and the head injuries. *World Neurosurg.* 2020 Jan;133:127–34.
- 2 Gabarin RS, Li M, Zimmer PA, Marshall JC, Li Y, Zhang H. Intracellular and extracellular lipopolysaccharide signaling in sepsis: avenues for novel therapeutic strategies. *J Innate Immun.* 2021 May:1–10.
- 3 Olinder J, Ehinger D, Liljenborg E, Herwald H, Rydén C. Plasma levels of hepcidin and reticulocyte haemoglobin during septic shock. *J Innate Immun.* 2020;12(6):448–60.
- 4 Linder A, Fjell CD, Inghammar M, Hsu J, Walley KR, Boyd JH, et al. The specific organism: not bacterial gram type: drives the inflammatory response in septic shock. *J Innate Immun.* 2020;12(2):182–90.
- 5 Beenakker KG, Westendorp RG, de Craen AJ, Chen S, Raz Y, Ballieux BE, et al. Men have a stronger monocyte-derived cytokine production response upon stimulation with the gram-negative stimulus lipopolysaccharide than women: A pooled analysis including 15 study populations. *J Innate Immun.* 2020;12(2):142–53.
- 6 Siemens N, Oehmcke-Hecht S, Hoßmann J, Skorka SB, Nijhuis RH, Ruppen C, et al. Prothrombotic and proinflammatory activities of the β -hemolytic group B Streptococcal pigment. *J Innate Immun.* 2020;12(4):291–303.
- 7 Fulkerson PC, Rothenberg ME. Eosinophil development, disease involvement, and therapeutic suppression. *Adv Immunol.* 2018;138:1–34.
- 8 Luo XQ, Liu J, Mo LH, Yang G, Ma F, Ning Y, et al. Flagellin alleviates airway allergic response by stabilizing eosinophils through modulating oxidative stress. *J Innate Immun.* 2021 Jul:1–12.
- 9 Sivapalan P, Jensen JU. Biomarkers in chronic obstructive pulmonary disease: emerging roles of eosinophils and procalcitonin. *J Innate Immun.* 2021 Aug:1–9.
- 10 Michailidou Z, Gomez-Salazar M, Alexaki VI. Innate immune cells in the adipose tissue in health and metabolic disease. *J Innate Immun.* 2021 Apr:1–27.
- 11 Odoardi N, Kourko O, Petes C, Basta S, Gee K. Tlr7 ligation inhibits tlr8 responsiveness in il-27-primed human thp-1 monocytes and macrophages. *J Innate Immun.* 2021 May:1–14.
- 12 Zyzak J, Mitkiewicz M, Leszczyńska E, Reniewicz P, Moynagh PN, Siednienko J. HSV-1/TLR9-mediated IFN β and TNF α induction is Mal-dependent in macrophages. *J Innate Immun.* 2020;12(5):387–98.
- 13 Liu Y, Mo CF, Luo XY, Li H, Guo HJ, Sun H, et al. Activation of Toll-like receptor 3 induces interleukin-1 receptor antagonist expression by activating the interferon regulatory factor 3. *J Innate Immun.* 2020;12(4):304–20.
- 14 Grahner A, Weiss R, Schilling E, Stanslowsky N, Sack U, Hauschildt S. CD14 counterregulates lipopolysaccharide-induced tumor necrosis factor- α production in a macrophage subset. *J Innate Immun.* 2019;11(4):359–74.
- 15 Dang CP, Issara-Amphorn J, Charoensapakit A, Udompornpitak K, Bhunyakarnjanarat T, Saisorn W, et al. Bam15, a mitochondrial uncoupling agent, attenuates inflammation in the LPS injection mouse model: an adjunctive anti-inflammation on macrophages and hepatocytes. *J Innate Immun.* 2021 Jun:1–17.
- 16 Khalili D, Kalcher C, Baumgartner S, Theopold U. Anti-fibrotic activity of an antimicrobial peptide in a drosophila model. *J Innate Immun.* 2021 May:1–15.
- 17 Lum GR, Mercado V, van Ens D, Nizet V, Kimmey JM, Patras KA. Hypoxia-inducible factor 1 α is dispensable for host defense of group B streptococcus colonization and infection. *J Innate Immun.* 2021 May:1–13.