MEETING REPORT

“Novel insights into the roles of mast cells and basophils”: Joint Webinar of the Japanese and the European Histamine Research Societies (JHRS/EHRS)

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Received: 2 April 2022 / Accepted: 10 April 2022 / Published online: 4 May 2022
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Abstract
The joint webinar of the Japanese (JHRS) and the European (EHRS) Histamine Research Society focusing on “Novel insights into the roles of mast cells and basophils” was organized in hybrid format on January 7, 2022 during the 23rd meeting of the JHRS held in Kyoto, Japan. Tissue mast cells and circulating basophils are the primary sources of histamine, and they are considered to be pivotal components shaping inflammatory and immune-related processes. The webinar comprised four lectures delivered by experts in the field from Japan and the European Mast Cell and Basophil Research Network (EMBRN) that exposed novel insights into the contribution of basophils and mast cells in inflammatory and (auto)immune diseases, including allergies, asthma, and urticaria. Several targets were also highlighted in terms of developing novel and improved treatments for these pathologies.

A webinar on “Novel insights into the roles of mast cells and basophils” was co-organized by the Japanese Histamine Research Society (JHRS) [1] and the European Histamine Research Society (EHRS) [2] on January 7, 2022. This was the second joint JHRS/EHRS event and took place during the 23rd meeting of the JHRS held in Kyoto, Japan. The webinar was organized and chaired by the President of the Organizing Committee of the 23rd JHRS meeting, Professor Satoshi Tanaka (Kyoto, Japan), and the President of the EHRS, Professor Katerina Tiligada (Athens, Greece), with contributions from renowned experts in the field of mast cell (MC) and basophil (patho)physiology from Japan and the European Mast Cell and Basophil Research Network (EMBRN) [3].

Pluripotent MCs [4] and their circulating counterparts, basophils, are the primary sources of histamine in the immune system and they are considered as professional histamine-synthesizing cells [5]. MCs and basophils were identified by Paul Ehrlich in the late 1870s. A pivotal breakthrough in recognizing the ‘intimate relationship’ between histamine and tissue MCs was first described by JF Riley and GB West in 1950s [5]. In fact, GB West was one of the founders of the EHRS and the ‘GB West lecture’, delivered at the annual EHRS meetings by prominent scientists and clinicians working in the field, has been established in recognition of his work [5].

The celebration of the 50th anniversary of the EHRS in 2021 has been long awaited by all histaminologists working in academia, research institutions, and industry in many countries across the world. Under the pressure of unprecedented measures to contain the spread of the severe acute respiratory syndrome–related coronavirus 2 (SARS-CoV-2) during the coronavirus disease 2019 (COVID-19) outbreak, the organization of the 50th EHRS conference had to be postponed. Hence, to mark its 50th anniversary, the EHRS organized a 1 year-long series of online events that was completed with the Joint JHRS/EHRS Webinar on MCs and basophils. As parts of the world started to emerge from the COVID-19 pandemic, the webinar adopted a hybrid format, thus unlocking the possibility for many delegates from around the world to attend. Despite the barriers in global research and training and the disruption of in-person activities introduced by the COVID-19 pandemic, four inspiring
topics presented by four talented invited speakers exposed novel insights into the importance of basophils and MCs in inflammatory and immune-related processes. The success of the webinar was also facilitated by the input from a highly interactive audience.

In the first talk, Professor Bernhard F. Gibbs (Department of Human Medicine, University of Oldenburg, Germany), EMBRN Vice-president and EHRS Council Officer, reviewed our current understanding of basophils in allergy and autoimmunity and provided new insights into how these somewhat neglected cells regulate inflammation and contribute to tissue remodeling and wound healing. Basophils are strongly associated with the severity of allergic reactions. They can invade tissues affected by allergic inflammation from the circulation and contribute to both late phase as well as to acute allergic reactions. Moreover, basophils release a number of key pro-inflammatory mediators such as histamine, leukotriene (LT) C₄, and the pruritic cytokine interleukin (IL)-31 that drive, at least in part, the symptoms of allergic and autoimmune inflammation. They also majorly contribute to the release of IL-4 and IL-13, cytokines which crucially support the T helper cell (Th) 2-type immunity and immunoglobulin (Ig) E synthesis. Indeed, basophils are implicated in many different diseases that are largely IgE-mediated, including bullous pemphigoid, systemic lupus erythematosus, and chronic spontaneous urticaria (CSU).

Supportive clinical evidence on the importance of basophils in CSU was provided by Professor Naotomo Kambe, (Department of Dermatology, Kyoto University Graduate School of Medicine, Japan) who presented a case of CSU refractory to antihistamines in which no peripheral basophils were detected for more than a year, while the rash was uncontrolled. Urticaria is an immediate allergic reaction involving the skin, but there are still many mysteries surrounding this disease. In the presented case, treatment with omalizumab, a therapeutic monoclonal antibody (mAb) which neutralizes circulating IgE, improved rash and resulted in peripheral blood basophil recovery. Similar responses related to basophil counts have been confirmed following treatment with antihistamine drugs targeting the H₁ histamine receptor (H₁ antihistamines) [5]. Based on the presented evidence, it was suggested that the decrease in peripheral blood basophil count is associated with their migration to the skin, thus reflecting disease activity in urticaria. Consequently, basophil count could be a marker of the clinical progression of CSU following omalizumab administration.

The next two talks focused on MCs and their contribution to diseases with different aetiopathological profiles [4]. EMBRN President, Professor Francesca Levi-Schaffer (Institute for Drug Research, School of Pharmacy, The Hebrew University of Jerusalem, Israel) presented novel therapeutic target molecules expressed on MCs that could be valuable for the development of more effective strategies for combating allergic diseases. In particular, the pro-inflammatory physical cross-talk between MCs and eosinophils, referred to as the Allergic Effector Unit (AEU), presents a challenging framework for the identification of several druggable components on both cell types. Among them, cluster of differentiation (CD) 48 is a co-activating/activating receptor expressed on both MCs and eosinophils. Importantly, MC CD48 is a main player as it binds to 2B4 (CD244) expressed on eosinophils in the AEU pro-inflammatory outcome. Moreover, CD48 interacts with Staphylococcus aureus/S. aureus exotoxins, further activating MC and eosinophil pro-inflammatory functions during allergic diseases. Notably, in asthmatic patients, CD48 is preferentially increased on peripheral blood eosinophils and released in its soluble form (sCD48) acting as a decoy receptor. Therefore, it was suggested that targeting CD48 could potentially lead to the development of novel options for the management of allergic inflammation.

The last talk was delivered by EMBRN Past President, Professor Marcus Maurer (Allergie-Centrum-Charité, Charité–Universitätsmedizin Berlin, Germany) who focused on MC-driven diseases and non-allergic MC activation contributing to, for instance, chronic inducible urticarias. These diseases allow the investigation of autoallergic pathways and, importantly, the study of MC-targeting treatments. The most novel MC-targeting urticaria treatments focus on silencing and depleting MCs, rather than inhibiting their activation or the actions of their mediators. For example, targeting sialic acid-binding Ig-like lectin (Siglec)-8, an inhibitory MC receptor, silences MC activation. Yet, the most radical approach is to kill MCs by targeting the receptor tyrosine kinase KIT (CD117), which is normally activated by binding of the stem cell factor (SCF), with an anti-KIT mAb producing MC-deficient human skin.

The experts’ panel concluded that the successful exchange of valuable new knowledge during this webinar showed the necessity of organizing similar events more often and marked the beginning of more productive interactions between the JHRS, the EHRS, and EMBRN.

Author contributions ET and BFG wrote the manuscript. All authors reviewed the manuscript.

Declarations

Competing interests The authors declare no competing interests.

Conflict of interests The authors declare no competing interests.
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