



ELSEVIER

Available online at www.sciencedirect.com
 ScienceDirect

Current Opinion in
Immunology

Allergy and hypersensitivity

Editorial overview

Bruce S Bochner and Rafeul Alam

Current Opinion in Immunology 2008, 20:1–2

0952-7915/\$ – see front matter

© 2008 Elsevier Ltd. All rights reserved.

DOI 10.1016/j.coi.2008.10.001

Bruce S Bochner

Division of Allergy & Clinical Immunology,
 Department of Medicine, Johns Hopkins
 University School of Medicine, Johns Hopkins
 Asthma & Allergy Center, 5501 Hopkins Bayview
 Circle, Room 2B.71, Baltimore, MD 21224, USA
 e-mail: bbochner@jhmi.edu

Bruce Bochner is an allergist and immunologist as well as a professor of Medicine and Cosner Scholar in Translational Research at the Johns Hopkins University School of Medicine. He is the director of the Division of Allergy & Clinical Immunology at Johns Hopkins. His research interests involve mechanisms of eosinophil, basophil, and mast cell recruitment, activation and survival in human allergic inflammatory responses.

Rafeul Alam

Division of Allergy and Immunology, Department
 of Medicine, National Jewish Medical and
 Research Center and University of Colorado
 Denver Health Sciences Center, 1400 Jackson
 Street, Denver, CO 80206, USA
 e-mail: alamr@njc.org

Rafeul Alam is a professor of Medicine and Veda and Chauncey Ritter Chair in Immunology at National Jewish Medical and Research Center. He is the director of the Division of Allergy and Clinical Immunology at National Jewish Medical and Research Center. His research focuses on the signaling mechanisms of the activation of eosinophils and T cells in asthma and allergic diseases.

Since the discovery of IgE in the late 1960s by Kimishige and Teruko Ishizaka and SGO Johansson [1] and the delineation of the Th2 paradigm focused on cytokines like IL-4, IL-5, and IL-13 in the 1980s by Mosmann and Coffman [2], it seemed as though all of the key players in allergic diseases had been delineated. Yet, the recent decade has witnessed the failure of IL-4 and IL-5 targeted therapies [3,4], and the approval of IgE-directed therapies for the treatment of moderate-to-severe persistent asthma inadequately controlled with inhaled corticosteroids [5]. These failures and successes point to both the importance of translational research and the imperfect nature of existing animal models in predicting human allergic disease pathophysiology and responses to pharmacotherapies. The failures also point to the gaps in our knowledge in understanding the pathogenesis of human asthma and allergic diseases.

The overall theme of this section on allergy and hypersensitivity focuses on our evolving understanding of allergic and allergic-like human disease pathophysiology. For example, Wang and Liu review the IL-17 cytokine family and its potential role in regulating allergic inflammatory responses. The discovery of this new cytokine family has led to the revision of the classic Th1/Th2 paradigm with the identification of a third major subset of CD4⁺ T cells capable of making a range of cytokines that can influence the pathogenesis of allergic and other inflammatory disorders. The importance of IL-17 is underscored by another recent finding that STAT3 mutation, which is associated with increased IgE production, also leads to impaired IL-17 production [6].

Once IgE is produced, it binds with high affinity to FcεRI on mast cells, basophils, and other cells expressing lower levels and various forms of FcεRI. The chapter by Donald MacGlashan Jr. focuses not on the regulation of IgE production *per se*, but instead reviews the consequences of IgE binding to FcεRI and how IgE/FcεRI triggering, through either monomeric or aggregation-related events, activates signal transduction pathways that regulate secretion and other functions of mast cells and basophils.

Another disorder that has been potentially linked to mast cell activation through IgE and FcεRI is chronic urticaria, a disabling disorder involving generalized hives of unknown cause. Vonakis and Saini cover the potential autoimmune etiology of this disorder, which may affect up to half of the patients with chronic idiopathic urticaria, and also review recent science implicating inappropriate mast cell and basophil activation, the role of signaling molecules as well as studies successfully using an IgE-lowering agent to understand disease pathophysiology and new ways to treat this condition.

Skipak and Sampson cover our current state of knowledge regarding the diagnosis and treatment of food allergy with an emphasis on promising and

2 Autoimmunity

emerging treatments beyond avoidance and emergency management. They review approaches involving careful, slow escalating oral delivery of allergens as well as IgE-directed therapies and other novel agents that may soon play an important role in the treatment of established food allergy. This may, for the first time, allow allergic individuals to safely ingest foods to which they are sensitized.

In addition to the food allergy epidemic, there also appears to be an epidemic of another possibly food-related disorder, namely eosinophilic esophagitis. [DeBrosse and Rothenberg](#) review what is known about the mechanisms of esophageal-specific inflammation that accompanies this unusual disorder, the role of eosinophil and mast cell activation in perpetuation of this disorder, and the potential role of allergens in disease pathogenesis.

Finally, [Lee and colleagues](#) explore the role of chitins, chitinases, and chitinase-like proteins in innate and adaptive immune and inflammatory responses, including its adjuvant role in allergic inflammation. The fact that this plentiful, nonmammalian polysaccharide alters allergic responses lends credence to the longstanding notion that allergic airways disease is one of mistaken identities in which the immune system views aeroallergens as an invader and mounts an immune response specific for this attack.

In pulling together what is seemingly a wide array of topics on allergy and hypersensitivity, our goal has been to update the reader in emerging concepts of allergy and hypersensitivity, especially those that have a bench-to-bedside or preclinical-to-clinical translational component, thereby providing reviews on some of the most promising and cutting edge research that is shaping our understanding, diagnosis, and treatment of allergies and related disorders.

References

1. Bennich HH, Ishizaka K, Johansson SG, Rowe DS, Stanworth DR, Terry WD: **Immunoglobulin E: a new class of human immunoglobulin.** *Immunology* 1968, **15**:323-324.
2. Mosmann TR, Coffman RL: **TH1 and TH2 cells: different patterns of lymphokine secretion lead to different functional properties.** *Annu Rev Immunol* 1989, **7**:145-173.
3. Steinke JW: **Anti-interleukin-4 therapy.** *Immunol Allergy Clin North Am* 2004, **24**: 599-614, vi.
4. Bochner BS: **Verdict in the case of therapies versus eosinophils: the jury is still out.** *J Allergy Clin Immunol* 2004, **113**:3-9.
5. Deniz YM, Gupta N: **Safety and tolerability of omalizumab (Xolair), a recombinant humanized monoclonal anti-IgE antibody.** *Clin Rev Allergy Immunol* 2005, **29**:31-48.
6. de Beaucoudrey L, Puel A, Filipe-Santos O, Cobat A, Ghandil P, Chrabieh M, Feinberg J, von Bernuth H, Samarina A, Jannière L *et al.*: **Mutations in STAT3 and IL12RB1 impair the development of human IL-17-producing T cells.** *J Exp Med* 2008, **205**:1543-1550.