INTRODUCTION

Immunopathology of lung diseases: introduction for the special issue

Tracy Hussell1 · Aleksander M. Grabiec 1

Received: 8 May 2016 / Accepted: 9 May 2016 / Published online: 19 May 2016
© Springer-Verlag Berlin Heidelberg 2016

This issue of Seminars in Immunopathology focuses on lung innate immunity and the recently identified mechanisms contributing to this unique environment. It was in the 1980s that T-cell subsets were first described by the cytokines that induced them and the cytokines they then produced [1, 2]. This segregation allowed more flexibility in the immune system, fine-tuning responses to eliminate very different antigens or pathogens. Sub-division to define optimal function, however, has now expanded to natural killer (NK) cells, innate lymphoid cells (ILCs), dendritic cells (DCs) and macrophages. Though polarising conditions in vitro provide clarity in our understanding of influencing forces, they do not tell us how this occurs in vivo, how it is regulated, or whether it contributes to common pathological conditions.

The discovery of tissue-specific regulation of innate and adaptive immunity has transformed our understanding of the immune system, provided clarity for otherwise unexplainable phenomena, and opened up a new area for scientific discovery [3]. Immunity adapts to tissue-specific cues that in turn maintain or restore homeostatic physiology. Forces driving the tissue adaptation in disease alter immune phenotype and reactivity, which can have deleterious consequences. The lung is a prime example of site-specific forces dictating the balance between health and disease. In this issue we examine lung innate immunity in this precise tissue-specific context, the impact of ILCs and neutrophils on health and disease, macrophage and DC adaptation and the consequences of disturbances in chronic lung disease and infection.

To some extent, tissue-specific influences on innate immunity should depend on what the tissue requires of that innate immune cell. Alveolar macrophages reside in a prime location for interaction with environmental and commensal microorganisms. Their role appears to be to sift the harmless from the dangerous and also perform domestic duties, keeping airspace clutter within tolerable margins [4]. These duties include removal of surfactant proteins, cellular and matrix debris, and apoptotic cells. Cell turnover by apoptosis is necessary, and removal of apoptotic bodies is essential to prevent inflammation-inducing secondary necrosis. In this issue, Grabiec and Hussell detail the mechanisms and impact of apoptotic cell uptake (efferocytosis) on airway macrophage function. Clearly, clearance of self-cells or proteins must be performed without activating the macrophage, otherwise peripheral tolerance will be overcome, leading to chronic inflammation or autoimmunity. The process of efferocytosis therefore triggers anti-inflammatory cascades. On the other hand, clearance of pulmonary pathogens by airway macrophages may require assistance from other cells, which necessitates macrophage production of chemokines that culminates in inflammatory cell recruitment. Eventually these recruited cells will themselves undergo apoptosis and require efferocytosis. Here we have a conundrum where two opposing functions are requested of airway macrophages: efferocytosis and inflammation. Writing in this issue, Robb and colleagues discuss the impact of neutrophil and eosinophil apoptosis and their clearance from the airways on the resolution of the inflammatory response.

Despite the considerable advances made in recent years in our understanding of airway macrophage origin, heterogeneity, longevity and turnover, there are still many unanswered questions [5]. Do original airway macrophages perform
Uncontrolled production of inflammatory cytokines, predominantly by innate immune cells and resident cells of the respiratory tract, plays a key role in driving airway damage not only in COPD, but also in many other lung diseases [10]. While the contributions of IL-1β to several lung immune pathologies were identified more than a decade ago, experimental evidence has accumulated in recent years showing that other pro- and anti-inflammatory members of the IL-1 family, including IL-33, IL-18 and IL-37, also play pivotal roles in controlling these pathological processes. In this issue, Borthwick details the impact of this cytokine family on lung immunopathology, with special focus on lung fibrosis.

In summary, this issue of *Seminars in Immunopathology* will provide the readers with an overview of key processes controlling the immune homeostasis of the lung and the consequences of dysregulation of these processes, which leads to chronic inflammation, lung tissue injury and/or fibrosis. Great advances have been made in recent years in our understanding of the molecular mechanisms underlying immune-mediated lung pathologies due to the introduction of mouse models mimicking certain aspects of human disease. However, future translational work on primary patient material is required to validate these findings and to tackle the challenge posed by the growing impact of chronic and acute lung diseases on public health.

References

1. Fernandez-Botran R, Sanders VM, Mosmann TR, Vitetta ES (1988) Lymphokine-mediated regulation of the proliferative response of clones of T helper 1 and T helper 2 cells. *J Exp Med* 168:543–558
2. Mosmann TR, Cherwinski H, Bond MW, Giedlin MA, Coffman RL (1986) Two types of murine helper T cell clone. I. Definition according to profiles of lymphokine activities and secreted proteins. *J Immunol* 136:2348–2357
3. Hu W, Pasare C (2013) Location, location, location: tissue-specific regulation of immune responses. *J Leukoc Biol* 94:409–421. doi:10.1189/jlb.0413207
4. Russell T, Bell TJ (2014) Alveolar macrophages: plasticity in a tissue-specific context. *Nat Rev Immunol* 14:81–93. doi:10.1038/nri3600
5. Ginhoux F, Guilliams M (2016) Tissue-resident macrophage ontogeny and homeostasis. *Immunity* 44:439–449. doi:10.1016/j.immuni.2016.02.024
6. Kopf M, Schneider C, Nobs SP (2015) The development and function of lung-resident macrophages and dendritic cells. *Nat Immunol* 16:36–44. doi:10.1038/ni.3052
7. Snegurov RJ, Godlee A, Russell T (2011) Airway immune homeostasis and implications for influenza-induced inflammation. *Trends Immunol* 32:328–334. doi:10.1016/j.it.2011.04.006
8. Licona-Limon P, Kim LK, Palm NW, Flavell RA (2013) TH2, allergy and group 2 innate lymphoid cells. *Nat Immunol* 14:536–542. doi:10.1038/ni.2617
9. Cosio MG, Saetta M, Agusti A (2009) Immunologic aspects of chronic obstructive pulmonary disease. *N Engl J Med* 360:2445–2454. doi:10.1056/NEJMra0804752
10. Barnes PJ (2006) The cytokine network in asthma and chronic obstructive pulmonary disease. *J Clin Invest* 118:3546–3556. doi:10.1172/JCI36130