Series introduction: innate host defense of the respiratory epithelium

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Abstract: This series overviews the current knowledge of the innate-immune system of the lung. Special emphasis is put on mechanisms used by epithelial cells of the respiratory tract to contribute to host defense. This defense function is important, as the lung is especially prone to microbial exposure. The exchange of oxygen and carbon dioxide requires the ventilation of a large volume of environmental air that may contain respiratory pathogens. Furthermore, the digestive pathway shares with the airways the pharynx, opening another possibility for the uptake of microorganisms into the respiratory tract. Host defense is provided by a multilayered and complex system that aims to avoid colonization and infection of the lung. A classic view separates the inborn, innate-immune system from adaptive mechanisms that involve antigen-specific lymphocytes [1]. J. Leukoc. Biol. 75: 3–4; 2004.

Key Words: innate immunity · antimicrobial peptide · chronic obstructive pulmonary disease · pattern recognition receptor · pathogen-associated molecular pattern

INTRODUCTION

In recent years, it became clear that airway epithelial cells are actively involved in host defense of the lung. The pseudostratiﬁed epithelium of the larger airways is composed of ciliated, basal, goblet, brush, and small-granule cells [2–4]. The walls of the larger airways contain glands composed of two secretory cell types: the serous and the mucous cell. The epithelium of the distal airways, the bronchioles, consists mainly of ciliated and Clara cells. The alveoli are covered by alveolar epithelial cells, types I and II. The goblet and Clara cells of the conducting airways, the submucosal glands, and the alveolar epithelial type II cell are parts of the secretory apparatus of the lung. In addition to cells lining the airways and alveoli, other cells of the innate- and adaptive-immune system contribute to host defense, including alveolar macrophage, neutrophil, eosinophil, dendritic cell, mast cell, natural killer cell, and lymphocytes [5, 6]. The respiratory epithelium is actively involved in inflammation and host defense in multiple ways: providing a physical barrier; constituting the structural basis of mucociliary clearance aiming at the physical removal of inhaled bacteria; recognition of microbial exposure by pattern recognition receptors expressed on epithelial cells and detection of pathogen-associated molecular patterns; secretion of a variety of pro- and anti-inflammatory mediators; and secretion of a variety of antimicrobial substances including antimicrobial peptides. Thus, airway epithelial cells are equipped with a large arsenal of receptor and effector mechanisms [4]. These mechanisms are important to maintain the structure and function of the respiratory tract but also likely contribute to the development of respiratory disease. Activation of airway epithelial cells is documented in asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, and respiratory infection.

The meeting reviews that constitute this series are based on two recent meetings that highlighted innate immunity at epithelial surfaces: the European Respiratory Society Research Seminar, Host Defense Function of The Airway Epithelium (November 2002, Noordwijkhout, The Netherlands), and the symposium, Antimicrobial Peptide Mediators of Host Defense, organized during the annual meeting of the British Society for Immunology and British Society for Allergy and Clinical Immunology (December 2002, Harrogate, UK). A clinical background for studying the host defense function of the airway epithelium is provided by Message and Johnston. Their contribution focuses on the innate-immune function of the lung using viral infections as examples. The paper by Immler and Zheng reviews receptor mechanisms that are used to detect the presence of microorganisms, highlighting the role of the Toll receptor family. The following articles focus on specific families of host defense molecules: Hickling et al. review the collectins and their role in lung immunity. One spotlight in this article is on surfactant proteins that fulfill multiple functions in the host defense of the lung. Another group of host defense molecules is the antimicrobial (poly)peptides reviewed by Ganz. Zanetti focuses on cathelicidins, a specific family of multifunctional, antimicrobial peptides. Finally, Cunliffe and Mahida summarize the current knowledge about expression and regulation of antimicrobial peptides in the gastrointestinal tract.

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The biological systems described in the series interact in a complex manner to maintain the function of the lung by means of mechanical, chemical, and cellular strategies. Usually, pathogens are cleared from the lung without inflammation or disturbance of the local function or structure. In case this first line host-defense system fails to clear the microorganism, secondary layers of the system are activated that are accompanied by an inflammatory reaction. The devastating effects of respiratory infection in patients with cystic fibrosis are a clear example of the serious consequences of impaired host defense. Deficient or overwhelming and uncontrolled host defenses and inflammatory responses also contribute to pulmonary disorders such as asthma or COPD. Detailed knowledge of these mechanisms and pathways will improve the understanding of respiratory physiology and pathology and potentially lead to novel diagnostics and therapies. It is our aim that this series of meeting reviews provides the reader with an overview of recent developments in research on innate immunity of the (respiratory) epithelium and thus stimulates further research in this area.

REFERENCES