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EDITORIAL

Airway secretions: new concepts and functions

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The editorial board of the European Respiratory Journal has decided to set up in the Journal several series of reviews covering areas of current interest in clinical, as well as in more fundamental molecular and cellular aspects.

The first series deals with "Airway secretions: new concepts and functions". Four reviews dealing with this topic will, therefore, appear in succession in the European Respiratory Journal. They will concentrate on the following: 1) human airway secretory cells during development and in mature airway epithelium; 2) human respiratory mucins; 3) functions of proteins and lipids of human airway secretions; and 4) role of the physicochemical properties of human airway mucus in the protection of the respiratory epithelium.

The last decade has brought significant advance in the knowledge of airway epithelium defence mechanisms, related to airway secretory cells and their secretory products released at the surface of the mucosa and in the airway lumen. The airway secretions, also known as respiratory mucus, are identified in all vertebrates, where they form a continuous lining filter on the epithelium surface. This mechanical and biochemical barrier protects the epithelial cells from invasion and injury by microorganisms and noxious agents present in the environment. Airway secretions play multiple key roles in airway epithelial protection, probably the most important being to preserve an aqueous environment at the airway epithelial surface.

Airway secretions represent a mixture of mucous components synthesized and secreted by different types of cells, including surface and glandular mucous and serous cells and other cell types, such as Clara cells, ciliated cells and brush cells [1]. The respiratory mucus forms a biphasic fluid composed of an aqueous "sol" phase, also described as "epithelial lining fluid", containing ions, proteins and lipids, where the cilia beat and relax and a "gel" phase, 0.5–2 μm thick, which is located at the tips of the cilia and is composed of high molecular weight (HMW) macromolecules mainly represented by mucins. The latter HMW macromolecules are characterized by the diversity of their carbohydrate chains, which represent a mosaic of potential binding sites for bacteria and viruses, chemically recognized and trapped and then mechanically eliminated by means of the mucociliary clearance [2, 3]. Mucins, in association with other biochemical components present in airway secretions, are directly involved in their physicochemical properties [4]. Phospholipids have recently been shown to be present at the surface of the epithelial cells and in the secretory granules of airway glandular cells [5, 6]. Tracheobronchial surfactant probably plays a key role in respiratory epithelial protection and in mucus transport, either by mucociliary activity or cough. The barrier of protection formed by the airway secretions is present very early in human foetal airways, where they have a mucociliary defence function for transporting cell debris and for regulating the ionic composition of the amniotic fluid [7].

Apart from their transport function, the airway secretions fulfil a variety of functions, such as airway hydration, lubrication (at the gel-sol phase interface and at the surface of the epithelial cells), waterproofing and epithelial insulation. Airway secretions also possess barrier functions by acting as a selective macromolecular sieve, able to neutralize toxic gases and protect the epithelium from oxidants and proteases by appropriate biochemical constituents [8].

The macromolecular gels, like respiratory mucus, possess fascinating properties characteristic of a network of connected molecules which can rapidly alter the conformation and arrangement of its molecular strands [9]. Respiratory mucus can swell very rapidly and the swelling can reverse. The capacity and degree of swelling is a determinant factor in the control of the rheological properties of mucus. Mucus hydration is carefully controlled by the movement of ions and proteins present in the epithelial lining fluid [10]. Serum proteins and ions are normally present at the surface of airway epithelial mucosa, but their concentration can undergo marked changes with parallel alterations in mucus hydration and rheology, particularly in chronic inflammatory diseases of the airways, such as cystic fibrosis, acute and chronic bronchitis and asthma. Albumin, normally found on the surface of the mucosa, plays a critical role in mucin hydration and mucus rheology because of its size and polyionic properties [11, 12]. Nevertheless, during inflammatory processes, its marked increase is responsible for the hyperviscous and adhesive properties of the mucus found in the airways of these patients [4]. Abnormalities of mucus hydration occur in a variety of diseases, such as asthma and cystic fibrosis. Mucus plugging results from a

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marked imbalance between a decreased, inefficient, or even absent sol layer and a marked inflammatory exudation with increased plasma derived protein transudation. It is clear that the periciliary sol phase represents a permanent source of water, which can be used to replace the volume lost during mucus swelling [9], to keep an optimal thickness of the sol layer surrounding the cilia. Mucin secretion *via* mucus exocytosis and ion-water secretion are probably concomitant events, mediated by intracellular calcium concentration changes.

During development and wound repair, polyionic macromolecules (such as mucins and proteoglycans) may have informative functions on the ionic homeostasis of the pericellular microenvironment of epithelial cells [13]. Speculative function of the gel network formed by mucus concerns its ability to allow the molecules, which are in solution in the mucous gel, to diffuse through channels in the gel. These molecules can be temporarily adsorbed by the gel and then further re-released. Conversely, large macromolecules cannot enter the gel. It can be speculated that the gel mucus network may be implied in the maturation of epithelial cells as well as in epithelial wound repair. During development or repair, polypeptide growth factors may be temporarily restrained in the gel mucus, then transported by mucociliary clearance, later interacting with specific receptors present on still undifferentiated epithelial cells. We speculate that cell-surface proteoglycans, present at the apical surface of the epithelial cells, may either help present some polypeptide growth factors to their receptors or may act as a reservoir for others [11, 14].

The rapid and recent advances in cell biology, using secretory cell culture biochemistry and biomolecular techniques, will contribute to a better understanding of the functions of the airway secretions. The contributors for this series of reviews, devoted to the functions of airway secretions, have been chosen for their indisputable expertise, with the idea of throwing light on the functional and physiopathological roles of the airway secretions. Such a contribution should be helpful in the development of new therapeutic orientations in the area of mucous epithelial protection.

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