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SIXTH INTERNATIONAL CONGRESS OF BIORHEOLOGY SYMPOSIUM ON CELLULAR AND MOLECULAR BASIS OF MUCUS RHEOLOGY

FOREWORD

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The rheological characteristics of mucus seem to be determined by a high molecular weight glycoprotein built up from a similar structural unit based on a protein chain some 800 amino acids long. A section of some 500 amino acids of this chain is densely covered by carbohydrate side chains. It is likely that depending only slightly upon the specifics of the epithelium this protein is the same, but the length and nature of the sugar side chains, the arrangement of the basic units in the aggregate and the overall concentration of the glycoprotein are variable and dictated by the local functional requirements. These variations in the very dense and thick carbohydrate protective cover are introduced by the secretory cells of the epithelium, not only by altering the level of glycosylation, but also by adjusting the level to which the mucus glycoprotein stored in the cell at high concentration in lipid covered granules is admixed with glycoprotein-free, serous secretions from other epithelial cell types. In the case of ciliated epithelia the mucus, so produced, forms a layer above, but in contact with the cilia, and is rheologically so adjusted as to cause optimal transport and clearance.

We have reason to think that mucus is not normally present over this kind of epithelium and that the cilia are not normally in motion. The secretion of mucus glycoprotein and the formation of mucus is stimulated mechanically at the local level when loads impinge or pass over a particular section of the epithelium. Ciliary

motion is initiated by the presence of mucus and dies off when the patch of mucus has moved over and beyond the cells in question. According to this picture, therefore, a particular mucus sample has only a transient presence over the epithelium. It is formed from its ingredients, mucus glycoprotein and secreted support fluid, when mucus producing cells are stimulated mechanically. The fresh mucus always constitutes the undermost layer, the layer which interacts with the ciliary tips to maintain transport. Some of the freshly formed mucus, at each site,is left behind, is degraded and is re-absorbed; the remainder is eliminated as part of the load, possibly while losing water to the air. Ciliary beat, it is postulated, occurs only where mucus is present, i.e., where loads have to be moved. The effectiveness of ciliary beat for this purpose depends upon the mucus being rheologically matched.

The great difficulty in studies of respiratory mucus structure and function is that we are dealing with a defense mechanism which, under normal circumstances, will only very occasionally be engaged. The amounts of normal respiratory mucus which can be harvested may thus well be insignificant. Much larger quantities are normally present in the stomach, intestines and cervix and more representative samples can be collected. Mucus production has to be engineered into some well defined steady state, not necessarily physiological, before a reliable source of mucus is established. This may not be feasible in the case of all epithelia.

Bearing these difficulties in mind it has proved to be very convenient to regard all mucus as a single system based on the same gene product, i.e., the protein backbone, which is differentially handled only during glycosylation, storage and secretion. Most indicators so far are in support of this approach and it continues to make sense to follow this working hypothesis. The Symposium, so elegantly assembled by Professor Verdugo and published in the following pages, is conceived in this spirit. It represents a very comprehensive overview of the state of the art. The discussion touches a broad variety of systems and while we should look for what is common, we must not forget that important differences are involved. With respect to our working hypothesis,therefore, both wishful thinking and a high level of objective criticism are in place.