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Molecular mechanisms of epithelial host defense in the airways

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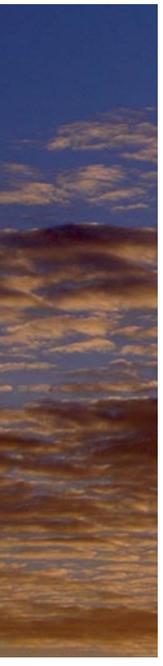

Molecular Mechanisms of Epithelial Host Defense in the Airways

Airway epithelial cells are indispensable for the host defense system in the lungs. A number of strategies by which epithelial cells protect the lungs against inhaled pathogens have been described. Despite, the molecular mechanisms by which epithelial cells initiate and control in thehost defense response have not been explored systematically. In this thesis, the molecular mechanisms underlying the initiation and regulation of the early epithelial host defense response in the airways were investigated.

Using genomics technology, genes were identified to be associated with the early inflammatory response in airway epithelial cells exposed to pro-inflammatory stimuli. Many of these genes had previously not been associated with the host defense response against pathogens in the airways. The early epithelial host defense response is rapidly induced and transient of nature and can be divided into two phases. The initial phase is characterized by a strengthening of the physical barrier and is accompanied by the production of immune signaling molecules. In the proceeding phase, production of specialized antimicrobial agents occurs. Following a comparative genomics approach, striking similarities were found in the molecular mechanisms of host defense in epithelial tissues of the airways and skin. Due to these similarities, genetic alterations in epithelial host defense mechanisms may explain the occurrence of inflammatory disorders at multiple sites of the body at the sametime. These observations provide the basis for future investigations to further unravel the molecular mechanisms underlying epithelial host defense, both in the human airways and other epithelial tissues.

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Joost B. Vos 2006

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