Microbiome and Innate Immunity in Respiratory Mucosa

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The innate immune system of the respiratory epithelium serves as a first line of defense against invading respiratory viruses. It senses microbial molecules, such as single- and double-stranded viral RNA, and initiates production of antiviral mediators such as interferon (IFN).

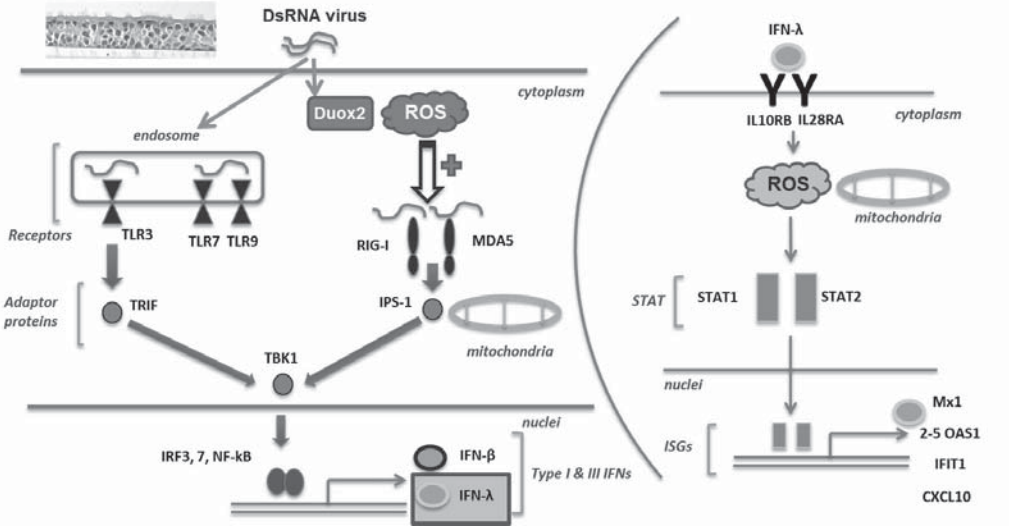
Initiation of antiviral response

Initiation of these innate immune responses is achieved through the recognition of invading viruses by pattern recognition receptors (PRRs) and virus-derived nucleic acids are considered to activate various PRRs, including members of the membrane-bound Toll-like receptor (TLR) family such as TLR3, 7, and 9, and the recently identified cytoplasmic retinoic acid-inducible gene 1 (RIG-I)-like receptors (RLRs), including RIG-I and melanoma differentiation-associated protein 5 (MDA5). Following the recognition of viral RNAs, the antiviral innate immune response is activated, mainly through the rapid expression of IFNs in nasal epithelium.

Innate Immune Response to Respiratory Virus

Secreted IFNs bind to their receptors and induce expression of IFN-stimulating genes that have antiviral activities via the JAK/STAT signaling pathway. IFNs are defined by their ability to induce resistance to viral infection. There are three distinct types of IFNs such as types I, II, and III that are classified based on their structural features, target receptors, and biological activities. Type I and type III IFNs are directly produced in response to virus infection and

contribute to the clearance of viral infections in epithelial cells. Until now, it has been thought that type I IFNs (IFN-α and β) played an exclusive role as early mediators of the innate immune response to viruses, as well as regulators of the subsequent response of the adaptive immune system. Recently, a group of proteins functionally similar to type I IFNs was discovered and designated as type III (IFN-λ1, λ2, and λ3). It has been widely accepted that the induction, signaling and biological activities of type III IFNs are very similar to those of type I IFNs and type I and III IFNs are directly produced in response to viral infections. However, there are emerging evidences that the activation signaling of type I and type III IFNs is likely to be quite different based on the unique distribution of their target receptors and especially, the receptors for type III IFNs are found primarily on epithelial cells. Recently, it has been verified that type III IFNs are primarily responsible for protection against viral invaders in the respiratory tract and play an important role in local antiviral innate immunity.

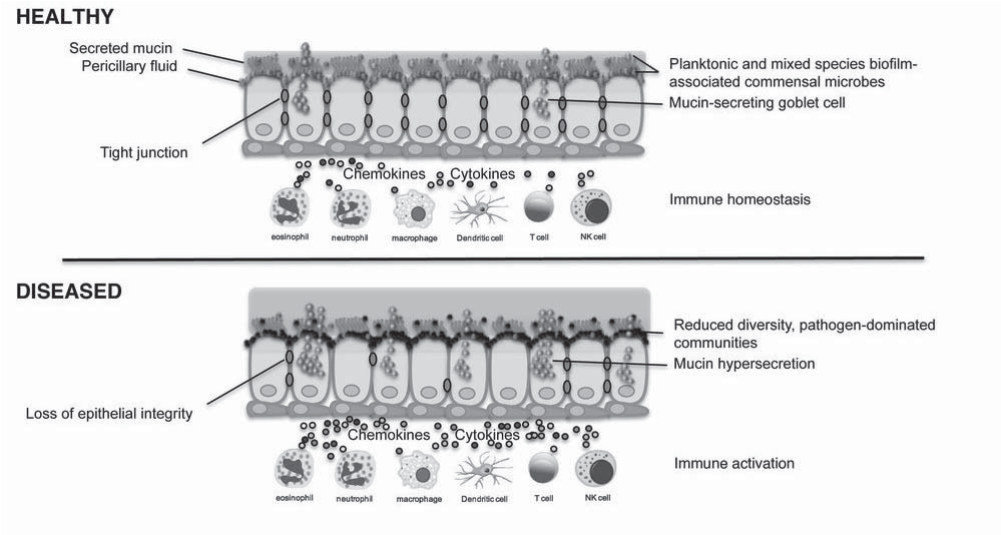


The presence of microbiota at respiratory mucosa,

- Constituent dependent on the health status of the individual,
- Chronic lung diseases, such as asthma, chronic obstructive pulmonary disease, cystic fibrosis and lung transplantation
- Further studies need to be conducted to verify the potential application or modification of the airway microbiota in nasal mucus
- Evidence points towards a contribution to disease progression and exacerbation.

* The alteration of the airway microbiota might influence on the consequences of respiratory diseases and

microbial balance provides new **insights into the pathogenesis of respiratory diseases** and **new conception about fundamental therapeutic strategies.**



*** Clinical importance of Microbiome in respiratory mucus**

- First target tissue for environmental pathogens
- Suppression of Pathogen colonization
- Diverse and direct immune responses against bacterial or viral invasion
- Environmental stimulation and Maintain homeostasis / Pathogen and Immunity
- Interferon-related innate immunity / Distribution of microbiome in respiratory mucus

Dysbiosis of microbial communities colonizing the human airway has been described for a variety of chronic diseases and characterization of human microbiome in states of health and disease is challenging for understanding the role of microbiome.

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