The non-unified airway: Different triggering factors in allergic rhinitis and asthma

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Allergic rhinitis (AR) and asthma are two entities of allergic airway diseases that frequently occur together, which is referred to as ‘united airways’. In contrast to this general concept, we hypothesized that innate immunity of the upper and lower airways is respectively distinctive, because the immunologic conditions of the nasal and lung mucosa as well as the functions of the immune cells within their epithelia are different. To identify distinctive mechanisms of innate immunity in the nose and lung mucosa, which are responsible for house dust mite (HDM)-induced AR and allergic asthma (AA), respectively. We constructed a mouse model of AR or AA induced by sensitization and consequent provocation with HDM extracts. HDM-derived β-glucans, rather than LPS, were proven to be essential to activating innate immunity in the nasal mucosa and triggering AR, which was dependent on Toll-like receptor 2 (TLR2), but not on TLR4; however, the LPS/TLR4 signaling axis, rather than β-glucans/TLR2, was critical to HDM-induced AA. These differences were attributed to the specific role of β-glucans and LPS in inducing the surface expression of TLR2 and TLR4 and their translocation to lipid rafts in nasal and bronchial epithelial cells, respectively. We also showed that dual oxidase 2 (DUOX2)-generated reactive oxygen species (ROS) mediate both β-glucan-induced TLR2 activation and LPS-induced TLR4 activation. We describe a novel finding of distinctive innate immunity of the nose and lungs, respectively, which trigger AR and AA, by showing the critical role of HDM-induced TLR activation via DUOX2-mediated ROS.