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Children Asthma; The Role of Molecular Pathways and Novel Saliva Biomarkers Assay

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Abstract : Introduction: Allergic asthma is a heterogeneous immuno-inflammatory disease based on Th-2-mediated inflammation. Histopathologic abnormalities of the airways characteristic of asthma include epithelial damage and subepithelial collagen deposition. Objectives: Human bronchial epithelial cell genome expression of TNF-α, IL-6, ICAM-1, VCAM-1, nuclear factor (NF)-κB signaling pathways up-regulate during inflammatory cascades. Moreover, immunofluorescence assays confirmed the nuclear translocation of NF-κB p65 during inflammatory responses. An absolute LDH leakage assays suggestedLPS-inducedcells injury, and the associated mechanisms are co-incident events. LPS-induced phosphorylation of ERKand JNK causes inflammation in epithelial cells through inhibition of ERK and JNK activation and NF-κB signaling pathway. Furthermore, the inhibition of NF-κB mRNA expression and the nuclear translocation of NF-κB lead to anti-inflammatory events. Likewise, activation of SUMF2 which inhibits IL-13 and reduces Th2-cytokines, NF-κB, and IgE levels to ameliorate asthma. On the other hand, TNFα-induced mucus production reduced NF-κB activation through inhibition of the activation status of Rac1 and IκBα phosphorylation. In addition, bradykinin B2 receptor (B2R), which mediates airway remodeling, regulates through NF-κB. Bronchial B2R expression is constitutively elevated in allergic asthma. In addition, certain NF-κB -dependent chemokines function to recruit eosinophils in the airway. Besides, bromodomain containing 4 (BRD4) plays a significant role in mediating innate immune response in human small airway epithelial cells as well as transglutaminase 2 (TG2), which is detectable in saliva. So, the guanine nucleotide-binding regulatory protein α-subunit, Gα16, expresses a κB-driven luciferase reporter. This response was accompanied by phosphorylation of IκBα. Furthermore, expression of Gα16 in saliva markedly enhanced TNF-α-induced κB reporter activity. Methods: The applied method to form NF-κB activation is the electromobility shift assay (EMSA). Also, B2R-BRD4-TG2 complex detection by immunoassay method within saliva with EMSA of NF-κB activation may be a novel biomarker for asthma diagnosis and follow up. Conclusion: This concept introduces NF-κB signaling pathway as potential asthma biomarkers and promising targets for the development of new therapeutic strategies against asthma.

Keywords : NF-κB, asthma, saliva, T-helper
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