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Title: Corticosteroid plus long-acting beta$_2$-agonist prevent virus-associated upregulation of B7-H1/PD-L1 on airway epithelium

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Body: Background: Airway viral infections exacerbate asthma and chronic obstructive pulmonary disease. B7-H1/PD-L1 is a coinhibitory molecule implicated in an escape mechanism of viruses from the host immune systems. This escape may induce viral persistence and lead to exacerbation of the underlying diseases. We previously showed that an analog of viral double-stranded RNA, polyinosinic-polycytidylic acid (poly IC), upregulated the expression of B7-H1 on airway epithelial cells, which was corticosteroid-resistant. We investigated the effects of corticosteroid plus long-acting beta$_2$-agonist (LABA) on the expression of B7-H1. Methods: BEAS-2B cells were stimulated with poly IC or the respiratory syncytial virus. B7-H1 expression was assessed by flow cytometry. Results: Poly IC-induced upregulation of B7-H1 was suppressed by high-concentration fluticasone but not by salmeterol. The upregulation was suppressed by low-concentration fluticasone when used in combination with salmeterol. Similar results were obtained from experiments using other combination of corticosteroid and LABA. Their combination also suppressed the virus-induced upregulation of B7-H1. Poly IC stimulation induced the nuclear translocation of the nuclear factor kB (NF-kB). The inhibitors of NF-kB activation prevented the poly IC-induced upregulation of B7-H1. The corticosteroid in combination with LABA enhanced the de novo induction of IkBa, the endogenous inhibitor of NF-kB activation. Conclusion: Corticosteroid plus LABA attenuates virus-associated upregulation of B7-H1 on airway epithelial cells via suppression of NF-kB activation.