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Abstract (poster session)

The live attenuated B. pertussis vaccine strain BPZE1 subverts the immune functions of RSV-infected human dendritic cells

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Objectives The respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection in infants. The immune response to RSV is still not fully understood and many data suggest an activation of innate immunity mainly focussed on the induction of a cytokine storm and a consequent tissue damage. Despite several efforts to develop effective vaccines, none have been successful to date. Recently, BPZE1, a live attenuated Bordetella pertussis vaccine strain, has been developed and entered a phase I safety trial (www.ChildINNOVAC.org). Immunization with BPZE1 protects mice challenged with influenza virus, suggesting potent adjuvant properties. To support the potential application of BPZE1 as adjuvant in a future RSV vaccine, we evaluated the immunomodulatory properties of BPZE1 in a model of human dendritic cells (DC) infected with RSV. Methods GM-CSF and IL-4 monocytes-derived DC (mDC) were exposed to RSV and/or to BPZE1. Functions of infected mDC were assessed, including cytokine production and polarization of T helper cells in co-culture experiments with allogeneic T cells. The phosphorylation of mitogen-activated protein kinases (MAPKs) p38, ERK1-2 and IkBalfa was evaluated by Western Blot. RT-PCR was used to measure IFNbeta, IRF-8, RANTES and IL-12p35 and IL-12p40 gene expression. Results BPZE1 was able to induce the production of IL-10, IL-23, and low level of IL-12p70 while RSV infection did not induce any of these cytokines. BPZE1 and RSV induced two different signal pathways: BPZE1 triggered the activation of p38 and ERK ½ MAPKs phosphorylation and expression of IL-6, IL12p40 and low level of IL-12p35 subunits; RSV triggered the activation of STAT1 phosphorylation and the expression of IFNbeta and several IFN-regulated genes, including IRF-8, RANTES and high levels of IL-12p35 subunit. Remarkably, in BPZE1/RSV co-infection the intracellular pathways complement each other as demonstrated by the enhanced production of IL-12p70. In vitro polarization experiments showed that RSV-primed mDC drive the expansion of a mixed Th1/Th2. Strikingly, the co-infection greatly decreased Th2 and increased Th17 expansion. Conclusion BPZE1 is able to re-direct the RSV immune response by modification of the cytokine profile that has a profound effect on polarization of T helper cells. These results support a potential application of BPZE1 as adjuvant in a future RSV vaccine. Supported by EC grant agreement 201502 (ChildINNOVAC).