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Title: LSC 2013 abstract - TLR7 decreases and TLR9 increases the airway responses in mice with established allergic inflammation

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Body: Toll-like receptor (TLR) 7 and TLR9 are localized in the endosomal compartment of the cell sharing the same adaptor protein. Their effect on an established allergic airway inflammation remains to be described. To this end, mice with an established ovalbumin (OVA)-induced allergic airway inflammation were given R848, a TLR7 agonist and CpG, a TLR9 agonist intranasally during four consecutive days. At day five the methacholine induced airway reactivity (AR) and the numbers of inflammatory cells in lung tissue and bronchial lavage fluid as well as presence of various mediators were assessed. OVA treatment enhanced AR. R848 had no effect on airway reactivity among control mice, but decreased the OVA-induced hyperresponsiveness. CpG increased AR in controls but did not affect the increase in airway reactivity caused by OVA treatment. OVA augmented the number of eosinophils and macrophages in bronchial lavage fluid. These increases were reduced by R848 and CpG. CPG enhanced the number of neutrophils and lymphocytes in control pulmonary tissue. The increase of neutrophils was not affected by an established allergic inflammation. In contrast, R848 did not influence pulmonary cell infiltration regardless of treatment. Enhanced pulmonary levels of IL-5 and leukotriene B_4 were seen after OVA, an effect reversed by R848-treatment. CpG increased the levels of pro-inflammatory mediators like IL-12, CXCL1 and CXCL9 in both control and OVA-treated mice. The conclusion from this study is that TLR7 activation interact with and decrease the outcome whereas TLR9 activation mainly does not react with and are not affected by an established allergic reaction.