A selective 7 nicotinic acetylcholine receptor agonist, PNU-282987, attenuates ILC2s activation and Alternaria induced airway inflammation

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Abstract

Background: The anti-inflammatory effect of the α7nAChR agonist, PNU-282987, has previously been explored in the context of inflammatory disease. However, the impact of PNU-282987 on type 2 innate lymphoid cells (ILC2s)-mediated allergic airway inflammation has not been established. Aims: To determine the effects of PNU-282987 on the function of ILC2s in the context of IL-33 or Alternaria Alternata (AA)-induced airway inflammation. Methods: PNU-282987 was administered to mice that received recombinant IL-33 or AA intranasal challenge. Whole lung was collected from mice for histological analysis, and ILC2 populations were quantified in the lungs and BALF of these mice. Additionally, ILC2s were isolated from murine lung tissue and cultured in vitro in the presence of IL-33, IL-2 and IL-7 with or without PNU-282987, and the expression of the transcription factors GATA3, IKK, and NF-ϰB was determined in these cells. Results: PNU-282987 significantly reduced airway goblet cell hyperplasia, eosinophil infiltration, and ILC2s numbers in BALF in response to IL-33 or AA. In vitro IL-33 stimulation of isolated lung ILC2s showed a reduction of GATA3 and Ki67 in response to PNU-282987 treatments. When compared to the established α7nAChR agonist, GTS-21, there was a notable reduction in IKK and NF-ϰB phosphorylation in the PNU-282987 treated group when compared to the GTS-21 treated ILC2s. Conclusion: PNU-282987 inhibits ILC2s-associated airway inflammation by inhibiting ILC2s cell proliferation and the initiation of inflammatory cascades.

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