PCI-10

IL-33-dependent eosinophilia in the lung mediated by natural helper cells

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Abstract

Natural helper (NH) cells are Th2-type innate lymphocytes producing large amounts of Th2 cytokines IL-5, IL-6 and IL-13 during infection of helminth such as *Nippostrongilus brasiliensis*, which results in eosinophilia and goblet cell hyperplasia in the lung and intestine. Induction of NH cells and eosinophilia were observed in the lung during an early phase of *N. brasiliensis* infection and by intratracheal administration of IL-33 or a combination of IL-2 and IL-25. Eosinophilia was not induced in γc-/-Rag-2-/- mice lacking NH cells but adoptive transfer of NH cells restored the accumulation of NH cells and eosinophilia in the lung. NH cells express CCR2 in fat-associated lymphoid cluster (FALC) in visceral adipose tissue in naïve mice but stimulation by IL-33 or a combination of IL-2 and IL-25 downregulates CCR2 and induces CCR4 and CCR5, which are involved in the migration of cells to the lung. NH cells thus play an important role during helminth infection in the induction of goblet cell hyperplasia and eosinophilia in the lung, which are also characteristics of pathophysiology of asthma.