Dogal Lenfoid Hucreler
Mübeccel Akdis

Despite detailed descriptions of the mechanisms through which ILC subsets contribute to various adaptive and innate immune processes, their involvement in immunoregulation has not been delineated. Retinoic acid receptor–related orphan receptor gt (RORgt)–expressing type 3 innate lymphoid cells (ILC3s) in adult mice and human subjects play a role in innate immune defense at mucosal barrier surfaces and tissue regeneration after damage, mainly through secretion of their signature cytokine, IL-22. ILC3s are also involved in limitation of pathologic adaptive immune responses against commensal bacteria in the gut. ILC3s have a dedicated role in the maintenance and restoration of homeostasis at the interface of the environment and the body. Human circulating $Lin^{-}CD4^{-}CD56^{-}IL\text{-}7Ra^{+}CD161^{+}$ c-Kit^{+} ILC3s were able to differentiate into the recently identified activated form of ILC3s, $CD40L^{+}$ ILC3s, in response to IL-15. $CD40L^{+}$ ILC3s reside on the border of the T-cell–B-cell areas in tonsils and are in close contact with B cells in vivo. $CD40L^{+}$ ILC3s and B cells are in mutually beneficial relationship with each other because $CD40L^{+}$ ILC3s strongly support the survival and proliferation of B cells and promote IgM secretion and IL-10–producing, programmed death ligand 1 (PD-L1)–expressing itBreg cell differentiation in aCD40L- and BAFF-dependent manner, whereas B cells upregulate IL-15, a growth factor for ILC3s, on interaction with $CD40L^{+}$ ILC3s. ILC3s can contribute to the maintenance of immune tolerance through itBreg cell induction. However, significantly reduced circulating ILC3 numbers was found within all lymphocytes in highly selected patients with moderate-to-severe allergic asthma (GINA steps 3-4) compared with those in healthy control subjects. There was a significant positive correlation between peripheral blood ILC3 and itBreg cell percentages, and the lower ILC3 levels in allergic asthmatic patients were accompanied by lower itBreg cell counts.