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Developmental Options and Functional Plasticity of Human Innate Lymphoid Cells

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Innate lymphoid cells (ILC) comprise a family of hematopoietic cells that lack antigen-specific receptors but can be activated to promptly produce immunomodulatory cytokines (including interleukin (IL)-5, -13, -17A, -22, TNF-α and interferon-γ) and thereby contribute to the immediate, first-line immune defense against viral, bacterial, and parasitic infections. ILCs include the previously described natural killer (NK) cells and have a similar 'natural' effector function which is immediately available during immune responses and prior to that of adaptive immunity. Three groups of ILC (ILC1, ILC2, ILC3) have been described that share biological activities of T helper (Th)1, Th2 and Th17/22 subsets and CTL. ILCs are active during both fetal and adult life and play important roles in the homeostasis of mucosal and non-mucosal tissues. How ILCs develop from hematopoietic precursors is poorly defined. We have embarked on a series of ILC studies in humans in an effort to understand how these innate cell subsets may impact on disease. We uncovered novel functional properties (‘plasticity’) of human group 2 ILCs in the context of intestinal inflammation, and recently identified human ILC precursors (ILCP). These observations suggest a novel model for ILC development in which ILCP enter tissues and differentiate in situ under the influence of environmental signals. Our current efforts aim to understand how tissue ILCP are activated. The discovery of human ILCP opens a path to novel therapies using adoptive transfer of defined ILC subsets as cellular immunomodulators.