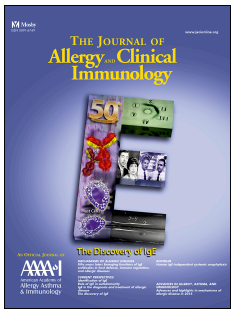
Accepted Manuscript



The Cellular Immune System Comes of Age

René A.W. van Lier, Taco W. Kuijpers

PII: S0091-6749(17)30420-7

DOI: 10.1016/j.jaci.2017.02.023

Reference: YMAI 12695

To appear in: *Journal of Allergy and Clinical Immunology*

Received Date: 18 January 2017

Revised Date: 17 February 2017

Accepted Date: 27 February 2017

Please cite this article as: van Lier RAW, Kuijpers TW, The Cellular Immune System Comes of Age, *Journal of Allergy and Clinical Immunology* (2017), doi: 10.1016/j.jaci.2017.02.023.

THE CELLULAR IMMUNE SYSTEM COMES OF AGE

René A.W. van Lier[1,4] and Taco W. Kuijpers[2,3]

[1]Departments of Hematopoiesis and [2]Blood Cell Research, Sanquin Research and Landsteiner Laboratory, Academic Medical Center (AMC), University of Amsterdam, the Netherlands.
[3]Department of Pediatric Hematology, Immunology, and Infectious Disease, Emma Children's Hospital, AMC.
[4]Correspondence: RAW van Lier, Sanquin Blood Supply Foundation, Plesmanlaan 125, 1066CX Amsterdam, the Netherlands
Phone: +31205123450
Fax: +31205123303
Email: r.vanlier@sanquin.nl

In this issue of the journal Van den Heuvel and colleagues[1] present data on a unique longitudinal study in which almost 1200 children were analyzed for immune cell numbers and phenotypes between birth and six years of age. Hierarchical clustering of 62 immune cells revealed that changes in immune cell numbers can be described in 4 distinct patterns and non-genetic factors could be identified that co-determine immune cell numbers. Importantly, but non unexpectedly, infectious disease history (notably herpes viruses) have a strong impact on numbers and phenotype of CD4+ and CD8+ T cell subsets and NK cells[2].

This type of study is essential to begin to understand the gradual and ordered acquisition of immune competence. Interestingly, Van den Heuvel et al[1] show that innate immune cell numbers are high at birth at drop rapidly in the first months of life. On the other hand, the development of the adaptive immune cell system follows distinct waves. Naïve lymphocytes rapidly and transiently accumulate in the first months of life, whereas likely after microbe encounter cells with features of antigen priming emerge somewhat later and these populations continue to increase in size. The relative predominance of innate immune cells shortly after birth corroborates the notion that these cells, also from an phylogenetic perspective, form a first line of defense, whereas it takes time for the adaptive lymphoid system to fully mature. Indeed, in the first months of extra-uterine life maternal antibodies may incite critical effector functions thereby in collaboration with the innate system providing a sufficient barrier to many pathogens. Notably, this protection has limitations as e.g. infections with CMV can be held in check by an initial NK cell response but depend on adaptive T cell reaction for long-term suppression and clearance[3].

The current study is highly controlled for infections with a number of specific pathogens but at the same time reveals an intrinsic problem with performing infection studies in healthy humans. In experimental mouse studies, timing and dosage of exposure to the (primary) infectious agents are known and consequently protocols can be developed that accurately depict the impact of the particular infection on different aspects of the immune system. In human studies, we are faced with a number of problems. Not only can neither the dose and exact time point of