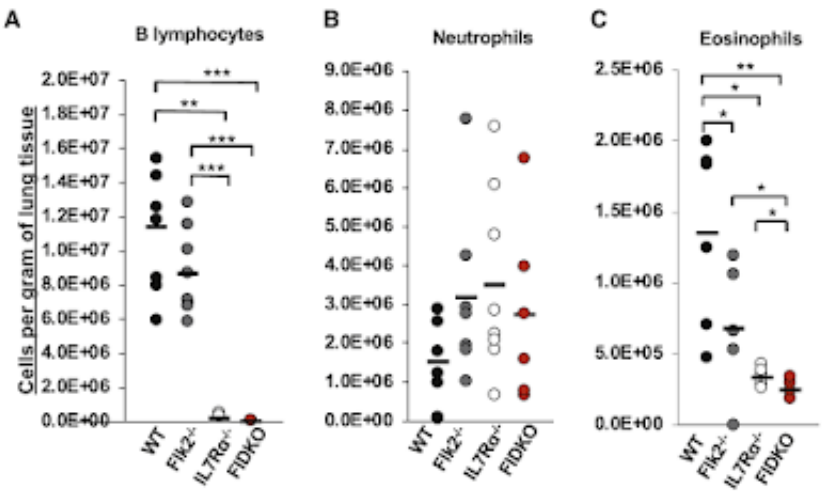
simply blood
Deconstructing Blood Cell Research
Building the Hematology Community

Exploring Experimental Hematology: November 2020 (Volume 42)

- November 12, 2020

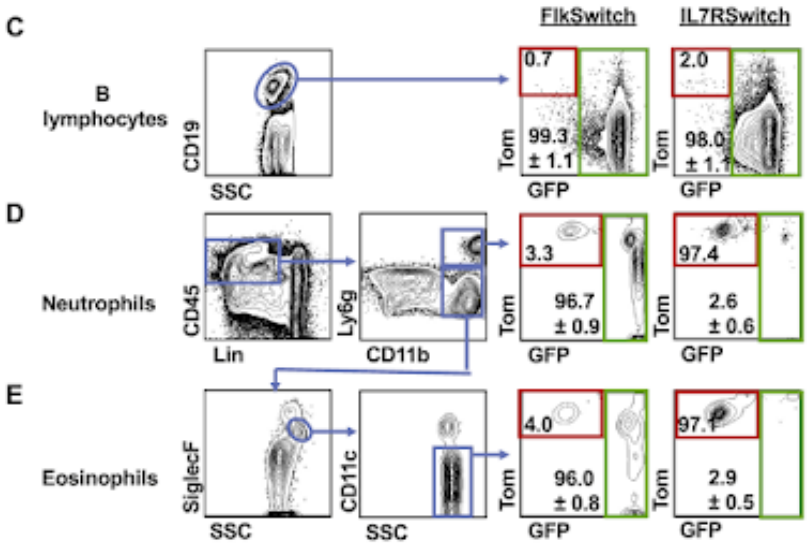
In this issue of *Simply Blood*, we are deconstructing an invited perspective from Experimental Hematology as Dr. Forsberg and colleagues build on their interesting prior work on differentiation of tissue resident macrophages (trMacs) via an interleukin-7α receptor (IL7Rα)-positive progenitor (Leung et al. 2019). trMac differentiation follows a 'nontraditional' pathway of myeloid cell specification occurring in fetal hematopoiesis. In this study, they now examine the role of IL-7 signaling in the maintenance of other tissue myeloid cells - neutrophils and eosinophils - in the lung, work directed at better understanding the immune system of the lung and its relationship to respiratory diseases.

First, the authors examined lung B-cell, neutrophil, and eosinophil content in Flk2$^{-/-}$, IL7Rα$^{-/-}$, or combined knock-out mice. Dr. Forsberg had previously shown that all 'traditional' adult myeloid and lymphoid cells, but not trMacs, develop via a Flk2-positive progenitor (Beaudin et al. 2014). Here, as expected, they found that IL7Rα was required for B-cell residence in the lung, but surprisingly, they also found that lung eosinophils also depended on IL7Rα.

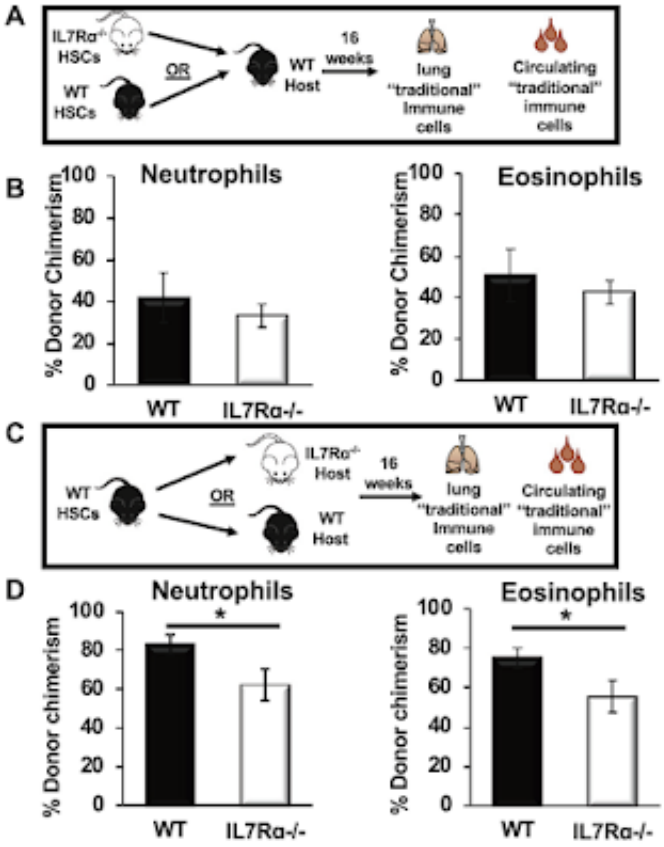


The authors next use lineage tracing to determine whether, like B-cells, eosinophils developed via an IL7Rα-expressing progenitor. Here, they modified their prior 'FlkSwitch' transgenic system to develop IL7RSwitch. In these transgenic systems, if a mature cell developed via a progenitor expressing Flk2

(FlkSwitch) or IL7Rα (IL7RSwitch), cells would transition from Tomato to GFP expression. As expected, they found that B-cells, neutrophils, and eosinophils were all labeled with GFP in the FlkSwitch system, and that B-cells were labeled with GFP in the IL7Switch system. However, despite their dependence on IL7Rα, eosinophils were not significantly labeled with GFP in the FlkSwitch system, suggestive of a cell extrinsic mechanism of eosinophil regulation by IL-7.



To test this possible mechanism, the authors performed hematopoietic stem cell (HSC) transplantation studies using their knock-out mice. They found that transplantation of IL7Rα$^{-/-}$ HSCs into wild-type recipients did not affect neutrophil or eosinophil population of the lungs. However, transplantation of wild-type HSCs into IL7Rα$^{-/-}$ recipients resulted in impaired neutrophil and eosinophil population of the lungs. IL7Rα$^{-/-}$ mice showed altered levels of cytokines that regulate eosinophil development.



This paper is an important advance in understanding the ontogeny of tissue immune cells, with important implications for pulmonary disease. Further studies should focus on uncovering the mechanism by which IL-7 extrinsically regulates eosinophil populations in tissues.

Beaudin AE, Boyer SW, Forsberg EC. 2014. Flk2/Flt3 promotes both myeloid and lymphoid development by expanding non-self-renewing multipotent hematopoietic progenitor cells. Exp Hematol 42: 218-229 e214.

Leung GA, Cool T, Valencia CH, Worthington A, Beaudin AE, Forsberg EC. 2019. The lymphoid-associated interleukin 7 receptor (IL7R) regulates tissue-resident macrophage development. Development 146.

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- *March 11, 2025*

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- *November 14, 2024*

Each month, Simply Blood spotlights a lab contributing to the fields of hematology, immunology, stem cell research, cell and gene therapies, and more. Get to know groups doing cutting edge research from around the world! This month, we are featuring the Vanuytsel Lab which is based out of the Center for …

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