
The lymphoid-associated interleukin 7 receptor (IL7R) regulates tissue-resident macrophage development.

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Public Summary:

The discovery of a fetal origin for tissue-resident macrophages (trMacs) has inspired an intense search for the mechanisms underlying their development. Here, we performed in vivo lineage tracing of cells with an expression history of IL7Ralpha, a marker exclusively associated with the lymphoid lineage in adult hematopoiesis. Surprisingly, we found that Il7r-Cre labeled fetal-derived, adult trMacs. Labeling was almost complete in some tissues and partial in others. The putative progenitors of trMacs, yolk sac (YS) erythromyeloid progenitors, did not express IL7R, and YS hematopoiesis was unperturbed in IL7R-deficient mice. In contrast, tracking of IL7Ralpha message levels, surface expression, and Il7r-Cre-mediated labeling across fetal development revealed dynamic regulation of Il7r mRNA expression and rapid upregulation of IL7Ralpha surface protein upon transition from monocyte to macrophage within fetal tissues. Fetal monocyte differentiation in vitro produced IL7R(+) macrophages, supporting a direct progenitor-progeny relationship. Additionally, blockade of IL7R function during late gestation specifically impaired the establishment of fetal-derived trMacs in vivo. These data provide evidence for a distinct function of IL7Ralpha in fetal myelopoiesis and identify IL7R as a novel regulator of trMac development.

Scientific Abstract:

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