

Embryonic white blood cells needed in adulthood

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Leukocytes which arise during the embryonic period regulate iron metabolism and the growth of the mammary gland in adults.

Leukocytes of the macrophage series are needed for defence reactions against microbial infections. In addition, they participate in the development and maintenance of organs and tissues and destroy tumour cells.

It was previously thought that the tissue-resident [macrophages](#) originate from bone marrow-derived precursors which migrate via the blood into different organs. However, new research has uncovered that a significant proportion of macrophages are distributed to the tissues already before the onset of bone marrow function. These long-lived embryo-derived macrophages maintain themselves in the adult tissues through stem cell-like renewal.

Finnish researchers at the University of Turku were the first to identify the molecular mechanism which controls the migration of early macrophages.

"While studying other topics, we incidentally noticed that a defect in a certain blood vessel selective protein causes major alterations in the macrophage distribution. In the absence of this protein, known as Plvap, the production of the earliest macrophages in the yolk sac and the development of macrophages after birth were completely normal. In a striking contrast, the macrophage production in the fetal liver failed in

the absence of Plvap," states Dr Pia Rantakari.

She and her collaborators found out that the Plvap protein immobilised attractant cues which guide the migration of macrophage precursors from the liver to the blood and thereby regulate their dissemination to different target organs. According to Dr Rantakari, the macrophage precursors are in a sense stuck in the liver without the Plvap protein.

"It was very exciting to learn that a defect in the generation of such a small macrophage population has dramatic consequences even in adults. The lack of these macrophages causes an aberrant accumulation of iron which is continuously released from old red blood cells. Moreover, the absence of the Plvap protein prevents the maturation of the [mammary gland](#) at puberty almost entirely. These data indicate that it is precisely these macrophages which are required for the development of the milk-producing ductal system in the mammary glands," says Dr Rantakari.

Dr Rantakari and her collaborators are now busy studying what other physiological functions are dependent on fetal liver-derived macrophages. Since macrophage targeting therapies are developed very actively worldwide, it is also essential to analyse how this particular macrophage subset is involved in the defence reactions against bacteria and tumour cells.

The study was recently published in the esteemed science periodical *Nature*. The work has mainly been funded by the Academy of Finland and Sigrid Juselius Foundation and has been performed in MediCity Research Laboratory at the University of Turku in Finland.

More information: Pia Rantakari et al. Fetal liver endothelium regulates the seeding of tissue-resident macrophages, *Nature* (2016). [DOI: 10.1038/nature19814](https://doi.org/10.1038/nature19814)

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