Leibniz Institute on Aging – Fritz Lipmann Institute

Media Release
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Embryonic macrophages in the bone marrow: regulators for normal hematopoietic stem cell numbers

Scientists at the Leibniz Institute on Aging - Fritz Lipmann Institute (FLI) in Jena discovered a previously unknown function of immune cells in the bone marrow. Embryonic macrophages - specialized phagocytes of the immune system - regulate the formation of blood stem cells and therefore the lifelong production of blood cells. They play a crucial role in the regulation of the size of the hematopoietic stem cell pool, which is essential for the continuous production of blood cells and the maintenance of a healthy immune system.

Jena. Our immune system is continuously renewed, as immune and blood cells have a limited lifespan and must therefore be constantly replaced. This is ensured by hematopoietic stem cells, which are found in the bone marrow. The process of blood cell formation is very important for the maintenance of a functional immune system and therefore for healthy aging. However, the process of blood cell formation requires a special micro-environment to function smoothly: the hematopoietic niche, which consists of supporting cells. How this niche is formed during development is still largely unknown.

A recent study of the team headed by Prof. Claudia Waskow at the Leibniz Institute on Aging - Fritz Lipmann Institute (FLI) in Jena has discovered that macrophages, which are produced before birth (embryonic development), play a key role in this process. These cells regulate the number of blood stem cells in the bone marrow through the orchestration of the set-up of the stem cell niche during development. These findings have now been published in the renowned journal “Nature Communications” (DOI: 10.1038/s41467-025-59059-9).

Macrophages - A heterogeneous stem cell population

The research team was able to show that two different groups of macrophages exist in the bone marrow: one with an embryonic origin and one that only arises from hematopoietic stem cells after birth. “The macrophage cell population is heterogeneous and, depending on age, consists of macrophages of different origins, so that they are either derived from embryonic sources or are formed with increasing age from adult blood-forming stem cells,” explains Prof. Waskow, head of the “Immunology of Aging” research group at the FLI.

Embryonic macrophages regulate the number of stem cells

Although they have a similar morphology (external characteristics), these macrophages differ significantly in terms of their function. “In particular, embryonic macrophages are essential for the correct number of blood stem cells in the bone marrow but are not required for the initial formation of stem cells in the embryo,” emphasizes Dr. Gülce Perçin, the first author of the study. “If these macrophages are missing, the number of blood stem cells is reduced and there are fewer progenitor cells for new blood cells. This has an impact on the body's ability to form new blood cells throughout life.”

Migration of hematopoietic stem cells is dependent on embryonic macrophages

But how do embryonic macrophages achieve this? Their absence affects the migration of hematopoietic stem cells into the bone marrow. The stem cells develop in other areas of the embryo and migrate to the bone marrow around birth, where they stay for the rest of the lifetime of the organism. The stem cells find their “destination” through chemical signals from the bone marrow - comparable with a special “smell” - which the stem cells recognize and thus know where they are needed. Mesenchymal stromal cells, which occur in the niche environment, can secrete these important signals for stem cells. The number of these specialized stromal cells as well as the production of the signals is coordinated by the embryonic-derived macrophages located in the bone marrow. If the embryonic macrophages are missing, the process of blood stem cell migration will no longer function optimally.

New insights into hematopoiesis and immune defense

“Our results show how complex the interactions are during the establishment of hematopoietic activity in the bone marrow and emphasize the importance of ontogenesis, i.e. the origin of the macrophages. They underline that bone marrow macrophages are not just simple immune cells, but actively control the conditions for healthy hematopoiesis,” the authors of the study summarize the results. “If we can better understand the role of embryonic macrophages, this would have wide-ranging implications for research into age-related diseases. In addition, the identification of the regulatory mechanisms underlying the establishment and maintenance of adult hematopoiesis could offer new therapeutic approaches to promote healthy aging.”

Publication

Embryonic macrophages orchestrate niche cell homeostasis for the establishment of the definitive hematopoietic stem cell pool. Perçin G, Riege K, Fröbel J, Metz J, Culemann S, Lesche M, Reinhardt S, Höfer T, Hoffmann S, Waskow C. *Nat Commun* **16**, 4428 (2025). https://doi.org/10.1038/s41467-025-59059-9

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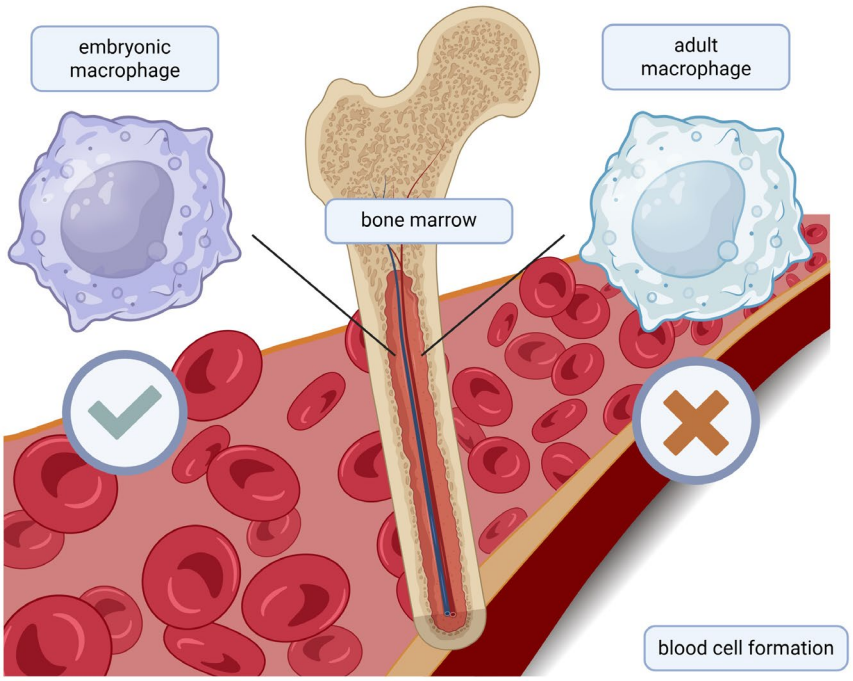
Picture



Embryonic macrophages - specialized phagocytes of the immune system - influence the formation of blood stem cells in the bone marrow and thus the lifelong production of blood cells. (Source: FLI / Kerstin Wagner; Created with *BioRender.com*)

Background

The **Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)** – upon its inauguration in 2004 – was the first German research organization dedicated to research on the process of aging. Around 350 employees from around 40 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit www.leibniz-fli.de.

The **Leibniz Association** connects 96 independent research institutions that range in focus from natural, engineering, and environmental sciences to economics, spatial, and social sciences and the humanities. Leibniz Institutes address issues of social, economic, and ecological relevance.

They conduct basic and applied research, including in the interdisciplinary Leibniz Research Alliances, maintain scientific infrastructure, and provide research-based services. The Leibniz Association identifies focus areas for knowledge transfer, particularly with the Leibniz research museums. It advises and informs policymakers, science, industry, and the general public.

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