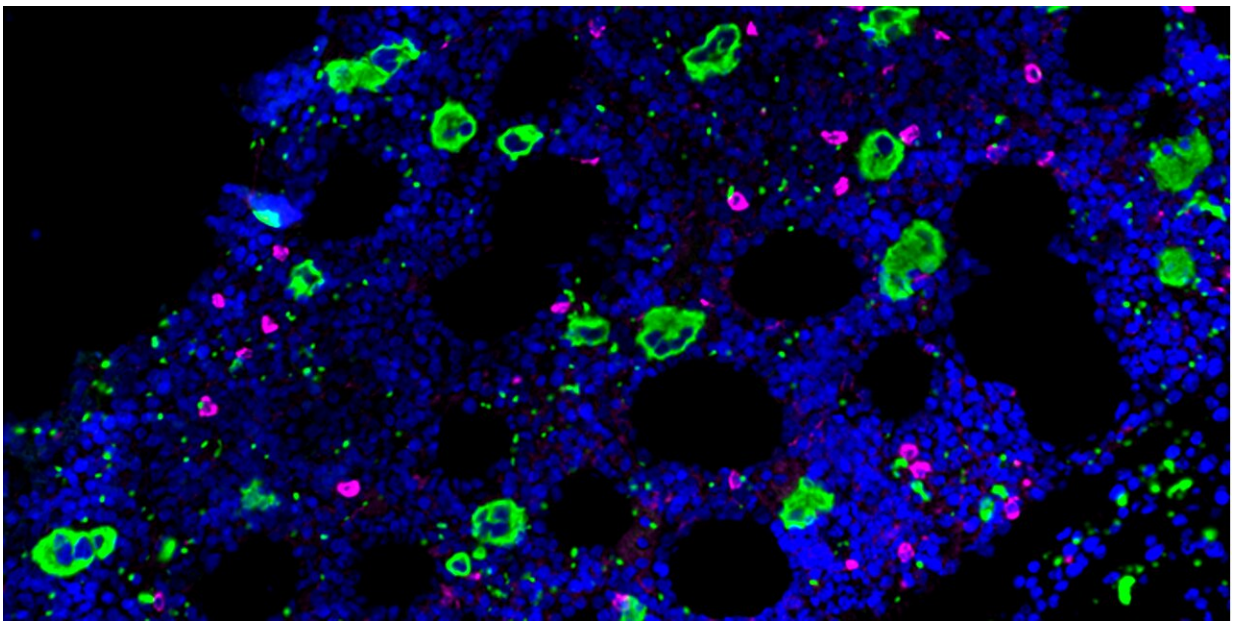
Immune cells monitor blood platelet maturation in bone marrow, researchers discover

July 17 2024



Tissue homeostasis: plasmacytoid dendritic cells monitor bone marrow, initiating on-demand megakaryocyte formation. Uniform distribution of megakaryocytes (green) controlled by plasmacytoid dendritic cells (magenta) within a human bone marrow section. Credit: Hellen Ishikawa-Ankerhold

Platelets play an essential role in wound healing. Underproduction can cause devastating bleeding, while overproduction increases the deadly risk of thromboses. Maintaining a constant level of platelets in the blood

(homeostasis) is therefore vitally important. Platelets are continuously formed by megakaryocytes (MKs) and released into the blood.

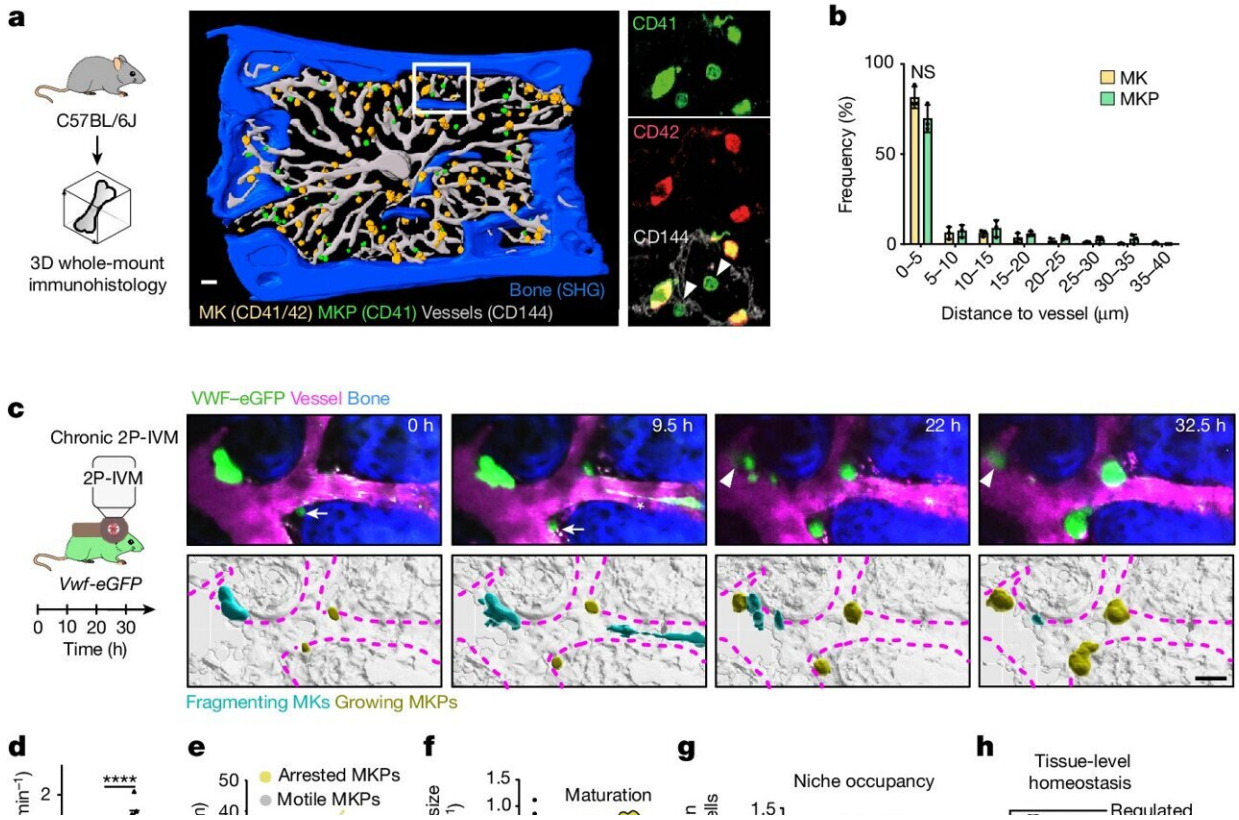
Researchers at LMU University Hospital and the Biomedical Center Munich (BMC) have now made a groundbreaking discovery: innate immune system cells known as plasmacytoid dendritic cells (pDCs) are substantially responsible for controlling the maturation of new MKs and therefore the formation of platelets. Moreover, pDCs precisely adjust the quantity of MKs to the needs of the body. The researchers published their findings in the journal *Nature*.

To find out how MKs develop (megakaryopoiesis), the lead authors—namely, Florian Gärtner, Hellen Ishikawa-Ankerhold, Susanne Stutte and Wenwen Fu,—studied the place where MKs originate: the bone marrow.

Innate immune system cells control megakaryopoiesis

They discovered that the progenitor cells of MKs are fully consumed and constantly replaced during platelet formation (thrombopoiesis). This decisive process is regulated by the innate immune system cells known as pDCs. It was already known that pDCs patrol the blood in small quantities so that they can act swiftly as one of the first immune cells to initiate viral defenses.

"We've identified a new process whereby pDCs also patrol inside the bone marrow and continuously 'measure' the stock of megakaryocytes being consumed," say the lead authors. "By releasing mediators, pDCs stimulate megakaryopoiesis from progenitor cells when required. And the immune system controls the homeostasis of MKs on this basis."



Spatiotemporal coordination of thrombopoiesis and megakaryopoiesis. Credit: *Nature* (2024). DOI: 10.1038/s41586-024-07671-y

Possible approach for therapies

As pDCs also play a role in defending the body against viral pathogens and can be activated by viral infections accordingly, this is where we find a previously unknown connection between infections such as COVID-19 and influenza and their effects on platelet formation.

"In patients with severe COVID-19, we identified an accumulation of activated pDCs in bone marrow tissue," says Gärtner. "The pDCs were in close contact with MKs, which correlated moreover with an excessive MK quantity in these patients."

The researchers hypothesize that pharmacological modulation of the pDC-mediated homeostatic circuit could benefit these patients. The discovery of this mechanism could form the basis for research into new treatment methods for COVID-19 and other diseases that are associated with dysregulated platelet production.

"The targeted modulation of pDC-controlled megakaryopoiesis offers possibilities for boosting or suppressing platelet production in various clinical scenarios," explains Gärtner.

More information: Florian Gaertner et al, Plasmacytoid dendritic cells control homeostasis of megakaryopoiesis, *Nature* (2024). DOI: 10.1038/s41586-024-07671-y

Provided by Ludwig Maximilian University of Munich