The Secret Life of Blood Stem Cells

New research reveals how blood stem cells cope with chronic inflammation

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A research team led by Meritxell Alberich-Jordà at the Institute of Molecular Genetics of the Czech Academy of Sciences has uncovered an unexpected protective strategy used by blood stem cells during chronic inflammation. In a study published in *Science Advances*, the researchers show that when persistent inflammation damages bone marrow function, blood stem and progenitor cells leave their usual home and settle directly in unexpected tissues. There, they actively cooperate with regulatory immune cells to limit inflammation and preserve blood formation, revealing a previously unknown partnership between stem cells and the immune system that may help explain how the body copes with inefficient blood cell formation during chronic inflammation.

Chronic inflammation and painful bone disease

Chronic inflammation is not only an abstract medical term — for patients, it often means persistent pain, limited mobility, and repeated flare-ups that interfere with everyday life. One example is chronic recurrent multifocal osteomyelitis (CRMO), a rare autoinflammatory bone disease that primarily affects children and adolescents. Patients experience recurring inflammation in one or more bones, leading to deep bone pain, swelling, fatigue, and, in severe cases, bone deformities or growth problems. There is currently no cure, and treatment focuses on long-term control of inflammation rather than its cause. In such chronic conditions, inflammation can also disrupt the bone marrow, the tissue responsible for producing blood and immune cells. How the body manages to maintain blood cell production when its primary system is compromised has long remained unclear.

When blood stem cells are forced to adapt

The research team discovered that under sustained inflammatory stress, blood stem and progenitor cells do not simply fail or disappear. Instead, they adapt. When the bone marrow environment becomes dysfunctional, these cells leave their usual niche and establish alternative sites of blood formation — a process known as extramedullary hematopoiesis. Surprisingly, this does not happen only in classical organs such as the spleen. The scientists found that blood stem cells can settle directly inside previously inhabited bone tissue, where they remain functional and capable of sustaining blood cell production. To study this process in detail, the researchers used an

experimental model of chronic autoinflammatory bone disease that mirrors key features of human CRMO, allowing them to track how stem cells respond to long-lasting inflammation.

"We were surprised to find fully functional blood stem cells in places where they were never expected to be," says Maria Kuzmina, first author of the study from the Institute of Molecular Genetics of the Czech Academy of Sciences. *"Instead of breaking down under inflammatory stress, these cells adapt, change their behavior, and actively contribute to maintaining blood production outside the bone marrow."*

A built-in emergency plan

When the bone marrow can no longer do its job, blood stem cells activate a kind of biological backup plan. Much like emergency generators that power essential services during a blackout, these cells relocate to unexpected tissues and set up temporary outposts that keep blood formation going under difficult conditions.

Importantly, they do not act alone. At inflamed sites, blood stem cells work closely with regulatory T cells — immune cells that function like peacekeepers, preventing inflammatory responses from running out of control. The stem cells help generate these regulatory T cells, creating a calmer local environment, while the regulatory T cells, in turn, shield the stem cells from inflammatory damage.

"This is a true two-way relationship," explains Maria Kuzmina. *"Stem cells help boost regulatory T cells that suppress inflammation, and those same immune cells protect the stem cells from becoming exhausted or destroyed."*

A shift in perspective

Although the findings do not point to an immediate therapy, they challenge long-held assumptions about how blood stem cells behave during chronic disease. *"Blood stem cells are usually seen only as factories for producing blood cells,"* says Meritxell Alberich-Jordà, group leader at the Institute of Molecular Genetics of the Czech Academy of Sciences and corresponding author of the study. *"Our work shows that under chronic inflammatory stress, these cells also actively help regulate inflammation and stabilize damaged tissue."*

By revealing that blood stem cells can directly influence immune environment, the study underscores the value of fundamental research. *"You cannot design effective treatments without first understanding how the system adapts and survives,"* Alberich-Jordà adds. *"This research lays the groundwork for rethinking how inflammation, immunity, and blood formation are interconnected."*

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