Infections can trigger hematopoiesis at sites outside the bone marrow – in the liver, the spleen or the skin. LMU researchers now show that a specific type of immune cell facilitates such "extra medullary" formation of blood cells.

Balanced hematopoiesis is essential for the function of the immune system. During fetal development, hematopoiesis takes place mainly in the liver and the spleen. Later the process is delegated to the bone marrow, and this tissue normally serves as the sole source of blood cells for the rest of one's lifetime. However, certain infections can reactivate hematopoiesis at sites other than the bone marrow, a process which is referred to as "extramedullary" hematopoiesis. One of the best known inducers is the so-called cytomegalovirus (CMV), a member of the herpesvirus family, which is widespread in human populations worldwide, and can lead to serious illness in individuals with immature or otherwise compromised immune systems.

An international team led by Professor Ulrich Koszinowski at LMU's Max von Pettenkofer-Institute has now examined how this virus activates hematopoiesis in tissues other than the bone marrow. "Herpesviruses are highly species-specific," explains Dr. Stefan Jordan, the lead author on the new paper. "So, in order to study the phenomenon of extramedullary hematopoiesis in an animal model, we were forced to turn to the mouse virus." The murine CMV induces extramedullary hematopoiesis principally in the spleen.

Killing of infected cells paves the way

The new findings reveal a hitherto unsuspected link between natural killer (NK) cells and hematopoiesis. NK cells play an important role in combating CMV infections, because they are the immune system's first line of defense against the virus. In the first place, they are able to recognize and eliminate CMV-infected cells and, secondly, they synthesize and secrete signal molecules that mobilize other types of immune cells to mount a concerted attack on the pathogen.

"The decisive factor that leads to hematopoiesis at otherwise dormant sites is the ability of NK cells to find and destroy virus-infected cells," says Jordan. Extramedullary hematopoiesis is actually initiated by the inflammatory reaction that occurs as an early response to infection with CMV. But when the virus can replicate and spread to other cells, the pathogen suppresses the process. "The development of extramedullary hematopoiesis in the spleen is dependent on the capacity of NK cells to prevent virus spread by effectively eliminating infected cells," Jordan explains.

Extramedullary hematopoiesis itself thus appears to be an antiviral reaction. This in turn has obvious implications for the development of novel therapies. Thus, targeted stimulation of the mechanism that triggers the process could help to fight and resolve viral infections. Conversely, there are situations in which the immune system overshoots, and the spleen becomes so enlarged that it has to be...
surgically removed. “In this context, it would be particularly useful to understand how CMV suppresses extramedullary hematopoiesis – then one might be able to exploit the mechanism to prevent rupture of the splenic capsule and life-threatening internal bleedings,” Jordan concludes. *(Cell Host and Microbe 2013)*


---

Provided by Ludwig Maximilian University of Munich


*This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.*