Unveiling the secret of blood regeneration: New insights into stress responses in hematopoietic stem cells

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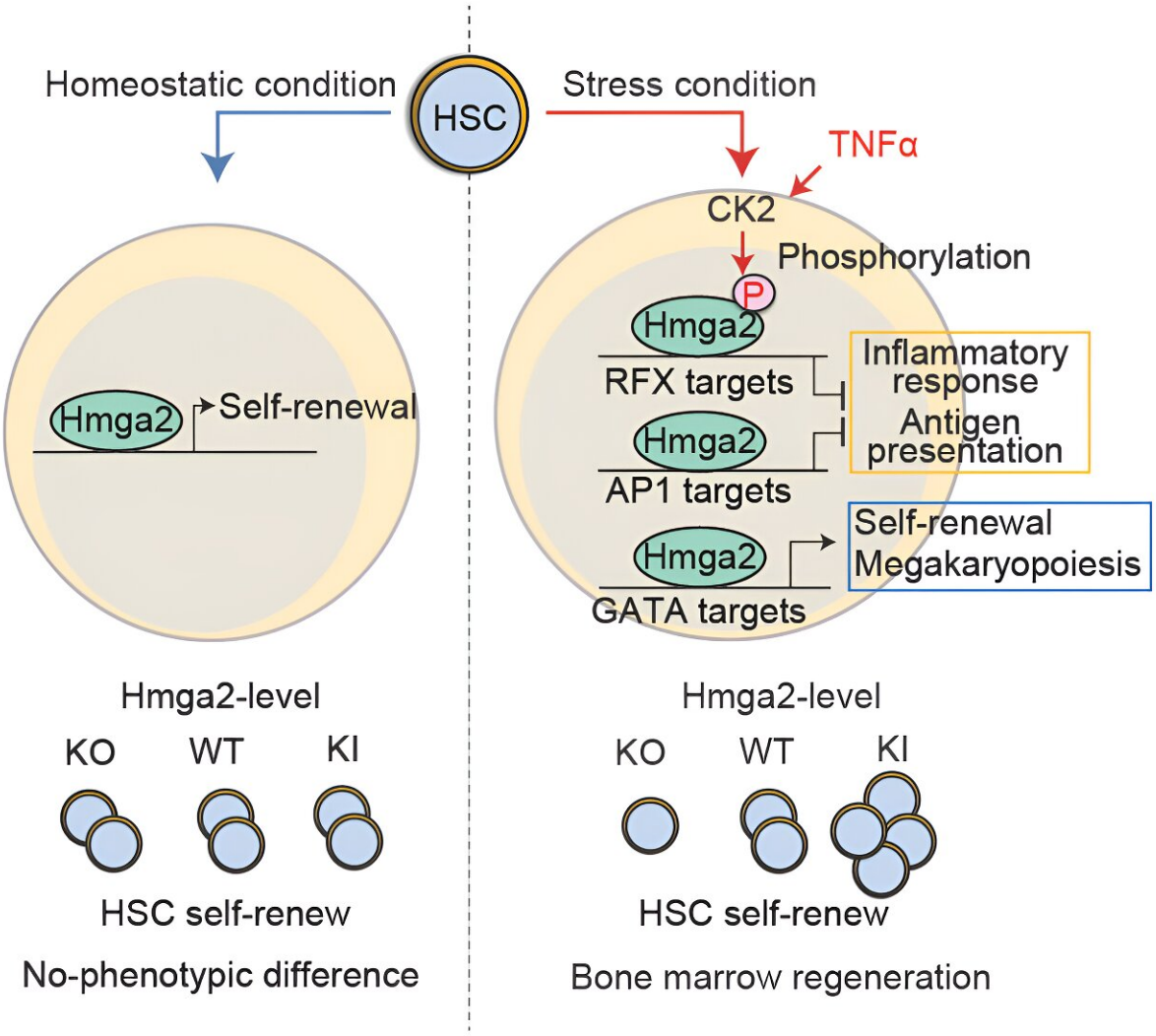

Kubota S, et al. EMBO J 2024

Chromatin modifier Hmga2 promotes adult hematopoietic stem cell function and blood regeneration in stress conditions. Credit: Goro Sashida, Kumamoto University

Kumamoto University researchers have made a discovery that sheds light on how the HMGA2 gene—an essential transcriptional activator involved in chromatin modification—regulates stress responses in hematopoietic stem cells (HSCs), thereby enhancing blood cell production recovery.

The study is published in *The EMBO Journal*.

Exposure to infections or treatments such as chemotherapy often leads to a rapid decline in blood cells, including red blood cells and platelets. HSCs, which reside in the bone marrow that can develop into various types of blood cells, are crucial for recovering from these stress-induced blood disorders.

Under stressed conditions, these stem cells proliferate and differentiate to produce blood cells. However, the exact mechanisms of this process have remained unclear.

The research team, led by Professor Goro Sashida from Kumamoto University's International Research Center for Medical Sciences (IRCMS), focused on HMGA2, a gene highly active in proliferating fetal hematopoietic stem cells.

HMGA2 has been well known for its role in binding to DNA and modifying chromatin structure to activate gene expression. In addition, it

is also critical for enhancing the stem cells' self-renewal capacity. This significance prompted the researchers to further investigate its role in this study

Using conditional knock-in (cKI) and knock-out (KO) mice, the researchers analyzed HMGA2's role in HSC function under both normal and stress conditions, such as exposure to chemotherapy and inflammatory cytokines.

They found that overexpression of HMGA2 significantly accelerates the recovery of HSCs and blood production under stress. Conversely, HMGA2 KO mice showed a reduced number of HSCs and platelet precursor cells.

Professor Sashida explained, "Our studies reveal that HMGA2 interacts with chromatin in response to inflammatory cytokines. It is phosphorylated by casein kinase 2 (CK2), which promotes its binding to chromatin and suppresses inflammation-related transcription factors, thereby modulating the inflammatory response."

This discovery not only enhances our understanding of blood cell regeneration mechanisms but also holds promising potential for developing therapies to rapidly restore blood cell production in individuals suffering from severe infections or post-cancer treatment blood disorders.

More information: Sho Kubota et al, Chromatin modifier Hmga2 promotes adult hematopoietic stem cell function and blood regeneration in stress conditions, *The EMBO Journal* (2024). DOI: 10.1038/s44318-024-00122-4

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