

Study uncovers key player contributing to healthy maintenance of bone marrow niche

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A study led by scientists from the Cancer Science Institute of Singapore (CSI Singapore) at the National University of Singapore (NUS) has uncovered a key player contributing to the maintenance of hematopoietic stem cells (HSCs), blood cell precursors which have the ability to become any type of blood cell in the body.

The research team, which includes Professor Toshio Suda and Dr Ayako Ishizu, who are respectively Senior Principal Investigator and Visiting Senior Research Scientist from CSI Singapore, found that the CLEC-2 protein was able to mediate the activity of the bone marrow (BM) niche where HSCs reside, and contribute to the health of the BM niche by influencing the production of Thrombopoietin (Thpo) protein.

While earlier studies have established the requirement of Thpo for the regular activity of HSCs in the BM niche, this study is the first to identify CLEC-2's role in the regulation of Thpo production, which contributes to the regular activity of HSCs in the BM niche. The team found that deficiencies in CLEC-2 result in a reduction of Thpo levels, as well as irregularities in BM niche and HSC maintenance, thus leading to abnormal blood cell production and activity.

The findings of the study were published in the *Journal of Experimental Medicine* in November 2015.

The healthy maintenance of the BM niche is significant given that HSCs are able to replenish all types of blood cells in the body, and are hence responsible for the regenerative abilities of the blood cells. While a <u>bone marrow transplant</u> remains the most promising therapy option for sufferers of many blood disorders, post-transplant prognoses are largely dependent on the quality and amount of donor HSCs which are transplanted into the recipient.

"As leukaemia stem cells are known to hijack the healthy <u>bone marrow</u> niche and rely on niche signals for disease progression, results from this study may point to these irregularities influencing the development and progression of blood diseases. We are hopeful that our findings from this study will contribute towards a better understanding of the underlying causes of the development and progression of hematopoietic diseases such as leukaemia and lymphoma, and ultimately, to the advancement of treatment for such diseases," said Prof Suda.

More information: A. Nakamura-Ishizu et al. CLEC-2 in megakaryocytes is critical for maintenance of hematopoietic stem cells in the bone marrow, *Journal of Experimental Medicine* (2015). DOI: 10.1084/jem.20150057

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