New insight into how immune cells are formed

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In contrast to what has been previously believed, development of blood stem cells into mast cells, a type of specialised immune cell, does not depend on stem cell factor. This has been demonstrated in a new collaborative study by researchers at Karolinska Institutet and Uppsala University, and published in the scientific journal *Blood*. The results could pave the way for new treatments for certain types of blood diseases.

Allergy and asthma affect a high percentage of the population. Mast cells are specialised immune cells that play an important role not only in these conditions but also in other diseases such as mastocytosis, a haematologic disease involving an increased number of mast cells. It has been commonly understood that the growth factor stem cell factor, which stimulates mast cell development, is essential for the formation of mast cells. Now researchers at Karolinska Institutet and Uppsala University have shown that this is not the case. The researchers analysed mast cells and their progenitors in blood from patients with chronic myeloid leukaemia, a disease of the blood.

"When the patients were treated with the drug imatinib (Glivec), which blocks the effect of stem cell factor, the number of mature mast cells dropped, while the number of progenitor cells did not change. We were thus able to conclude that mast cell progenitors did not require stem cell factor", says Professor Gunnar Nilsson at the Department of Medicine, Solna, and the Centre of Excellence for Systemic Mastocytosis at Karolinska Institutet, and visiting professor at the Department of Medical Sciences, Uppsala University, who led the study.

By culturing the mast cell progenitor cells present in blood, which are relatively uncommon (about 10 cells per million white blood cells), the researchers found that mast cell progenitors could survive, divide and partially mature without stem cell factor. Instead, development can take place with the factors interleukin 3 and 6.

"The study increases our understanding of how mast cells are formed and could be important in the development of new therapies, for example for mastocytosis for which treatment with imatinib/Glivec is not effective. One hypothesis that we will now test is whether interleukin 3 can be a new target in the treatment of mast cell-driven diseases", comments Joakim Dahlin, researcher at the Department of Medicine, Solna, at Karolinska Institutet and first author of the study.

More information: Joakim S. Dahlin et al. KIT signaling is dispensable for human mast cell progenitor development, *Blood* (2017). DOI: 10.1182/blood-2017-03-773374

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