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Mapping the metabolism of blood stem cells

Researchers from the Max Planck Institute of Immunobiology and Epigenetics in Freiburg and ETH Zürich have created the first integrated map detailing the metabolic and molecular changes in human blood stem cells as they age, specialize, or turn cancerous. Their innovative research, made possible by highly sensitive low-input techniques, identifies the nutrient choline, as a key player in preserving youthful stem cell traits. This work offers profound insights into stem cell health and disease, suggesting promising directions for nutritional and therapeutic interventions to maintain a healthy blood system.

Hematopoietic stem cells (HSCs) are rare cells tucked away in the bone marrow. They hold the unique capability to produce every type of blood cell, from oxygen-carrying red blood cells to infection-fighting immune cells. HSCs are essential for keeping us healthy. However, as we age or in conditions like leukemia, their remarkable regenerative powers can decline or become disrupted, leaving our blood and immune systems vulnerable to attacks – especially under stress conditions.

But how do blood stem cells change as we grow older or when disease strikes? A new study from the Max Planck Institute of Immunobiology and Epigenetics in Freiburg and the ETH Zürich now offers the first integrated view of metabolism and molecular programs in these rare cells revealing how these inner features shift as the cells specialize, age, or become cancerous.

A combination of highly sensitive »low-input« methods

Studying these cells is no easy task. Until now, gaining an in-depth understanding of the metabolic profile of hematopoietic stem cells has been an enormous challenge. Due to their rarity and the limited availability of human bone marrow samples, it has been difficult to perform comprehensive analyses. "To overcome this, we developed highly sensitive techniques which enable the acquisition of meaningful metabolic data from an extremely small number of cells. This allowed us to measure hundreds of metabolites and lipids using far fewer cells than typical approaches require", says Maria-Eleni Lalioti, one of the two first authors of the study.

A Venn diagram shows data integration from RNA-seq, metabolomics, and lipidomics for the analysis of HSPCs and progenitors during differentiation, aging, and leukemia.
By integrating the collected metabolic data with gene expression profiles, the team created a comprehensive "map" of the cell's chemical processes and gene activity enabling them to trace how blood stem cells change during different stages of health, aging, and disease. "We could find, for instance, that human stem cells are less metabolically active than their more developed descendants. We find fewer metabolites needed for energy production, building cell parts, and making amino acids. This fits with the fact that stem cells usually stay in a resting state to protect themselves and their capabilities", says Professor Nina Cabezas-Wallscheid.

The stem cell booster

The most striking discovery involves choline, an essential nutrient found in foods such as eggs, soybeans, and fish. Healthy stem cells had high choline levels, which decreased as cells specialized, and declined further with aging and leukemia. "Our lab experiments revealed that choline supplementation boosted lipid production and helped preserve a more youthful, stem-like identity, suggesting that specific nutrients may be key to maintaining stem cell function", says the co-first author Mari Carmen Romero-Mulero.

The study also revealed changes in the lipid composition of blood stem cells which alter the membrane structure of the cells and affect how they sense and respond to their surroundings. "These findings provide new directions for exploring how metabolism not only shapes a cell's internal machinery but also its interactions with the environment", says co-corresponding author Jörg Büscher.

The study clearly demonstrates that human blood stem cells undergo fundamental metabolic changes as they specialize, age, or become diseased. These shifts can reshape both their identity and behavior. "This raises intriguing questions about whether

targeted nutrition could help preserve stem cell health, and whether metabolic interventions might support leukemia therapies or promote healthy aging", says Nina Cabezas-Wallscheid.

The data from the Cabezas-Wallscheid lab provide a comprehensive resource for further research into this field. By charting how metabolism guides the fate of human blood stem cells, this study lays the groundwork for future therapies aimed at maintaining stem cell function – helping to keep our blood system healthier for longer.

Publication:

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Further information

- Max Planck Institute of Immunbiology and Epigenetics