Breakthrough in Artificial Blood Production

Scientists have been working on the artificial production of blood for several decades. Making a new discovery, researchers from the Institute for Cellular Biology and Immunology Thurgau at the University of Konstanz, in collaboration with Queen Mary University of London, have come an important step closer to this goal.

Roughly 15,000 units of blood are needed daily in Germany, most of which currently come from donations. Research into developing alternative sources, such as large-scale artificial blood production, has been ongoing for decades but is still far from reaching its widespread utility. The main challenge lies in the complex and still not fully appreciated means how our bodies naturally produce this vital fluid.

Julia Gutjahr is a biologist at the Institute for Cellular Biology and Immunology Thurgau (BITG), an associated institute of the University of Konstanz. The BITG is funded by the Foundation for Science and Research of the Canton Thurgau. Gutjahr carries out research into the process of blood production, and, together with colleagues from Queen Mary University of London, she has deciphered a further intermediate step towards a complete understanding of the cellular processes: the molecular signal, chemokine CXCL12, triggers the expulsion of the nucleus by the red blood cell precursors, a key step in the development of red blood cells.

Blood Production Requires Perfect Timing

In the body, natural blood production takes place in the bone marrow. Stem cells develop into erythroblasts, which are precursor cells to erythrocytes — the red blood cells. “In the final stage of an erythroblast’s development into an erythrocyte, the erythroblast expels its nucleus. This process only occurs in mammals, allowing to make more room for haemoglobin involved in the transport of oxygen”, Gutjahr explains.

While the process of stem cell maturation into erythrocytes is now nearly optimised, it was previously unclear what factors induce the expulsion of the nucleus. “We discovered that the chemokine CXCL12 found mainly in bone marrow can trigger such nucleus expulsion, albeit in an interplay with several factors. By adding CXCL12 to erythroblasts at the right moment, we were able to artificially induce the expulsion of their nucleus,” says Gutjahr.

This finding is a scientific breakthrough that in the future should help make artificial blood production much more efficient. However, further research will still be necessary. Gutjahr began this work in 2019 as a postdoctoral researcher in the Lab of Professor Antal Rot at Queen Mary University of London. She is now continuing her research at the University of Konstanz. Since 2023, she has led her own research groups at the Institute of Cellular Biology and Immunology Thurgau, where she continues the studies on CXCL12.

“We are currently investigating how to use CXCL12 to optimize the artificial production of human erythrocytes,” Gutjahr explains. “Importantly, apart from immediate practical application for the industrial production of red blood cells, our results brought a completely new understanding of cell biological mechanisms involved in erythroblast responses to chemokines. While all other cells migrate when stimulated by CXCL12, in erythroblasts this signalling molecule is transported into the interior of the cell, even into the nucleus”, adds Rot. “There, it accelerates their maturation and helps to expel the nucleus. Our research shows for the first time that chemokine receptors not only act on the cell surface but also inside the cell, thus opening entirely new perspectives on their role in cell biology,” says Rot.

Optimized Production for Broader Applications

Stem cells are currently the most effective method for producing artificial blood with nuclear expulsion taking place in about 80% of cells. However, stem cell sources are limited relying on isolation from umbilical cord blood or bone marrow donations for the treatment of specific diseases, not feasible for mass production of blood to fulfil the clinical need.

However, recently it became possible to reprogram different types of cells into stem cells and use them to generate red blood

cells. This approach offers an almost unlimited cell source for artificial blood production, but takes much longer, and the success rate for nucleus expulsion is only about 40%. "Based on our new findings highlighting the key role of CXCL12 in triggering nuclear expulsion, we can expect that using CXCL12 should bring significant improvement in producing red blood cells from reprogrammed cells," says Gutjahr.

If large-scale production becomes possible, a wide range of applications could emerge. "Even though body cells are readily available, the lab-based production process will remain complex. But it would enable the targeted generation of rare blood types, help bridge shortages, or allow individuals to reproduce their own blood for specialized treatments in many different diseases," says Gutjahr.

Publication:

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Further information

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