Last step leading to blood cell formation elucidated

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A team of scientists led by Dr. Timm Schroeder of Helmholtz Zentrum Muenchen, Germany, has proved the existence of hemogenic endothelial cells. The findings answer the question -- unsolved until now -- of how blood cells are generated during embryonic development and will enable scientists in the future to produce blood cells in the laboratory in a more target-specific manner.

These new insights represent an important contribution to future clinical therapeutic approaches. The study was published in the prestigious science journal *Nature* and will be a central topic of the international symposium on the molecular mechanisms of hematopoiesis, which will take place in Munich from April 2nd to 4th.

The findings on the molecular mechanisms of blood formation (hematopoiesis) will be presented in Munich at the international symposium "Molecular Mechanisms of Normal and Malignant Hematopoiesis" from April 2nd to 4th. A question that has puzzled researchers for decades could now be solved: How are the first blood cells generated in the embryo? In particular, Dr. Timm Schroeder, research group leader at the Institute of Stem Cell Research of Helmholtz Zentrum Muenchen and his team found out that a special type of endothelial cells exists that can transform themselves into blood cells. Endothelial cells line the interior surface of blood vessels.

Dr. Timm Schroeder explained: "It is extremely difficult to investigate the blood cell generation process. It occurs only very briefly, hidden

from view in the embryo within the mother's uterus."

The scientists first had to create the technical means to continually observe the transformation process of endothelial cells into blood cells on the single-cell level over a longer period of time. Dr. Schroeder and his colleagues developed novel bioimaging techniques with which the behavior of large numbers of individual cells can be recorded and tracked. They combined optimized microscopy, incubation and imaging technology as well as novel software programs to track individual cells in time-lapse videos with sophisticated cell purification and cell culture techniques. Thus, the scientists could observe the behavior of many differentiating mesodermal cells over a period of up to one week.

By carefully analyzing thousands of cells and the molecules expressed by them, Dr. Schroeder and PhD student Hanna Eilken were able to detect several very rare endothelial cells that indeed transformed themselves into blood cells.

"As a next step, we will focus on the identification of molecules that regulate the specification of blood cells," Dr. Schroeder went on to say. "Ultimately, our objective is to understand the precise molecular mechanisms. Identifying the exact cell type generating blood cells is an important prerequisite for understanding what combination of molecules makes a cell a blood cell."

Besides giving more insight into the mechanisms of blood formation, the findings of this just-published study are important for improving production of blood cells in the laboratory for clinical therapies. A possible in vitro production of unlimited numbers of blood cells from embryonic stem cells holds great promise for new therapy approaches. However, to enable targeted, efficient and pure production of specific blood cells that are safe for clinical therapy, it is essential to precisely understand the necessary differentiation steps. Dr. Schroeder concluded:

"Our study has now elucidated the last of these steps."

Directed by Professor Magdalena Götz, the Institute of Stem Cell Research at Helmholtz Zentrum München combines research on stem cells of the nervous system, the hematopoietic system and of the endoderm. Especially in view of clinical applications, the objective of the Institute is to elucidate the underlying mechanisms for the specification of stem cells in order to utilize these in a targeted manner to repair damaged cells.

More information: Original Publication: Eilken HM, Nishikawa SI and Schroeder T (2009), Continuous single-cell imaging of blood generation from haemogenic endothelium *Nature*, 457: 896 - 900

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