

# Environmental factors instruct lineage choice of blood progenitor cells

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The research team led by Dr. Timm Schroeder, stem cell researcher at Helmholtz Zentrum Muenchen, Germany, has developed a new bioimaging method for observing the differentiation of hematopoietic progenitor cells (HPC) at the single-cell level. With this method the researchers were able to prove for the first time that not only cell-intrinsic mechanisms, but also external environmental factors such as growth factors can control HPC lineage choice directly.

The findings, published in the current issue of the prestigious journal *Science*, provide an essential building block for understanding the molecular mechanisms of hematopoiesis and are an important prerequisite for optimizing therapeutic stem cell applications.

For decades scientists from various disciplines have discussed to what respective extent genetic predisposition and [environmental factors](#) influence human development. Likewise, the same 'nature vs. nurture' issue is debated by hematologists and stem cell researchers: Is multipotent progenitor [cell differentiation](#) influenced solely by cell-intrinsic mechanisms or is it also influenced by the environment of the cell? What role do growth factors such as cytokines play? Do they influence HPC lineage choice directly or do they merely regulate the survival of the cell after the lineage choice has been made? Despite the immense importance of cytokines for day-to-day clinical research - and not least their far-reaching significance commercially - this issue has been one of the key unknown factors in the stem cell biology of blood.

"This is simply because until now we did not have the suitable technology to observe the processes of cell differentiation and to measure them quantitatively," explained Dr. Timm Schroeder, research group leader at the Institute of Stem Cell Research of Helmholtz Zentrum München. "We didn't know exactly what happens during this time span," Dr. Schroeder said. "That is why until now we could not prove what role cytokines play."

With the new bioimaging techniques developed by Dr. Schroeder's team, [progenitor cells](#) could be observed for a longer period and on the single-cell level. Depending on the kind of cytokines present, after a few days the HPC cultures contained only one cell type. The question remained unanswered whether this was a consequence of direct cytokine regulation or merely the result of sorting out "erroneously differentiated" cells by cell death. Using the new bioimaging techniques for continuous single-cell observation, Dr. Michael Rieger and students in Dr. Schroeder's research group showed for the first time that no cell death could be detected during the entire cell differentiation process. This proves unambiguously that HPC lineage choices can be steered by external environmental factors such as in this case by cytokines. The hematopoietic progenitor cells are "instructed" by cytokines.

"These findings confirm that signaling pathways that are activated by cytokine receptors influence the lineage choices of the cells," Dr. Schroeder said. "The new method offers us the unique chance to observe the effect of all the molecules involved in the differentiation process separately and to better understand their role. This is an important requirement for optimizing the therapeutic use of [stem cells](#)."

Source: Helmholtz Zentrum München

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