New study reveals how human embryo develops the precursor to blood-forming stem cells

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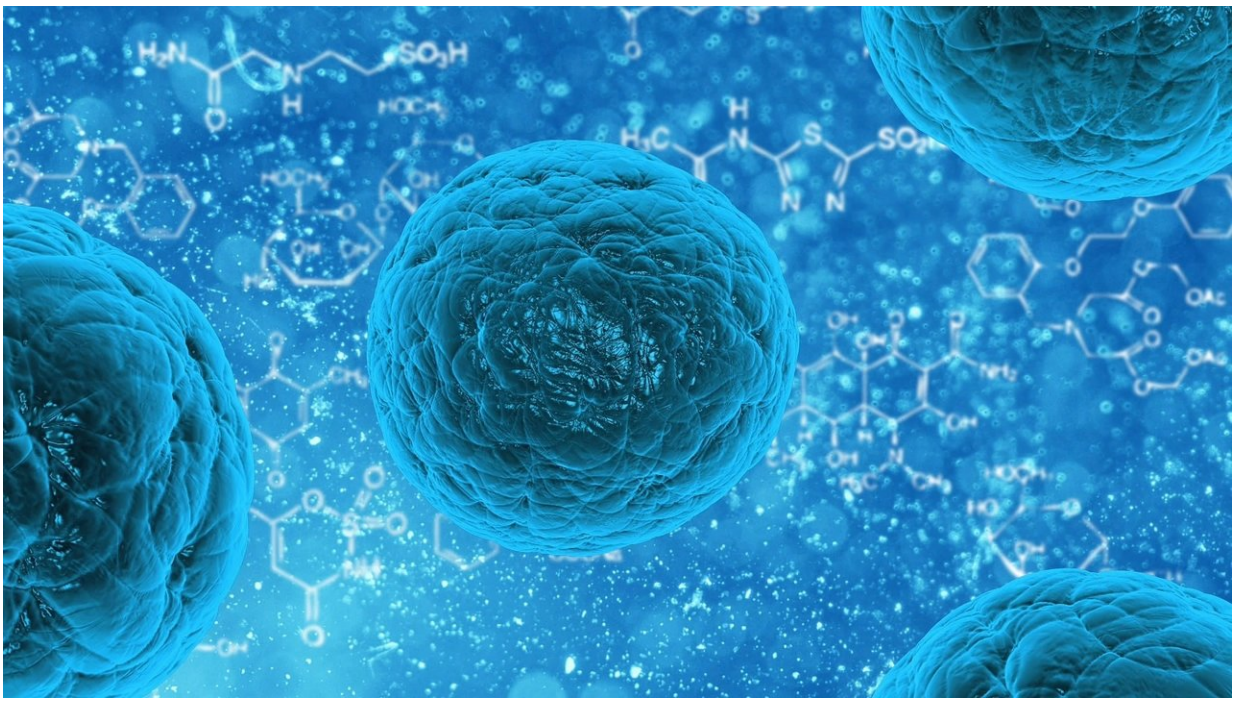

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Blood-forming stem cells found in bone marrow are the life-saving component used in bone marrow transplants. However, suitable donors cannot be found in many cases. A new study reveals how the human embryo develops the precursor to blood-forming stem cells, which

researchers say can be used in the novel method they developed to generate blood-forming stem cells from cells in a tissue culture.

The study, led by researchers from Mount Sinai and the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy, confirms many aspects of cell development, including origins and regulation, which are known to occur within both the mouse and human embryo. In the mammalian embryo, blood-forming stem cells emerge from a specialized cell type called hemogenic endothelium. These cells develop in response to a critical signal pathway known as retinoic acid, which is essential for growth. Their analysis found that stem cell populations derived from human pluripotent stem cells were transcriptionally similar to cells in the early human embryo.

For years, researchers in the field of regenerative medicine have been able to obtain hemogenic endothelium from embryonic stem cells, but these cells do not produce blood-forming stem cells. In the embryo, blood-forming stem cell development requires signaling by retinoic acid. But, current state-of-the-art methods for deriving blood progenitors from human pluripotent stem cells do so in the absence of retinoic acid.

In this latest study, researchers examined the dependence on retinoic acid in early cell types derived from human pluripotent stem cells. They performed single cell RNA sequencing of stem cells in vitro to better understand patterns of mesodermal cell types during early development. The research team identified a new strategy to obtain cells that are transcriptionally similar to those hemogenic endothelial cells found in the human embryo by stimulating a very discrete original population with retinoic acid.

This new method brings researchers and scientists closer to developing blood-forming stem cells in tissue culture, but also provides a pathway to establishing specialized blood cell types for transfusions and other

treatments for cancer since the new method makings it possible to obtain the same original cells in adult blood that are found in a developing embryo.

Mount Sinai's Dr. Christopher Sturgeon says that they "have made a major breakthrough in our ability to direct the development of stem cells in a tissue culture dish into cells that have the same gene expression signature as the immediate progenitor of a blood-forming stem cell found in the developing embryo. With this, now we can focus our efforts at understanding how to capture embryonic blood-forming stem cells, with the goal of using them as a substitute for bone marrow."

The research was published in *Nature Cell Biology*.

More information: Andrea Ditadi, Identification of a retinoic acid-dependent haemogenic endothelial progenitor from human pluripotent stem cells, *Nature Cell Biology* (2022). DOI: 10.1038/s41556-022-00898-9

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