

Researchers succeed in converting human skin cells into blood stem cells

Researchers have succeeded in converting human skin cells into blood stem cells in an international collaboration project. "This is a first step on the way to generating fully functional blood stem cells in a petri dish which, in the future, could be transplanted into patients with blood diseases", says Filipe Pereira, the researcher from Lund University in Sweden who led the study now published in *Cell Reports*.

Transplantation of blood stem cells, isolated from mobilized peripheral blood or bone marrow, is a widely utilized therapy for a range of inherited and acquired blood disorders. Allogeneic transplantation, when using stem cells from a donor, depends on genetic matching to avoid graft rejection and a severe disease called graft versus host disease.

Autologous transplantations, using the patient's own blood stem cells, may not always be possible to perform due to previous therapies and the nature of the specific disease. There remains a need for alternative strategies to generate patient-specific transplantable blood stem cells in a test tube. A couple of years ago, researchers managed to convert mouse skin cells into blood stem cells. Now, the same researchers have shown that the approach also functions with human cells.

"Skin cells are easily accessible and simple to reproduce in test tubes, which means that they could constitute an unlimited source of cells for transplantation. Blood stem cells, on the other hand, lose important properties when they are cultivated. This is why we wanted to investigate whether

it was possible to use skin cells as material to produce blood stem cells”, says Filipe Pereira, researcher at Lund University and in charge of the international collaboration between Swedish, American, Russian and Portuguese researchers.

The process takes between 15 and 25 days and cells undergo a dynamic transition mirroring the birth of blood stem cells during embryonic development. To succeed, the researchers used different transcription factors; proteins that function as a sort of gene regulator and that control the cells' identity.

By using the same combination of the three proteins that had successfully converted the mouse skin cells into blood stem cells, the researchers were able to activate the genes that make human skin cells reprogram into blood stem cells.

“It is interesting that just three proteins can cause such a major change. The same transcription factors work in both mice and humans, showing that their combined function has been preserved through evolution”, says Filipe Pereira.

The researchers also observed that the collaboration between the transcription factors was important; together they induce the process of blood stem cell formation called *hemogenesis*. One of the transcription factors, GATA2, leads the process and is the one that recruits the two other players into accessible regions of the genome. This cooperation leads to silencing of the skin cell program and activation of hemogenesis, which results in the reprogramming of the skin cell into a blood stem cell. This is the first time that the mechanism of blood stem cell reprogramming is described.

“When we transplanted the new blood stem cells into mice, we observed that the cells survived over three months. The next step will be to improve their capacity to regenerate blood production long-term. We now know much more about the underlying mechanisms of this process which will allow us to make this a reality in the future”, says Filipe Pereira.

The aim is to generate blood stem cells that in the future will be suitable for clinical use in patients affected by blood diseases, such as leukaemia.

“So far, this is basic research, but it has great potential for development into treatment. Before we get to that stage, we are learning quite a lot about the genetic program of blood stem cells”, concludes Filipe Pereira.

Source:

<https://www.lunduniversity.lu.se/article/mechanism-for-turning-skin-cells-into-blood-stem-cells-uncovered>