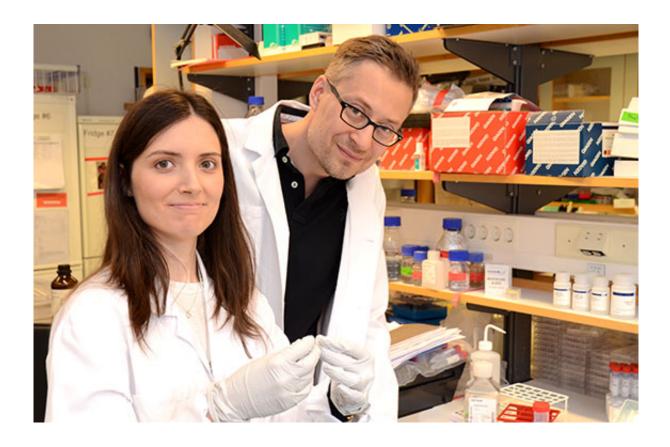


Genetic code of red blood cells discovered

June 2 2016



Johan Flygare and Sandra Capellera. Credit: Åsa Hansdotter / Lund University

Eight days. That's how long it takes for skin cells to reprogram into red blood cells. Researchers at Lund University in Sweden, together with colleagues at Center of Regenerative Medicine in Barcelona, have successfully identified the four genetic keys that unlock the genetic code of skin cells and reprogram them to start producing red blood cells



instead.

"We have performed this experiment on mice, and the preliminary results indicate that it is also possible to reprogram skin cells from humans into red blood cells. One possible application for this technique is to make personalised red blood cells for blood transfusions, but this is still far from becoming a clinical reality", says Johan Flygare, manager of the research group and in charge of the study.

Every individual has a unique genetic code, which is a complete instruction manual describing exactly how all the cells in the body are formed. This instruction manual is stored in the form of a specific DNA sequence in the cell nucleus. All human cells—brain, muscle, fat, bone and skin cells—have the exact same code. The thing that distinguishes the cells is which chapter of the manual the cells are able to read. The research group in Lund wanted to find out how the cells open the chapter that contains instructions on how to produce red blood cells. The skin cells on which the study was based had access to the instruction manual, but how were the researchers able to get them to open the chapter describing red blood cells?

With the help of a retrovirus, they introduced different combinations of over 60 genes into the skin cells' genome, until one day they had successfully converted the skin cells into red blood cells. The study is published in the scientific journal *Cell Reports*.

"This is the first time anyone has ever succeeded in transforming skin cells into red blood cells, which is incredibly exciting", says Sandra Capellera, doctoral student and lead author of the study.

The study shows that out of 20,000 genes, only four are necessary to reprogram skin cells to start producing red blood cells. Also, all four are necessary in order for it to work.



"It's a bit like a treasure chest where you have to turn four separate keys simultaneously in order for the chest to open", explains Sandra.

The discovery is significant from several aspects. Partly from a biological point of view—understanding how red blood cells are produced and which genetic instructions they require - but also from a therapeutic point of view, as it creates an opportunity to produce red blood cells from the skin cells of a patient. There is currently a lack of blood donors for, for instance, patients with anaemic diseases. Johan Flygare explains:

"An ageing population means more blood transfusions in the future. There will also be an increasing amount of people coming from other countries with rare blood types, which means that we will not always have blood to offer them".

Red <u>blood cells</u> are the most common cells in the human body, and are necessary in order to transport oxygen and carbon dioxide. Millions of people worldwide suffer from anaemia—a condition in which the patient has an insufficient amount of <u>red blood cells</u>. Patients with chronic anaemia are among the most problematic cases. They receive regular blood transfusions from different donors, which can eventually lead to the patient developing a reaction to the new blood. They simply become allergic to the donor's blood. Finding a feasible way to make blood from an individual's own <u>skin cells</u> would bring relief to this group of patients. However, further studies on how the generated blood performs in living organisms are needed.

More information: Defining the Minimal Factors Required for Erythropoiesis through Direct Lineage Conversion. Published in *Cell Reports* on June 2, 2016



Provided by Lund University

Citation: Genetic code of red blood cells discovered (2016, June 2) retrieved 23 June 2024 from https://phys.org/news/2016-06-genetic-code-red-blood-cells.html

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