Cell transformation a la carte

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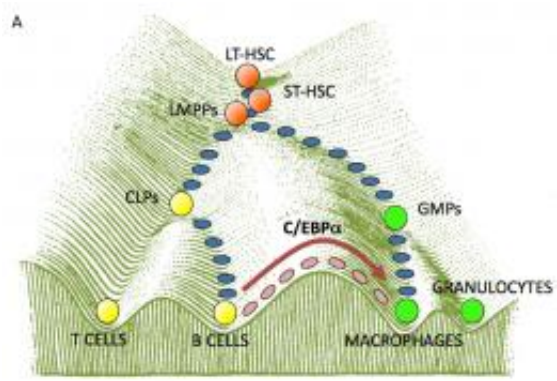

This figure shows how stem cells (in orange) generate specialised cells (blue pathway), such as B lymphocytes (yellow) and macrophages (green), and what occurs when the cells transdifferentiate (arrow and pink pathway). The work of the researchers shows how the C/EBPα transcription factor makes the lymphocytes convert into macrophages without first transforming into stem cells.

Researchers from the Haematopoietic Differentiation and Stem Cell Biology group at the Centre for Genomic Regulation (CRG), have described one of the mechanisms by which a cell (from the skin, for example) can be converted into another which is completely different (e.g., a neuron or hepatic cell). They have discovered that the cell transcription factor C/EBPα is a determinant factor in cell transdifferentiation. This differentiation mechanism can be applied to any of the cells of an organism. The scope of the study, published in the *Proceedings of the Natural Academy of Sciences* (*PNAS*), could profoundly influence the development of cell therapies. In all tissues,

stem cells specialise to produce very different cell types.

This specialisation is, to a great extent, regulated by transcription factors, proteins responsible for activating or repressing the transcription of various genes. The study of these factors is essential for understanding how a stem cell is converted into a specialised cell as well as the reverse path, that is, how a specialised cell is converted into a stem cell. This process, which reveals all the steps of specialisation, is known as "dedifferentiation".

This reversal of the cell differentiation process had already been described in skin cells by a group of Japanese researchers, and cases of skin cells being converted into cardiac cells, neurones and liver cells (hepatocytes) have been reported. However, until now it hadn't been possible to see if, during this process, the cell was reconverted into a stem cell for later specialisation, or if it simply transformed into another cell. This process of direct transformation is what is known as "transdifferentiation".

Investigators from the CRG, led by Thomas Graf, research professor at the ICREA, have studied this process for years. In this research they used immune system cells and saw that it was possible to convert a leukocyte (white blood cell) into a macrophage (cells which engulf and digest any foreign particle), without the need to reconvert into a stem cell, that is, following the reverse specialisation pathway. The results of this research show that dedifferentiation and transdifferentiation are completely different processes.

The scope of these findings is currently restricted to the fields of research and academia, but they will be relevant for the development of treatments with cell therapy. The possibility of obtaining cells of any type at the moment that they are required is getting nearer all the time.

More information: Di Tullio, A. et al. (2011). CCAAT/enhancer binding protein α (C/EBP α)-induced transdifferentiation of pre-B cells into macrophages involves no overt retrodifferentiation. *Proc Natl Acad Sci* USA 108: 17016- 17021. DOI:10.1073/pnas.1112169108