Notch activation determines signals necessary to generate hematopoietic stem cells in laboratory

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An international study led by researchers from IMIM (Hospital del Mar Medical Research Institute) published in the journal *Nature Communications* has revealed that the intensity or efficiency of the activation of a protein called Notch, which is involved in the different phases of embryonic development, determines the fate of cells, i.e. if cells will form the aorta artery or blood (hematopoietic) stem cells. For artery cells, many Notch molecules need to be activated, whereas for hematopoietic cells many fewer are needed.

According to Dr. Anna Bigas, the coordinator of the group on stem cells and cancer at IMIM "to reach these levels of activation, we have proven that there is a competition between two proteins that activate the Notch molecule, i.e. between two ligands, in a way that one limits the activation generated by the other to form hematopoietic stem cells".

Until now it was known, thanks to the studies conducted by this same group and others, that the Notch activation was essential to form arteries and hematopoietic stem cells. It was also known that the proteins responsible for this activation were ligands Delta4 and Jagged1, respectively. With this study, researchers have shown how this signal works to reach a certain level of activation and form the two different types of cells.

This is important to determine the signals that are necessary to generate hematopoietic stem cells in a laboratory, whether this is done with embryonic stem cells or from other sources. " Currently stem cells are being obtained from laboratory with the features of stem cells, but the process is still not very efficient or reproducible. This study will help to improve the quality and efficiency in obtaining hematopoietic stem cells and this could mean that, in the future, it may be possible for many patients with no compatible donors to get a transplant", the researcher comments.

Researchers carried out this study using mice cells. Now, the next step will be to reproduce the study using human embryonic cells or programmed endothelium cells, where researchers are confident it will work in a similar way. Moreover, it is highly possible that similar mechanisms will also work to generate other types of cells.

"Although this is not immediately applicable because not all signals are known, nor how to regulate them, we are gradually drafting a more precise protocol to learn how to generate cells that can then be transplanted", the researchers conclude.

Source:
IMIM (Hospital del Mar Medical Research Institute)
