Atlas of Science
another view on science
http://atlasofscience.org

A new kind of human immune cell that cannot leave the liver

Natural Killer (NK) cells are immune cells that are found in the blood and protect the body by killing infected and cancerous cells. NK cells can also be found in large numbers in some organs, including the liver. These NK cells are different from those found in the blood in that they are not very good at killing dangerous cells. What they do is not yet clear. Recent work in mice has shown that some of the NK cells in the liver cannot leave it: they are "resident". We wanted to find out if humans also have liver-resident NK cells.

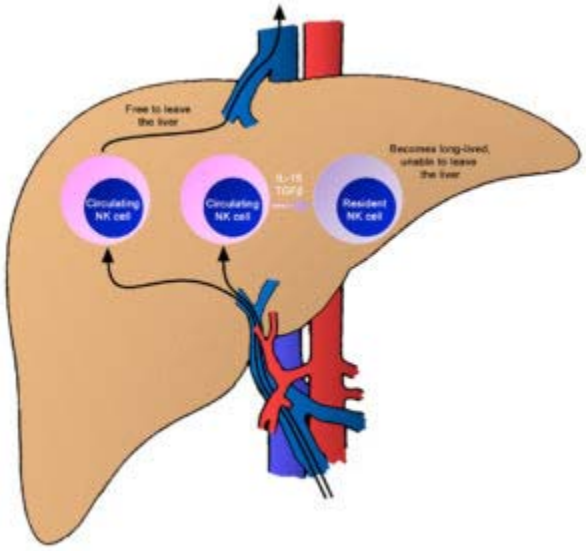

Fig. 1.

Transcription factors are molecules that bind to DNA in cells and tell the cell which genes it should activate to carry out its functions. Different kinds of cell have different transcription factors. We found two large groups of NK cells in the human liver: one group has low levels of a transcription factor called Eomes and is similar to blood NK cells; the other has high levels of Eomes and is only found in the liver, not the blood.

To work out if the Eomes-high NK cells were able to leave the liver, we looked at liver transplant recipients. Sometimes there is a genetic mismatch between the transplant recipient and the transplanted liver that means we can tell whether any given cell has come from the patient's blood or their new liver. In these cases, we can look at the recipient's blood shortly after the transplant to see which cells have been able to leave the liver. By doing this, we discovered that the Eomes-low NK cells were able to leave the liver ("circulating NK cells") whereas the Eomes-high NK cells were not ("liver-resident NK cells").

By looking at genetically mismatched transplanted livers that were removed between 8 day and 13 years after the transplant, we were also able to show that liver-resident NK cells are long-lived in the liver, surviving up to 13 years, whereas the circulating NK cells rapidly left the liver and/or died. We also found that some of the liver-resident NK cells derive from the patient's blood, even as early as 8 days after transplant. This was surprising because in mice liver-resident NK cells are thought to come from the fetal liver, not the adult blood. We then took circulating NK cells from the blood and kept them in a dish for 8 days with two immune molecules, called IL-15 and TGFβ, that are found at high levels in the liver. By doing this, we were able to turn circulating NK cells into cells similar to liver-resident NK cells, with high levels of Eomes and molecules on the surface of the cells that would be expected to stop them leaving the liver.

In the past, doctors and scientists have often looked at NK cells in the blood and assumed that these were representative of NK cells throughout the body. Our finding that human liver contains a large group of resident NK cells means that this assumption is mistaken, in the liver at least, and probably also in other organs. The existence of these cells may also have implications in liver transplantation. It could suggest that treatments aimed at immune cells should be focused on the donor liver before transplantation, instead of or as well as the patient, in order to target liver-resident immune cells.

Victoria Male
Institute of Immunity and Transplantation, UCL Medical School, London, United Kingdom

Publication

Eomeshi NK Cells in Human Liver Are Long-Lived and Do Not Recirculate but Can Be Replenished from the Circulation.
Cuff AO, Robertson FP, Stegmann KA, Pallett LJ, Maini MK, Davidson BR, Male V
J Immunol. 2016 Dec 1