

The role of Natural Killer cells in Liver Transplantation

Department of Gastroenterology and Hepatology

Background:

Liver transplantation (LTx) is a life-saving procedure for end-stage liver diseases such as auto-immune diseases, acute liver failure, and cirrhosis. In the context of solid organ transplantation, liver transplantation is unique in that the incidence of chronic rejection is much lower compared to other organ grafts. Moreover in around 20% of liver transplant recipients immunosuppressive medication can be stopped a few years after LTx without occurrence of graft rejection. These features of LTX led to the hypothesis that liver grafts have unique tolerogenic properties. However, still 80% of LTx-recipients need life-long immunosuppressive therapy, and suffer from severe adverse side effects of these drugs (cancer, infections and kidney failure).

We hypothesized that Natural Killer (NK) cells, that are present in large number in the liver, are responsible for its tolerogenicity. From our study, many interesting differences between these NK cells and their counterpart in blood are emerging. We aim to study the role of these NK cells in inducing tolerance to liver grafts after LTX, and to exploit donor-derived NK cells to promote tolerance to liver grafts in transplanted patients.

Project:

The student's project consists of performing functional assays to assess if donor-derived liver NK cells can kill Dendritic Cells (DCs) or reactive T-cells from recipients. If this effect will be proved, the following step will be designing a protocol allowing expansion *ex vivo* of NK cells from the donor, followed by injection of the expanded cells into the recipient. This way tolerance to the liver graft will be induced by exploiting the beneficial effects of donor liver-derived NK cells. The student will be working within the liver transplant research group, consisting of about 10 young and enthusiastic researchers.

Techniques:

Isolation of leukocytes from blood and from liver perfusion fluid (the fluid used in the operating room to "wash" the liver graft right before it is transplanted in the recipient); magnetic isolation of NK-cells; cell culture; flow cytometry (FACS), cell sorting, ELISA, RT-qPCR.

Contacts:

For more information: Viviana Moroso (PhD student), tel: +31.10-7032585, email: v.moroso@erasmusmc.nl or Dr. Jaap Kwekkeboom, tel: +31.10-7034776, email: j.kwekkeboom@erasmusmc.nl (group leader). More information about the laboratory: www.gastrolab.nl