

Modulation of dendritic cells and regulatory T cells by Intravenous Immunoglobulins

Laboratory of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands

Liver Transplantation unit

The Laboratory of Gastroenterology and Hepatology consists of multiple research groups, working on liver transplantation (LTx), hepatitis immunology, inflammatory bowel disease, Barrett's esophagus, and intestinal carcinogenesis. The LTx group, consisting of approximately 16 people (postdocs, PhD-students, technicians, undergraduate students), strives to combine fundamental and translational research, to keep a close link to the clinic.

Project:

Currently, liver transplantation is the treatment of choice for patients with acute and chronic liver failure. Survival is excellent on the short term, with patient survival rates of approximately 85% one year after surgery. At present, life-long treatment with immunosuppressive drugs is needed in order to prevent rejection of transplanted organ grafts. However, the side effects of current immunosuppressive drugs are severe and thereby impair the long-term survival of transplant patients significantly. It is therefore of major importance to find an alternative immunosuppressive drug that is safe for life-long use.

Intravenous immunoglobulin (IVIg) is a standardised pharmaceutical preparation of human immunoglobulin G prepared from pools of plasma. High-dose IVIg therapy is an established treatment for several autoimmune diseases. Importantly, life-long treatment with IVIg does not show significant side-effects. Interestingly, we have shown that IVIg treatment is also capable in preventing acute rejection in liver transplant patients. As long-term IVIg treatment is safe and effective in preventing rejection, using IVIg as long-term immunosuppressive therapy is promising.

We have established that the mechanisms behind the immunosuppressive effects of IVIg are different from current immunosuppressive drugs. While current drugs can only inhibit effector T-cells, IVIg can target Dendritic Cells (DC) and Regulatory T-cells (Treg), which subsequently inhibit effector T-cells. By targeting these pivotal cells involved in transplant rejection, IVIg might be superior to current immunosuppressant in the control of transplant rejection. However, the mechanism by which IVIg interacts with DC and Treg is still unknown. The aim of this project is to explore these mechanisms and further explore the machinery by which IVIg modulates these cells. This new insight may enable a novel highly-specific therapy for prevention of transplant rejection.

Methods and techniques used in this project:

1. DC and Treg purification from human blood
2. Cell culture
3. Flow cytometry
4. ELISA

The following meetings will take place weekly:

- Department of Gastroenterology and Hepatology seminars
- LTx lab meetings
- LTx clinical meetings (optional)

We are looking for an enthusiastic Biology, Life Sciences (or equivalent) Master student who is highly motivated to do laboratory work, has an active interest in participating in scientific discussions and is willing to perform an internship of a minimum of 5 months at the Dept of Gastroenterology and Hepatology of the Erasmus MC, Rotterdam, the Netherlands.

For further information, please contact:

Jaap Kwekkeboom, PhD; j.kwekkeboom@erasmusmc.nl
Angela Tjon; s.tjon@erasmusmc.nl