

**Report of European Society for Organ Transplantation (ESOT) meeting 30 August – 2 September 2009 Paris for the Novartis Transplantation Advisory Board Grant**

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This year, the 14<sup>th</sup> congress of the European Society for Organ Transplantation (ESOT) was held in Paris. Notable, Paris was the city where J. Hamburger and his team performed one of the first renal transplantation more than 50 years ago! The ESOT Congress is designed for physicians, surgeons, scientists, nurses, organ procurement personnel, and pharmacists who are interested in the clinical and research aspects of solid organ and tissue transplantation. Every two years the ESOT will hold its congress in a European city. The program aim to encourage the exchange of new scientific and clinical information and support an interchange of opinions regarding care and management issues, as well as socioeconomic, ethical, and regulatory issues relevant to organ and tissue transplantation. This year's congress, delegates came from 80 different countries worldwide, demonstrating the major international aspect of this meeting. My main interest field was liver transplantation, particular in basic science. In this report, I will highlight my topics of interest.

The congress started on Sunday 30 August. The day started with post graduate courses organized by different committee and associations of ESOT, including Eurorpean Liver and Intestine Transplant Assocation (ELITA), European Pancreas and Islet Transplant association (EPITA), Thoracic committee, European Donation Committee (EDC), Basic science committee (EBSOT) and Ethical, Legal and Psychosocial Aspects of organ Transplantation (ELPAT). As my main PhD project is performing research in basic science and I aim to gain more knowledge in this field, I joint the Basic Science post graduate course, named 'Novel research tools in transplantation: tips and tricks'. During this course, novel tools and methods were presented including laser-microdissection for cell type- and compartment-specific analyses and the reprogramming of human cells to generate pluripotent stem cells. For me, the lecture about Multicolor flowcytometry was most interesting, as this technique I use most often and there were some tips provided that can be practical.

In the evening, the opening session started, with the celebration of honorary memberships followed by the introduction of a new extensive project on education, named 'The Tree of Life'.

Thereafter, plenary session 1 was opened, started with a presentation about suppressor T cells. This presentation was interesting, as the title suggests that the subject will be about the CD4+ regulatory T cells. But instead, the presentation was about the CD8+ regulatory T cells, of which is less known. The main difference between the regulatory CD8+ and the conventional CD8+ was demonstrated, which is their specific recognition of MHC-Ib (=Qa-1-a class Ib MHC). Thereafter, an interesting presentation was shown of the usage of tissue engineering in clinical trachea transplantation, which was visualized with video material. The procedure that was shown was the removement of cells and MHC antigens from a human donor trachea, which was then readily colonised by epithelial cells and mesenchymal stem-cell-derived chondrocytes that had been cultured from cells taken from the recipient. This graft was then used to replace the recipient's left main bronchus. The graft immediately provided the recipient with a functional airway, improved her quality of life, and had a normal appearance and mechanical properties at 4 months. The patient had no anti-donor antibodies and was not on immunosuppressive drugs. This finding suggests that autologous cells combined with appropriate biomaterials might provide successful treatment for patients with serious clinical disorders. Due to its clinical approach, this lecture was very fascinating!

On the second day, 31 August, several interesting presentations took place.

First, from our research group, a presentation was presented about plasmacytoid dendritic cells (pDC) as a tool for immune-conditioning therapy of organ transplant recipients. In this presentation, pDC was demonstrated to inhibit allogeneic memory T cells responses by induction of profound anergy in conventional T-cells and de novo generation of CD8+ regulatory T-cells. Then, during the state of the art- 'Infections in transplantation' session, a session about 'new emerging viruses in transplantation' was interesting, under which the H1N1 virus.

In parallel session 7, named 'Liver transplantation and tumors', I had to present my abstract. My presentation was entitled 'Increased incidence of de novo cancer in liver graft recipients transplanted in recent years'. The occurrence of de novo malignancy after liver transplantation (LTx) is mainly related to the chronic use of immunosuppressants. Whether changes of immunosuppressive regimens over the years had influenced the incidence of cancer is unknown. The objectives of our retrospective study were to describe the incidence of de novo malignancy after LTx in the Rotterdam liver transplant cohort and to determine whether this incidence has changed over time. The main results of our study were as followed. In total, we have found a de novo cancer incidence of 13% in all LTx patients and the relative risk of de novo cancer compared to the matched Dutch population was 2.2. Over time, we observed a considerable decline in the incidence of de novo cancer. Strikingly, patients transplanted in the recent LTx period (2005 till 2007) showed an increased incidence of early *de novo* cancer ( $P=0.022$ ). Multivariate analysis revealed that cyclosporine (CsA) was associated with this higher cancer risk, which was 9.9-times higher compared to tacrolimus (TAC) treatment in the same period (95% CI 1.2 – 80.5,  $P=0.030$ ). During this transplantation period, a clinical trial was conducted comparing CsA with C<sub>2</sub> monitoring versus TAC. In previous LTx-periods, when CsA was monitored by conventional C<sub>0</sub> levels, a higher cancer risk for CsA could not be found. These data suggest that CsA-C<sub>2</sub> treatment was associated with a higher early *de novo* cancer risk in patients transplanted in recent years, indicating that CsA-C<sub>2</sub> might cause over-immunosuppression.

This presentation yielded a great discussion with good questions. Main questions included whether the CsA-C<sub>2</sub> group and the TAC-group were comparable (=yes), whether the increase in cancer incidence was due to more awareness (=no), which type of cancer was increased (=all cancer types) and did the survival differ between CsA- and TAC- group (=no).

In the plenary session 2, a presentation entitled 'Immunosuppression: does one regimen fit all?' was of interest. In this presentation, the tailoring of immunosuppressive regimen for individual patients is demonstrated the focus on: 1) stratification of clinical risk factors, 2) post-transplant monitoring and 3) identification of pre-transplant risk factors.

Then, during the parallel sessions, several interesting presentations came ahead. One of these presentation took place in the 'Operational tolerance: approaches & mechanisms' session, a presentation entitled 'Th17 and regulatory T cells relationship during allograft rejection' showed that Tregs do not prevent, but rather strengthen Th17 alloreactivity in vivo. IL-17 becomes an important player in case of shrunk alloreactive repertoire. This is controversy, as Th17 and Treg have been known as competing fates of naive T cells differentiation, so the one should inhibit the other. Thus, further research should be progressed to understand this mechanism. Perhaps, in the next meetings we will hear more about the generation mechanism of Treg versus Th17.

On the third day, 1<sup>st</sup> of September, the most interesting part of this day was the plenary session named 'The emerging role of T cells in transplantation'. In this big session, a major overview was presented of memory T-cells, Th17 in transplantation and Treg and its usage as a therapeutic tool for inducing or re-establishing tolerance. It was an honour to hear the expert opinion from famous researchers, such as Kathryn Wood and Manuela Battaglia.

However, other sessions were fascinating too, such as the 'Pharmacology & immunological monitoring' session. One of the presentations was the study about the JAK-inhibitor CP-690,550. This is currently being investigated for prevention of allograft rejection; however, whether it has differential effect on effector and regulatory T cells is unknown. In this study, the investigators showed that CP-690,550 inhibits the effector T cell function, but spares the suppressive activity of CD4+CD25<sup>high</sup>FoxP3 T cells. This means that JAK/STAT inhibition can provide a novel mechanism for modulation of anti-donor responses.

Furthermore, another presentation showed that the use of Basiliximab (anti-CD25), which is successfully and routinely used after organ transplantation, directly decreases the amount of CD4+CD25<sup>high</sup>FoxP3 T cells. So the use of Basiliximab in tolerance promoting protocols might be questioned.

At last, arriving the last day, 2<sup>nd</sup> of September, there were some interesting sessions. One of these sessions was the state-of-the-art session of Basic science. Topics that crossed ahead were innate allorecognition, the role of dendritic cells, Toll-like receptors and the new roles of complements in transplantation.

Then, last but not least, I attended the 'What's hot, what's new' session, in which all new scientific findings in the transplantation field presented during the ESOT 2009 meeting were reviewed. Revision of currently used immunosuppressive protocols and the results of randomized clinical trials of new therapeutics were presented. And the most impressive part of the day, were the presentations of the Biotest award winners. Most fascinating study was, to my opinion, the study of the ability of NK cells to drive dichotomous T cell response. The investigators suggest that NK cells may directly function as antigen presenting cells and thereby regulating peripheral T cell homeostasis in autoimmunity and transplantation. I think attending this outstanding session was very motivating for my future work.

Apart from high quality presentations, the ESOT meeting also provides a great opportunity to meet experts in ones research field. For me, I was very honoured to be able to meet dr. Kaveri, one of the biggest expert on immunoglobulines, particular the therapeutic drug intravenous immunoglobuline, which is the main topic of my PhD-project. It was great to hear his opinion and to discuss about our projects.

To conclude, I really enjoyed and learned a lot about different aspects in the transplantation medicine during the ESOT 2009. This congress not only provides you more knowledge of current and new practice in transplantation, but also provides the opportunity to meet other experts. I think after attending this congress, I was once again encouraged to perform great research!