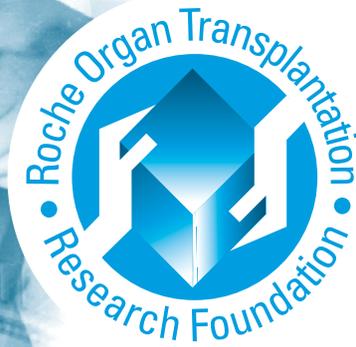


R O T R F

*Roche Organ Transplantation  
Research Foundation*



***ANNUAL  
REPORT 2011***



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## *The Roche Organ Transplantation Research Foundation*

The mission of the Roche Organ Transplantation Research Foundation (ROTRF) is to advance the science of organ transplantation in order to improve the care of the thousands of patients undergoing transplantation every year. The results of the funded research projects will contribute to an understanding of many aspects of the clinical and scientific transplantation, such as the mechanisms of long-term organ deterioration and the consequences of tissue injury, and will provide the opportunities to intervene in these processes.

The Foundation is an independent medical research charity that provides operating funds to established academic staff at universities, transplant centres and research institutes. The Foundation supports research in organ transplantation, particularly where there is an unmet medical need.

The funding of the Foundation consists of donations from F. Hoffmann-La Roche Ltd, with an initial sum of 25 million Swiss francs over the first five years and renewal donations of 15, 10 and 17.5 million Swiss francs for the following eight and a half years (a total of 67.5 million Swiss francs over 13.5 years). The funds are distributed as grants of up to 200,000 Swiss francs distributed over two years. The foundation is legally independent from F. Hoffmann-La Roche Ltd and is guided solely by the Board of Trustees according to its charter.





## 1. Preface

It is my pleasure as chairman of the Roche Organ Transplantation Research Foundation (ROTRF), to inform you about the highlights of our activities in 2011.

Beside the traditional grant award competitions, which saw 17 investigators being awarded grants, which I will discuss later, this year has seen the recognition of 11 ROTRF grantees with a *ROTRF Recognition Prize*.

In 2010, the Trustees invited all ROTRF grant recipients to participate in a survey presenting the results of their ROTRF-funded projects. The Trustees were very impressed with the overwhelming amount and quality of data and publications produced by ROTRF grant recipients over the years. The Trustees were pleased to have been able to fund areas of transplantation that are often not funded and young investigators who would have otherwise faced difficulties pursuing their ideas and establishing their research programmes. From the time of the first awards in March 1999 until the end 2011, the ROTRF has supported almost 260 important and innovative projects in basic science and clinical research applicable to the understanding and care of human organ transplant recipients and related tissue transplants. The *ROTRF Recognition Prizes* were awarded to investigators whose ROTRF-funded projects had a major impact on the field of transplantation and whose achievements best exemplify the mission of the ROTRF. The award-winning projects spanned a wide range of topics, such as induction of tolerance, the role of regulatory T cells and anti-inflammatory molecules in graft acceptance, the role of innate and adaptive immunity in allograft rejection, and immunology of CMV infection and T cell allo-recognition. The Trustees also recognise that there are several promising and important projects currently ongoing, which will likely impact on clinical practice in the years to come.

The recipients of the *ROTRF Recognition Prize* were invited to present the results of their ROTRF-funded research at the ROTRF-sponsored satellite symposium „*ROTRF Recognition Prize – Recognising Excellence in Organ Transplantation Research*“ at the American Transplant Congress 2011 in Philadelphia. As in the past, this symposium was very well attended and the audience was rewarded with excellent and very interesting presentations, which prompted questions and stimulating discussions.

As for the grant award competitions in 2011, 8 grants were awarded in Cycle XXV while the ROTRF Board of Trustees and the Scientific Advisory Committee selected 9 outstanding projects for funding in Cycle XXVI. The main criteria for the evaluation of the proposals were scientific merit and originality, with particular attention being paid to the relevance of the question addressed to organ transplantation, and the realistic potential for clinical application of the results in the near term. Projects selected for a ROTRF grant award in Cycle XXV focused on the identification of rejection markers after cardiac transplantation, investigations of inflammatory

processes in the small airways of transplanted lungs, hepatitis C recurrence after liver transplantation, Epstein Barr virus malignancies after transplantation, cardiovascular risk in children and young adults after renal transplantation, and dynamics of bacterial colonisation after lung transplantation.

As highlighted by the many publications in peer-reviewed journals, presentations at congresses and meetings, and the *ROTRF Recognition Prize*, previous awards have led to very interesting and important data in disparate research areas of organ transplantation. We are looking forward to updates on the progress of the projects funded in 2011.

Grants in Cycle XXVII, for which the preliminary submission was in November 2011, will be awarded in spring 2012 and we are currently accepting applications for Cycle XXVIII until the deadline on 1 October 2012. Once again, we will welcome submission of proposals for clinically oriented research projects, such as observational clinical studies or studies that use human transplant samples for laboratory examinations to investigate the pathogenesis of human disease states in organ transplantation. We are also looking forward to receiving applications for collaborative partnerships, for developing and evaluating novel techniques or addressing currently under-studied areas of clinical transplantation research.

We are very grateful to F. Hoffmann-La Roche Ltd for their continuous support. With their generous gift, the ROTRF has been able to support research into organ transplantation for over 13 years. We also like to thank the ROTRF Scientific Advisory Committee, ad hoc reviewers and the grantees for their excellent work and support, which have contributed to the overall success of the Foundation.

Finally, we wish the newly granted investigators of Cycles XXV and XXVI good luck with their research!

A handwritten signature in black ink, appearing to read 'Philip F. Halloran', written in a cursive style.

On behalf of the Board of Trustees

Philip F. Halloran, MD, PhD, OC  
Chairman, ROTRF Board of Trustees



## 2. Facts and Figures

### **Funding Cycles XXV and XXVI – Letters of Intent Submission in October 2010 and April 2011**

In 2011, the Roche Organ Transplantation Research Foundation (ROTRF) had the pleasure of awarding 3.8 million Swiss francs to 17 investigators. The focus in these cycles, as in the previous two since the announcement of the new 5-year plan, was on clinical research, and all grants awarded support clinically orientated research projects.

For Cycle XXV, the ROTRF received 103 eligible Letters of Intent (LOIs) up to the submission deadline (1st October 2010) from prospective applicants around the world. North American teams submitted 51.5% of all LOIs (USA 45.6%, and Canada 5.8%). European proposals accounted for 36.9%: mostly from UK, Switzerland and the Netherlands (6.8% each) and French and German researches accounted for 3.9% each. 9.7% of the total applications received were submitted from investigators from Australasia. One LOI was received from Africa (Egypt) and one from South America (Argentina) (<1% each).

In Cycle XXVI applications were accepted until up the 1st April 2011 LOI deadline. The ROTRF received 147 eligible Letters of Intent (LOIs). Most of the applications were received from North America (59.2%): USA (53.1%) and Canada (6.1%). European research teams accounted for 32.6% of applications; for the most part from the UK (8.2%), The Netherlands and France (4.8% each), and Italy (4.1%). Germany, Switzerland and Belgium each submitted 2.7% of LOIs. Of the remaining applications received, Australasia accounted for 4.8%, Asia for 2.0% and Africa 1.4%.

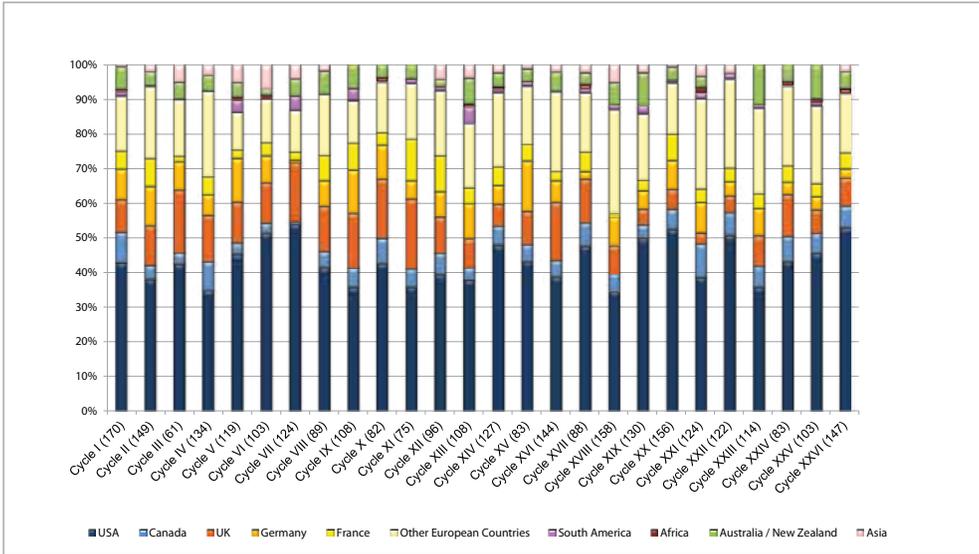
Based on the Scientific Advisory Committee review, the Board of Trustees invited 21 applicants in Cycle XXV and 24 applicants in Cycle XXVI to submit Full Paper Applications (FPAs), of which 8, respectively 9 received the award.

The research funded in Cycle XXV focuses on clinical issues affecting organ transplantation patients, including the role cytokines in graft rejection; identification of lung allografts at risk of rejection; viral kinetics after transplantation; specificity and mechanism of B cell graft rejection; predictors of EB virus -associated PTLD, novel hepatitis C virus therapy, and cardiovascular risk in children and young adults after renal transplantation. Applicants awarded a grant in Cycle XXVI will address questions such as recurrence of malignancies after liver transplantation and molecular assessments of transplanted livers, novel reperfusion methods in lung transplantation, clinical outcome of HIV-positive patients transplanted with kidneys from HIV-positive donors, immune response against viruses and effects of immunosuppressive regimens on allo- and viral-specific immunity in transplant patients, role of memory T cells in immune rejection, and cross-reactivity of allogeneic T cells.

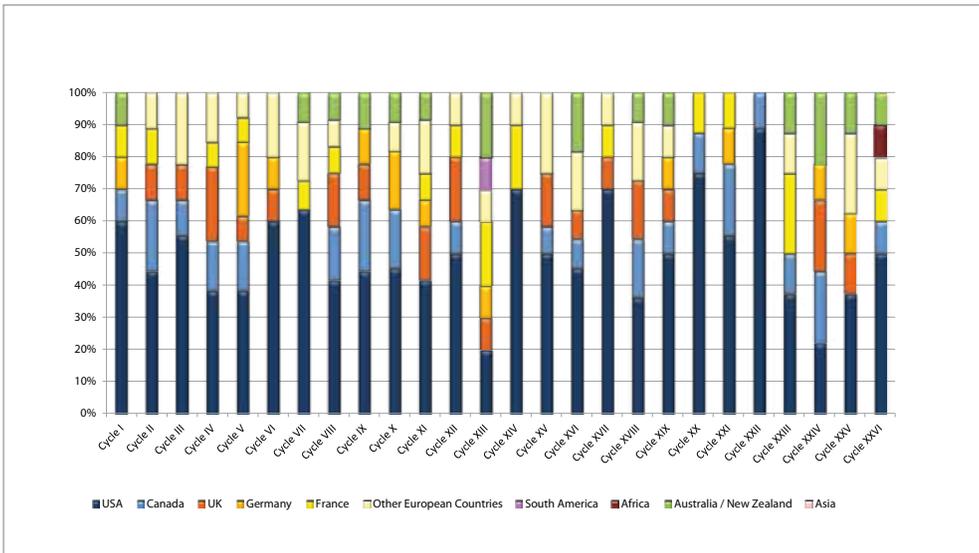
Abstracts of all funded projects are available on the ROTRF homepage.



# Statistics on Applications to the ROTRF

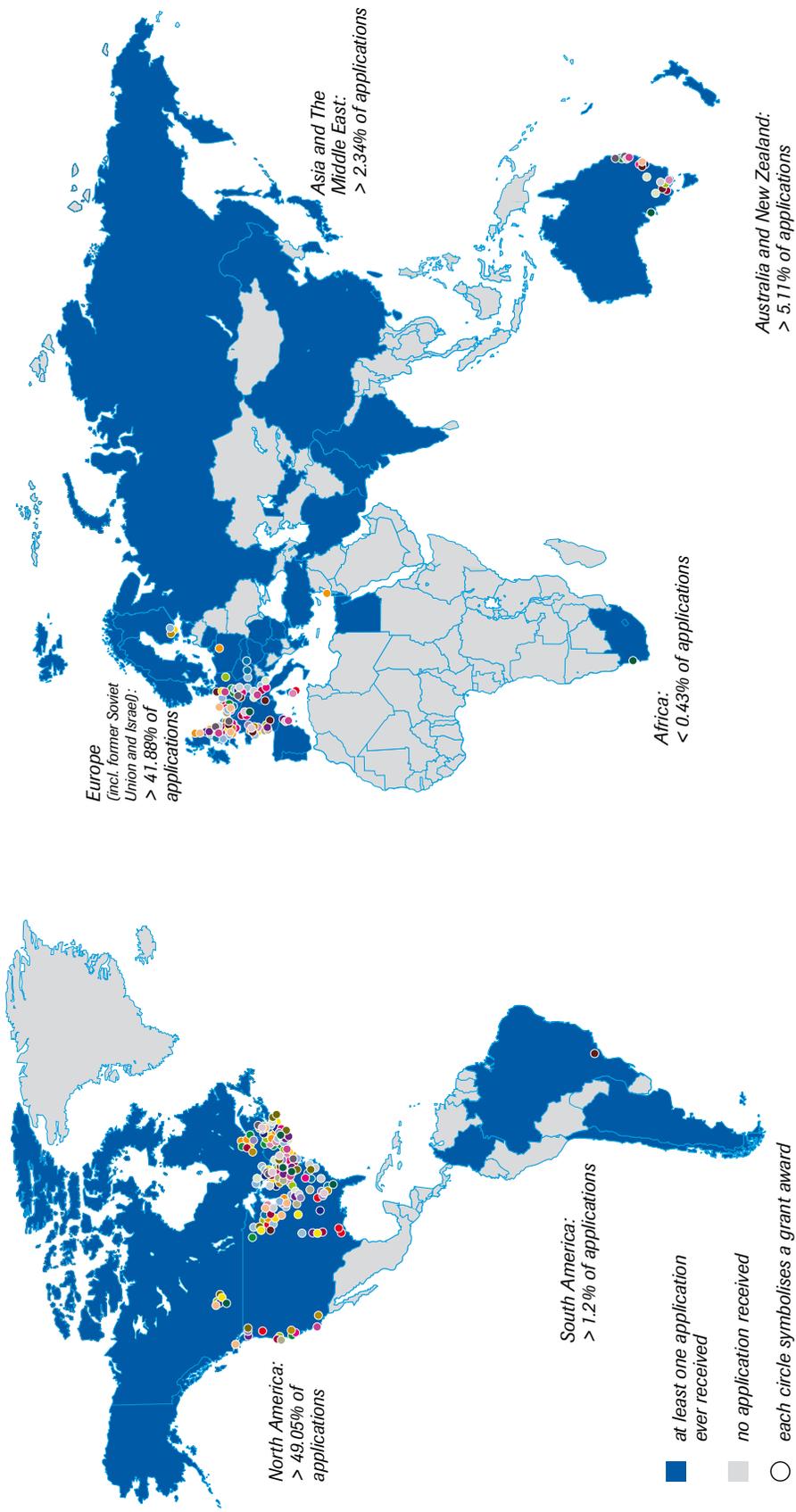


**Figure 1.** Geographical distribution of the applicants who submitted Letters of Intent (LOI) during the first twenty-six ROTRF funding cycles. The total number of LOIs submitted per cycle is shown in brackets.



**Figure 2.** Geographical distribution of the applicants who were awarded ROTRF grants during the first twenty-six ROTRF funding cycles.

## The Global View: Distribution of the ROTRF Applications and Grant Awards Worldwide





## 3. ROTRF Grant Awards in Cycle XXV and Cycle XXVI

*The abstracts of these projects are available on the ROTRF homepage.*

### **3.1. Research Grant Awards – Cycle XXV**

Dr William Baldwin, Cleveland Clinic, Cleveland, USA

*“Adiponectin, a Natural Anti-inflammatory Molecule, Decreases Heart Graft Rejection”*

Dr Daniel Chambers, University of Queensland, Chermside, Australia

*“Assessment of Airway Rejection in Lung Transplantation – No Longer B Grade?”*

Dr Xavier Forns, Fundació Clínic, Barcelona, Spain

*“Identification of Hepatitis C Recurrence after Liver Transplantation”*

Dr Joren Madsen, Massachusetts General Hospital, Boston, USA

*“Early Understanding How Immune Cells Reject Heart Transplants”*

Dr Olivia Martinez, Stanford University School of Medicine, Stanford, USA

*“Understanding the Cause of Malignancy in Transplant Recipients”*

Prof. Jane McKeating, University of Birmingham, Birmingham, UK

*“Do HCV-Receptor Interactions Determine the Outcome of Liver Transplant?”*

Dr Bernhard Schmidt, Hannover Medical School, Hannover, Germany

*“Cardiovascular Risk in Children and Young Adults after Renal Transplantation”*

Dr Christian van Delden, University of Geneva, Geneva, Switzerland

*“Dynamics of Bacterial Colonization after Lung Transplantation”*

### **3.2. Research Grant Awards – Cycle XXVI**

Prof. Christopher Barry, University of Rochester, Rochester, USA

*“MicroRNA Expression Predicts Liver Cancer Recurrence after Transplant”*

Prof. Irving Kron, University of Virginia, Charlottesville, USA

*“Improving Lung Transplantation Outcomes with Novel Reperfusion Methods”*

Prof. James McCluskey, University of Melbourne, Parkville, Australia

*“To Monitor the Mechanism and Tissue-specificity of Cross-reactive, Allogeneic T Cells”*

Prof. Nuala Mooney, INSERM, Paris, France

*“Regulation of Endothelial Cell Allogenicity by HLA Class II Alloantibodies”*

Dr Elmi Muller, University of Cape Town, Cape Town, South Africa

*“Transplanting HIV-positive Kidneys into HIV-positive Recipients”*

Dr Emilio Poggio, Cleveland Clinic, Cleveland, USA

*“Role of a Subtype of Memory T Cells in Immune Rejection of Transplanted Kidneys”*

Dr Banu Sis, University of Alberta, Edmonton, Canada

*“Molecular Assessment of Liver Transplant Biopsies”*

Dr Chen Tan, Beth Israel Deaconess Medical Center, Boston, USA

*“The Role of the Cellular Immune Response against BK Virus in Kidney Transplant Recipients”*

Dr He Xu, Emory University, Atlanta, USA

*“Belatacept and Rapamycin Regimen on Allo- and Viral-specific Immunity in Renal Allografts”*



## 4. ROTRF Recognition Prizes

Eleven ROTRF grantees were awarded a *ROTRF Recognition Prize* in 2011. This prize was awarded to investigators whose ROTRF-funded projects had a major impact on the field of transplantation and whose achievements best exemplify the mission of the ROTRF.

From the time of the first awards in March 1999 until the end 2011, the ROTRF has supported almost 260 important and innovative projects in basic science and clinical research applicable to the understanding and care of human organ transplant recipients and related tissue transplants.

In 2010, the Trustees invited all ROTRF grant recipients to participate in a survey presenting the results of their ROTRF-funded projects and selected 11 outstanding projects to receive an *ROTRF Recognition Prize*. The Trustees were very impressed with the overwhelming amount and quality of data and publications produced by ROTRF grant recipients over the years and were pleased to have been able to fund areas of transplantation that are often not funded and young investigators who would have otherwise faced difficulties pursuing their ideas and establishing their research programmes.

The award-winning projects addressed disparate topics relevant to organ transplantation, including induction of tolerance, the role of regulatory T cells and anti-inflammatory molecules in graft acceptance, the role of innate and adaptive immunity in allograft rejection, immunology of CMV infection and T cell allorecognition. The Trustees also recognise that there are several promising and important projects currently ongoing, which will likely impact on clinical practice in the years to come.

The ROTRF Recognition Prizes were awarded to the selected investigators at the ROTRF-sponsored satellite symposium "*ROTRF Recognition Prize – Recognising Excellence in Organ Transplantation Research*" at the American Transplant Congress 2011 in Philadelphia. At the symposium recipients of the *ROTRF Recognition Prize* had the opportunity to present the results of their ROTRF-funded research to an interested and appreciative audience.



### ***Recipients of a ROTRF Recognition Prize***

*The abstracts of these projects are available on the ROTRF homepage.*

Dr David Adams, University of Birmingham, Birmingham, UK  
*“Human Hepatic Dendritic Cells Induce Tolerance via Notch Signalling”*

Dr Simi Ali, Newcastle University, Newcastle-upon-Tyne, UK  
*“Anti-Rejection Therapy: Modifying Intra-graft Immunity by Specific Blockade of Th1 Cell Recruitment”*  
*“Non-Glycosaminoglycan-Binding Chemokine Receptor Agonists: a Novel Route to Anti-Rejection Therapy?”*

Dr Anita Chong, The University of Chicago, Chicago, USA  
*“Pathogenesis and Protective Activities of anti-Gal Antibodies”*  
*“Bacterial Infections and Allograft Tolerance”*  
*“Bacterial Infections and Transplantation Tolerance”*

Dr Julie Déchanet-Merville, CNRS, Bordeaux, France  
*“Study of the Role of Gamma-Delta T Lymphocytes in the Immune Response Directed against Human Cytomegalovirus”*

Dr Leszek Ignatowicz, Medical College of Georgia, Augusta, USA  
*“Visualizing the Role of Individual CD4+ T Cell Clones in Response to Allograft”*  
*“Origin and Dynamic Allocation of Foxp3+ Regulatory T Cells upon Graft Rejection or Acceptance”*

Dr Megan Levings, University of British Columbia, Vancouver, Canada  
*“Manipulating FOXP3 to Induce Transplantation Tolerance in Humans”*

Dr James McCluskey, The University of Melbourne, Parkville, Australia jointly with Prof. Jamie Rossjohn, Monash University, Clayton, Australia  
*“Defining the Molecular Basis of T Cell Allorecognition”*  
*“Understanding the Structural Basis of T Cell Allorecognition”*

Dr Miguel Soares, Instituto Gulbenkian de Ciência, Oeiras, Portugal  
*“Heme Oxygenase-1: an Anti-inflammatory Molecule that Promotes Organ Graft Survival”*

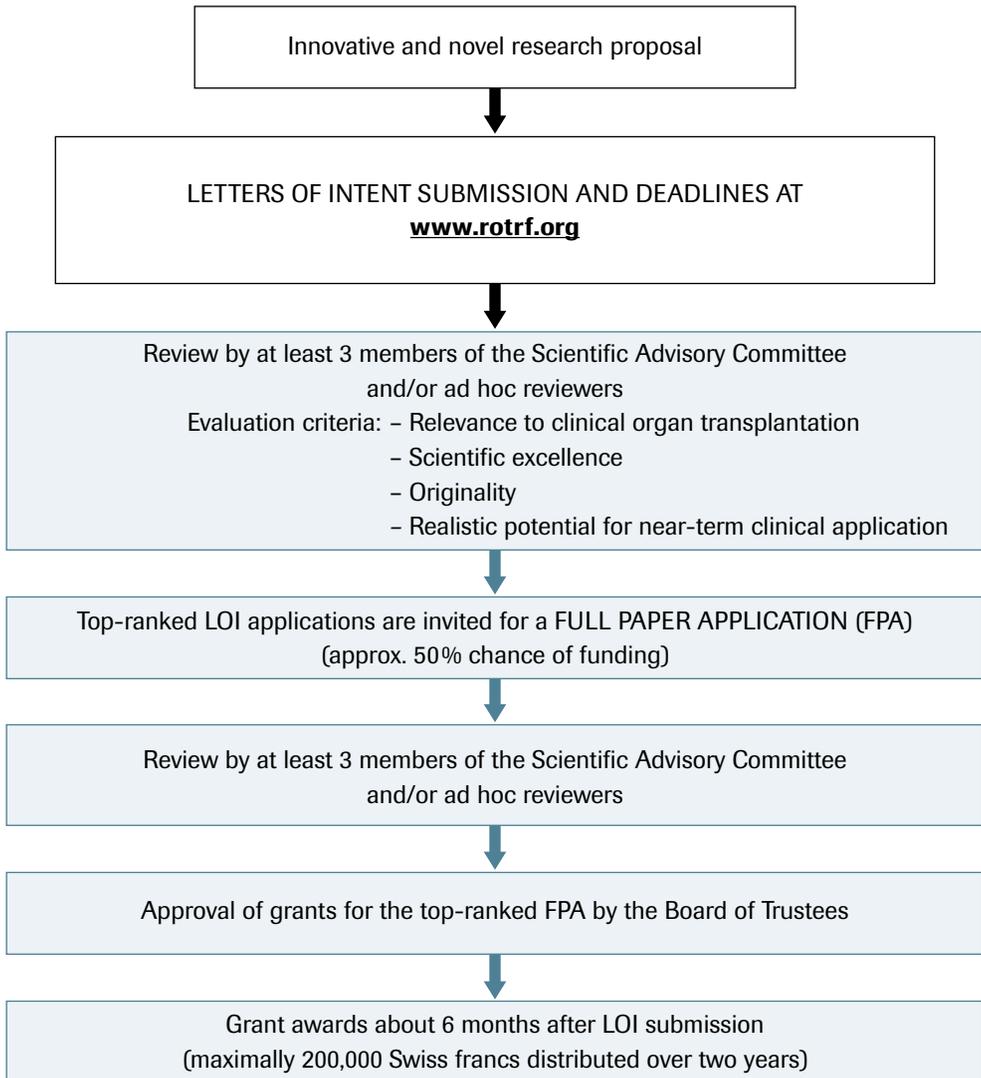
Dr Peter Terness, University of Heidelberg, Heidelberg, Germany  
*“Prevention of Allograft Rejection by Local Expression of the IDO Gene”*  
*“Using the Immunosuppressive IDO Gene for Prevention of Allograft Rejection”*

Dr Joost van Meerwijk, Toulouse University, Toulouse, France  
*“Induction of Allograft Tolerance with Regulatory T Cells in Mice Harboring a Humanized Immune System”*

Dr Barbara Wasowska, Johns Hopkins University, Baltimore, USA  
*“Activation of Macrophages and Endothelium by Non-complement Fixing Antibodies in Allograft Rejection”*  
*“Sialylated IgG Antibodies Inhibit Inflammation and Graft Rejection”*



## 5. How Do I Apply for a ROTRF Grant?



## **ROTRF Priority**

Our priority is to support clinically oriented research projects, such as observational clinical studies or studies that use human transplant samples for laboratory examinations, and focusing on understanding the pathogenesis and prevention of human transplantation diseases, including organ injury and rejection, viral infection, and late graft deterioration. Furthermore, the ROTRF may consider funding research that addresses related clinical issues in non-transplant patients, including hepatitis C infection and other viral infections, and inflammatory processes relevant to human organ transplantation. These related clinical issues should demonstrate their relevance to disease phenotypes in organ transplant patients. The Trustees will also consider funding studies that investigate transplant populations, ethics, organ preservation and allocation, and healthcare delivery. Moreover, the ROTRF will welcome research in new emerging technologies that examine the pathogenesis of human disease states in organ transplantation.

## **Project Proposals**

Project proposals submitted to the ROTRF should include work with clinical transplant material or with organ transplant patients, e.g. in human organ preservation, human transplant pathology, or other human transplant areas, and should be focused on issues relevant to clinical organ transplantation. If animal models are used to complement the clinical research, a higher priority will be given to those that simulate pathological states and mechanisms operating in human organ transplantation. To be considered for a grant award, applications should demonstrate practical applicability to human organ transplantation in the near term.

*\* Please note that the ROTRF cannot fund interventional clinical trials and projects involving interventions that would add risk to the patient or alter patient management. However, the Trustees may consider funding non-invasive scientific studies that complement an ongoing, approved clinical trial or projects proposing diagnostic clinical examinations posing minimal risk to the patients, e.g. laboratory investigations with a biopsy core obtained as an additional sample during biopsy procedures performed as standard of care. The Trustees will evaluate the clinical risk and take the final decision on the suitability of the project for ROTRF funding.*

## Research Areas Funded by the ROTRF\*

- Improvement of long-term graft survival and prevention of chronic organ dysfunction
- Relevant immune recognition, regulation and effector mechanisms
- Histocompatibility
- Inflammation and tissue injury in transplantation
- Development of new agents for use in transplantation
- Prospective and specific analysis of human organ transplant populations
- Induction of antigen-specific unresponsiveness
- New clinical trial methods and surrogate endpoints
- Tissue injury and organ preservation relevant to transplantation
- Cell or tissue transplantation relevant to organ transplantation
- While the ROTRF does not support operating costs for registries, it will consider providing limited support for unique initiatives such as international databases of general interest to transplant researchers.

**\* OF NOTE:**

*Research in human cloning is not considered for funding.*

*Applications for funding of research into transplantation of organs that are not yet transplanted in the clinic will not be considered.*



## 6. Board of Trustees

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**Professor Philip Halloran**

---

*Director, Alberta Transplant Institute  
Division of Nephrology & Immunology  
University of Alberta  
Edmonton, Canada*

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Professor of Surgery  
Department of Surgery  
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King’s College London  
King’s College Hospital London  
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**Dr Laurence Peterson**

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*Research Leader  
Inflammation Discovery  
Investigative and Translational Pharmacology  
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## 7. Scientific Advisory Committee

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Pittsburgh, USA



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