R O T R F

Roche Organ Transplantation Research Foundation

ANNUAL REPORT 2013

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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 300,000 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.

The ROTRF is a charity registered in Switzerland, no. CH–270.7.022.678–7.

1. Preface

For over fifteen years, the Roche Organ Transplantation Research Foundation (ROTRF) has supported research in organ transplantation. During these years, the ROTRF has changed its funding priorities from primarily basic laboratory science to areas more centred on clinical issues. At the same time, the ROTRF has played an educational role and has pushed forward a number of initiatives that have helped shape today's organ transplantation research into a science that is more responsive to the real challenges of the clinic.

Over 270 investigators have received ROTRF support totalling more than 53 million Swiss francs (over 57 million US dollars) across the 15 years. Many studies have increased our knowledge and understanding of biological issues intrinsic to transplantation, from which patients are benefitting. These investigations have led to numerous articles published in peer-reviewed journals and to ROTRF grantees receiving important awards.

In 2013, the ROTRF selected ten projects to receive ROTRF operating grants. The ROTRF has always distinguished itself by supporting novel ideas and innovative approaches, characterised by scientific excellence and relevance to important issues in transplantation, and by potential impact on clinical practice. The projects selected in this review cycle aim at identifying non-invasive biomarkers to evaluate graft function and monitor graft senescence after transplantation as a means to detect early rejection events and impaired organ function, and to prevent graft loss. Other investigations will attempt to identify molecular markers to assess organ quality at procurement to reduce risks of unsuccessful transplantation and increase organ utilisation. Further topics addressed include mechanisms of betalacept-resistant rejection in renal and liver transplantation, the effects of ischaemia-reperfusion damages and the risk of rejection in intestinal transplantation, and the factors influencing graft outcome in HCV/HIV-co-infected liver transplant patients. Finally, genetic factors and mechanisms leading to metabolic syndrome and weight gain after transplantation are also the subject of investigation.

None of this would have been possible without the generous gift from F. Hoffmann-La Roche Ltd, the unconditional commitment of the Trustees, the exceptional support of the Scientific Advisory Committee, ad hoc reviewers, and the grantees to which we wish to express our most sincere gratitude.

We also wish the newly awarded grantees of Cycles XXVIII every success in their investigations and are looking forward to hearing about the outcomes of their projects!

On behalf of the Board of Trustees

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

2. Facts and Figures

Funding Cycle XXVIII – Letters of Intent Submission in October 2012

The Roche Organ Transplantation Research Foundation (ROTRF) is pleased to announce that 1'698'180 Swiss francs were awarded to ten clinical research projects in 2013. As in previous years, the projects funded by the ROTRF focus on important issues in transplantation and have the potential for near-term clinical application.

In Cycle XXVIII, Letters of Intent (LOI) for research projects were accepted up until the deadline of 1 October 2012, and the ROTRF received 104 eligible applications. The majority was received from Europe (49%), with the major countries being the UK, Italy, Spain and Switzerland (6.7% each), Germany and the Netherlands (5.8% each), and France (3.8%). LOI's from North America accounted for 46.1% (USA: 39.4%; Canada: 6.7%) and of the remaining applications, 3.9% were received from Australasia and 1% from South America. No applications were submitted from Asia or Africa. Based on the Scientific Advisory Committee's review, the Board of Trustees invited 25 applicants to submit a Full Paper Application (FPA) and ten grants were awarded.

The newly awarded investigators will focus their efforts on the identification of non-invasive biomarkers of organ rejection in kidney, paediatric heart, and intestinal transplant patients; on assessing cellular senescence of transplanted grafts; and on the prediction of graft performance before transplantation. Other projects will address the problem of weight gain after transplantation or will aim to identify genetic markers of metabolic syndrome in transplant patients. Finally, the Trustees also awarded grants to support investigations on factors influencing HCV/HIV orthotopic liver transplantation outcome, immunosuppressive mechanisms of betalacept action, and the role of Paneth cells and microbiota alterations in the pathology of intestinal transplantation-related complications.

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

Statistics on Applications to the ROTRF

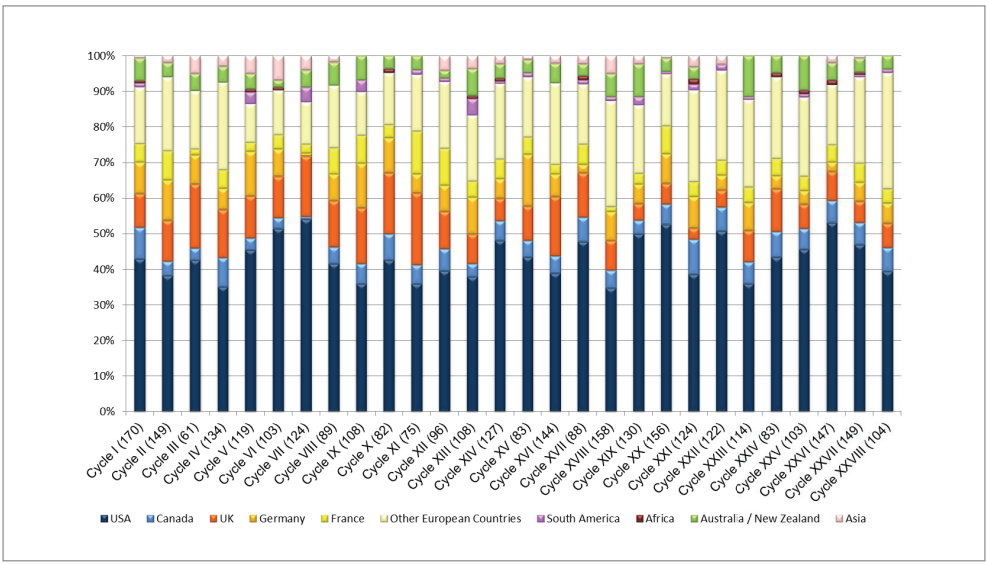


Figure 1. *Geographical distribution of the applicants who submitted Letters of Intent (LOI) during the first twenty-eight ROTRF funding cycles. The total number of LOIs submitted per cycle is shown in brackets.*

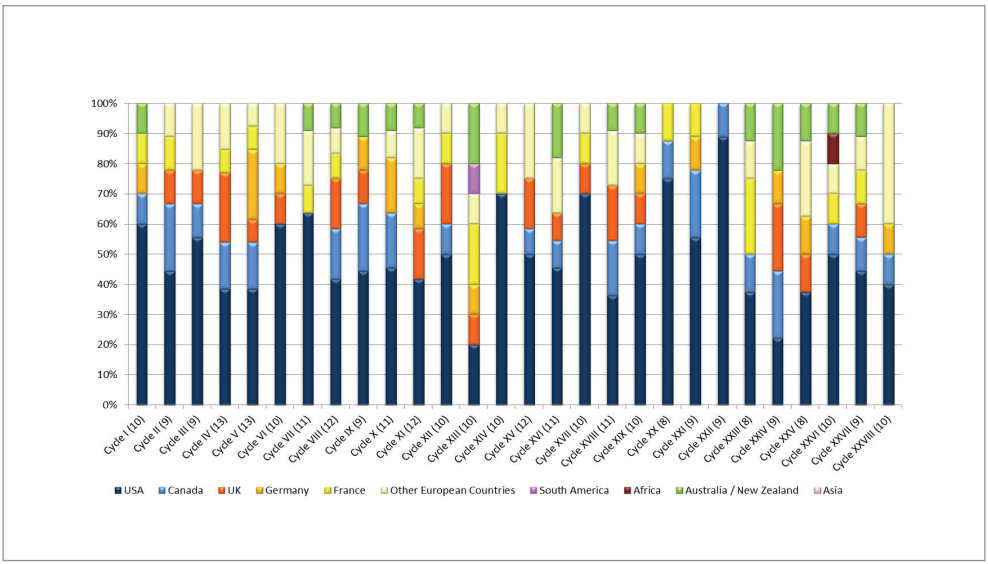
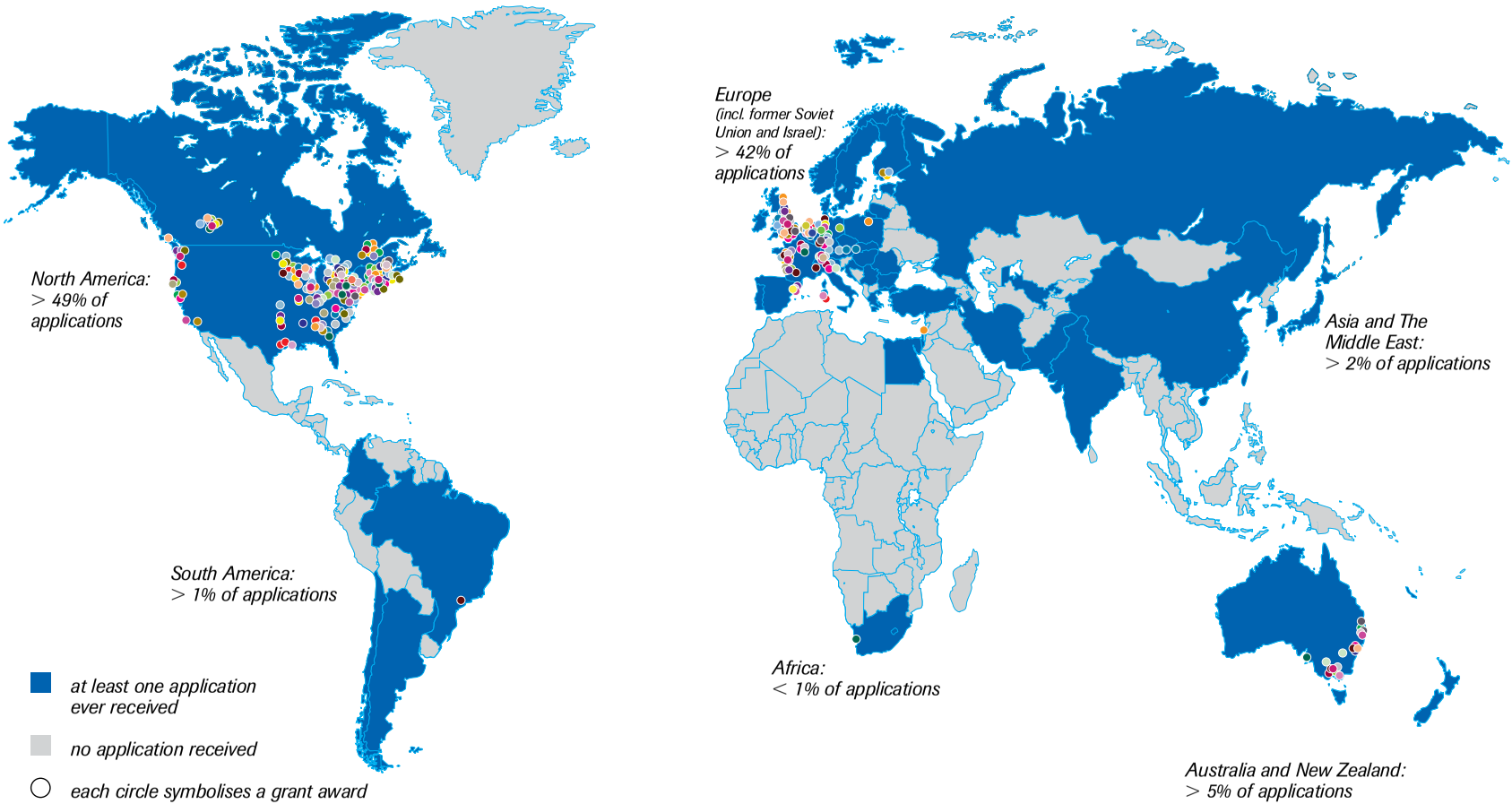


Figure 2. *Geographical distribution of the applicants who were awarded ROTRF grants during the first twenty-eight ROTRF funding cycles. The total number of grants awarded per cycle is shown in brackets.*

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



3. ROTRF Grant Awards in Cycle XXVIII

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

Research Grant Awards – Cycle XXVIII

Prof. Chin Eap, Hospital of Cery, Prilly, Switzerland
"Genetic Markers of the Metabolic Syndrome in Transplantation"

Dr Michael Eikmans, Leiden University Medical Center, Leiden, The Netherlands
"Diagnosing and Predicting Kidney Allograft Rejection by Biomarkers in Urine and Blood"

Dr Konrad Famulski, University of Alberta, Edmonton, Canada
"Identification of the Biomarkers of Tissue Injury and Age-Related Changes in Deceased Donor Kidneys at the Time of Donation"

Prof. Thomas Fishbein, MedStar Georgetown University Hospital, Washington DC, USA
"Does a Successful Intestinal Transplant Harbor a Special Population of Bacteria?"

Dr Mandy Ford, Emory University, Atlanta, USA
"Targeting Recently Identified T Cell Subsets Using Novel Immunosuppression"

Dr Kaatje Lenaerts, Maastricht University Medical Centre, Maastricht, The Netherlands
"Impact of Small Bowel Transplantation on the Intestinal Immunological Barrier"

Prof. Anette Melk, Hannover Medical School, Hannover, Germany
"Urinary Exosome Analysis for the Study of Kidney Transplant Aging"

Dr José Miro, Hospital Clinic – IDIBAPS, Barcelona, Spain
"Biological Factors Influencing Outcome HCV/HIV Co-Infected Liver Transplant Recipients"

Prof. William Mitch, Baylor College of Medicine, Houston, USA
"Characterizing Weight Gain after Kidney Transplantation"

Dr Heth Turnquist, University of Pittsburg, Pittsburg, USA
"Prognostic Value and Function of IL-33/ST2 in Transplant Recipients with Infection"

4. Board of Trustees

Chairman: **Professor Philip Halloran**	*Director, Alberta Transplant Institute* Division of Nephrology & Immunology University of Alberta Edmonton, Canada
Professor Andrew Bradley	*Clinical Director of Transplantation Services* *Professor of Surgery* Department of Surgery University of Cambridge Cambridge, UK
Professor Robert Colvin	*Director, Immunopathology Research Laboratory* Department of Pathology Harvard Medical School Massachusetts General Hospital Boston, USA
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Professor Alberto Sanchez-Fueyo	*Professor, Institute of Liver Studies* King’s College London King’s College Hospital London London, UK

5. Scientific Advisory Committee

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