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Roche Organ Transplantation Research Foundation

ANNUAL REPORT 2009



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 three 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.



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1. Preface

On behalf of the Board of Trustees of the Roche Organ Transplantation Research Foundation (ROTRF), I am pleased to announce that the ROTRF grant awards for Cycles XXI and XXII have been awarded to 14 clinical and 4 conventional research projects, including 9 clinical projects that were awarded in Cycle XXI as part of the special competition promoting clinical research in organ transplantation*. In total, 3.95 million Swiss francs were awarded in these two application cycles.

In this past year, the Board of Trustees and the Scientific Advisory Committee (SAC) of the ROTRF took on the difficult task of selecting 18 projects that were to be funded from an impressive number of highly original and interesting applications. The results from many funded projects have already been presented at national and international congresses, published in peer-reviewed journals and on the ROTRF homepage. The Trustees are looking forward to even more new and exciting data from the newly funded projects.

In 2007, the ROTRF announced a 5-Year Plan focusing on the understanding of the pathogenesis and prevention of human transplantation diseases. Two years into the Plan, the emphasis continues to be on supporting research involving transplant patients and material, addressing clinical issues relevant to organ transplantation in non-transplant patients, and on the development and clinical implementation of new technologies to examine the pathogenesis of disease states in transplant patients. In line with the 5-Year Plan, in 2008, the Board of Trustees marked the 10th Anniversary of the ROTRF with a special grant award competition promoting clinical research in organ transplantation. The response to this special competition was overwhelming, with many innovative applications received by the October 2008 deadline. The grants were awarded in March 2009 and are presented in the grant award overview of Cycle XXI.

Based on the success of the special competition and of its clinical grant award programme in the past, the ROTRF has now decided to concentrate its efforts on exclusively supporting clinical research. This new focus aims to promote research specifically addressing problems in human transplantation and having a realistic potential for clinical application in the near term. The Trustees hope to promote collaborative work between clinicians and research investigators and to support areas of clinical transplantation research that are currently under-studied, and that may open new research frontiers.

Starting with Cycle XXIII, the Trustees encourage investigators to submit proposals for clinically oriented research projects, such as observational clinical studies or studies that use human transplant samples for laboratory examinations. Investigators working in areas such as antibody-mediated rejection and antibody formation, graft pathology during rejection

events, histocompatibility, infectious agents, and disease phenotypes in transplant patients are encouraged to apply. The Trustees will also consider funding studies that investigate transplant populations, ethics, organ preservation and allocation, and healthcare delivery. Furthermore, the ROTRF will welcome research in new emerging technologies that examine the pathogenesis of human disease states in organ transplantation. The first Letters of Intent under this new focus were received by the 1 October 2009 deadline for Cycle XXIII, and have been of outstanding breadth and quality. The Trustees are anticipating a number of exciting and competitive grant applications in Cycle XXIII.

In 2009, the ROTRF sponsored a satellite symposium at the American Transplant Congress in Boston entitled "The Systems Biology of Clinical Organ Transplantation". This symposium highlighted new technologies and approaches to the analysis of patient material that can be used alongside the more traditional approaches to ensure a better understanding of the disease state of transplant patients. This informative symposium was chaired by the ROTRF Trustees, Prof. J. Andrew Bradley and Prof. Allan D. Kirk and included presentations on analysis, storage and interpretation of complex data related to the disease states in organ transplantation, emerging technologies and bioinformatic approaches for identifying key regulatory molecules. Novel technologies for quantifying human B cell responses in highly sensitized patients were also discussed and preliminary results of the Long-term Deterioration of Kidney Allograft Function (DeKAF) study that examined the prognostic value of cluster analysis based on BANFF score were presented. The symposium was very well attended and received. The ROTRF is looking forward to bringing important and exciting developments in transplantation to congresses in the future.

The ROTRF is grateful to F. Hoffmann-La Roche Ltd for their continued support of research in organ transplantation over the last 10 years. The Board of Trustees would like to thank the ROTRF Scientific Advisory Committee for their dedication to this cause, and the grantees for their excellent work and support, which have contributed to the overall success of the Foundation.

Finally, the ROTRF wishes the newly granted investigators of Cycles XXI and XXII good luck with their research.

On behalf of the Board of Trustees

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

^{*} At the time of going to press two grant awards in each cycle were still pending due to administrative reasons and are not listed in the grant award overview.



2. Facts and Figures

Funding Cycles XXI and XXII – Letters of Intent Submission in October 2008 and April 2009

The Roche Organ Transplantation Research Foundation (ROTRF) is very pleased to announce that 9 grants have been awarded for the 10th Anniversary Clinical Transplantation Research Grant Award Competition (Cycle XXI) and in Cycle XXII, 4 grants have been awarded for conventional and 5 for clinical research applications. In Cycle XXI, 1.97 million Swiss francs were allocated to the 9 clinical research projects*, whereas in Cycle XXII, 1.98 million Swiss francs were distributed to the 9 clinical and conventional projects*.

The ROTRF received 124 Letters of Intent for the 10th Anniversary Clinical Transplantation Research Grant Award Competition up to the submission deadline (1 October 2008) from scientists around the world. Of the applications, 41.9% were received from Europe, the major countries being Germany (8.9%), Italy (8.1%), and France and The Netherlands (4.0% each). Belgium, Switzerland and the UK accounted each for 3.2% of the applications submitted. The majority of the applications was received from North America (48.4%): United States (38.7%) and Canada (9.7%). Australia/New Zealand (3.2%), Asia (3.2%), South America (1.6%) and Africa (1.6%) accounted for the remaining 9.6% of the applications. Based on the reviews of the Scientific Advisory Committee (SAC), the Board of Trustees invited 27 applicants to prepare Full Paper Applications. After a thorough review of the 23 received applications, grants were awarded to 9 clinical research projects.

In Cycle XXII, 122 Letters of Intent were received up to the submission deadline (1 April 2009). Applications from Europe accounted for 38.5% and those from North America for 57.4% of all applications received. The European submissions were received mainly from Switzerland (8.2%). Italy, The Netherlands and UK accounted each for 4.9%, and France and Germany each for 4.1% of the total applications. Applications from the USA and Canada accounted for 50.8% and 6.6% of applications, respectively. The remaining applications were received from Asia (2.5%) and South America (1.6%). Following review by the SAC, the Board of Trustees invited 24 applicants to prepare Full Paper Applications and after reviewing the 20 received applications, grants were awarded to 9 research projects, including 4 conventional and 5 clinical projects.

The research funded in these two cycles will focus on clinical and scientific aspects of organ transplantation, such as molecular markers of graft rejection, molecular diagnostic strategies for donor selection, innate immunity, induction of tolerance, effects of viral infections on graft rejection and development of preclinical protocols for induction of mixed chimerism. Abstracts and progress reports of the projects supported by the ROTRF are available on the ROTRF homepage.

^{*} At the time of going to press two grant awards in each cycle were still pending due to administrative reasons and are not listed in the grant award overview.



Statistics on Applications to the ROTRF

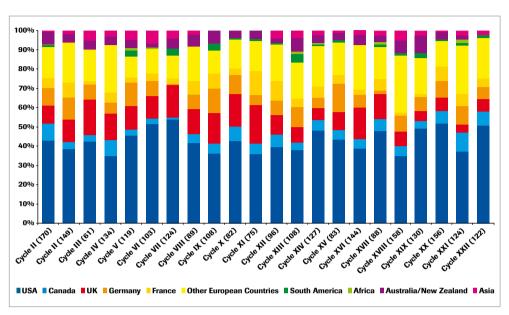


Figure 1. Geographical distribution of the applicants who submitted Letters of Intent (LOI) during the first twenty-two ROTRF funding cycles. The total number of LOIs submitted per cycle is shown in brackets.

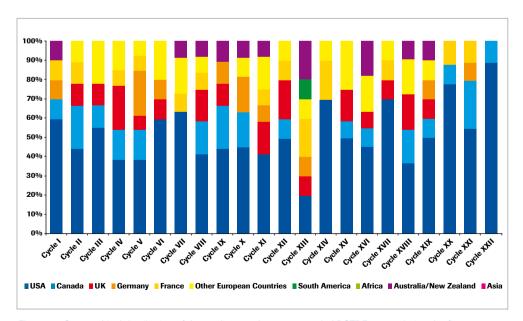
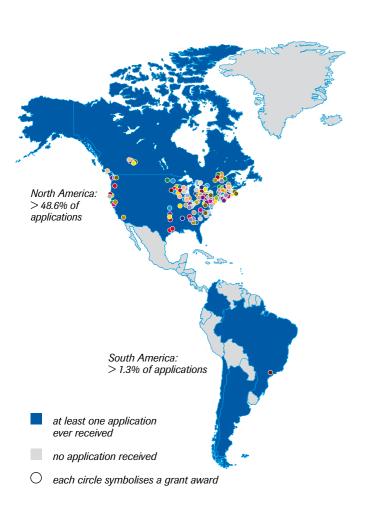
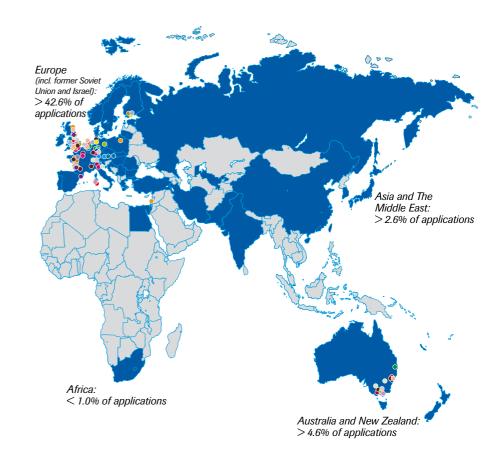


Figure 2. Geographical distribution of the applicants who were awarded ROTRF grants during the first twenty-two ROTRF funding cycles.

The Global View of Applications to the ROTRF: Distribution of the ROTRF Applications Worldwide







3. ROTRF Grant Awards in Cycle XXI and Cycle XXII

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

3.1.1 ROTRF Conventional Research Grant Awards - Cycle XXII

"How Antibodies from B Cells Lead to Rejection of Organ Transplants"

Dr Geetha Chalasani, University of Pittsburgh, Pittsburgh, USA

"Immune Tolerance to Face and Hand via Mixed Chimerism"

Dr David Mathes, Fred Hutchinson Cancer Research Center, Seattle, USA

"Bone Marrow Transplantation with Regulatory Cells to Achieve Tolerance in Monkeys" Prof. Megan Sykes, Principal Investigator Massachusetts General Hospital, Boston, USA

3.2.1 ROTRF Clinical Research Grant Awards - Cycle XXI

10th Anniversary Clinical Transplantation Research Grant Award Competition

"Innate Immunity of the Transplanted Human-small Intestine"

Dr Thomas Fishbein, Georgetown University, Washington DC, USA

"Can Cells from a Transplant Recipient Integrate into a Transplanted Organ?" Dr A. John Iafrate, Massachusetts General Hospital, Boston, USA

"Molecular Techniques to Improve Safety of Donor Lungs for Transplantation" Dr Shaf Keshavjee, University Health Network, Toronto, Canada

"Integrins in Fibrosis and Atrophy in Human Renal Allografts"
Dr Michael Mengel, University of Alberta, Edmonton, Canada

"Improving Management of Cytomegalovirus Complications after Transplantation"

Dr Martina Sester, University of the Saarland, Homburg, Germany

"Use of a Unique Marker to Identify T Cells that Can Control Transplant Rejection" Dr Mark Siegelman, University of Texas Southwestern Medical Center, Dallas, USA

"Identifying Viral Infections in Kidney Transplant Patients" Dr David Wang, Washington University, St. Louis, USA

3.2.2 ROTRF Clinical Research Grant Awards - Cycle XXII

"Cytomegalovirus: from Bench to Bedside"

Dr Atul Humar, The University of Alberta Hospital, Edmonton, Canada

"Development of Novel Tools to Diagnose Kidney Injury in Transplantation"

Dr John Iacomini, Brigham and Women's Hospital Transplantation Research Center,
Boston, USA

"Role of Fibroblasts in Lung Dysfunction after Lung Transplantation"
Dr Scott Palmer, Duke Medical Center, Durham, USA

"The Role of Dendritic Cell Dysfunction in BK Nephropathy"
Prof. Karl Womer, Johns Hopkins University, Baltimore, USA



4. How Do I Apply for a ROTRF Grant?

Innovative and novel research proposal









Submission of LETTER OF INTENT (LOI) at http://www.rotrf.org



Review by at least 3, normally 4, members of the Scientific Advisory Committee and/or ad hoc reviewers

Evaluation criteria: - Relevance to clinical organ transplantation

- Scientific excellence
- Originality
- Realistic potential for near term clinical application



Top-ranked LOI applications are invited for a FULL PAPER APPLICATION (FPA) (approx. 50% chance of funding)



Review by at least 3, normally 4, members of the Scientific Advisory Committee and/or ad hoc reviewers



Approval of grants for the top-ranked FPA by the Board of Trustees



Grant awards about 6 months after LOI submission (maximally 300,000 Swiss francs distributed over three years)



5. Board of Trustees

| Chairman: | | |
|--------------------------------|---|--|
| Professor Philip F. Halloran | Director, Alberta Transplant Institute | |
| - Tolessor Fillip I. Hallorali | Division of Nephrology & Immunology | |
| | University of Alberta | |
| | Edmonton, Canada | |
| | Edinoritori, Odridda | |
| Professor Andrew Bradley | Clinical Director of Transplantation Services | |
| | Professor of Surgery | |
| | Department of Surgery | |
| | University of Cambridge | |
| | Cambridge, UK | |
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| Professor Robert Colvin | Director, Immunopathology Research Laboratory | |
| | Department of Pathology | |
| | Harvard Medical School | |
| | Massachusetts General Hospital | |
| | Boston, USA | |
| | Boston, Gov | |
| Professor Allan Kirk | Scientific Director of the | |
| | Emory Transplant Center | |
| | Professor of Surgery | |
| | Emory University | |
| | Atlanta, USA | |
| Duefe a con Ocale and Ocale | Director, Department of | |
| Professor Gerhard Opelz | Transplantation Immunology | |
| | University of Heidelberg | |
| | Heidelberg, Germany | |
| | Tioladisolg, admining | |
| Professor Giuseppe Remuzzi | Director, Department of Immunology and | |
| | Clinical Transplantation | |
| | Ospedali Riuniti di Bergamo and Istituto di | |
| | Ricerche Farmacologiche "Mario Negri" | |
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| D. M | VP, Head CRED Inflammation | |
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| | Nutley, USA | |
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| | | |



6. Scientific Advisory Committee

Prof. Maria-Luisa Alegre

Dept of Medicine The University of Chicago Chicago, USA

Prof. Anthony d'Apice

Dept of Clinical Immunology St. Vincent's Hospital Melbourne. Australia

Prof. Jeremy Chapman

University of Sydney Westmead Hospital Westmead, Australia

Prof. Henrik Ekberg

Dept of Nephrology and Transplantation Lund University Malmö, Sweden

Prof. Sandy Feng

UCSF Medical Center Transplant Surgery University of California San Francisco, USA

Prof. Christiane Ferran

Harvard Medical School Immunobiology Research Center Boston, USA

Prof. Gregg Hadley

The Ohio State University Division of Transplant Surgery Columbus, USA

Prof. Bruce Kaplan

Arizona Health Science Center Dept of Medicine Tucson, USA

Prof. John Kirby

Dept of Surgery
University of Newcastle-upon-Tyne
Newcastle-upon-Tyne, UK

Prof. Philip O'Connell

Westmead Hospital Transplantation Westmead, Australia

Prof. Richard III Pierson

Cardiac Surgery
University of Maryland Medical Center
Baltimore, USA

Prof. Jeffrey Platt

Surgery and Microbiology and Immunology University of Michigan Ann Arbor, USA

Prof. Heinz Regele

Clinical Institute of Pathology and Department of Internal Medicine III University of Vienna Vienna, Austria

Prof. Alberto Sanchez-Fueyo

Unidad de Hepatologia y Transplante Hepático Hospital Clinic Barcelona Barcelona, Spain

Prof. Angus Thomson

Thomas E. Starzl Transplantation Institute University of Pittsburgh Pittsburgh, USA



To apply, please visit our website, http://www.rotrf.org

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