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Roche Organ Transplantation Research Foundation

ANNUAL REPORT 2008



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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 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.



1. Preface

On behalf of the Board of Trustees of the Roche Organ Transplantation Research Foundation (ROTRF), I am pleased to announce that in Cycles XIX and XX, ROTRF grants have been awarded to 12 conventional and 6 clinical research projects, including 3 projects that were awarded as part the joint grant award initiative with the Juvenile Diabetes Research Foundation International (JDRF). In total, 3.8 million Swiss francs were awarded in these two application cycles.

The Board of Trustees and the Scientific Advisory Committee (SAC) of the ROTRF were once again impressed with the quality and originality of the applications received. This continues to translate into high-quality research and stimulating new findings, which are presented at national and international congresses and published in high-impact peer-reviewed journals.

In 2007 the ROTRF announced a 5-Year Plan focusing on the understanding of the pathogenesis and prevention of human transplantation diseases, emerging techniques for the investigation of diseases related to transplantation and clinical issues in non-transplant patients applicable to transplantation.

In line with the 5-Year Plan's aim of promoting clinical research and new emerging technologies in transplantation, the Board of Trustees marked the 10th Anniversary of the ROTRF with a special grant award competition promoting clinical research in organ transplantation and inviting investigators to study their patients. With the "10th Anniversary Clinical Transplantation Research Grant Award Competition", the Trustees wished to promote research in antibody-mediated rejection and antibody formation, pathology of the graft during rejection events, and other areas in clinical research that promote the understanding of the critical events in patients with organ transplants. This includes studies of transplant populations, ethics, organ preservation and allocation, and healthcare delivery. The response to this special competition was overwhelming, with many innovative applications received by the October 2008 deadline. These applications are currently being evaluated and the funded projects will be announced in 2009.

To further celebrate the 10th Anniversary of its conception, the ROTRF sponsored symposia at two major transplantation congresses in 2008. At the American Transplant Congress in Toronto, the ROTRF symposium "CSI – Clinical Science Investigations: Where Science Meets the Bedside" focused on immunosuppression, antibody-mediated rejection and cytomegalovirus infection in organ transplantation and included a discussion of clinical cases. The ROTRF early morning workshop at The XXII International Congress of the Transplantation Society in Sydney was entitled "Mechanisms of Graft Rejection and Acceptance: Pathways

to a New Clinical Era". In this informative workshop, ROTRF Trustees Dr Robert Colvin and Dr Gerhard Opelz chaired talks about cell- and antibody-mediated rejection and operational tolerance in liver transplantation. Both symposia were very successful and drew large audiences. The ROTRF plans to continue bringing to the forefront important issues in transplantation at future congresses.

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. The ROTRF also wishes to thank the JDRF for the excellent collaboration for the joint grant award competition. The Trustees would like to acknowledge the excellent work of the ROTRF Secretariat, in particular Dr Claudia Ellenrieder.

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

On behalf of the Board of Trustees

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



2. Facts and Figures

Funding Cycle XIX and XX – Letter of Intent Submission in October 2007 and April 2008

The Roche Organ Transplantation Research Foundation (ROTRF) is very pleased to announce that in Cycles XIX and XX grants have been awarded to 12 conventional and 6 clinical research applications, including 2 conventional grants and 1 clinical grant for the joint ROTRF/JDRF grant award competition. In Cycle XIX, 1.85 million Swiss francs were allocated to 10 research projects, whereas in Cycle XX, 1.95 million Swiss francs were distributed to 8 projects.

The ROTRF received 130 Letters of Intent in Cycle XIX up to the submission deadline (1 October 2007) from scientists around the world. Of the applications, 32.3% were received from Europe, the major countries being Germany and The Netherlands (each 5.4%), UK (4.6%) and France, Switzerland and Spain (each 3.1%). The majority of the applications were received from North America (53.9%): United States (50.0%) and Canada (3.9%). Australia/New Zealand (9.2%), Asia (2.3%) and South America (2.3%) accounted for the remaining 13.9% of the applications. Based on the reviews of the SAC, the Board of Trustees invited 25 applicants to prepare Full Paper Applications. After a thorough review of the 24 received applications, grants were awarded to 10 research projects, including 2 from the ROTRF/JDRF Joint Initiative.

In Cycle XX, 156 Letters of Intent were received up to the submission deadline (1 April 2008). Applications from Europe accounted for 36.5% and those from North America for 58.3% of all applications received. The European submissions were received mainly from Germany (8.3%), France (7.7%), UK (5.8%) and Italy (4.5%). Applications from the USA and Canada accounted for 52.6% and 5.8% of applications, respectively. The remaining applications were received from Australia/New Zealand (3.9%), Asia (0.6%) and South America (0.6%). Following review by the SAC, the Board of Trustees invited 25 applicants to prepare Full Paper Applications and after reviewing the 22 received applications, grants were awarded to 8 research projects, including 1 from the ROTRE/JDRE Joint Initiative.

The research funded in these two cycles will focus on clinical and scientific aspects of organ and islet transplantation, such as induction of tolerance, viral infection, imaging and diagnostic techniques for the detection of graft rejection, post-transplant lymphoproliferative disease, islet cell isolation and survival, and the role of histocompatible stem cells in transplantation.

Abstracts and progress reports of the projects supported by the ROTRF are available on the ROTRF homepage.



Statistics on Applications to the ROTRF

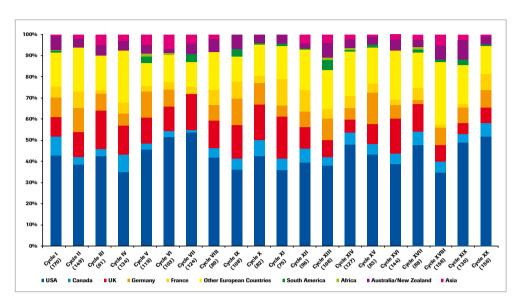


Figure 1. Geographical distribution of the applicants who submitted Letters of Intent (LOI) during the first twenty ROTRF funding cycles. The total number of LOIs submitted per cycle is shown in brackets.

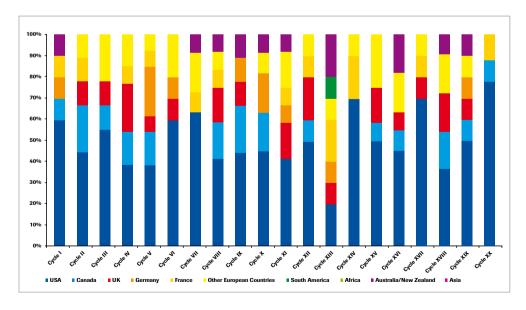
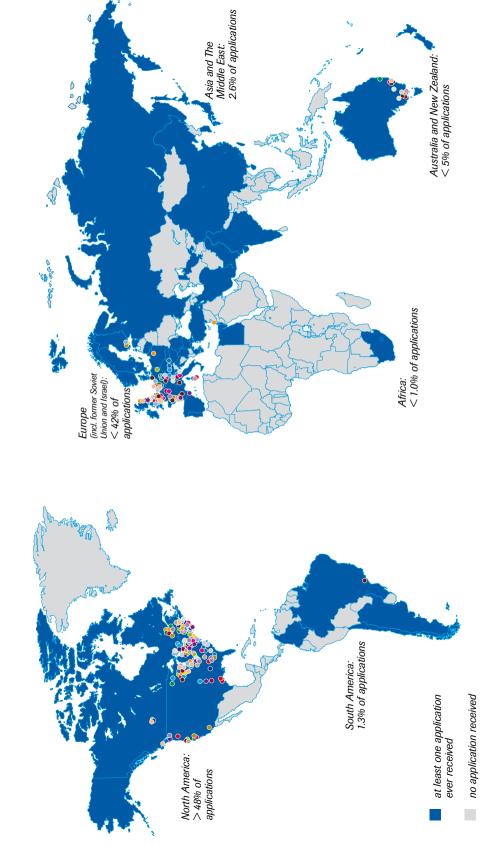


Figure 2. Geographical distribution of the applicants who were awarded ROTRF grants during the first twenty ROTRF funding cycles.

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



Grant Awards in:

| 2008 | | | | | | | 2003 | | | | | | |
|-----------------|----------------------------------|-----|------------------------------|-----|-----------------------------------|-----|-------------|---------------------------------------|-----|---|-----|---|-----|
| ək XX | Atlanta, USA | • | Hannover, Germany | • | Pittsburgh, USA | • | | Birmingham, USA | • | Herston, Australia | | Sainte-Foy, Canada | |
| ς γ | Baltimore, USA | • | Melbourne, Australia | • | Zurich, Switzerland | • | | Boston, USA | | lowa City, USA | | Stanford, USA | |
| X) | Boston, USA | | Milwaukee, USA | • | | | IX C | Brussels, Beiglum | | London, Canada | | sydney, Australia | |
| IX | Charlestown, USA | • (| Montreal, Canada | | | | | Columbus, USA | • | Newcastle-upon-Tyne, | | | |
| | Cleveland, USA | • | Oxford, UK | • | | | | Edmonton, Canada | • | UK Mour House 1194 | • | | |
| 2007 | | | | | | | 2006 | neideberg, dermany | | wew ridgell, COA | | | |
|) | Edmonton, Canada | • | Dallas, USA | | Newcastle-upon-Tyne, | | I | | | | | | |
| ΛΙ ()C | Augusta, USA | • | Edinburgh, UK | • | CK | | | Baitimore, USA | | Columbus, USA | • (| Montreal, Canada | • (|
| X C | Baltimore, USA | | Groningen, | | Oxford, UK | • | \ | Bergamo, Italy Roston 11SA | | neideiberg, Australia London Canada | | Names, France New York 11SA | • |
| 8 | Barcelona, Spain | | The Netherlands | • (| Pittsburgh, USA Scottle, USA | | 3 I 3 I | Brussels, Belgium | • | London, UK | | Oxford, UK | |
| | BOSIOII, USA Rrissels Retrium | | Madison 11SA | | Sydney Australia | | IΛ | Cagliari, Italy | | Madison, USA | | Paris, France | |
| X | Chicago, USA | • | Nantes, France | • | Vancouver, Canada | • | | Chicago, USA | | Melbourne, Australia | • • | Pittsburgh, USA | |
| 2006 | | | | | | | 1006 | , , , , , , , , , , , , , , , , , , , | | , | | (00000000000000000000000000000000000000 | |
| 1/ ə | Amsterdam. | | Columbus 11SA | • | New Haven USA | • | 700 | | | | | | |
| X/ | The Netherlands | • | Helsinki, Finland | • | Nijmegen, | | IA Əl: | Augusta, USA | | Edgbaston, UK | | Munich, Germany | |
| C) & | Baltimore, USA | • | Leeds, ÚK | • | The Netherlands | • | % ;λc | Bergamo, Italy | | Hanover, Germany | | Nantes, France | |
| ٨ | Bergamo, Italy | • | London, Canada | • | Parkville, Australia | • | Λ C | Boston, USA Brussele Belgium | | Heidelberg, Germany | | Okianoma City, USA Regenshira | |
| X | Boston, USA | • | London, UK | • | Philadelphia, USA | • (| | Chapel Hill. USA | | Madison, USA | | Germany | |
| | Chicago, USA | • | Newcasue-upon-ryne, UK | n). | Zunch, Switzenand | • | | Chicago, ÚSA | | Manchester, UK | | Toronto, Canada | |
| 2005 | | | | | | | Ī | Durham, USA | | Minneapolis, USA | | Vienna, Austria | |
| | | | | | | | 5000 | | | | | | |
| ΛI) | Atlanta, USA | • | Leiden, | | Sydney, Australia | | \ \ | Atlanta USA | | Laval. Canada | • | Niime aen. | |
| χ Y | Boston, USA Cambridge 11K | • | The Netherlands Madison 11SA | | St. Louis, USA Toulouse France | • (| § 1 \c | Birmingham, UK | | Madison, USA | | The Netherlands | |
|) 8 I | Cleveland, USA | • | Nantes, France | • | Utrecht. | | | Boston, USA | • | Montreal, Canada | | Philadelphia, USA | |
| | Columbus, USA | • | Pittsburgh, USA | | The Netherlands | • | | Cagliari, Italy Chicago 1184 | • • | Nantes, France | • | Portland, USA Rehovot Israel | • |
| | Fitzroy, Australia | • | San Francisco, USA | • (| | | | Dundee. UK | • | Newcasuc-upon-ryne, UK | • | Warsaw. Poland | • |
| | негаегрегд, Germany | | Sao Paulo, Brazil | | | | | Houston, USA | | Oxford, UK | | Winnipeg, Canada | |
| 2004 | | | | | | | 1999 | | | | | | |
| ək II) | Augusta, USA | | Giessen, Germany | | Nantes, France | | II | Berlin Germany | | Madison 11SA | | Pittshurdh 11SA | |
| | Baltimore, USA | | Helsinki, Finland | • (| New Haven, USA | • (| S. | Bordeaux, France | • | Melbourne, Australia | • | San Francisco, USA | • |
| | Boston, USA | | Leiden. | | Pittshurah USA | | l C | Boston, USA | • | Montreal, Canada | • | | |
| | Cambridge, UK | | The Netherlands | | Stanford, USA | | | Cincinnati, USA | • (| Nantes, France | • (| | |
| | Chapel Hill, USA | | London, UK | | Sydney, Australia | | | Famonion, Canada Helsinki, Finland | • | New Haven, USA New York, USA | • | | |
| | Cleveland, USA | | Los Angeles, USA | | | | | London, Canada | • | Oxford, ÚK | • | | |



3. ROTRF Grant Awards in Cycle XIX and Cycle XX

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

ROTRF Conventional Research Grant Awards - Cycle XIX

"Origin and Allocation of Regulatory T Cells upon Graft Rejection or Acceptance" Prof. Leszek Ignatowicz, Medical College of Georgia, Augusta, USA

"Prevention of Lung Transplant Injury by Adenosine Receptor Activation" Prof. Victor Laubach, University of Virginia, Charlottesville, USA

"Chemokine-Mediated Control of Effector and Regulatory T Cells in Lung Rejection"
Dr Andrew Luster, Massachusetts General Hospital, Charlestown, USA

"Overcoming Senescence Mechanisms Will Lead to Better Renal Graft Survival"

Prof. Anette Melk, Medizinische Hochschule Hannover, Kinderklinik, Hannover, Germany

"Prevention of Organ Injury and Rejection in Transplantation"
Prof. Wei-Ping Min, University of Western Ontario, London, Canada

"Prevention of Virus-associated Nephropathy after Renal Transplantation" Prof. Andrey Sorokin, Medical College of Wisconsin, Milwaukee, USA

ROTRF Conventional Research Grant Awards - Cycle XX

"Analysis of Cells That Inhibit Anti-graft Immune Responses" Dr Ignacio Anegon, INSERM U643, Nantes, France

"Histocompatible Stem Cells for Transplantation"

Dr David Russell, University of Washington, Seattle, USA

"Alloantibody Production in Sensitized Transplant Recipients"
Dr Anna Valuiskikh, Cleveland Clinic, Cleveland, USA

"Sialylated IgG Antibodies Inhibit Inflammation and Graft Rejection" Dr Barbara A. Wasowska, Johns Hopkins University, Baltimore, USA

ROTRF Clinical Research Grant Awards - Cycle XIX

"Confocal Microscopy after Lung Transplantation: Specific Findings during Rejection?" Prof. Annette Boehler, University Hospital, Zurich, Switzerland

"Immune Cells for Therapy of Post-transplant Lymphoproliferative Disorders in Pediatric Transplant Patients"

Dr Diana Metes, University of Pittsburgh, Pittsburgh, USA

ROTRF Clinical Research Grant Awards - Cycle XX

"Transplant Rejection Mediated by Antibody"

Dr Neal N. Iwakoshi, Emory University, Atlanta, USA

"Predictive Modeling of Outcomes in Lung Transplantation" Dr David Neujahr, Emory University, Atlanta, USA

"Characterization of Immune Cells Contributing to the Rejection of Transplanted Kidneys in Humans"

Dr Emmanuel Zorn, Massachusetts General Hospital, Boston, USA

4. ROTRF/JDRF Joint Initiative Grant Awards in Cycle XIX and XX

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

ROTRF/JDRF Conventional Research Grant Awards - Cycle XIX

"Prolonging Pancreatic Islet Cell Survival Following Transplantation" Dr Karen Dwyer, St. Vincent's Hospital, Melbourne, Australia

ROTRF/JDRF Conventional Research Grant Awards - Cycle XX

"New Immunological Avenues to Improve Allograft Survival"

Dr Jacques Thibodeau, University Montreal, Montreal, Canada

ROTRF/JDRF Clinical Research Grant Awards - Cycle XIX

"Optimisation of Human Pancreatic Islet Isolation" Mr Paul Johnson, University of Oxford, Oxford, UK



5. Addendum to Grant Awards in Cycle XVII and XVIII (ROTRF Annual Report 2007)*

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

ROTRF Conventional Research Grant Awards - Cycle XVIII

"Do Blood Platelets Affect Quality of Organs to be Transplanted from a Brain-dead Organ Donor?"

Dr Johannes Lisman, University Medical Centre Groningen, Groningen, The Netherlands

ROTRF/JDRF Conventional Research Grant Awards - Cycle XVIII

"Using Cells to Prevent the Rejection of Transplanted Organs"

Dr Megan K. Levings, University of British Columbia, Vancouver, Canada

^{*} These grant awards were pending at the time of publication of the ROTRF Annual Report 2007.



6. How Do I Apply for a ROTRF Grant?

Innovative and novel research proposal

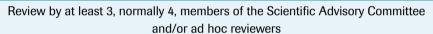








Submission of LETTER OF INTENT (LOI) at http://www.rotrf.org



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)



7. Board of Trustees (BT)

| Chairman: | | |
|---------------------------------|--|--|
| Professor Philip F. 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 | |
| D (All 10) | 2001011, 0071 | |
| Professor Allan Kirk | Scientific Director of the | |
| | Emory Transplant Center | |
| | Professor of Surgery | |
| | Emory University Atlanta, USA | |
| | Allanta, USA | |
| Professor Gerhard Opelz | Director, Department of | |
| | Transplantation Immunology | |
| | University of Heidelberg | |
| | Heidelberg, Germany | |
| Professor Giuseppe Remuzzi | Director, Department of Immunology and | |
| | Clinical Transplantation Ospedali Riuniti di Bergamo and Istituto di | |
| | | |
| | Ricerche Farmacologiche "Mario Negri" | |
| | Bergamo, Italy | |
| | | |



8. Scientific Advisory Committee (SAC)

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. Sophie Brouard

ITERT-INSERM U643 CHU Jean Monnet Nantes. France

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. 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

Questions? Please contact us.

E-mail: admin@rotrf.org
Tel.: +41 41 377 53 35
Fax: +41 41 377 53 34
Mail: ROTRF, P.O.Box 222

6045 Meggen, Switzerland