**This website is under construction, and information since 2008 is being updated.**

## BIOSKETCH: Prof. Randall E. Morris, M.D., F.R.C.P. (Glasgow)

Before Dr. Morris joined Novartis AG, he collaborated with over 20 pharmaceutical and biotechnology companies to discover and study new immunosuppressants for transplantation. Dr. Morris was the President of the International Congress on New Trends in Experimental and Clinical Immunosuppression. He served two terms as a Councilor of The Transplantation Society (third term ongoing). Dr. Morris has also presented the results of his research in over 400 lectures and has published over 400 articles, reviews, book chapters and published abstracts on immunosuppression, effects of immunosuppressants on immune cells in the blood of treated subjects (pharmacodynamics), chronic rejection, lung transplantation and xenografting. Awards include N.I.H. Medical Scientist Trainee, Stanford Medical Alumni Award, American College of Surgeons Schering Research Award, Karolinska Institute & Huddinge Hospital (Stockholm) Transplant Medal, Royal Society of Medicine (United Kingdom) Visiting Fellowship, Honorary Fellow of the Royal College of Physicians and Surgeons (Glasgow) as well as named Lectureships.

## Selected Laboratory and Clinical Research Projects:

**1989 - 2004**: Initiated experiments that led to the discoveries and the first publications that reported the efficacies of the IMPDH inhibitor, mycophenolate mofetil (RS-61443, CellCept®; Syntex/Roche) for prevention of acute and chronic transplant rejection in rodents and non-human primates (See Bibliography for selected citations). MMF became

the most prescribed immunosuppressant for acute rejection in solid organ and bone marrow transplant recipients.

**1989 - 2003**: Initiated experiments that led to the independent discoveries and the first publications that reported the efficacies of the mTOR inhibitor, sirolimus (rapamycin, Rapamune®; Wyeth) for prevention of acute and chronic transplant rejection (graft vascular disease) as well as treatment of ongoing chronic rejection in rodents and non-human primates (See Bibliography for selected citations). Rapamune was approved for use in kidney transplant recipients; its analog, everolimus (Certican®; Novartis), was approved for use to prevent chronic rejection (graft vascular disease) in heart transplant recipients.

**1993 - 1995**: Initiated experiments that led to the co-invention and the first publications to report the efficacy of sirolimus for prevention of restenosis after arterial balloon angioplasty. These studies were the foundation for the development and widespread use of sirolimus and other mTOR inhibitors in drug-eluting stents for patients after coronary artery balloon angioplasty (See Bibliography for selected citations).

**1992 - 2000:** Initiated experiments that led to the discoveries and the first publications to report the efficacies of monotherapy with mouse anti-LFA-1 monoclonal antibodies for prevention of acute transplant rejection and a humanized form of anti-LFA-1 monoclonal antibody (efalizumab, Raptiva®) for prevention of non-human primate heart transplant rejection, which was, at one time, approved for the treatment of psoriasis (See Bibliography for selected citations).

**1992 – 2000:** Research on the pyrimidine synthesis inhibitor, leflunomide, Arava®; Hoechst, Sanofi) and published the first

paper on suppression of transplant rejection by its analogue, MNA-715 (FK778). Leflunomide is approved for treatment of rheumatoid arthritis.

**2003 - 2004**: First to publish results showing the immunosuppressive efficacy of the Janus kinase 3 (JAK3) inhibitor, CP-690, 550 (tafocitinib, Xeljanz®; Pfizer), for prevention of acute transplant rejection. Tafocitinib completed Phase II trials in renal transplant recipients and was approved by the FDA for the treatment of rheumatoid arthritis. (See Bibliography for selected citations).

**2002 - 2005**: Oversaw the preclinical development and early clinical development of the novel protein kinase C inhibitor, sotrastaurin (NVP AEB071) that has completed Phase II trials in renal transplant recipients. (See Bibliography).

**1995 – Present**: Developed new methods to measure the effects of systemically administered immunosuppressive drugs on circulating immune cells in animals and humans (pharmacodynamics) (See Bibliography for selected citations).

## Professional Responsibilities, Training and Education:

**2010-Present:** Non-Exclusive consultant in the fields of transplantation, autoimmune diseases and medical devices.

**2009-2010:** Exclusive consultant to Novartis AG in the field of transplantation.

**2006-2008**: Head of Therapeutic Sciences for Transplantation and Immunology in the Infectious Diseases, Transplantation & Immunology Business Unit/Franchise, Novartis Pharma AG, Basel, Switzerland.

**2002-2006:** Global Head of Transplantation Research and Head of Translational Medicine for Transplantation (2004-2006), Novartis Institutes for BioMedical Research, Basel, Switzerland.

**2004-Present:** Emeritus Professor of Cardiothoracic Surgery and (by courtesy) Medicine and Surgery, Stanford University School of Medicine, Stanford, California.

**1983-2004:** Director of the Laboratory for Transplantation Immunology, and subsequently, Research Professor of Cardiothoracic Surgery and (by courtesy) Depts. of Surgery and Medicine Stanford University School of Medicine, Stanford, California.

**1977-1983:** General Surgical Residency Training (including transplant surgery) and Postdoctoral fellow in Immunology at the University of Wisconsin Health Sciences Center, Madison, Wisconsin.

**1976-1977:** Surgical Internship, Stanford University School of Medicine, Stanford, California.

**1969-1976:** M.D., Stanford University School of Medicine and Transplantation Immunology Trainee in the NIH Medical Scientist Training Program in the Department of Cardiothoracic Surgery.

**1966-1969:** A.B. (Honors in Molecular Biology), Stanford University.

**1963-1966:** Westminster School, London, United Kingdom.

## Bibliography (selected citations):

### Mycophenolate Mofetil (CellCept®; IMPDH inhibitor) Suppresses Acute and Chronic Transplant Rejection


1. Prolongation of Rat Heart Allograft Survival by RS-61443. **Morris RE**, Hoyt G, Eugui E, Allison A: Surgical Forum. 40: 337, 1989.

2. Mycophenolate Acid Morpholinoethyl Ester (RS-61443) is a New Immunosuppressant that Prevents and Halts Heart Allograft Rejection by Selective Inhibition of T and B Cell Purine Synthesis. **Morris RE**, Hoyt G, Murphy M, Eugui E, Allison A: Transplant. Proc. 22: 1659, 1990.

3. Immunosuppressive Effects of the Morpholinoethyl Ester of Mycophenolic acid (RS-61443) on Rat and Non-Human Primate Recipients of Cardiac Allografts. **Morris RE**, Wang J, Blum J, Flavin T, Almquist S, Chu N, Lam Y, Kaloostian M, Allison A, Eugui E: Transplant. Proc. 23 (Suppl 2): 19, 1991.

4. Treatment by Mycophenolate Mofetil of Advanced Graft Vascular Disease in Non-Human Primate Recipients of Orthotopic Aortic Allografts. Klupp J, Dambrin C, Hibi K, Luna J, Suzuki T, Hausen B, Birsan T, van Gelder T, Fitzgerald P, Berry G, **Morris RE**: Amer. J. Transplant. 3: 817, 2004.

**Sirolimus (Rapamycin, Rapamune®; mTOR inhibitor) Suppresses Acute and Chronic Transplant Rejection**


1. A New Pharmacologic Action for an Old Compound. **Morris RE**, Meiser B: Medical Science Research. 17: 609, 1989 (Republished with corrected type setting: Medical Science Research. 17: 877, 1989).

2. Rapamycin: A New and Highly Active Immunosuppressive Macrolide with Efficacy Superior to Cyclosporine. Meiser B, **Morris RE**: Progress in Immunology. 7: 1195, 1989**.**

3. A Study of the Contrasting Effects of Cyclosporine, FK506 and Rapamycin on the Suppression of Allograft Rejection. **Morris RE**, Wu J, Shorthouse R: Transplant. Proc. 22: 1638, 1990.

4. Use of Rapamycin for the Suppression of Alloimmune Reactions in Vivo: Schedule Dependence, Tolerance Induction, Synergy with Cyclosporine and FK506 and Effect on Host-versus-Graft and Graft-versus-Host Reactions. **Morris RE**, Meiser B, Wu J, Shorthouse R, Wang J: Transplant. Proc. 23: 851, 1991.

5. Sirolimus (Rapamycin) Halts and Reverses Progression of Allograft Vascular Disease in Non-Human Primates. Ikonen T, Gummert J, Hayse M, Honda Y, Hausen B, Christians U, Berry G, Yock P, **Morris RE**: Transplantation. 70: 969, 2000.

6. Sirolimus (Rapamycin) Monotherapy Prevents Graft Vascular Disease in Non-Human Primate Recipients of Orthotopic Aortic Allografts. Dambrin C, Klupp J, Birsan T, Luna J, Suzuki T, Stahr P Hausen B, Christians U, Fitzgerald P, Berry G, **Morris, RE**: Circulation. 107 (18): 2369, 2003.


**Sirolimus (Rapamycin, Rapamune®) Suppresses of Post Angioplasty**

**Restenosis**

1. Effects of Treatment with Cyclosporine, FK506, Rapamycin, Mycophenolic Acid and Deoxyspergualin on Vascular Smooth Muscle Proliferation in Vitro and in Vivo. Gregory C, Pratt R, Huie, P, Shorthouse R, Dzau V, Billingham M, **Morris RE**: Transplant. Proc. 25: 770, 1993.

2. Rapamycin Inhibits Arterial Intimal Thickening Caused by Both Alloimmune and Mechanical Injury: Effect on Cellular Growth Factor and Cytokine Responses in Injured Vessels. Gregory C, Huie P, Billingham ME, **Morris RE**: Transplantation (Rapid Communication). 55: 1409, 1993.

3. Treatment with Rapamycin and Mycophenolic Acid Reduces Arterial Intimal Thickening after Balloon Catheter Injury and Allows Endothelial Replacement. Gregory C, Huang X, Pratt R, Dzau, V, Billingham M, **Morris RE**: Transplantation (Rapid Communication). 59: 655, 1995.

**Anit-LFA-1 Monoclonal Antibody Suppresses Acute Transplant Rejection**

1. An Anti-Adhesion Molecule (LFA-1, CD11a) monoclonal antibody suppresses ongoing rejection and prolongs heart allograft survival indefinitely without lymphocyte depletion. Nakakura E, Jardieu P, Zheng B, **Morris RE**: J. Heart Lung Transplantation. 11: 223, 1992.

2. Prolongation of Heart Allograft Survival by Anti-LFA-1 Monoclonal Antibody Monotherapy: Mechanisms of Action of Antigen-Specific Unresponsiveness. Nakakura E, Shorthouse R, Zheng B, McCabe S, Jardieu P, **Morris RE**: Transplantation. 62: 547, 1996.

3. Effects of Humanized Monoclonal Antibody to Rhesus CD11a in Rhesus Monkey Cardiac Allograft Recipients. Postern R, Robbins R, Chan B,

Simms P, Presta L, Jardieu P, **Morris RE**: Transplantation. 69: 2005, 2000.

**CP-690, 550 (Janus Kinase 3 [JAK3] Inhibitor) Suppresses Acute Transplant Rejection**

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2. JAK3 Inhibition as a New Concept for Immune Suppression. Borie D, Ming-Sing S, **Morris RE**, Reitz B, Changelian P: Current Opinion in Investigational New Drugs. 4 (11): 1297, 2003.

3. Immunosuppression by the JAK3 Kinase Inhibitor CP-690, 550 Delays Rejection and Significantly Prolongs Kidney Allograft Survival in Nonhuman Primates. Borie D, Changelian P, Larson M, Si, M-S, Paniagua R, Higgins J, Holm B, Campbell A, Lau M, Zhang S, Flores M, Rousvoal G, Ball D, Hawkins J, Kudlascz E, Brissette W, Elliott E, Reitz B, **Morris, RE**: Transplantation. 79: 791, 2005.

**Sotrastaurin (NVP-AEB071; Protein Kinase C Inhibitor) Suppresses T-Cell Responses in Vitro and Suppresses Acute Transplant Rejection**

1. The First-In-Class Oral Protein Kinase C (PKC) Inhibitor, NVP-AEB071, Prolongs Renal Allograft Survival in Non-Human Primates (NHP) and Suppresses Lymphocyte Proliferation at Safe Exposures in Human Proof-of-Concept Studies. Wagner J, Evenou J-P, Zenke G, Brinkmann V, Pally C, Bigaud M, Burkhart C, Cottens S, Jung T, Rordorf C, **Morris, RE**: American J. Transplant. 6, Suppl 2: 86, Abstract 57, 2006.

2. NVP-AEB071 (AEB), A Novel Oral Inhibitor of Early T-Cell Activation, Prolongs the Survival of Non-Human Primate (NHP) Kidney Allografts When Used As Monotherapy or At Non-Effective Doses Combined With a Non-Effective Dose of Cyclosporine (CsA). Bigaud M, Wieczorek G, Reisen S, Menninger K, Barbet I, Jean, C, Beerli, C, Audet M, Blancher A, Heusser C, Wagner J, **Morris, RE**: American J. Transplant. 6, Suppl 2: 250, Abstract 546, 2006.

3. NVP-AEB071 (AEB), The Novel Oral Inhibitor of Early T-Cell Activation, Prolongs the Survival of Non-Human Primates (NHP) Kidney Allografts Survival When Combined with Everolimus (RAD), ERL080 (ERL) or FTY720 (FTY) Without Calcineurin Inhibitor. Bigaud M, Wieczorek G, Preussing E, Reisen S, Cordoba F, Audet M, Blancher A, Heusser C, Bruns C, Wagner J, **Morris, RE** : American J. Transplant. 6, Suppl 2: 251, Abstract 550, 2006.

4. NVP-AEB071 (AEB), A Novel Oral Inhibitor of Early T-Cell Activation, Prolongs Rat Cardiac Allograft Survival When Used Alone and In Combination With Cyclosporine, Everolimus, or FTY720. Bruns C, Pally C, Beerli C, Wieczorek G, Wagner J, **Morris RE**: American J. Transplant. 6, Suppl 2: 316, Abstract 741, 2006.

5. Pharmacodynamics (PD) of T-Cell Inhibition by the New Protein Kinase C (PKC) Inhibitor, NVP-AEB071 (AEB) in Non-Human Primates (NHP).

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8. Enzymatic & Cellular Characterization of NVP-AEB071 (AEB), A Novel & Selective Protein Kinase C (PKC) Inhibitor That Blocks Early T-Cell Activation, and Its Use to Define the Role of PKC in T Cells. Evenou J-P, Brinkmann V, Towbin H, Welzenbach K, Cottens S, Wagner J, **Morris R**, Zenke G: American J. Transplant. 6, Suppl 2: 1026, Abstract 2954, 2006.

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5. Pharmacodynamics of Mycophenolate Mofetil after Heart Transplantation: New Mechanisms of Action and Correlations with Histologic Severity of Rejection. Barten M. van Gelder T, Gummert J, Boeke K, Shorthouse R, Billingham M, **Morris RE** : Amer. J. Transplant. 2 (8): 719, 2002.

6. Sustained Suppression of Peripheral Blood Immune Functions by Treatment with Mycophenolate Mofetil Correlates with Reduced Severity of Cardiac Allograft Rejection. Klupp J, van Gelder T, Dambrin C, Regiel J, Boeke K, Billingham M, **Morris RE** : J. Heart and Lung Transplant. 23 (3): 334, 2004.

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2. New Immunosuppressive Drugs. **Morris RE**: In "Transplantation of the Liver" R Busuttil, G Klintmalm (Eds). WB Saunders. Pp 760-786, 1996.

3. Molecular Mechanisms of Action of New Xenobiotic Immunosuppressive Drugs: Tacrolimus (FK506), Sirolimus (Rapamycin), Mycophenolate Mofetil and Leflunomide. Brazelton T, **Morris RE**: Current Opinion in Immunol. 8: 710, 1996.

4. Leflunomide and Malononitrilamides. Silva H, **Morris RE**: Expert Opinion in Investigational Drugs. 6: 51, 1997.

5. Unapproved Nonbiologic Immunosuppressants. Klupp, J, **Morris RE**: In "Primer on Transplantation." D Norman, L Turka (Eds). American Soc. of Transplantation. Pp 165-172, 2001.