Molecular Medicine Ireland was established under the Higher Education Authority’s Programme for Research in Third Level Institutions.
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MMI Highlights 2010

Molecular Medicine Ireland Board

MMI welcomed the appointment of a new chair and two new directors to the Board during 2010. Thomas Lynch was appointed Chair in December and Professor Jonathan Hourihane, Professor of Paediatrics and Child Health at UCC and Professor Michael Keane, Professor of Medicine and Therapeutics at UCD, became Directors in November and December, respectively.

MMI Clinical & Translational Research Scholars Programme

In 2010, MMI was awarded funding under PRTLI Cycle 5 for the Clinical & Translational Research Scholars Programme (CTRSP), led by NUI Galway and with partners TCD, UCC and UCD. The CTRSP is a structured 4-year PhD programme, integrated with industry and clinical research centres, which will prepare graduates for careers in industry, academic medical centres and as biomedical entrepreneurs.

Dublin Centre for Clinical Research

In 2010, the DCCR with ICRIN facilitated the development of the Standard Application Form. This initiative involved the participation of research ethics committee administrators and other stakeholders including the Data Protection Commission, Irish Medicines Board, Council for Bioethics and the Clinical Indemnity Scheme to develop a research ethics application form for research studies and clinical trials not subject to SI 190/2004. Also during the year, the DCCR delivered on one of its objectives with the graduation of the first cohort of research nurses with a certificate in Research Nursing from the RCSI School of Nursing.
MMI Highlights 2010

MMI Guidelines for Standardised Biobanking

In 2010, the MMI Guidelines for Standardised Biobanking were published in the internationally peer-reviewed ISBER journal, Biopreservation and Biobanking (Volume 8, Number 1). The guidelines aim to ensure sample quality, consistency and integrity of bio-collections across different clinical and research centres in Ireland. MMI partner institutions have adopted the MMI Guidelines for Standardised Biobanking for all new bio collections and the European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) has also accepted them as a first version of the BBMRI laboratory manual.

MMI Clinician Scientist Structured PhD Curriculum

The Clinician Scientist Fellowship Programme structured training curriculum is the basis of a sustained resource, accessible via the MMI website, for all medical graduates undertaking PhD studies. Over sixty graduate education modules have been assembled from MMI partner institutions and aligned to curriculum topics. Participants can select modules of interest taking place in their own or other institutions and register to attend.

ICRIN Clinical Research Roadmap

The Clinical Research Roadmap was published in May and launched in the presence of Mary Harney TD, Minister for Health and Children, in the Royal College of Physicians, Dublin in June. The Roadmap is the product of extensive stakeholder consultation and highlights the strategic and operational changes needed to improve Ireland’s capacity to undertake high quality, multicentre clinical research. It is aligned to and complements the stated goals of both the Action Plan for Health Research, published by the Minister for Health and Children, and the HRB’s Strategic Business Plan.

MMI/ICRIN Courses and Workshops

MMI and its business unit ICRIN organised a number of very successful courses and workshops during 2010. These comprised the Irish Biomarker Network Inaugural Workshop (see page 29), the SFI/MMI Technology Platform Workshop (see page 32), the Research Governance and Sponsorship Seminar (see page 44), Health Technology Assessments, Procurement and Reimbursement Process for Medical Devices (see page 45), and the educational courses and workshops entitled Human Disease Genomics: SNPs, GWAS and Next-Gen Sequencing, Molecules to Medicines: How Biopharma Delivers, and Techniques & Strategies in Molecular Medicine (see pages 25 -27).
**Chairman’s Statement**

MMI’s mission is to enable clinical and translational research in Ireland by mobilising the strengths of the five partner institutions and their associated hospitals. Despite the unprecedented challenges facing the country, MMI made progress with its mission in 2010. We were particularly pleased that, faced with such pressing economic and fiscal problems, the Government’s commitment to funding for research remained firm. In July 2010, MMI was awarded funding of €4.3m under the Programme for Research in Third Level Institutions - Cycle 5 to coordinate a PhD programme in clinical and translational research. This structured PhD will equip at least 20 science graduates with the skills to translate their bench research into advances in diagnostics and therapies in the clinic and in industry. The PhD programme, with strong clinical and industry input, will train a cadre of researchers who understand the challenge of translating research ideas from the bench to the clinic and into the commercial sphere and who will advance the mission of MMI.

MMI was also pleased with the publication of the Report of the Innovation Taskforce, launched by An Taoiseach on 11 March, which aims to position Ireland as an innovation hub in Europe. From an MMI perspective, the Report endorses the need for strong alliances between third level institutions as part of creating the eco-system for innovation in the lifesciences. The Report highlights the opportunities for this country to capture innovation from convergent technologies in the pharma and biotech sectors and from our strengths in research on food and health and expertise in medical device technologies. It points out that ‘the development of a clinical trials research system is critical for the future growth and development of this sector in Ireland (both indigenous and MNCs) and to ensure that we leverage investments in research and development - translating from bench to bedside’ (Page 59) It recognises that the

**In response to our stakeholders’ needs for access to information about resources for clinical and translational research in Ireland, we launched a number of web portals on the MMI website.”**

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Damian O’Connell MD BSc PhD is Vice President of Clinical Research and Development, Pfizer. Damian has been a Medical Faculty member of The University of Virginia Health Sciences Center as well as of the Clinical Pharmacology & Therapeutics Department at University College Cork. He started his career in industry with Elan Pharmaceuticals as Director of Clinical Research (US) and was previously Executive Director and Clinical Research Group Head at Pfizer.
creation of such a system requires a cultural shift and commitment to research within the hospital environment, consistent with the objectives of the Action Plan for Health Research. The Report recommends a 'one stop shop' website with information on all aspects of research expertise and support for innovation and greater access by companies to specialised equipment in HEIs.

During 2010, MMI took a number of steps in harmony with the recommendations of the Innovation Taskforce. We launched the Clinical Research Roadmap in June 2010 in the presence of the Minister for Health and Children. The Roadmap, the product of much consultation and analysis among those involved in clinical research in this country, outlines what is needed if Ireland is to achieve its potential in clinical research, including the conduct of clinical trials. In June MMI set itself the objective of supporting scientifically relevant, industry sponsored multi-centre studies. To this end MMI established the Irish Clinical Research Infrastructure Network (ICRIN) Working Group; ICRIN being a business unit of MMI. Under the Chair of Professor Larry Egan, ICRIN Clinical Director, the group will build capacity to support scientifically relevant industry sponsored trials as well as investigator led, multi-centre studies. Working with Enterprise Ireland, we made progress in assisting SMEs and start-ups navigate the clinical and regulatory steps to bring their products to the market. We were also pleased to secure additional funding from the Health Research Board for the coordination and support activities of ICRIN until March 2012.

In response to our stakeholders’ needs for access to information about resources for clinical and translational research in Ireland, we launched a number of web-portals on the MMI website. The MMI Technology Platform Web-Portal was launched, providing easy access to information on over 70 technologies across the island of Ireland that are available for clinical and translational research by both academic and industry researchers. The MMI Bioreource Web-Library provides access to the internationally peer reviewed and published biobanking standards developed by MMI. These standards have been adopted by MMI partner institutions for all new bio-collections. Our hope is that these standards will provide the basis for a strategic, national approach to biobanking, driven by the research funders and underpinned by legislation. With the close involvement of principal investigators from our partner institutions, we also established the Irish Biomarker Network to facilitate researchers overcome the many hurdles in the way of translating biomarker research from the bench to the clinic and into clinical practice. We believe that all these initiatives are central to building the eco-system for innovation recommended by the Innovation Taskforce.

I would like to express my thanks to my fellow directors and my appreciation for their contribution to MMI. During the year Professor Peter Kennedy, Vice president for Research at UCC, Professor David Kerins, Dean of the School of Medicine at UCC, and Professor Des Fitzgerald, Vice-President for Research at UCD, stepped down as Directors of the Board. I would like to thank them for their commitment to MMI. It was my pleasure to welcome Dr Jonathan Hourihane, Professor of Paediatrics and Child Health at UCC, Dr John Climax, former CEO and Chair of ICON, and Dr Michael Keane, Professor of Medicine and Therapeutics at UCD, as directors and to wish them well on their appointment. Professor Hourihane also joins the Executive Management Team.

In December, I stepped down as chairman of MMI after four years as a director and two years as chair, to take up the position of Clinical Director of the UCC Clinical Research Centre. I would like to take this opportunity to wish my successor Tom Lynch every success as he leads MMI during its next period of development. I look forward to being involved in the mission of MMI in my new capacity.

May I also take the opportunity to thank John Coman, Secretary to the Board, for his support and advice to me as Chair and to Dr Ruth Barrington, CEO, and the staff of MMI for their expertise and commitment to working collaboratively to achieve MMI’s mission.

Damian O’Connell MD BSc PhD Chair of Molecular Medicine Ireland
Message from the CEO

The vision of Molecular Medicine Ireland's Strategy 2009-11 is improved healthcare through the development of diagnostics and therapies from concept to realisation. The mission of MMI is to mobilise the strengths of the five partner institutions and their associated hospitals to build a sustainable national system to coordinate, support and promote translational and clinical research to achieve its vision.

MMI's unique selling point continues to be its potential to mobilise the strengths of the partner institutions and associated hospitals, to build a national system for clinical and translational research. This national system is necessary to translate research into innovative diagnostics, therapies and devices and provide an ecosystem for innovation. In MMI we believe that the same system can serve the needs of academic investigators and industry as well as SMEs and start-ups that need access to clinical resources to bring their prototypes to market. MMI's greatest contribution to innovation is to integrate the capacity and expertise of the partner institutions and associated hospitals to complete this national system and make it accessible to all who need access to clinical resources to improve outcomes for patients and increase economic value for this country.

Given the scale of the problems facing the country, it was not surprising that the National Recovery Plan, 2011-14, published in November, confirmed expected significant reductions in public expenditure and increases in taxation. MMI welcomed the recognition in the Plan of the contribution of ‘productive, high quality research, undertaken by highly skilled research teams working closely with industry partners’ to national recovery and the indications that support for such research will continue to be a core investment priority for Government. MMI was also pleased to see the commitments in the Plan to deliver the long promised Health Information Bill to ‘speed up ethical review of health research trials and investigations’ and to investment in R&D industry/third level sector collaboration.

MMI was also pleased that the Health Research Group (HRG), co-chaired by the Departments of Health and Children and Enterprise, Trade and Innovation made progress with the implementation of the Action Plan for Health Research. MMI actively contributed to the HRG group charged with developing a national

"In 2008, MMI and Enterprise Ireland agreed to work together to speed up the time required for SMEs and start-ups to bring their prototypes to market”

Ruth Barrington took up her appointment as CEO of the DMMC/MMI in October 2007. She was previously CEO of the Health Research Board, a position she held from 1998 to 2007. She is a graduate of University College Dublin, the College of Europe in Bruges, Belgium and was awarded her doctorate by the University of London.
strategy for biobanking, with Dr Jan Guerin providing scientific advice to the group based on her contribution to the design phase of GeneLibrary Ireland and the compilation of MMI’s internationally peer-reviewed, biobanking standards.

Building capacity for clinical and translational research is a key activity of MMI. Based on the experience of the PRTLI Cycle 4 funded Clinician Scientist Fellowship Programme, the MMI partners agreed a structured curriculum for the training of clinical scientists into the future. The curriculum is founded on courses developed in each institution and can be accessed by medical graduates undertaking PhDs in clinical and translational research in any of the partner institutions. The MMI website provides all the information the PhD student needs in order to access the most appropriate course for his or her needs. MMI continued to organise its popular courses and workshops in molecular and translational medicine, with 265 attendances recorded at the 5 courses and workshops held during the year. Demand for training in good clinical practice continued to grow and MMI and ICRIN responded by organising courses during the year attended by over 350 participants. It was particularly exciting that the MMI Clinical and Translational Research Scholars Programme was awarded funding under the PRTLI Cycle 5. The award endorses MMI’s assessment of the need to train scientists in the clinical and commercial application of their research. It also recognises MMI’s unique experience of delivering collaborative PhD programmes.

The Clinical Research Roadmap launched by MMI in June 2010 as a contribution by the academic community to the work of the HRG, identified the underdeveloped nature of research governance and the reluctance of academic institutions and hospitals to act as sponsors of clinical trials as factors that are constraining the development of investigator led clinical trials in Ireland. MMI organised a seminar on 16 September to draw attention to the need for more developed systems of research governance in academic hospitals, including the capacity to sponsor investigator led clinical trials. Participants at the seminar heard how the emergence of the academic medical centre in both Ireland and the UK is enhancing research governance and providing a solution to the challenge of sponsorship of investigator led clinical trials. The proceedings of the seminar are available on MMI’s website at http://www.molecularmedicineireland.ie/show/item/1/1565. MMI hopes that these proceedings will inform the work being undertaken by the HRG on research governance for the health system as a whole. The Dublin Centre for Clinical Research (DCCR), an ambitious project funded by the Health Research Board and the Wellcome Trust to create a network for multi-centre clinical studies in Dublin and to construct a new clinical research facility in St James’s Hospital, got into its stride in 2010. MMI plays a critical role in the coordination of the DCCR, providing programme and financial management and hosting governance arrangements. A new contract was agreed with the HRB and a number of changes were made in the organisation to reflect the new agreement.

In 2008, MMI and Enterprise Ireland agreed to work together to speed up the time required for SMEs and start-ups to bring their prototypes to market. Since joining MMI in 2009 as Clinical Trials Liaison Officer, Fionnuala Gibbons has been advising companies, start ups and research groups on how to navigate the regulatory and clinical requirements for successful translation of products to the market. In 2010 the value of the position of the CTLO to the innovation agenda was confirmed by the number of indigenous companies and start ups that were connected to clinical providers and/or advised on regulatory and technology assessment requirements, thus helping them on their way to market.

It was with regret that at the end of 2010 I accepted the resignation of Dr Jan Guerin as Programme Manager for Translational Research. I would like to acknowledge the outstanding contribution made by Jan to the work of MMI. On her appointment in 2008, she quickly identified those deficits in the eco-system for translational research which could be addressed by collaborative initiatives and she worked assiduously with the MMI research community to build that collaboration. The design phase of GeneLibrary Ireland, the MMI Guidelines for Standardised Biobanking, the MMI Technology Platform Web-Portal and the Irish Biomarker Network are her legacy to MMI. I know I speak for all in MMI when I wish her every success in her new post of Assistant Head of the School of Biological Sciences at the Dublin Institute of Technology.

May I also acknowledge the contribution of Dr Damian O’Connell, the outgoing Chairman, to the development of MMI and thank him for his leadership of the company over the past two years. On a personal note, I would like to thank him for his wise advice and continuous encouragement to me and my staff. May I also thank the directors who stepped down this year – Professor Peter Kennedy, Professor David Kerins and Professor Des Fitzgerald for their support and commitment to MMI.

Ruth Barrington PhD
Chief Executive
Molecular Medicine Ireland (MMI) is a collaborative biomedical research partnership between National University of Ireland Galway (NUI Galway), Trinity College Dublin (TCD), University College Cork (UCC), University College Dublin (UCD) and The Royal College of Surgeons in Ireland (RCSI). MMI, established in 2008, replaced the Dublin Molecular Medicine Centre.

MMI was established in response to the need to create in Ireland a critical mass of excellence in molecular medicine research and education and to deploy a clinical research infrastructure to facilitate the transfer of advances in molecular medicine into new and more effective diagnostics, therapies and devices for patients. MMI is committed to supporting translational and clinical research, best described as research from ‘bench to bedside’ - ‘bench’ experiments being driven by clinical questions and findings at the ‘bench’ being put into practice through better diagnosis and treatment at ‘the bedside’ of the patient.

MMI is a joint venture company controlled by NUI Galway, TCD, UCC, UCD and RCSI and established with funding from the Higher Education Authority’s Programme for Research in Third Level Institutions, Cycle 4. Formally incorporated in 2008, MMI is a company limited by guarantee and has been registered without the world ‘Limited’ in its name. It is a registered charity founded for the promotion of molecular medicine research. MMI is governed by a Board of Directors (see page 12 – this page no may change) supported by an Executive Management Team (EMT: see page 10) The EMT comprises the CEO of MMI and five directors who are leaders in medical research in the partner institutions.

At the end of 2010, the business of MMI was supported by a staff of 11 people, of whom 6.5 were funded from sources other than by the partner institutions. MMI also received the welcome assistance of a FAS graduate work placement programme participant from February to October and an overseas student of statistics who supported the organisation for 12 weeks from April to June.

MMI has been successful in attracting funding from the Health Research Board, the Health Service Executive and the European Union to develop clinical research capacity in Ireland. The organisational structure of MMI is shown in the diagram below and the names of the members of staff are listed on page 45. Staff work closely with senior investigators in the partner institutions and associated hospitals to put MMI programmes into effect, including the Clinician Scientist Fellowship Programme, MMI’s suite of courses and workshops, the deployment of the Dublin Centre for Clinical Research, the preparatory phase of ICRIN and MMI’s support for biobanking, biomarker development and technology platforms.
VISION

In December 2008, MMI adopted a strategy to guide its direction and activities to the end of 2011. The strategic vision of MMI is improved healthcare through the development of diagnostics and therapies from concept to realisation.

The strategic mission of MMI is to mobilise the strengths of the five partner institutions and their associated hospitals to build a sustainable national system to coordinate, support and promote translational and clinical research.

MMI achieves this mission by:

- connecting the key players in health, research and industry
- attracting, training and retaining world-class researchers
- working to provide state-of-the-art facilities, bio-resources and harmonised processes
- representing Ireland in clinical and translational research infrastructures/networks in Europe and internationally, and building collaborative research initiatives and opportunities.

MMI’s unique selling point is its potential to mobilise the strengths of the partner institutions and their associated hospitals to build a national system for clinical and translational research. This national system is necessary to translate research into innovative diagnostics, therapies and devices that will improve the health of the population, contribute to economic development and create employment. A national system for clinical and translational research is a virtuous circle for innovation. The same system can serve the needs of academic researchers, industry-led research and those SMEs and start-ups that need access to clinical resources to bring their prototypes to market. MMI’s greatest contribution to innovation over the next few years will be to integrate the capacity and expertise of the partner institutions and associated hospitals to complete this national system and make it accessible to all who need access to clinical resources.

A focus on building a national system for clinical research maps well with the Health Research Action Plan’s deliverable of ‘fully functional and networked clinical research facilities in our main academic teaching hospitals, with a focus on accelerating research advances into benefits for patients and the population’.

OUTPUTS

The output of MMI’s activities are:

- the deployment of a sustainable system for clinical and translational research to support trans-disease, multi-site studies nationally and as part of the European Clinical Research Infrastructures Network (ECRIN)
- the creation of an internationally recognised community in molecular medicine and clinical research
- the creation of skilled translational and clinical researchers, both medical graduates and scientists
- the creation of high quality and standardised biological collections for patient and disease-focused research linked with the European Biobanking and Biomolecular Resources Infrastructure (BBMRI)
- the generation of new intellectual property to fuel Ireland’s biotechnology, biomedical device and pharmaceutical industry
- new diagnostics, devices and therapeutics and more effective patient intervention strategies.
The Executive Management Team (EMT) guides the scientific and operational strategy of MMI. The EMT comprises five MMI Board Directors, one each from NUI Galway, RCSI, TCD, UCC and UCD and the Chief Executive Officer of MMI.

**Professor Larry Egan**

Professor of Clinical Pharmacology, Head of the Department of Pharmacology and Therapeutics at NUI Galway and Consultant Clinical Pharmacologist with the HSE Western Region

Larry Egan took up his appointment with NUI Galway and the HSE in 2005 after having gained specialist experience in the USA in the areas of gastroenterology, internal medicine and clinical pharmacology and gastroenterology at the Mayo Clinic in Minnesota (1994-1999) and in the Laboratory of Mucosal Immunology at the University of California in San Diego. Currently, his research focuses on molecular characterization of signalling pathways involved in intestinal epithelial cell stress, death and malignant transformation. Larry is the ICRIN Clinical Director.

**Professor Jonathan Hourihane**

Professor of Paediatrics and Child Health and Head of the Department of Paediatrics, University College Cork.

Jonathan Hourihane specialised in allergy, immunology and infectious diseases at the Institute of Child Health and Great Ormond Street Hospital. His primary area of clinical and research interest is in paediatric food allergy and anaphylaxis with ongoing projects in areas which include the clinical and proteomic characterisation of emerging food allergy syndromes, and exploration of the link between skin barrier dysfunction and systemic allergic disorders. Jonathan is co-investigator in the groundbreaking BASELINE birth cohort study.

**Professor Dermot Kelleher**

Vice-Provost for Medical Affairs, Head of the School of Medicine & Director of the Institute of Molecular Medicine, Trinity College Dublin & St James’s Hospital

Dermot Kelleher was appointed Wellcome Senior Fellow in Clinical Science in 1989 at Trinity College Dublin and subsequently Professor of Clinical Medicine in 2001. With specialist training in Gastroenterology, Professor Kelleher’s widely published research has focused on the cell biology both of immune responses and of the inflammation-cancer sequence. He co-founded MMI’s predecessor, the Dublin Molecular Medicine Centre, in 2003 and obtained funding from the Wellcome Trust and Health Research Board to establish the Dublin Centre for Clinical Research.
Professor Gerry McElvaney
Professor of Medicine, Chairman of the Department of Medicine, Royal College of Surgeons in Ireland and Director of the Respiratory Research Unit, Beaumont Hospital

Gerry McElvaney has a strong track record in translational research both in Ireland and the USA in the areas of Cystic Fibrosis, emphysema and lung inflammation with an emphasis on protease/anti protease interactions, signal transduction in bronchial epithelium, innate defences of the lung and gene therapy for lung diseases. He co-founded the Respiratory Research Unit in Beaumont Hospital in 1997 and the Alpha One Foundation of Ireland in 2003, both of which have attracted significant national and international funding and have resulted in a large number of publications as well as interactions with pharmaceutical companies interested in translational research.

Professor Bill Powderly
Head of School of Medicine & Medical Science and Professor of Medicine & Therapeutics at University College Dublin and the Mater Misericordiae University Hospital and Chief Academic Officer of Dublin Academic Health Care

Bill Powderly has been actively involved in HIV-related research in both Ireland and the USA and is widely published in this area. His recent research focuses on the emerging toxicities of treatment of HIV, especially the metabolic complications seen in patients receiving effective therapy, including the development of diabetes, lipid abnormalities and bone disease. Professor Powderly is a Fellow of the Infectious Diseases Society of America, the Royal College of Physicians of Ireland and the American Association for the Advancement of Science.

Dr Ruth Barrington
Chief Executive of Molecular Medicine Ireland

Dr Ruth Barrington was appointed Chief Executive to the DMMC (now MMI) in October 2007. She was awarded a PhD from the London School of Economics and an honorary degree in laws by NUI Maynooth, and she is the author of Health, Medicine and Politics in Ireland, 1900-1970 and other publications on health, research policy and EU affairs. She was Chief Executive of the Health Research Board from 1998 to 2007. She is on the board of IPPOSI (Irish Platform for Patients’ Organisations, Science and Industry), the Conway Institute (UCD) and CRANN (TCD) and she is Chair of the Irish Times Trust.
MMI Board of Directors

CHAIR

Thomas Lynch

DIRECTORS

Dr Willard Dere
Senior Vice-President and International Chief Medical Officer of Amgen

Dr David Lloyd
Head of the Molecular Design Group, School of Biochemistry & Immunology and Dean of Research, Trinity College Dublin

Professor Larry Egan
Chair of Clinical Pharmacology and Head of the Department of Pharmacology and Therapeutics, NUI Galway

Prof Gerry McElvaney
Professor of Medicine, Royal College of Surgeons in Ireland

Professor Jonathan Hourihane
Professor of Paediatrics and Child Health and Head of Department of Paediatrics, University College Cork

Prof Tim O' Brien
Professor of Medicine and Director of the Regenerative Medicine Institute, NUI Galway

Dr Hannah McGee
Dean of Faculty of Medical and Health Sciences and Professor of Psychology, Royal College of Surgeons in Ireland

Dr Helen Ryan
Chief Executive, Creganna

Prof Dermot Kelleher
Professor of Clinical Medicine and Head of the School of Medicine, Trinity College Dublin and Director of the Institute of Molecular Medicine, Trinity College Dublin and St James’s Hospital

Prof Bill Powderly
Head of the School of Medicine & Medical Science at UCD and Professor of Medicine & Therapeutics at UCD and the Mater Misericordiae University Hospital

Professor Michael Keane
Professor of Medicine and Therapeutics, University College Dublin, and Consultant Respiratory Physician at St Vincent’s University Hospital

Mr David Shanahan
Global Head of Life Science, IDA

Dr Marina Zvartau-Hind
Director, Neurosciences Medicines Development Centre and Clinical Leader of Alzheimer Disease Projects, GlaxoSmithKline

Mr John Coman
Corporate & Legal Affairs Secretary, University College Dublin
MMI Board Appointments

**Thomas Lynch - Chairman**

Tom Lynch was appointed Chair of Molecular Medicine Ireland in December 2010. He currently serves on the Board of Icon plc, a major clinical research organisation, as well as on a number of public and private biotechnology firms and pro-bono boards in healthcare, the arts and academia.

Mr Lynch is a graduate in economics from Queen’s University Belfast and qualified as a Chartered Accountant with KPMG in 1983, becoming a partner in 1990. He entered the pharmaceutical industry three years later, initially as Chief Finance Officer with Elan Corporation plc. Mr Lynch continued at Elan working in a variety of capacities until 2004 when he acquired the company’s stake in Amarin Corporation plc.

Mr Lynch served on the Board of Amarin from 2000, first as Elan’s nominee and from 2004 as principal shareholder. He was subsequently appointed CEO and successfully turned the company around by repositioning it into cardiovascular disease and establishing a clinical development operation in Connecticut, USA. He stepped down as CEO in October 2009 after gaining approval from the Food and Drugs Administration to embark on Phase 3 clinical trials and he resigned as Chair in January 2010.

**Professor Michael Keane**

Professor Keane was appointed to the MMI Board of Directors in December 2010. He is Professor of Medicine and Therapeutics and Consultant Respiratory Physician at St Vincent’s University Hospital. He is also a member of the management team of the Dublin Centre for Clinical Research.

After initial training following his graduation in medicine from University College Dublin in 1989, Professor Keane completed a fellowship in pulmonary and critical care medicine at the University of Michigan, USA. He remained on the faculty at the University of Michigan until 2000 when he moved to University College Los Angeles where he was Director of the Medical Intensive Care Unit, the Interstitial Lung Disease Clinic and the Pulmonary and Critical Care Fellowship Training Programme. He returned to Dublin in 2007 to take up the positions he currently holds.

Professor Keane’s clinical interests include all aspects of interstitial lung disease, and he has published widely on this subject, while his research interests include the mechanisms of pulmonary fibrosis and acute lung injury. He has an active research laboratory at the Conway Institute in UCD which is funded by Science Foundation Ireland.

**Professor Jonathan Hourihane**

Professor Jonathan Hourihane joined the Board of Directors in November 2010. He is Professor of Paediatrics and Child Health at University College Cork. His primary area of clinical and research interest is in paediatric food allergy and anaphylaxis, with ongoing projects in clinical and proteomic characterisation of emerging food allergy syndromes, exploration of the link between skin barrier dysfunction and systemic allergic disorders, threshold doses of food allergens, immune-modulation of established allergic responses, prevention of allergic sensitisation including use of pre-and probiotic-enhanced infant formulae, and evaluation of quality of life in food allergic children.

Professor Hourihane is a co-investigator in the BASELINE study which is the first birth cohort study to be undertaken in Ireland in which babies are followed from birth and studied to determine why some go on to develop disease, whilst others remain healthy. He is an Associate Editor of *Clinical and Experimental Allergy and Paediatric Allergy and Immunology*. 
NUI Galway, Regenerative Medicine Institute

The Regenerative Medicine Institute (REMEDII) was established at NUI Galway in 2004 as a Science Foundation Ireland funded Centre for Science, Engineering and Technology with a central focus on the development of novel therapies for treating major human diseases involving adult stem cell therapy and gene therapy.

It has developed a translational research effort with an emphasis on the delivery of therapeutic products to patients and is an integral part of the National Centre for Biomedical Engineering Science. It consists of a large multidisciplinary team of scientists, clinicians, engineers, technicians and veterinarians lead by Professor Tim O’Brien (Director) and Professor Frank Barry.

REMEDII has significant interest in addressing diseases of the vasculature and to this end, is currently looking at stents as a platform from which to deliver a therapeutic product to blood vessels. www.nuig.ie/remedi/

RCSI Research Institute

The RCSI Research Institute is a multi-site infrastructure encompassing the research activities of RCSI at the St Stephen’s Green campus and the RCSI Education and Research Centre (ERC) at Beaumont Hospital. This comprises a network of research centres and core facilities in peptide synthesis and labeling, solid phase chemistry, proteomics, clinical research and biobanking, molecular, live cellular and human imaging.

Through this infrastructure of laboratories, core technology platforms and staff, the RCSI Research Institute aims to facilitate and develop sustainable research programmes in translational research in the areas of Neuroscience, Cancer Cell Biology and Genetics, Vascular Biology, Imaging and Molecular Medicine, Population Health, Bio-Engineering, Infection and Immunity.

The Clinical Research Centre (CRC) at Beaumont Hospital, which combines dedicated research beds and laboratories equipped for cell and molecular biology, enables an integrated bench-to-bedside approach to biomedical research. www.rcsi.ie/research

TCD Institute of Molecular Medicine

The Institute of Molecular Medicine (IMM) was established in 2003 as a state-of-the-art facility housed in a 4,500 sq metre building within the Trinity Centre for Health Sciences at St James’s Hospital. IMM is primarily designed as a molecular research facility. To date, IMM has been successful in bringing key research groups into a single location promoting interdisciplinary and complementary synergies.

IMM is a facility dedicated to research into the molecular basis of human disease with significant core technology platforms in: High Content Screening Analysis in association with the siRNA Library, Cell Signalling, High Throughput Genomics, Transcriptomics and houses the Irish Gene Bank. IMM's key research themes are: Infection & Immunity, Cancer and Neurosciences. IMM offers structured postgraduate education programmes in Molecular Medicine at Diploma, MSc,
and PhD level, the latter a prestigious Health Research Board funded 4-year PhD scheme.

IMM’s location on the St. James’s Hospital site permits close interaction between basic and clinical sciences promoting the bench to bedside approach in molecular medicine. IMM has strategically targeted the aggregation of research teams within the institute, and as a result, an excellent pool of academic researchers, clinician scientists, technologists and teaching resources has been assembled and aligned around a molecular level approach to medicine. Currently, IMM houses approximately 180 residents in 16 research teams. [www.tcd.ie/IMM](http://www.tcd.ie/IMM)

UCD Conway Institute of Biomolecular & Biomedical Research

The UCD Conway Institute of Biomolecular & Biomedical Research is located on the Belfield campus of University College Dublin, the largest university in Ireland. This multidisciplinary centre for research brings together over 550 research staff from all over the University and its associated teaching hospitals.

The research focus of UCD Conway Institute is the identification of molecular mechanisms underlying human and animal diseases primarily in the areas of Infection, Immunity & Repair; Diabetes & Vascular Biology and Neuroscience. The close collaboration of scientists and clinicians underpins the translational nature of this research from the ‘bench to bedside’ which is supported by world-class proteomic, bioinformatic and transcriptomic core facilities.

The longer term objectives of the Institute are set on the integration of the biological sciences with those sciences not traditionally associated with biology with a view to realising the synergistic benefits of such associations. These include computer science, applied mathematics, systems biology, engineering and economics. [www.ucd.ie/conway](http://www.ucd.ie/conway)

UCC BioSciences Institute

Basic and translational research at UCC has been greatly enhanced by the opening, in 2002, of the Biosciences Institute (BSI). The BSI provides research space for active investigators in the biomedical area and fosters, through its design and governance, a collaborative and interdisciplinary approach to research questions.

The Institute incorporates six major research programmes, including Neuroscience, Cancer Biology, Cell Signalling and Cardiovascular Health, Plant Biotechnology and Integrative Genomics, Food for Health and Microbe Host Interaction. The BSI houses over 250 scientists from eight different departments, as well as three research centres (APC, CCRC and BIOMERIT). Technology platforms at the BSI include functional genomics, proteomics, bioinformatics, advanced microscopy, cell imaging and transgenics. In addition, BSI is also home to a number of state-of-the-art core facilities such as the Advanced Microscopy Unit, MALDI-TOF (mass spectrometry) and Flow Cytometry. The major unifying theme of the BSI is the improvement of quality of life for patients, while the underlying strategy that ties all research groups together is teamwork. Adjacent to the BSI, and directly linked to it, the School of Pharmacy incorporates a designated industry suite to allow transfer of new pharmaceuticals to industry. [www.bsi.ucc.ie](http://www.bsi.ucc.ie)
HRB Clinical Research Facility, Galway

The HRB Clinical Research Facility, Galway (CRFG) is a joint venture funded by the Health Research Board between Galway University Hospitals (GUH) and National University of Ireland, Galway (NUIG) and opened in temporary accommodation in March 2008. The CRFG provides the infrastructure, physical space, facilities, expertise and culture needed to optimally support patient-focused research studies and clinical studies aimed at understanding a range of diseases and translating the knowledge obtained through this research work into reimbursed, regulatory approved advances in patient care as speedily as possible.

The Department of Health has provided the Health Research Board with €7.5 million to fund the construction of a new building which is expected to commence in July 2011. This will provide Galway with world class facilities for researchers and industry and will enhance research development capacity in the medical device and pharmaceutical sectors. The CRFG will be built along with translational research laboratories which will provide facilities for processing and analysis of biospecimens.

HRB Discovery Centre, Cork

The HRB Discovery Centre is a paediatric clinical research facility based in Cork University Campus which opened in November. The HRB will provide funding of €58,000 to the new paediatric CRF which will conduct clinical assessments on more than 2000 babies and children over the next six years. One of the research programmes being conducted at the new facility is BASELINE. As Ireland’s first study to observe children from before birth up to two years of age, it will examine the development of allergies, metabolic problems, diabetes and neurodevelopmental problems. The facility will also be the Irish central point for the development of an international study called NEMO, which aims to understand the effects of hypotension on the foetus.

The HRB Discovery Centre is part of a much bigger HRB clinical research facility and research programme currently being developed by UCC, Cork University Hospital and Mercy University Hospital and both centres will be part of a national research network supported by the HRB. The CRF which is undergoing development and due to open in September 2011 will facilitate and promote high quality clinical research of an international standard.

UCD Clinical Research Centre

The UCD Clinical Research Centre is an academic-led integrated clinical research infrastructure located at the Mater Misericordiae University Hospital and St. Vincent’s University Hospital and which supports activity at several other Dublin hospitals. Purpose-built clinical investigation and laboratory support facilities were established in April 2006 at Mater and in 2007 at St Vincent’s with recurrent funding from PRTLI Cycle 3.

Since opening in April 2006, there have been over 18,000 research patient visits in core areas of clinical trials, population studies and mechanisms of disease based research. As well as providing the infrastructure for development of improved healthcare practice, the UCD CRC is also enhancing access to health services and new medicines. In addition to underpinning research, there is a substantial benefit to both the patient and the hospitals from rapid and early access to modern healthcare.
The UCD CRC has enabled Dublin Academic Medical Centre (DAMC) investigators to leverage over €12M in research funding comprising industry-funded clinical trial activity and competitive peer-reviewed research funding from charitable and public funding agencies. The UCD CRC is an active participant in the MMI coordinated Dublin Centre for Clinical Research.

**RCSI Clinical Research Centre**

2010 marked the 10-year anniversary of the opening of the RCSI Clinical Research Centre. In that time the CRC has grown significantly and now has a core staff of 15 research nurses in addition to administrative, medical and IT personnel. In the last decade, more than 13,000 patients have participated in clinical trials. Research activities at the centre span the research spectrum from patient registries, biobanking projects, and observational studies to device trials and clinical trials of medicinal products.

RCSI nursing personnel play significant operational roles in the DCCR and ICRIN working groups, as well as contributing to the ongoing development of the Irish Research Nurses Network. In partnership with the DCCR they are engaged in a number of collaborative disease group studies in the areas of respiratory, gastrointestinal, neurology and endocrinology, and have contributed to the development of research protocols.

The RCSI CRC also has a leading role in the provision of educational courses and support for the professional development of clinical research nurses. The first ever Postgraduate Certificate in Nursing (Clinical Research), provided through the RCSI Faculty of Nursing and Midwifery, is in its second year.

**Centre for Advanced Medical Imaging**

The Centre for Advanced Medical Imaging (CAMI) at St James’s Hospital (TCD) was funded by the Health Research Board and opened in the Autumn of 2008. CAMI, which is a national centre open to researchers from other institutions, focuses on three research themes:

1. Cardiovascular imaging techniques that allow visualisation of the vascular tree and assessment of heart function and the viability of heart tissue.
2. Brain MRI imaging techniques that help understand and assess conditions such as stroke, epilepsy, depression and multiple sclerosis.
3. Whole body screening of patients with cancer through new methods that identify abnormal water diffusion in tumours. Prostate and breast imaging in particular have potential to benefit from MRI developments.

CAMI is located close to where the planned Wellcome Trust and HRB Clinical Research Centre and TCD’s Institute of Cardiovascular Science will be built.
Haplotype block: structure in the human genome

Recombination mostly takes place at late replication forks. Inter-chromosomal regions in these regions are called haplogene blocks.

The genome is composed of discrete haplotype blocks separated by recombination hot spots.
MMI Structured PhD Training Programmes

The *Molecular Medicine Ireland* partner institutions collaborate to train key groups in clinical and translational research through structured PhD programmes.

The MMI Clinician Scientist Fellowship Programme (CSFP), funded under the Programme for Research in Third Level Institutions (PRTLI) Cycle 4, is training clinician scientists through a 3-year structured PhD programme. In 2010, the first cohort of 22 medical graduates continued their PhD research in five academic institutions and participated in national structured training and the second Annual Scientific Meeting.

In 2010, MMI was awarded funding under PRTLI Cycle 5 for the Clinical & Translational Research Scholars Programme (CTRSP), led by NUI Galway and with partners TCD, UCC and UCD. The CTRSP is a structured 4-year PhD programme, integrated with industry and clinical research centres, which will prepare graduates for careers in industry, academic medical centres and as biomedical entrepreneurs.

MMI Structured PhD Curriculum

The Clinician Scientist Fellowship Programme structured training curriculum is the basis of a sustained resource, accessible via the MMI website, for all medical graduates undertaking PhD studies. Over sixty graduate education modules have been assembled from MMI partner institutions and aligned to curriculum topics. Participants can select modules of interest taking place in their own or other institutions and register to attend.

MMI Courses and Workshops Supporting Clinical and Translational Research

The widely-available MMI Courses & Workshops continue as a mainstreamed resource initiated through PRTLI Cycle 3 funding. Delivered by faculty from multiple institutions (including international keynote lecturers and industry staff), these short courses and practical workshops provide continuing professional development opportunities for all researchers.

In 2010, MMI offered Human Disease Genomics: SNPs, GWAS and Next-Gen Sequencing, a lecture course and practical workshop; Molecules to Medicines: How Biopharma Delivers, the fifth run of this collaboration with Pfizer (lecture course and problem-based workshop); and the eighth run of Techniques & Strategies in Molecular Medicine.

The MMI Structured Training Topics web resource provides an easily-navigated overview of all areas covered by MMI Courses and structured training since 2003:

http://www.molecularmedicineireland.ie/training_topics
Clinician Scientist Fellowship Programme (CSFP)

Since 2008, 22 medical graduates are undertaking PhD studies in five academic institutions as MMI Clinician Scientist Fellows. The CSFP is a structured PhD programme funded under PRTLI Cycle 4 which is training this key group of clinician scientists who will graduate with unique and specialised knowledge essential to fulfil Ireland’s research needs in translational medicine.

Fellows are carrying out research in areas including cancer, cystic fibrosis, autism, diabetes, heart disease, and disorders of pregnancy. Co-supervision by basic and clinician scientists creates a collaborative translational research training environment. See page 33 for a list of the MMI Clinician Scientist Fellows’ research projects, and for selected research highlights from 2010.

MMI Fellows come together for shared national structured training and present their research at Annual Scientific Meetings. In 2010, the structured training period and the second Annual Scientific Meeting took place in University College Cork.

CSFP Annual Scientific Meeting 2010

The second Annual Scientific Meeting of the CSFP took place on Friday 25 June 2010 at University College Cork. 19 MMI Fellows gave short presentations on their research. The 2010 MMI medal for best presentation was awarded to Dr Mark Coyne (NUI Galway). Second prize was awarded to Dr Damian McCartan (RCSI) and third prize was awarded jointly to Dr James Ryan (UCC) and Dr David Prichard (TCD).

Professor David H. Dockrell (Wellcome Senior Clinical Fellow, University of Sheffield) delivered the keynote lecture: ‘Macrophage cell death is tightly coupled with the performance of microbicidal function during innate immune responses’. Professor Dockrell also adjudicated the award of prizes for the best presentations.

For more information on the MMI Clinician Scientist Fellowship Programme, please visit: www.molecularmedicineireland.ie/csfp
MMI Clinician Scientist Fellows presented their research at the second Annual Scientific Meeting, held on 25 June 2010 in UCC

Top: MMI Fellows at the Annual Scientific Meeting with the organisers. Above: (Left to right): MMI medal for best presentation - Dr James Ryan speaking at the Annual Meeting - Professor David Dockrell presents second prize to Dr Damian McCartan.
CSFP Structured Training

The CSFP Annual Scientific Meeting was preceded by a 4 days of Structured Training (21-24 June 2010). The MMI Fellows were brought together for education modules covering innovation; commercialisation and career management and leadership in academic medicine (see Table below).

### Areas covered during the 2010 period of CSFP Structured Training

<table>
<thead>
<tr>
<th>Area</th>
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<tbody>
<tr>
<td>Funding Opportunities (including presentations from the Wellcome Trust and the Health Research Board)</td>
</tr>
<tr>
<td>Leadership, Stress Regulation &amp; Life Skills</td>
</tr>
<tr>
<td>Commercialisation of Research</td>
</tr>
<tr>
<td>Communicating your Research Message</td>
</tr>
<tr>
<td>Writing up your PhD</td>
</tr>
<tr>
<td>Research Creativity</td>
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<tr>
<td>Career Development</td>
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In July 2010, Molecular Medicine Ireland was awarded €4.3m funding for a collaborative structured PhD programme under Cycle 5 of the Government’s Programme for Research in Third-Level Institutions (PRTLI). The proposal was led by NUI Galway with partners Trinity College Dublin, University College Cork and University College Dublin. The MMI Clinical & Translational Research Scholars Programme (CTRSP) will begin in 2011.

The CTRSP will equip graduates with the knowledge, skills and know-how to discover and develop disease-focused research ideas directly linked to improved health. Scholars will come together to participate in a national structured curriculum developed with the engagement of the innovation and enterprise community; organisations working with MMI include Amgen, Creganna-Tactx Medical, Merrion Pharmaceuticals, Medtronic, Opsona, Pfizer and the Irish Medicines Board.

Research projects in this structured PhD programme will focus on:

- Drug discovery
- Discovery/validation of biomarkers
- Patient-oriented research in clinical research facilities

Twenty scholarships are available in the first year of this prestigious national programme.

In 2010 work commenced on the implementation of the programme and recruitment of students. Applications will be invited in 2011, followed by a rigorous selection process.

The CTRSP is being developed by a Steering Committee with representation from each of the partner institutions, from industry and from the Irish Medicines Board. Over 80 principal investigators from the four academic partners are involved in the programme.
The MMI Clinician Scientist Structured PhD Curriculum was launched on 17 November 2010, with access via a secure web portal.

In the pilot phase, the portal is offered as a resource that gathers together information on graduate education modules of particular relevance to clinician scientist trainees, available to all medical graduates undertaking PhD studies in clinical and translational research in the medical schools of the MMI partner institutions. It will be used as a resource to identify structured training that graduate students may wish to pursue in consultation with their research supervisors, and as part of existing institutional requirements with respect to graduate education module attendance and credits.

Professor Bill Powderly (Head of the UCD School of Medicine & Medical Science, Chief Academic Officer of Dublin Academic Medical Centre and Director of MMI) commented that the "MMI Clinician Scientist Structured PhD Curriculum is an exciting new resource that demonstrates the importance the MMI partners attach to the training of clinician scientists in Ireland. It is to be hoped that mainstreaming this key element of the PRTLI Cycle 4 funded MMI Clinician Scientist Fellowship Programme will lead to further strategic investment in clinician scientist training so that the gains of recent years are maintained".

In total there are currently 69 graduate education modules available through the portal, provided by all the MMI partner institutions to address the topics of the clinician scientist curriculum.
The cross-institutional MMI Courses & Workshops build on the research and teaching strengths of the partner institutions and the clinical expertise in the affiliated teaching hospitals to deliver continuing professional development opportunities for researchers.

The MMI Courses & Workshops began in 2003 as a Dublin Molecular Medicine Centre (DMMC) activity funded through PRTLI Cycle 3.

MMI Courses (lecture-based and practical courses) are designed specifically for a cross-institutional audience of postgraduate students and research staff (see attendances breakdown below).

Courses & Workshops Faculty

Since 2003, 256 individuals have assembled as faculty on over 60 DMMC/MMI courses and on structured training for the MMI Clinician Scientist Fellowship Programme. There were 27 faculty members in 2010.

Courses & Workshops Attendances

198 individuals from our partner institutions (NUI Galway, RCSI, TCD, UCC and UCD) and further afield attended three MMI Courses & Workshops in 2010 (see table below) with a total of 265 attendances (some individuals attended more than one course). See below for Institutional breakdown and Position Breakdown since 2003).

<table>
<thead>
<tr>
<th>Course/Workshop Title</th>
<th>Dates</th>
<th>Venue</th>
<th>Attendees (1 or more sessions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Disease Genomics: SNPs, GWAS and Next-Gen Sequencing (Course &amp; Workshop in collaboration with Ensembl Project)</td>
<td>22-23 June 2010</td>
<td>TCD Institute of Molecular Medicine</td>
<td>89</td>
</tr>
<tr>
<td>Molecules to Medicines: How Biopharma Delivers (Course &amp; Workshop in collaboration with Pfizer)</td>
<td>10-11 Nov 2010</td>
<td>Royal College of Surgeons in Ireland and MMI Directorate Offices</td>
<td>61</td>
</tr>
<tr>
<td>Techniques &amp; Strategies in Molecular Medicine*</td>
<td>1-2 Dec 2010</td>
<td>UCD Conway Institute</td>
<td>74</td>
</tr>
</tbody>
</table>

* Due to adverse weather conditions, only session 1 of this course took place on the morning of the 1st December 2010. The remaining sessions have been rescheduled for 2011.

Attendances breakdown for 2010 (Total=265): Institutional Affiliation

Attendances breakdown since 2003 (Total=3207): Position
Photos: Top (inset) - Dr Bert Overduin (Ensembl) and Human Disease Genomics workshop attendees. Above (Main Pic) - Dr Jonny Finlay (Pfizer) lecturing during the MMI/Pfizer Molecules to Medicines – How Biopharma Delivers course.
2010 Course Highlight

The MMI course ‘Human Disease Genomics: SNPs, GWAS and Next-Gen Sequencing’ took place in the Institute of Molecular Medicine, Trinity Centre for Health Sciences, St James’s Hospital, on 22-23 June 2010.

This course introduced researchers to key strategic considerations in designing and performing gene-mapping studies.

89 attendees from MMI partner institutions and further afield attended Day 1 of the course comprising lectures from a total of 9 speakers. Prof David Goldstein (Duke Institute for Genome Sciences & Policy, USA) delivered the keynote lecture on ‘Rare and Common Variants in Human Disease’.

A practical workshop took place on Day 2 (Wed 23 June), delivered by Dr Bert Overduin (European Bioinformatics Institute, Wellcome Trust Genome Campus). The workshop complemented the day 1 lecture material by focusing on the analysis of genetic variation with guided hands-on experience in the use of the Ensembl genome browser. The Ensembl project (http://www.ensembl.org) provides a comprehensive and integrated source of annotation of genome sequences.

Courses & Workshops Sponsorship

The commercial sector also participated in 2010 as sponsors of MMI education activities. This assistance is essential in order to provide the best experience for course attendees, including refreshment breaks providing opportunities for further discussion, and prestigious international keynote lectures. Our commercial partners interact with researchers based in the various MMI courses venues as well as course participants from multiple institutions.

2010 Course Sponsors

- Pfizer
- Roche
- Illumina
- Affymetrix
- Agilent Technologies
- Genologics
Throughout 2010, MMI worked towards the realisation of its vision for biobanking which is “the creation of an all-island, standardised and carefully phenotyped repository of biological specimens and associated clinical data, accessible to academic and industry researchers and to start-up and spin-out companies to underpin biomedical research and to fuel innovation and commercialisation”.

**MMI Guidelines for Standardised Biobanking**

An important milestone was the publication of the internationally peer-reviewed [MMI Guidelines for Standardised Biobanking](http://liebertonline.com/toc/bio/8/1) which appeared in Volume 8 Number 1 2010 of the ISBER journal [Biopreservation and Biobanking](http://www.liebertpub.com). To download this publication go to: liebertonline.com/toc/bio/8/1

Professor H-Erich Wichmann, Director and Chair of Epidemiology at the Institute of Epidemiology at Helmholtz Zentrum München and Chair of the European Biobanking and Biomolecular Resources Research Infrastructure’s (BBMRI) Work Package on Disease Oriented Biobanks, provided the guest editorial for the publication of the Guidelines in which he stated that 'Molecular Medicine Ireland has made an important step in developing SOPs which will be instrumental in standardising biobanking in Europe and in BBMRI’. He added that BBMRI was happy to accept them as a first version of the BBMRI laboratory manual.

MMI believes that the adoption of these Guidelines, for all new bio-collections would be a first step towards harmonising biological collections across different research centres and a contribution towards a more strategic approach to biobanking nationally.

The Guidelines, which were proposed by Dr Peter Doran, PI of the Design Phase of GeneLibrary Ireland, were compiled by Dr Jan Guerin, Programme Manager for Research at MMI with the assistance of Dr Peter Doran, Dr David Murray and Mary McGrath of UCD CRC, and Dr Joe McPartlin of Trinity Biobank. They can be accessed via the MMI Bioresource Web Library at [http://www.molecularmedicineireland.ie/page/g/s/5](http://www.molecularmedicineireland.ie/page/g/s/5).

**MMI Bioresource Web-Library**

MMI developed the Bioresource Web-Library to share standardised procedures for the collection, processing and storage of biospecimens with all those who are engaged in biobanking. It also serves to promote access to the [MMI Guidelines for Standardised Biobanking](http://liebertonline.com/toc/bio/8/1) and provides a central web-based portal to bring together standardised procedures in biobanking. Section One of the web-portal contains an electronic version of all the internationally peer reviewed standardised procedures published in the [MMI Guidelines for Standardised Biobanking](http://liebertonline.com/toc/bio/8/1) while Section Two contains electronic versions of individual standardised procedures specific for tissue biobanking which have been donated by those engaged in biobanking in Ireland.
Irish Biomarker Network

MMI established the Irish Biomarker Network at the request and with the close involvement of Professor Dolores Cahill of UCD; Professor Louise Kenny of UCC; Professor Mark Lawler of TCD, Dr Nicola Miller of NUIG and Professor Alice Stanton of RCSI, all of whom are principal investigators in MMI’s partner institutions. The objective of this network is to facilitate researchers to overcome the hurdles associated with translating biomarker research from the bench to the clinic and into clinical practice. MMI believes that this initiative is central to building the eco-system for innovation recommended by the Innovation Taskforce.

IBN Inaugural Workshop

MMI hosted the Irish Biomarker Inaugural Workshop on 4 November 2010 in Croke Park Conference Centre in Dublin. Considered a great success, the workshop brought together over 100 academics, clinicians and industry representatives united in their interest in biomarkers. The workshop aimed to address some of the key hurdles involved in translating biomarkers to the clinic, in particular, the European and FDA regulatory requirements, and to explore the value and key objectives of an Irish biomarker network.

MMI welcomed the attendance of guest chair, Don Black, Director of MHICC/Trialynx Inc and the International Partnership for Critical Markers of Disease, and keynote speaker, Dr Francis Kalush, Network Leader for the Diagnostics and Personalised Medicine Network of the Food and Drug Administration both of whom travelled from the US for the event.

The first session of the workshop featured presentations from Dr Francis Kalush and Dr Sarah O’Meara, IMB, who respectively gave overviews of the FDA and European regulatory requirements for biomarker validation and translation to the clinic. The session was followed by a number of interesting case study presentations from Professor Louise Kenny, Cork University Maternity Hospital and UCC; Professor Professor Joe Duffy, St Vincent’s University Hospital and UCD; Dr Thomas Barry, NUIG; Dr Isabella Bray, RCSI; and Professor Paul Harkin, Queen's University Hospital and Almac Diagnostics who shared their experiences in biomarker discovery, development and translation.

Professor Dermot Kelleher of TCD closed the workshop following an invigorating and constructive discussion on the value, focus and the key objectives of an Irish biomarker network which reaffirmed the need for such a network. It was agreed that the Irish Biomarker Network should be inclusive of all academics with an interest in biomarkers on the island of Ireland and should involve a relationship with industry, the regulatory authorities, patient organisations and ethicists.

To view the proceedings of the workshop, please go to: http://www.molecularmedicineireland.ie/page/g/t/44
Research highlights across MMI partner institutions

PCRC celebrate five years of research and collaboration
Professor Bill Watson (UCD)

The research achievements of the Prostate Cancer Research Consortium were celebrated at an event hosted by the Irish Cancer Society in May 2010. The event featured the launch of a report prepared by the PCRC highlighting the consortium’s research activities and achievements in the area of prostate cancer over the five year period since it was formed in 2004.

Some of the achievements of the PCRC include the establishment of a prostate cancer biobank, the first biobank in Ireland to be approved and licensed by the Data Protection Commissioners, the publication of over 30 articles in international peer-review journals and the development and fostering of key international collaborations with prostate cancer groups in Europe, Australia, Canada and the USA. In addition, researchers in the consortium have received 19 awards and have made a number of significant discoveries. The PCRC has also been involved in the training of 33 young dedicated prostate cancer researchers and doctors.

The PCRC was established with funding from the Irish Cancer Society and with support from the Dublin Molecular Medicine Centre, now Molecular Medicine Ireland. It comprises a co-ordinated group of researchers and clinicians from universities and hospitals in Dublin whose aim is to improve the diagnosis and treatment of prostate cancer. The consortium has also attracted funding from Science Foundation Ireland, the British Urological Foundation and the Health Research Board.

REMEDI collaborate in major European osteoarthritis project
Dr Mary Murphy (NUIG) and Dr Thomas Ritter (NUIG)

Researchers at REMEDI became involved in an EU-funded collaborative project in September 2010 known as GAMBA which is short for ‘Gene Activated Matrices for Bone and Cartilage Regeneration in Arthritis’. GAMBA which is coordinated by the University Hospital Rechts de Iser at the Munich Technical University in Germany with additional partners in France, Italy, the Netherlands and Switzerland, aims to use regenerative medicine therapies to find new treatments for osteoarthritis. REMEDI has received €382,000 in funding over three years from the project’s total budget of €3.2 million.

Dr Mary Murphy of the orthobiologics group leads the GAMBA project at REMEDI and works with the gene therapy group led by Dr Thomas Ritter to develop methods for immune-modulation in the osteoarthritic joint to prevent progression of osteoarthritis and pain. REMEDI aims to develop greater awareness and debate on the societal and ethical issues relating to osteoarthritis that affect patients and the public alike.
CERVIVA - Irish Cervical Screening Research Consortium
Dr Cara Martin (TCD) and Prof John J. O’Leary (TCD)

CERVIVA was originally established in 2005 and has since been conducting research in the area of cervical screening in Irish women. The consortium is funded by the HRB, Irish Cancer Society, Friends of the Coombe and the EU Seventh Framework Programme. In 2010, CERVIVA conducted new research on HPV population and genotype prevalence’s in the Irish cervical screening population, which is geographically representative of the entire country. It estimated an overall high risk HPV prevalence rate of 19.2% (n=3193, median age 39.1, age range 17-89), in the Irish screening population, with HPV 16 being the most prevalent HPV genotype detected. Other dominant genotypes included; HPV 31, HPV 52, HPV 18, HPV 51 and HPV 39/HPV 66.

In low grade cervical abnormalities presenting at colposcopy, CERVIVA discovered a HR HPV DNA prevalence rate of 62% compared with a 38% HPV E6/E7 mRNA prevalence rate. In this cohort an association between smoking and HPV mRNA status was found whereby HPV mRNA was detected in 35% of non-smokers (cotinine <50ng/ml) compared with 43% of smokers (cotinine >50ng/ml).

Together with partners at the NCRI, CERVIVA conducted a large–scale, nationwide population survey (n=>3,300) on women’s knowledge and views of cervical screening, HPV infection, HPV testing and vaccination. A psychosocial study aimed at quantifying levels of anxiety, depression and worries among women at 4, 8 and 12 months following colposcopy has just commenced with over 400 women recruited to date. Following a GP survey conducted by the consortium in 2007, a clinical trial called ATHENS commenced which aims to develop resources to support GPs and practice nurses in Ireland in the area of cervical screening, HPV infection, HPV vaccination and HPV testing. The consortium have leveraged additional funding from the EU FP7 (PASCA and AUTOCAST) and others to the value of €10 million.

Psychosis Research Group
Professor Aiden Corvin (TCD)

Understanding the molecular basis of the psychotic disorders (e.g. schizophrenia and bipolar disorder) is a critical step in improving diagnostics and developing novel therapeutics. The Psychosis Research Group encompasses gene discovery, bioinformatics and biostatistics, patient studies (e.g. using clinical, neuroimaging and electrophysiology studies), and investigation of gene function. 2010 was a year of progress for the research group on each of these fronts. Collaborating with international colleagues, a novel risk gene for schizophrenia was identified. Locally, evidence for involvement of molecular pathways related to cell adhesion and synaptic trafficking in psychosis aetiology was discovered and new research methods, e.g., to facilitate high-throughput DNA sequencing were developed.

In addition, the effects of risk genes in patients and healthy participants on cognitive performance and brain structure were reported. These help to unravel how risk genes differ in the effects they have on illness. Finally, an examination of the functional impact of key risk genes using cellular and animal systems has been initiated which will provide a deeper level of understanding of the molecular mechanisms involved in psychosis and how this affects the normal function of neurons and neural systems. The group which is funded by Science Foundation Ireland, the Health Research Board, the National Institute for Mental Health (US) and the Wellcome Trust published 23 peer-reviewed papers in 2010 in leading journals including Nature and Archives of General Psychiatry.
MMI in association with Science Foundation Ireland organised a Technology Platform Workshop in June at the Institute for Molecular Medicine in St James Hospital to showcase and highlight how these technologies:

- Operate as national and/or all-island facilities
- Contribute to Ireland’s innovation and commercialisation agenda
- Facilitate partnerships with industry.

The workshop was well attended with representation from many institutions in both Ireland and Northern Ireland. Dr Stephen Simpson of SFI and Dr Jan Guerin of MMI jointly opened the workshop, highlighting their shared interest in developing a better understanding of the contribution of technology platforms to research outcomes. Dr Guerin launched the MMI Technology Platform Web-Portal which has been developed with the input of the research community to promote and showcase the breadth of technology platforms and associated expertise that support clinical and translational research in Ireland. The web-portal which can be viewed at www.molecularmedicineireland.ie/tp_web_portal currently profiles over 60 technology platforms available for biomedical research including technologies for proteomics, genomics/transcriptomics, medical and pre-clinical imaging, mass spectrometry, flow cytometry, data management and IT.

Dr Eucharia Meehan of the HEA, whose Programme for Research in Third Level Education funded the establishment of many technology platforms throughout Ireland, chaired the first session which focused on how technology platforms operate as national and/or all-island facilities. Mr Martin Shanagher from the Department of Enterprise, Trade and Innovation, chaired a session which discussed how technology platforms are addressing the innovation and commercialisation agenda. Mr Shanagher led this session by highlighting the Government’s recognition that investment in science and research is central to Ireland’s economic recovery. Dr Brian Kelly of Celtic Catalysts and a member of the Innovation Task Force chaired a further session that highlighted how technology platforms facilitate partnerships with industry.

The keynote speaker was Dr. Christian Boulin, Head of Core Facilities at the European Molecular Biology Laboratory (EMBL), who provided a comprehensive overview of the state-of-art facilities available through EMBL to Irish researchers and who encouraged more Irish researchers to avail of EMBL’s technologies and expertise. The final session, chaired by Dr Ruth Barrington, provided a lively discussion around the use and sustainability of technology platforms. The panel members for this session were Sean Mulvany (EI), Stephen Simpson (SFI), Enda Connelly (HRB), Christian Boulin (EMBL), John Boland (CRANN) and Bert Rima (QUB) who shared their views openly on this important topic.

The presentations for all three sessions included researchers from a number of universities in Ireland who clearly demonstrated how technology platforms are actively contributing to Ireland’s research and innovation agenda and forging strong partnerships with industry. These presentations also highlighted the availability of these state-of-the-art technologies, many organised as national facilities, to researchers throughout Ireland.

In addition to the broad range of oral presentations, there were a number of posters showcasing the contribution of their technology platforms to these thematic areas. MMI and SFI prepared proceedings of the workshop with a view to promoting a more strategic approach to sustain the substantial investment in infrastructure and expertise of the past ten years. The proceedings are available at the following link: http://www.molecularmedicineireland.ie/page/g/t/40
The Clinician Scientist Fellowship Programme, funded under PRTLI Cycle 4 and coordinated by MMI, is training 22 medical graduates through a structured three-year PhD programme. The table below lists the MMI Clinician Scientist Fellows and their research projects. The research highlights of five MMI Clinician Scientist Fellows presented here provide a snapshot of the progress made by Fellows in 2010. See page 20 of this report and www.molecularmedicineireland.ie/csfp for more information.

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<tr>
<th>Host institution</th>
<th>Fellow</th>
<th>Title of project</th>
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<td>NUI Galway</td>
<td>Dr Aoife Lowery*</td>
<td>Analysis of micro-RNA expression and function in breast cancer</td>
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<td></td>
<td>Dr Aonghus O’Loughlin</td>
<td>Novel Cell-Based Approaches in the Treatment of Diabetic Foot Ulcers</td>
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<td>Dr Gerard Curley</td>
<td>Investigation of the role of inhibition of NF-kB activity in mediating effects of hypercapnic acidosis in Ventilation induced Lung Injury</td>
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<td>Dr Mark Coyne</td>
<td>Devising new Therapeutic Strategies for Multiple Myeloma: Cell Cycle Dysregulation</td>
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<td>Dr Ruth Morrell</td>
<td>The Potential Therapeutic role of BH3 mimetics in overcoming Bcl2 resistance in Haematological Malignancies</td>
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<td></td>
<td>Dr Nuala Healy</td>
<td>Investigation of microRNA expression patterns as novel biomarkers for breast cancer</td>
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<td>RCSI</td>
<td>Dr Damian McCartan</td>
<td>The developmental protein HOXc11 mediates endocrine resistance in breast cancer</td>
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<td>Dr Finian O’Brien</td>
<td>The Neurobiology of Psychogenic Non-Epileptic Seizures</td>
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<td>Dr Mazen Al-alawi</td>
<td>Modulation of ion transport and human airway epithelial physiology by two classes of anti-inflammatory molecules, lipoxins and glucocorticoids</td>
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<td></td>
<td>Dr Sanjay Chotirmall</td>
<td>Investigating the role of estrogen in cystic fibrosis</td>
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<td>TCD</td>
<td>Dr David Prichard</td>
<td>Ursodeoxycholic Acid – a Molecular Modulator of the Inflammation-Cancer Sequence in the Oesophagus?</td>
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<td></td>
<td>Dr Fionnuala Ní Áinle</td>
<td>Generation and Characterisation of Activated Protein C variants with Altered Functional Properties and Enhanced Therapeutic potential</td>
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<td></td>
<td>Dr Jane McGrath</td>
<td>Brain structure, function and connectivity in autism</td>
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<td></td>
<td>Dr Niall Conlon</td>
<td>The association of variations in the immune response with the development of idiopathic bronchiectasis</td>
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<tr>
<td>UCC</td>
<td>Dr James Ryan</td>
<td>Cellular mechanisms of insulin resistance due to the r482w mutation of the lmna gene in familial partial lipodystrophy, dunnigan variety (fpld)</td>
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<td>Dr John O’Sullivan</td>
<td>Paracrine mediators of progenitor cell function and myocardial repair post ischaemia</td>
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<td>Dr Fergus McCarthy</td>
<td>The role of PPAR-γ in the pathogenesis of pre-eclampsia</td>
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<td>Dr Daniel Schmidt</td>
<td>Do the dynamics of quasispecies complexity and IP-10 concentration in chronic hepatitis C provide an opportunity to individualise treatment strategies?</td>
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<td>Dr Brian Walsh</td>
<td>The investigation and validation of predictive biomarkers in hypoxic-ischaemic encephalopathy</td>
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<td>UCD</td>
<td>Dr Aidan Ryan</td>
<td>An investigation of the therapeutic potential of lipoxins and lipoxin analogues in diabetic nephropathy</td>
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<td>Dr Eoin Feeney</td>
<td>Human and in vitro studies examining the early effects of antiretroviral drugs on mitochondrial DNA and genes regulating lipid metabolism</td>
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<td>Dr Patrick Collier</td>
<td>The role of Endothelial to Mesenchymal Transition in Cardiac Fibrosis</td>
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*Dr Lowery was awarded a PhD in June 2010.*

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Dr Aoife Lowery (NUI Galway)

**Supervisors:** Professor Michael J Kerin / Dr Nicola Miller

**Title:** Analysis of micro-RNA expression and function in breast cancer

Breast cancer is a heterogenous disease, representing a number of distinct phenotypes. The discovery that mi(cro)RNAs regulate the expression of multiple target genes and are frequently dysregulated in breast cancer has placed them at the forefront of molecular research into the origins of tumourigenesis. High-throughput techniques such as microarray profiling are used to identify differentially expressed microRNAs that may provide insight into the mechanisms of breast cancer initiation and progression.

This study was undertaken to characterise miRNA expression in breast tumours, to examine relationships between miRNAs and clinicopathological parameters and to investigate the functional role of specific aberrantly expressed miRNAs in breast cancer.

Data from this study indicates that microarray technology and artificial neural network (ANN) analysis reliably identify biologically relevant miRNAs associated with specific breast cancer phenotypes. The association of specific miRNAs with ER, PR and HER2/neu status indicates a role for these miRNAs in disease classification of breast cancer and their detection in the circulation of breast cancer patients implicates potential as novel minimally invasive breast cancer biomarkers. Furthermore, the functional analysis of miR-342 and miR-183 reveals that not only are these miRNAs disregulated, but they also have potential tumour suppressor roles in breast cancer and represent attractive targets for therapeutic intervention.
Dr Damian McCartan (RCSI)

**Supervisor:** Dr. Leonie Young / Prof. Arnold Hill  
**Title:** Identifying Novel Transcriptional Targets for SRC-1 in Breast Cancer

SRC-1 is a nuclear receptor co-activator protein that has been implicated as a mediator of breast cancer metastasis. The aim of this work was to adopt an unbiased approach to identify new SRC-1 transcriptional targets. A combined approach using ChIP-sequencing and whole genome expression arrays in luminal B breast cancer cells was employed to perform this genome wide search for direct SRC-1 targets. SRC-1 peaks within the genome were focused near transcription starts sites, often in close proximity to an estrogen response element in keeping with the traditionally described role as an ER coactivator.

The most novel target selected for further validation is a transmembrane disintegrin protein that has been shown to mediate cell migration, confirmed in this work, but has yet to be implicated in tumourigenesis. Expression of the disintegrin was identified in 49% of patients with breast cancer and its expression was associated with an almost two fold increase in rate of disease relapse at 5 years follow up.

An unbiased, genome wide approach has identified a variety of novel, direct SRC-1 target genes including a clinically important disintegrin that may offer the first therapeutic target to disrupt the central role of SRC-1 in mediating breast cancer metastasis.

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Dr Niall Conlon (TCD)

**Supervisors:** Dr. John Jackson / Dr. Mary Therese Keogan / Prof. Con Feighery  
**Title:** The association of variations in the immune response with the development of idiopathic bronchiectasis

Bronchiectasis is a chronic suppurative lung disease that results in significant mortality and morbidity. While bronchiectasis represents the pathological endpoint of many disease processes the cause in the majority of cases is not clear. We examined a cohort of 101 Irish patients with High Resolution CT scan proven bronchiectasis for polymorphic variations of CD32A and compared with 115 healthy controls. CD32A H131 (HH) is the only human immunoglobulin receptor that binds IgG2 efficiently, while the R131 (RR) variant exhibits reduced binding.

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Figure 3 - A significant excess of the R131 (RR) variant was identified in patients with bronchiectasis (p<0.01, OR 2.46 (1.32-4.57)). Significantly fewer patients were heterozygote for CD32A (HR) (p=0.05, OR 0.51 (0.31-0.93))

Figure 4 - A significantly lower proportion of neutrophils bearing the R131 (RR) CD32A receptor phagocytose beads when compared to heterozygote (HR) (p<0.002) or H131 (HH) genotypes (p<0.001)
A significant excess of CD32A R131 was identified in the bronchiectasis cohort (p<0.01, OR 2.46 (1.32-4.57)). Review of patient clinical data indicated that the R131 polymorphism was associated with bilateral disease (p<0.05), more frequent infective exacerbations (p<0.05) and increased hospitalisation due to infection (p<0.001). Flow cytometric phagocytic analysis indicated R131 homozygote bearing control neutrophils phagocytosed significantly less serotype 14 beads (p<0.002) and serotype 14 bacteria (p<0.001) than other polymorphic variants. R131 neutrophils also generated less oxidative burst (p<0.01) and elastase (p<0.05).

This study demonstrates an association between CD32A R131 and the presence and severity of bronchiectasis in an Irish cohort. In addition we provide compelling functional evidence that CD32A polymorphisms affect neutrophil phagocyte function. We suggest that CD32A R131 may predispose to bronchiectasis due to impaired phagocyte clearance of infecting organisms. This predisposition to infection may foster more severe disease. We plan to further develop evidence for this argument by examining monocyte phagocytosis in a whole blood assay.

Dr Fergus McCarthy (UCC)

**Supervisors:** Dr Louise Kenny / Dr Sarah Walsh

**Title:** Peroxisome proliferator activated receptor gamma critically regulates the risk of pre-eclampsia

Pre-eclampsia is a major cause of maternal and perinatal mortality and morbidity world-wide causing approximately 15% of all direct maternal deaths and mediating a five-fold increase in perinatal mortality. Peroxisome proliferator activated receptors (PPARs) are ligand activated transcription factors, expressed in placental tissue, that regulate the expression of a number of genes involved in cell differentiation and proliferation.

We have shown that PPAR-γ critically regulates the risk of pre-eclampsia. Healthy pregnant rats treated with the PPAR-γ antagonist, T0070907, developed key features of pre-eclampsia including hypertension, endothelial dysfunction, proteinuria, reduced pup weight, increased platelet aggregation and an imbalance of angiogenic factors. To further investigate the role of PPAR-γ in
pregnancy and its potential as a therapeutic target we demonstrated that administration of the PPAR-γ agonist, rosiglitazone, to pregnant rats with surgically induced pre-eclampsia ameliorated hypertension, vascular dysfunction and abnormally elevated microalbumin creatinine ratios, effects that were abrogated in the presence of a heme-oxygenase 1 (HO-1) inhibitor.

Our studies indicate that pre-eclampsia may be critically regulated by PPAR-γ via a HO-1 pathway and the present findings have important implications regarding the underlying etiology of pre-eclampsia and potential therapeutic interventions.

Dr Eoin Feeney (UCD)
**Supervisor:** Dr Patrick Mallon / Dr Peter Doran
**Title:** Human and in vitro studies examining the early effects of antiretroviral drugs on mitochondrial DNA and genes regulating lipid metabolism

Mitochondrial toxicity (MtT) is a common side effect of highly active anti-retroviral therapy (HAART) for HIV infection. We are examining the risk factors and mechanisms of MtT with HAART.

Lactic acidosis (LA) and symptomatic hyperlactatemia (SHL) are life-threatening complications of severe MtT. Through a multicenter international collaboration with samples from the INITIO trial we are examining clinical and molecular risk factors for LA and SHL. In particular we are examining whether mitochondrial changes in peripheral blood mononuclear cells (PBMCs) predict MtT in other tissues. This is the largest randomized study to date of LA and SHL.

HIV lipodystrophy (HIVLD) occurs due to MtT in adipose tissue in individuals on HAART. We are investigating how different components of HAART alter adipose tissue function, with tissue samples from 3 international trials. We are examining changes in mitochondrial DNA and gene expression, and the expression of genes involved in adipose tissue differentiation, inflammation and glucose and lipid metabolism. We are correlating molecular data with clinical and histologic findings from subjects enrolled in these trials. We are validating these findings through adipose cell cultures established from samples obtained from elective abdominal surgery in the Mater Misericordiae University Hospital.

This research will allow a better understanding of mitochondrial and adipose tissue physiology, as well as the mechanisms of toxicity of HAART.
Dublin Centre for Clinical Research (DCCR)

In June 2006 a DMMC bid involving TCD, RCSI, UCD and the DMMC (forerunner of MMI) and led by Professor Dermot Kelleher secured investment from the Wellcome Trust and the Health Research Board for the Dublin Centre for Clinical Research (DCCR).

The aim of the DCCR is to provide the infrastructure, that is, the physical space, facilities and trained staff, needed to support collaborative clinical research studies across Dublin. The investment is of the order of €23m with the Wellcome Trust funding the building and equipping of a clinical research centre at St. James’s Hospital. The HRB funding is supporting the initial running costs of the St. James’s facility and the DCCR clinical research network which is a clinical research collaboration between TCD, UCD, RCSI, MMI and the associated Dublin area teaching hospitals.

A review was concluded in 2010 of the contractual arrangements between the HRB and the DCCR partners. This featured the development of a multi-year work plan establishing the distinct work packages to be delivered by the DCCR Programme over the period to 2014. It specifically delineates those work activities associated with establishing a clinical research centre at St. James’s Hospital and the activities of establishing a city-wide clinical research network in Dublin.
The Wellcome Trust - HRB Clinical Research Centre at St. James’s Hospital

In 2010 TCD and St James’s Hospital agreed to enter into a lease agreement that will allow for the CRC to be constructed in the very heart of St. James’s Hospital and the building works are expected to commence in 2011, with completion in 2012. At the end of 2010, three DCCR Research Nurses were based at St. James’s Hospital in temporary accommodation.

DCCR Educational Activities

In Autumn 2010, the DCCR delivered on one of its objectives with the graduation of the first cohort of research nurses with a certificate in Research Nursing from the RCSI School of Nursing. This Level 9 certificate programme aims to enhance the professional status of research nursing within the nursing profession.

DCCR Management and Operations

The DCCR Network Management Team is responsible for the management and development of the strategic direction of the network and comprises representatives from the three Dublin medical schools and MMI. Chaired by Professor Dermot Kelleher appointed in 2010, policies and procedures were agreed during the year in a number of areas including conflict of interest and a process for a study application form. By the end of 2010, the DCCR Network Management Team had approved the formation of the following new disease and clinical interest groups:

- Stroke Group (Chaired by Professor Peter Kelly)
- Neurodegeneration (Chaired by Professor Orla Hardiman)
- Ophthalmology (Chaired by Mr. David Keegan)

Also during the year, the DCCR Network Management Team held two meetings with the chairs of the DCCR’s disease groups to provide updates on the DCCR’s progress and to highlight common issues being faced by the disease groups.

The DCCR Network Operations Team is responsible for the day to day activities of the network and supporting the DCCR disease groups to achieve their research aims. In 2010 it developed a shared study adoption process that promotes a consistent approach to starting and managing networked clinical research studies across the city.

Standard Application Form

In 2010, the DCCR together with ICRIN facilitated an initiative of research ethics committee (REC) administrators and other stakeholders including the Data Protection Commission, Irish Medicines Board, Council for Bioethics and the Clinical Indemnity Scheme to develop a research ethics application form for the country so that investigators submitting applications to multiple RECs only have to complete one single form.

The Standard Application Form, as it is now known, is specifically for the ethical review of health-related research studies that do not involve medicinal products as defined in SI 190/2004. Approximately 70% of the country’s hospital RECs now accept this form for research studies involving multiple sites. Considered to represent ‘best practice’ in the Irish context, the Standard Application Form has helped to streamline the administration of clinical research and boost the effectiveness of research funding.

To access this form and for further information on how to use it please go to: http://www.molecularmedicineireland.ie/page/q/d/82
DCCR Disease and Clinical Interest Groups

The DCCR Network hosts and facilitates a number of disease and clinical interest groups. Scientists and clinicians with similar research interests come together to agree on research activity that is best conducted as a large group rather than in isolation. This is effective where large volumes of patients are required for a research project, or where a particular condition is rare and identifying suitable patients requires a collaborative effort. By the end of 2010, DCCR clinical research studies were underway at six Dublin teaching hospitals (see table above), some of which involved collaboration from further afield. The following comprises summaries of a sample of these studies.

Respiratory Medicine
Led by Professor Michael Keane this group continued to collect samples and clinical data from patients with idiopathic pulmonary fibrosis and sarcoidosis. Over 200 patients were recruited to this study by the end of 2010 and a trial of an asthma inhaler device developed jointly between the TCD Centre for Bioengineering and Dr. Richard Costello of Beaumont Hospital was initiated.

Gastrointestinal Medicine
Led by Dr Ross McManus this group continued with its citywide collection of whole blood samples with patients diagnosed with coeliac disease. Samples were contributed by consultants based in Beaumont Hospital, the Mater and SUVH as well as consultants in Galway University Hospital, and were the focus of a paper published in Nature Genetics (listed in the publications on page 41). Throughout 2010 the group contributed to a GWAS Study of Barret’s Oesophagus.
Prostate Cancer Research Consortium
One of the pioneers of multi-site clinical research in Ireland, the Prostate Cancer Research Consortium joined the DCCR network in 2010. Its expertise in biobanking and establishing a multi-site research database will be invaluable to the DCCR network as it develops.

HIV/TB
This group, chaired by Professor Colm Bergin, is comprised of infectious disease specialists in St. James's, the Mater and Beaumont hospitals as well as the HRB-funded Professor Joe Keane, a specialist in Respiratory Medicine. The group carried out research on interferon gamma release assays in various patient populations, and this work was presented at international conferences and submitted for publication as well as informing institutional practices.

Neuropsychiatry
Led by Professor Michael Gill, its collaborative activities span Dublin and also include collaborators from across Ireland. In 2010 this group started a large scale study funded by the National Institute of Mental Health and Virginia Commonwealth University both based in the US to identify gene mutations that give rise to schizophrenia. This study builds on work already funded by the Wellcome Trust.

Inflammatory Skin Disease
A Dublin citywide group of dermatologists agreed to come together to study inflammatory skin diseases such as eczema and psoriasis under the leadership of Professor Alan Irvine and Dr Brian Kirby. Following a successful application to the Wellcome Trust to undertake a GWAS Study into eczema, the group have been involved in the collection of samples from patients attending clinical sites across Ireland and the UK.

Other Groups
2010 saw the development of city-wide groups with interests in the areas of neurodegeneration (Prof. Orla Hardiman), ophthalmology (Mr. David Keegan), rheumatoid arthritis (Professor Doug Veale) and chronic kidney disease.

Publications
In terms of outputs the DCCR's clinical research infrastructure has contributed to the generation of a wide range of publications. Specific examples of publications in 2010 include:

1. Multiple common variants for celiac disease influencing immune gene expression. *Nature Genetics* 2010 42
3. Clinical symptomatology and the psychosis risk gene, ZNF804A. *Schizophrenia Research* 2010; 122
5. Evidence for cis-acting regulation of ANK3 and CACNA1C gene expression. *Bipolar Disorders* 2010; 12
6. Variation in memory function associated with the psychosis susceptibility gene ZNF804A. *Arch Gen Psychiatry* 2010; 67
7. Replicated genetic evidence supports a role for HOMER2 in schizophrenia. *Neuroscience Letters* 2010; 468
8. The Letter-Number sequencing test and its potential to work among people with psychotic illness. *European Psychiatry* 2010; 25
10. Microduplications of 16p11.2 are associated with schizophrenia. *Nature Genetics* 2009 41
11. Detecting soluble Clustering in in-vitro and in-vivo models of prostate cancer. *Neoplasma* 2010 57
The Irish Clinical Research Infrastructure Network (ICRIN) was established in 2006 by the MMI partners (NUI Galway, RCSI, TCD, UCC, UCD) to create a harmonised and coordinated clinical research infrastructure in Ireland. Such an infrastructure is needed to conduct multi-centre and multi-national clinical trials that enhance outcomes for patients, improve the health of the population and support the life sciences industry in Ireland. ICRIN’s preparatory phase is funded by the Health Research Board and the Health Service Executive. Additional support is being provided to ICRIN by Enterprise Ireland to support indigenous innovators and academics, small to medium enterprises (SMEs) and multi-national companies access clinical resources to bring their products to market. ICRIN operates as a business unit of Molecular Medicine Ireland and is the Irish scientific partner of the European Clinical Research Infrastructures Network (ECRIN).

2010 was a very successful year for ICRIN. In September, the HRB approved an award of €221,000 to MMI for an 18 month extension of ICRIN activities enabling ICRIN to continue its clinical research coordination activities and research readiness programme. The Clinical Research Roadmap was published and launched and the ICRIN Working Group was established. These and other activities are highlighted below.

Launch of the Clinical Research Roadmap

In May, MMI published the Clinical Research Roadmap. The Roadmap is the product of extensive stakeholder consultation and highlights the strategic and operational changes needed to improve Ireland’s capacity to undertake high quality, multi-centre clinical research. These changes are needed to develop new medicines, diagnostics, therapeutics and medical devices and to enable Ireland to participate in European research initiatives. It is aligned to and complements the stated goals of both the Action Plan for Health Research, published by the Minister for Health and Children, and the HRB’s Strategic Business Plan.

At the launch in June, guest of honour, Mary Harney TD, Minister for Health and Children, affirmed the Government’s commitment to building capacity for clinical research in Ireland and acknowledged the Roadmap as an important contribution in this regard. (For further information on the launch go to http://www.molecularmedicineireland.ie/show/item/1/1439)
ICRIN Working Group

Also in June, MMI established the ICRIN Working Group with the aim of increasing the number of scientifically relevant multi-centre clinical studies, and industry sponsored clinical trials in particular. Members of the Working Group who include leading clinical researchers held its first meeting on 13 August under the chairmanship of Professor Larry Egan, ICRIN Clinical Director. See list of members in table below.

The Working Group is addressing the following work streams:

- Streamlining trial approval and start-up systems - ethics, institutional, contractual, financial and improved feasibility
- CRC sustainability and research infrastructure assessment and proposals
- Process and systems harmonisation, with a focus on IT and data management, bio banking and quality management systems
- Training, education and resource assessment of research community – with an initial focus on research nurses
- Piloting multicentre clinical trials - industry and investigator-led
- Identification and focusing on research strengths

In order to progress the theme of process harmonisation, a quality management subgroup was also instituted drawing membership from all the CRCs, MIRA, Perinatal Ireland, the National Stoke and Cardiovascular research network, National Children’s Research Centre and the UCC neonatal group.

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<tr>
<td>Professor Larry Egan (Chair)</td>
<td>NUI Galway</td>
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<td>Paul Barry</td>
<td>Molecular Medicine Ireland</td>
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<tr>
<td>Ailbhe Cullen</td>
<td>Royal College of Surgeons in Ireland</td>
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<td>Dr Peter Doran</td>
<td>University College Dublin</td>
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<tr>
<td>Siobhan Gaynor</td>
<td>Irish Clinical Research Infrastructure Network</td>
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<td>Fionnuala Gibbons</td>
<td>Irish Clinical Research Infrastructure Network</td>
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<tr>
<td>Professor Dermot Kenny</td>
<td>Royal College of Surgeons in Ireland</td>
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<td>John McCourt</td>
<td>Dublin Centre for Clinical Research / RCSI</td>
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<td>Veronica McInerney</td>
<td>NUI Galway</td>
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<td>Marie Mellody</td>
<td>Irish Clinical Research Infrastructure Network</td>
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<td>Professor Patrick Murray</td>
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<td>Professor John Nolan</td>
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<td>Dr Aideen O’Doherty</td>
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<td>Professor George Shorten</td>
<td>University College Cork</td>
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<td>Jeremy Towns</td>
<td>Dublin Centre for Clinical Research</td>
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ICRIN commenced Research Readiness Programme

ICRIN commenced its Research Readiness Programme with the Mercer’s Institute for Research on Ageing (MIRA) and the Mater CRC in June 2010. The overall goals of the Research Readiness Programme are: to evaluate the research systems which are already functioning well; to identify the areas where more consistency of approach would be of benefit; (e.g. sharing best practice) and to gain information from the research teams on the research infrastructure elements which would be best addressed at a national level.

Research Governance and Sponsorship Seminar

The Clinical Research Roadmap identified the absence of a well developed system of research governance as one of the major obstacles to the development of clinical research in Irish hospitals, universities and the broader research community. In order to address this issue, MMI/ICRIN organised a seminar in September to investigate why it is so difficult for principal investigators in Ireland to act as sponsors of clinical trials. Professor Steve Smith, CEO of Imperial College Healthcare NHS Trust, London was invited as guest speaker to talk about the lessons learned in the establishment of the Imperial College NHS Trust, the first academic medical centre in the UK, and how a research governance system was developed within it. A report of the seminar is available at: http://www.molecularmedicineireland.ie/uploads/files/ICRIN/MMIICRIN_2010113_Seminar_Research_Governance&Sponsorship.pdf

Education and Training

The ICRIN team continued to deliver a successful GCP training programme in 2010 consisting of seven one-day training courses. GCP training is required for those involved in undertaking clinical research. The courses were attended by a total of 140 participants and were very well received. In addition four bespoke training courses were conducted at the request of individual research groups and attended by over 120 people.

ICRIN was also involved in providing lectures and modules to the following courses:

- RCSI research nurse certificate in clinical research
- The IMDAs ‘Medical Devices and Diagnostics Leadership Programme
- Dublin Academic Medical Centre Summer School course - Principles and Practices of Translational Research
- UCD Postgraduate Certificate in Clinical and Translational Research

Above: Members of the Quality Management Subgroup attending their first meeting at Newman House in December
ICRIN and ECRIN

ICRIN is the Irish scientific partner of the European Clinical Research Infrastructure Network (ECRIN) which is a sustainable, not-for-profit infrastructure established to build European capacity in multinational investigator-led clinical research. ECRIN does this by offering integrated support through its national partners to multinational clinical research projects by providing information, consultancy and a set of flexible services for any category of clinical research, in any medical field.

In Ireland, the support outlined above is provided by ICRIN. ICRIN also facilitates access by Irish principal investigators to ECRIN partners and where required, to the ECRIN Scientific Review Board. This Board is responsible for reviewing research proposals to assess whether they are suitable for ECRIN support and if there is interest by other ECRIN partners in participating in Irish-led projects. ICRIN assisted in establishing the new ECRIN Scientific Review Board and the revision of the review process to streamline review procedures for access to ECRIN services.

During the year, ICRIN contributed to an MMI position paper recommending Ireland’s continued membership of the next phase of ECRIN and also the Biobanking and Biomolecular Research Infrastructure (BBMRI). MMI is the Irish scientific partner of BBMRI. To facilitate the advancement of the next phase of both research infrastructures, the Council of Ministers agreed on a new legal instrument in 2009 known as the European Research Infrastructure Consortium or ERIC. The ERIC will provide both ECRIN and BBMRI with a permanent legal structure enabling them to make contracts and be a party in legal proceedings. BBMRI and ECRIN are at an advanced stage in preparing proposals for the adoption of the ERIC though the running costs for the research infrastructures fall to national governments. MMI argues that Irish membership of the ECRIN ERIC will be critical to the integration of the emerging national clinical research infrastructure with a wider European infrastructure and to the success of Irish PIs in leading and partnering in FP funded clinical studies.

ICRIN was a partner in an ECRIN application to the FP7 programme in December 2010 under its integrating activity call to deepen and expand clinical research support for multi-national clinical trials in Europe. ICRIN is contributing to work packages in the submission to build capacity at European level to support clinical research in medical devices and rare diseases and to expand the ECRIN network to other EU member states. Success in this call will underscore the importance of Irish membership of the ECRIN ERIC, when established.

Authors from the MMI partners contributed to an ECRIN paper in 2010 entitled ‘Heterogeneity prevails: the state of clinical trial data management in Europe - results of a survey of ECRIN centres’ and published in Trials 2010, 11:79 (21 July 2010).

ICRIN provided considerable assistance to principal investigators interested in applying for funding for investigator-led clinical trials under the FP7 Health call in July 2010. The aim of the call is “to boost innovative drugs and health solutions in Europe’ and is the first time the programme has funded investigator led trials on this scale. Several Irish consortia were invited to submit a Stage 2 proposal and one of these which is involved in developing an Alzheimers clinical trial, worked closely with ICRIN to develop its Stage 2 proposal. As a result of this process, Siobhan Gaynor of ICRIN was invited to lead the ECRIN task force on FP7 and to engage with the European Commission to clarify a number of issues, including subcontracting and the involvement of SME’s in multi-national, investigator driven clinical trials.

Advising companies on clinical trials

The ICRIN Clinical Trials Liaison Officer (CTLO), funded by Enterprise Ireland, worked with a number of indigenous pharmaceutical, medical device, biotech companies, spin off start-up companies from academic/university discovery connecting them to the people with the clinical skills to support their research ideas and exploit their commercial opportunities.

Among the workshops organised by the CTLO was the very successful Health Technology Assessments (HTAs), Procurement & Reimbursement Process for Medical Devices. With the assistance of Enterprise Ireland and NUI Galway this workshop was held in Dublin on 21 and 22 June. Professor Ciaran O’ Neill of the Department of Economics in NUIG was the key speaker. The aim of the workshop was to give participants from academia, SMEs and indigenous companies an overview of HTA requirements and the re-imbursement process for medical devices in Europe and Ireland. For further information please go to http://www.molecularmedicineireland.ie/show/item/1/1516. The CTLO works in close partnership with personnel from Enterprise Ireland.
Communication

**MMI Website, an interactive platform for collaborative research**

The MMI Website provides our visitors with up to date information on MMI activities, news, events and career opportunities.

MMI website users can register and maintain an up-to-date research profile, as well as apply for MMI Courses and Workshops. Collaborative groups working under the auspice of MMI can communicate and share documents via dedicated secure areas on the website.

Dedicated areas of the MMI website enable easy to navigate access to key collaborative resources in clinical and translational research.

**Traffic on the MMI Website**

| Mar - Dec 2009: 133,594 Page views | Mar - Dec 2010: 163,835 Page views (+22.64%) |

*Please note that due to a server transfer in March no statistics were recorded for January and February 2009.*
MMI Online Newsletter

The MMI Newsletter features quarterly updates on all MMI activities.

Above: Examples of secure group areas on the MMI website

Above: MMI Web Portals to access technology platforms and the MMI Clinician Scientist Structured PhD Curriculum.
## Financial Report

### UNAUDITED - DETAILED INCOME AND EXPENDITURE ACCOUNT

Year Ended 30th September 2010

#### INCOME

<table>
<thead>
<tr>
<th>Income</th>
<th>2010</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Course fees</td>
<td>12,255</td>
<td>26,740</td>
</tr>
<tr>
<td>Partners</td>
<td>678,350</td>
<td>769,149</td>
</tr>
<tr>
<td>Grants</td>
<td>476,026</td>
<td>480,188</td>
</tr>
<tr>
<td><strong>TOTAL INCOME</strong></td>
<td><strong>1,166,631</strong></td>
<td><strong>1,276,077</strong></td>
</tr>
</tbody>
</table>

#### EXPENDITURE

<table>
<thead>
<tr>
<th>Expences</th>
<th>2010</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel costs</td>
<td>907,075</td>
<td>947,440</td>
</tr>
<tr>
<td>Advertising and public relations</td>
<td>10,817</td>
<td>5,169</td>
</tr>
<tr>
<td>Professional and consultancy fees</td>
<td>8,844</td>
<td>60,072</td>
</tr>
<tr>
<td>Conferences and training</td>
<td>29,804</td>
<td>25,451</td>
</tr>
<tr>
<td>Rent and rates</td>
<td>94,923</td>
<td>127,618</td>
</tr>
<tr>
<td>Building – repairs, cleaning and canteen</td>
<td>8,410</td>
<td>12,055</td>
</tr>
<tr>
<td>Insurance</td>
<td>25,842</td>
<td>8,911</td>
</tr>
<tr>
<td>Communications : telephone, fax and postage</td>
<td>13,158</td>
<td>12,807</td>
</tr>
<tr>
<td>Website design and maintenance</td>
<td>9,395</td>
<td>18,383</td>
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<tr>
<td>Printing and stationery</td>
<td>10,747</td>
<td>12,262</td>
</tr>
<tr>
<td>Travel and subsistence</td>
<td>27,211</td>
<td>26,807</td>
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<tr>
<td>Bank interest and charges</td>
<td>1,261</td>
<td>753</td>
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<tr>
<td>Depreciation:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Fixtures and fittings</td>
<td>2,165</td>
<td>1,960</td>
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<tr>
<td>- Computer equipment</td>
<td>5,292</td>
<td>5,339</td>
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<tr>
<td>- Office equipment</td>
<td>524</td>
<td>523</td>
</tr>
<tr>
<td>Auditors’ remuneration</td>
<td>11,163</td>
<td>10,527</td>
</tr>
<tr>
<td><strong>TOTAL EXPENDITURE</strong></td>
<td><strong>1,166,631</strong></td>
<td><strong>1,276,077</strong></td>
</tr>
</tbody>
</table>

**Profit for the year**

- -

*unaudited
During 2010 MMI welcomed the assistance of Jonathan Coyle, a participant on the FAS graduate work placement programme, and Pauline Jestin, an overseas student of statistics.