Dublin Molecular Medicine Centre

Annual Report 2005

UCD DUBLIN

RCSI

The DMMC was established under the Higher Education Authority's *Programme for Research in Third Level Institutions*, in partnership with Atlantic Philanthropies, as part of the National Development Plan.

HEA
Higher Education Authority
An tÚdarás um Ard-Oideachas

NDP
NATIONAL DEVELOPMENT PLAN

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DMMC Highlights 2005

The Royal College of Surgeons in Ireland becomes equal owner of the DMMC

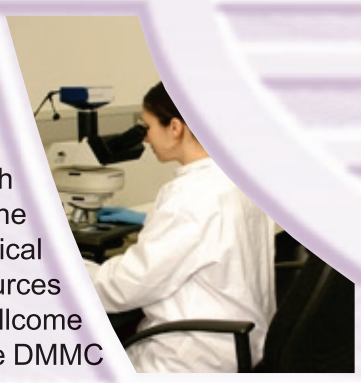
On 25 April 2005, the commitment to partnership was strengthened with The Royal College of Surgeons in Ireland formally joining University College Dublin and Trinity College Dublin as joint owners of the DMMC. The Irish Minister for Education & Science, Ms Mary Hanafin TD, attended the ceremony at which the new DMMC agreement was signed. RCSI brings excellent research capabilities, complementing those of UCD and TCD, and we look forward to building more disease-specific consortia where research and education are developed in parallel. **[page 12]**

Genome Resource Units

Two Genome Resource Units (GRU's) were completed at the Mater Misericordiae and St Vincent's University Hospitals in 2005. These are key developments in the establishment of citywide infrastructure for facilitating translational research. The GRU's will provide many scientists and clinicians with access to tissue collections, advanced and best practice operating procedures, informatics infrastructure and expertise, and skilled specialist staff including research nurses. Disease-specific bio-collections created within these facilities will be the cornerstone of our genetic epidemiology and translational research programmes. The GRU's will become an essential resource for elucidation of the molecular basis of disease pathogenesis, and will bring together clinicians and scientists in collaborative efforts to help realise the bench to bedside research goal of the DMMC. **[page 19]**

Research Programmes

Progress has been made on a number of cross-institutional research programmes including the Prostate Cancer Research Consortium, The Resource for Psychoses Genomics in Ireland, Hepatitis C, Autism, and Cervical Cancer. All of these initiatives are funded at least in part from external sources including the Health Research Board, the Irish Cancer Society and the Wellcome Trust. All use the infrastructure laid down during the PRTLI programmes of the DMMC and the Programme for Human Genomics. **[pages 13-17]**



DMMC Highlights 2005

DMMC Education & Training

2005 was a vibrant year in cross-institutional development, delivery, and usage of DMMC Courses. These are short taught courses used by postgraduate students to supplement research degrees and by postdoctoral workers and staff as career-long training across disciplines and institutions. By the end of 2005, the total number of individuals applying for DMMC Courses since their inception in December 2003 had risen to 879. This total includes 410 from UCD and affiliated hospitals, 234 from TCD and affiliated hospitals, and 161 from RCSI and affiliated hospitals. The DMMC's international Scientific Advisory Committee see the contracted provision and coordination of high quality postgraduate training in biomedicine, in a manner that would be more efficient and cost-effective than providing it at the individual institutional level, as a very powerful driver for the future success of the DMMC. **[page 21]**

Website developments and increased usage

The DMMC website *www.dmmc.ie* is the primary communication channel for all activities and information about the DMMC. News, events, careers, education and research information are profiled on the site and this year additional functionality and search facilities have been added to both our Programmes and Research sections. The site has become increasingly busy over time with a monthly average of over 7,000 visits. **[page 23]**

HRB & DMMC Translational Workshop

In conjunction with the Health Research Board, the DMMC organised a workshop on translational research, which took place on 13 December 2005. Attended by over 60 delegates, the audience included representatives of many stakeholder groups including patient advocates, clinician scientists, nurses, academic institutions, hospital managers, funding agencies, clinical research organisations, pharmaceutical and informatics companies. The workshop explored Ireland's position in this emerging field and formulated a strategy to overcome obstacles and identify key areas in need of additional resources. The DMMC will coordinate future workshops to ensure Ireland is positioned to be competitive in this research space. **[page 20]**

Technology Platforms

Many of the technology platforms have matured and developed further in 2005 and are the source of many collaborations across the city. DMMC workshops have been run to promote the use of these, including several on Proteomics, Bioinformatics, and Transcriptomics among others. The new High Content Cell Analysis (Cellomics KineticScan and GE INcell analyser) platform has been further developed at the IMM and is unique in Europe in an academic setting. A new histology core is also available at the Conway Institute. **[page 18]**

Chairman's Statement

In many developed countries huge efforts are being focussed on building the necessary infrastructure to perform translational research. This is a complex task as it involves the integration of activities at the interface between cutting edge research and clinical practice, and thus poses new challenges in the translation of innovation directly to patients. The UK, Singapore, France, Spain, the Netherlands and the USA in particular, are investing massively in this arena, in many instances using joint public/private strategies. There is a firm belief that this investment is key in being able to maintain healthcare costs at sustainable levels over the long term.

The Dublin based medical schools and teaching hospitals have an opportunity to seriously compete on the international scene as well as contributing to the national health research strategy. The collective agenda built through the DMMC over the past three years is maturing and has already allowed a joint bid to be put forward to the Wellcome Trust for the creation of the Dublin Centre for Clinical Research. Irrespective of the outcome of this funding application, which is competing with the best throughout the UK and Ireland, the effort has helped define a city-wide programme and an understanding of our strengths and weaknesses.

We reached a major milestone in April when RCSI officially became a joint owner of the DMMC, and the three colleges recommitted to the collaborative model until at least 2012. There is no alternative for Ireland but to play the collective game in translational research and I would go further in proposing that plans be drawn up for strategic links with Cork and Galway to create a truly national platform and become credible partners on the European scene, where the door is open for exciting collaborative programmes currently under discussion for FP7.

There is no alternative for Ireland but to play the collective game in translational research and I would go further in proposing that plans be drawn up for strategic links with Cork and Galway to create a truly national platform.

The integration of academia, industry and the clinical setting has just begun. It is hard to imagine how different healthcare delivery will be in 20 years time – the only certainty is that it will be much more informed by scientific knowledge than it is today and this will be the major driver for change in medical practice, education and training of healthcare professionals, and translational research. The DMMC now has the opportunity to raise the game and coordinate and facilitate the actors in their disparate disciplines to create real value for Ireland.

Dr Michael Kamarck
Chair of the DMMC Board

Michael Kamarck PhD, is Senior Vice President of TO&PS (Technical Operations and Product Supply) with Wyeth BioPharma and Vaccines at their Global Headquarters in Pennsylvania (USA). Dr Kamarck has a PhD from MIT Cambridge (USA) and has extensive experience in the Biopharmaceutical industry at the highest levels.

Message from the CEO

2005 has witnessed much progress towards achieving our aim of developing a city-wide infrastructure for modern translational research. The Programme for Human Genomics has delivered on many of its goals and will complete its mission on target in 2007. In particular we should note the completion of the RCSI Research building in York House and the Genome Resource Units at both the Mater and St. Vincent's Hospitals, which will be the hubs of clinical research at these sites.

In addition, the continuing collection of biomaterials from disease specific cohorts is progressing well, the most important ones being in Psychoses (RPGI, funded by the Wellcome Trust), Epilepsy, Autism, Inflammatory Bowel Disease, Rheumatoid Arthritis, Cardiovascular Diseases, and various cancers: Prostate (funded by the Irish Cancer Society), Breast, Oesophageal and Haematological malignancies. These collections are being interrogated by research groups using the proteomics, genomics, imaging and high-throughput cellular screening technology platforms that have been set up in the UCD Conway Institute, the TCD Institute of Molecular Medicine and in the RCSI Research Institute. Most platforms use a collaborative model for access which for the time being is the most appropriate and interactive for the researchers.

The DMMC Education & Training programme has continued to create new innovations, with 2005 seeing the planning of the first DMMC/industry collaborations and the internationalisation of some courses and workshops. The quality of the offering was once again commended by our International Scientific Advisory Committee.

Having consolidated the ownership structure, the DMMC can now build on successes to date and look to the future by preparing the next stage in its evolution.

Having consolidated the ownership structure, the DMMC can now build on successes to date and look to the future by preparing the next stage in its evolution.

As the next national development plan is rolled out and the EU prepares to kick off FP7 in 2007, we need to be prepared. FP7 in particular will give us an opportunity to leverage EU funds if we can organise ourselves nationally. The DMMC will be driving an ambitious plan that will bring Ireland to the European table with a platform for translational research which can link in to like-minded centres across Europe.

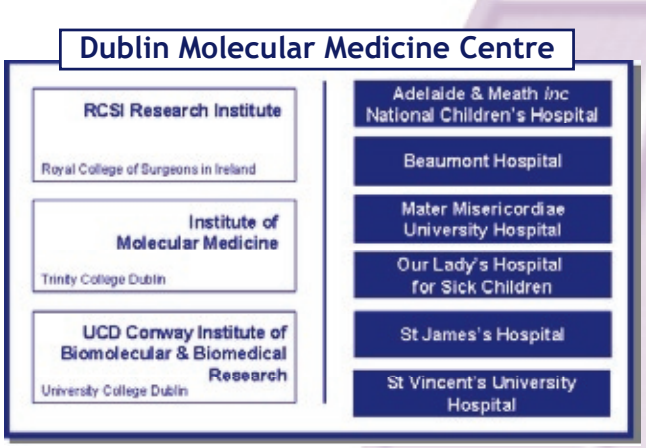
Dr Pierre Meulien
DMMC Chief Executive Officer

Pierre Meulien PhD was appointed as CEO of the DMMC in September 2002. Dr Meulien has a PhD in Molecular Biology from Edinburgh University (UK) and has 20 years of industrial R&D experience, most recently as Senior Vice President of R&D at Aventis Pasteur - Canada (now Sanofi Pasteur).

DMMC Overview: Structure & Governance

The Dublin Molecular Medicine Centre (DMMC) is a collaborative biomedical research partnership between Trinity College Dublin (TCD), University College Dublin (UCD), and The Royal College of Surgeons in Ireland (RCSI).

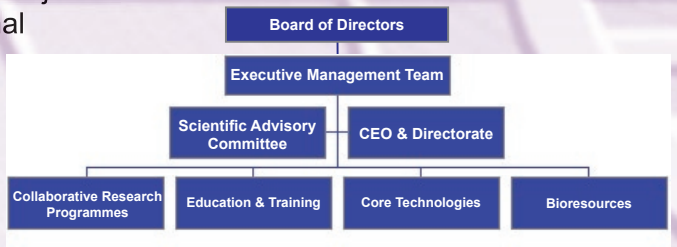
The DMMC was established to create a critical mass and centre of excellence in molecular medicine research and education. The DMMC has helped align the activities of Dublin's three premier biomedical research institutions and six affiliated teaching hospitals under a common framework designed to facilitate cross-institutional collaboration and enhance translational research capability. Translational research is best described as 'bench' experiments being driven by clinical questions, and the findings from the 'bench' being put into practise through better diagnosis and treatment at the 'bedside'. Traditionally, clinical and scientific research are rarely integrated in this way.



Above: the UCD Conway Institute (top) and the TCD Institute of Molecular Medicine.
Left: the DMMC Directorate Offices, Newman House.
Below: the RCSI Research Institute, York House.

The DMMC continues to defragment the research community, enabling fundamental academic investigators and clinician scientists to collaborate in research programmes and education & training activities regardless of their institutional affiliation.

Established through funding from the Higher Education Authority, the DMMC is a joint venture company controlled by TCD, UCD and RCSI. Formally incorporated in March 2002, DMMC is a company limited by guarantee and has been registered without the word "Limited" in its name. It is a registered charity founded for the promotion of molecular medicine research. The DMMC is governed by a Board of Directors (see page 10), with executive control vested in an Executive Management Team (EMT; see page 9). The EMT comprises the CEO of the DMMC and the three Heads of Medical Research in TCD, UCD and RCSI and it guides scientific and operational direction. The strategic direction and the scientific excellence of the DMMC and its constituent research institutions is subject to independent and objective critique from an international Scientific Advisory Committee (see page 11).



The DMMC operates in essence as a virtual organisation since, with the exception of the 6-person Directorate, all staff are employed by the parent academic institutions or teaching hospitals. This Directorate comprises Chief Executive Officer, a Senior Executive Assistant, a Financial Controller, a Programme Manager, an Education & Information Coordinator and an Education Administration Assistant (see page 26). The DMMC Directorate provides a focal point for trans-institutional activities and works in close cooperation with a range of University & Hospital appointed personnel. Central to the effective execution of the DMMC objectives is a group of senior investigators from across the constituent institutions. These individuals act in a variety of roles to ensure local implementation of collaborative programmes, establishment of DMMC-funded core technologies and development of cross-institutional educational resources.

DMMC Overview: Resources

RESEARCH INSTITUTES

UCD Conway Institute of Biomolecular & Biomedical Research

This 11,300 m^2 institute located on the University College Dublin Belfield campus includes the *Conway Proteome Research Centre* and the *Applied Neurotherapeutics Research Group*, together with bioinformatics and transcriptomics core facilities. Over 400 staff work within the institute and in affiliated centres and hospital sites. Research at the UCD Conway Institute is organised into three interactive multi-disciplinary centres: Synthesis & Chemical Biology, Integrative Biology, and Molecular Medicine. Collaborative research across these centres in the areas of cancer, vascular biology, neuroscience, and infection, immunity and inflammation aims to identify potential therapeutic targets for the treatment of human and animal diseases. Strong links with a number of major academic teaching hospitals have been developed to underpin this activity.

Above: the Clinical Research Centre at Beaumont Hospital.

RCSI Research Institute

Formerly the *Institute of Biopharmaceutical Sciences*, this is a multi-site research infrastructure encompasing the research activities of RCSI at the St Stephen's Green campus and the RCSI-Education and Research Centre (ERC) at Beaumont Hospital, including:

- Cellular neuroscience research labs in York House
- Molecular medicine research labs at Beaumont Hospital
- Centre for Advanced Drug Delivery
- Centre for Human Proteomics
- School of Pharmacy

Through this infrastructure of labs, 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, Respiratory Medicine, Cardiovascular and Tumour Biology. 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.

TCD Institute of Molecular Medicine

Located on the St James's Hospital Campus, the 4,500 m^2 Institute of Molecular Medicine (IMM) is well placed as a centre for collaborative translational research and postgraduate education in molecular medicine. Among the areas of active research in the IMM are cancer (prostate, haematological, oesophageal, cervical, and thoracic), infection & immunity (including TB and *Helicobacter pylori* research), genomic research into inflammatory disease, molecular histopathology, cell signalling (including multidisciplinary collaborations in microfluidics and quantum nanodot technology development), neuropsychiatric genetics, and nutrigenomics. The IMM also houses the Trinity Biobank (processing biological research collections including the Resource for Psychoses Genomics Ireland), a cellular High Content Analysis (HCA) core, and a gene expression array core facility. The 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.

ADDITIONAL TRANSLATIONAL RESEARCH INFRASTRUCTURE

Infrastructure to facilitate translational research across the DMMC, including Genome Resource Units located at various hospital sites, is described on page 19.

DMMC Overview: Strategy

VISION

The DMMC aims to create a dynamic, collaborative environment that fosters cross-institutional biomedical research and accelerates its translation to improved clinical practice leading to better patient healthcare.

It unites three of Ireland's premier academic institutions and the principal Dublin teaching hospitals within a focussed research partnership that respects the diversity & tradition of its constituent institutions. The DMMC will leverage the unique strengths and capabilities of all three institutions in order to position Dublin as an internationally recognised centre of excellence in molecular medicine by 2010.

MISSION STATEMENT

The DMMC will accelerate translational bioscience by:

1. Creating trans-institutional research clusters with focussed programmes that exploit state-of-the-art technologies to increase our knowledge of the pathogenesis and treatment of commonly acquired diseases.

2. Generating a network resource of tissue samples, genetic material, genotypic & phenotypic data that enable the evaluation of clinical hypotheses leading to earlier diagnosis and improved therapeutic strategies.

3. Developing, attracting & retaining world-class research and clinician scientists to an environment where multiple career track opportunities are promoted.

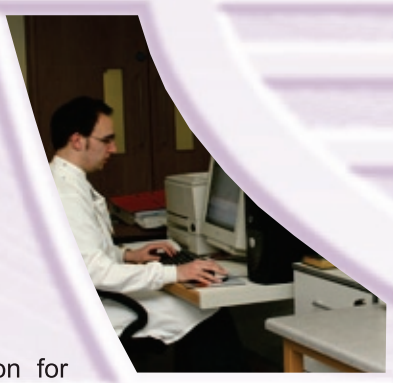
4. Building a multi-disciplinary education curriculum that is informed by the biopharmaceutical industry and which enables career-long learning.

5. Securing appropriate finance for competitive multi-investigator research proposals and making our combined resources (including citywide technology cores) available to enable academic researchers & clinician scientists attract individual funding.

6. Building strategic partnerships with the biopharmaceutical industry and international academic research centres.

7. Offering a professional, accessible interface that facilitates the exploitation of our research knowledge & educational resources on behalf of the participant institutions.

OUTPUTS



1. The creation of an internationally recognised community in molecular medicine.

2. Novel research programmes and enabling technologies resulting in increased international impact by the participant academic institutions.

3. New diagnostics, therapeutics and more effective intervention strategies.

4. The generation of valuable biological collections with high context information for individual investigators.

5. The creation of skilled human capital and the generation of new intellectual property to fuel Ireland's biotechnology & pharmaceutical industry.

DMMC Overview: Activities

With a cross-institutional perspective, the Dublin Molecular Medicine Centre seeks to advance translational biomedical research by bringing together research teams in targeted and coordinated programmes of research and education. The goal is to build the infrastructure and research excellence to compete globally and to develop collaborative links with like-minded academic centres and with the biotech and pharmaceutical industry.

The landmark completion of the Human Genome Project provided a unique resource for biomedical sciences. The *Programme for Human Genomics* (PHG) is a partnership between UCD, TCD and RCSI within the DMMC. It's over-riding goal is the application of human genomics and proteomics to the study of the pathogenesis, diagnosis and treatment of human disease with a view to identifying new diagnostic markers and therapeutic targets. The Programme, funded by the Higher Education Authority under cycle 3 of the *Programme for Research in Third Level Institutions* (PRTLI), includes the creation of technology cores and funding of demonstration research projects designed to advance the capability for translational research in the DMMC. Some of these projects are described in the context of themed research areas (pages 13-17).

The DMMC represents a *neutral space* where researchers can meet to discuss potential collaborative projects that may necessitate research expertise and technology platforms to be provided by more than one academic institution, and may include industry partners. Such collaborative research and infrastructure development is increasingly seen as an important factor by funding agencies when deciding strategic investment. This activity can build Research Consortia that capitalise on their multi-institutional, cross-disciplinary membership to obtain significant funding and a high profile.

In the sphere of *Education & Training*, the DMMC is helping to build a cross-institutional translational research environment by providing easily accessible means for all researchers to develop their skills and broaden their training. DMMC Education & Training broadens and adds structure to postgraduate research degrees in the biosciences, and offers research staff in universities and hospitals new opportunities, by enabling individuals to take time out from their laboratory research and enter a cross-institutional learning community. DMMC Education & Training capitalises on the research and teaching strengths of TCD, UCD, RCSI, and the clinical expertise in the affiliated teaching hospitals (pages 21-22).

DMMC Executive Management Team

The Executive Management Team (EMT) meets regularly to guide the scientific and operational strategy of the DMMC. In addition to the DMMC Chief Executive Officer, Dr Pierre Meulien, the EMT comprises key representatives of TCD, UCD, and RCSI:

Prof Dermot Kelleher Professor of Clinical Medicine & Director of the Institute of Molecular Medicine, Trinity College Dublin & St James's Hospital

Dermot Kelleher is Head of the Medical School at Trinity College Dublin. He graduated with First Class Honours in Medicine in 1978 and completed specialist training in Gastroenterology in Dublin. He subsequently received a Fogarty Scholarship for a research fellowship at University of California San Diego. In 1989 he was appointed as a Wellcome Senior Fellow in Clinical Science at Trinity College Dublin and was subsequently appointed as Professor of Clinical Medicine in 2001. Professor Kelleher's research has focussed on the cell biology both of immune responses and of the inflammation-cancer sequence. He is the author of approximately 200 publications including papers in journals such as Nature Immunology, Journal of Experimental Medicine, PNAS, Gastroenterology, Journal of Biological Chemistry and Journal of Immunology. He is also the author of 10 patents. Prof Kelleher has been successful in obtaining funding from NIH, Wellcome Trust, European Union, Health Research Board and Enterprise Ireland. Prof Kelleher obtained collaborative grant funding to establish the Dublin Molecular Medicine Centre and he has had a major involvement in interdisciplinary research including research into nanofluidic technology, high content analysis with siRNA screening, and nanoparticle delivery.

Prof William Powderly Professor of Medicine & Therapeutics at University College Dublin & the Mater Misericordiae University Hospital

William G. Powderly, MD, is Head of the School of Medicine and Medical Science at University College Dublin. Until July 2004, he was Professor of Medicine at Washington University School of Medicine in St. Louis, Missouri, USA where he was chief of the Division of Infectious Diseases. Prof Powderly has been actively involved in HIV-related clinical research for the last 18 years and has held many leadership roles in the US Adult AIDS Clinical Trials Group, including Vice-Chair of the Group and chair of its Scientific Steering Committee. He was a member of numerous Advisory groups for the National Institutes of Health and the Centers for Disease Control and Prevention in the USA. He was also the first Chairman of the HIV Medicine Association in the USA.

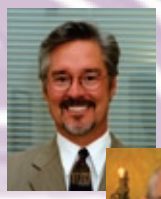
His own research originally focused on infections, especially fungal infections, in patients with AIDS and cancer. More recently, he and his group have concentrated on the emerging toxicities of treatment of HIV, especially the metabolic complications seen in patients receiving effective therapy, including the development of diabetes, lipid abnormalities, and bone disease.

Prof. Powderly is widely published in the areas of HIV and AIDS with over 300 original articles or book chapters. Together with Prof Jonathan Cohen from London, he has edited a major international textbook in Infectious Diseases that was published in 2004. He is a Fellow of the Infectious Diseases Society of America, of the Royal College of Physicians of Ireland and of the American Association for the Advancement of Science.

Prof Brian Harvey Professor of Molecular Medicine & Director of the RCSI Research Institute, The Royal College of Surgeons in Ireland

Professor Brian Harvey obtained his PhD at UCD in 1982 and spent the following 12 years in France where he became director of research at the CNRS molecular cell biology labs in Villefranche-sur-mer. In 1993 he returned to Ireland to take up the Chair of Cell Physiology at University College Cork (UCC) and direct the Wellcome Trust Cellular Physiology Research Unit. From 1998-2002 he was Vice-President for Research at UCC and co-ordinated UCC's successful PRTLI €130M funded infrastructural programmes. In 2003 he was appointed Professor of Molecular Medicine at The Royal College of Surgeons in Ireland and director of the Charitable Infirmary Trust Molecular Medicine Laboratories at Beaumont Hospital. His research programmes are focussed on rapid responses to steroid hormones in kidney, lung and intestine. Prof Harvey is currently Chair of the Royal Irish Academy Life Sciences Committee.

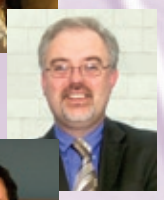
DMMC Board of Directors



CHAIR **Dr Michael Kamarck**
Senior Vice President, Wyeth Biopharma & Vaccines TO&PS

DIRECTORS

Prof Brian Harvey Professor of Molecular Medicine and Director of the RCSI Research Institute, The Royal College of Surgeons in Ireland



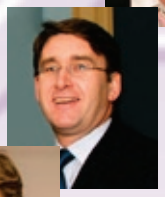
Prof William Powderly Professor of Medicine & Therapeutics and Head of the School of Medicine & Medical Science, University College Dublin

Prof Dermot Kelleher Professor of Clinical Medicine and Head of the School of Medicine, Trinity College Dublin

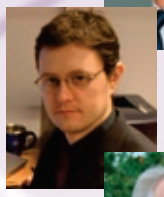
Mr Michael Gleeson
Secretary to the College, Trinity College Dublin

Prof Desmond Fitzgerald
Professor of Molecular Medicine & Vice President for Research, University College Dublin

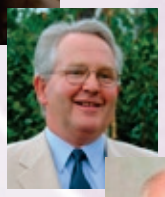
Prof Jochen Prehn
Head of the Department of Physiology & Medical Physics and Director of the Centre for Human Proteomics, The Royal College of Surgeons in Ireland



Mr Terry McWade
Deputy Chief Executive Officer, The Royal College of Surgeons in Ireland



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



Mr Frank Kenny
Founding Partner, Delta Partners

Mr Barry O'Leary
Senior Vice President, Life Sciences & Food
IDA Ireland

Mr Michael Lyons
Chief Executive, The Adelaide & Meath Hospital Incorporating the National Children's Hospital

Prof Janet Allen
Director of the UCD Conway Institute of Biomolecular & Biomedical Science, University College Dublin

COMPANY SECRETARY **Mr John Coman**
Corporate & Legal Affairs Secretary, University College Dublin

Scientific Advisory Committee Review

The Scientific Advisory Committee (SAC) provides an independent and objective critique of the strategic direction and the scientific performance of the Dublin Molecular Medicine Centre. This group is mandated with an advisory responsibility and plays no formal role in the decision-making or in the management of the DMMC.

The SAC convened on 3 June 2005 for their second review of DMMC activities. Dr Pierre Meulien (DMMC Chief Executive Officer) introduced the meeting and provided an overview of DMMC strategy and operations. This was followed by presentations on DMMC Education & Training (Dr Mark Watson), an overview of DMMC research programmes (Paul Harkin), and outlines on the research strategies of the UCD Conway Institute for Biomolecular & Biomedical Research, the TCD Institute of Molecular Medicine, and the RCSI Research Institute. The review continued with presentations on specific research programmes in the areas of cancer, infection & immunity, inflammation, neuroscience, and cardiovascular disease.

The DMMC Scientific Advisory Committee during their review. *From left*: Dr Hugh Brady, Dr John Sims, Prof Gordon Duff, Prof Garret FitzGerald, Dr Peter Ghazal, Prof Stephen O'Rahilly, Prof Martin Carey.

In their report, the SAC noted that the DMMC has been remarkably successful in pulling together the different academic institutions and healthcare centres in Dublin, enabling leverage of substantial funding for biomedical translational research, the creation of core facilities that will be available across institutions, and well-organised biobanks of tissue, DNA and clinical information that will be of enormous utility into the future. The SAC again noted that the DMMC has had great success in postgraduate education. They recognised the importance of the DMMC as a 'neutral space' in which investigators from different institutions could meet to discuss collaboration, and its potential as a 'first port of call' for industrial collaborators.

Among the areas for further development, the SAC recommended a more all-Ireland focus for the DMMC. They would like to see more clarity in what the DMMC is charged to do and oversee among the various bioscience enterprises of its parent institutions. Considering future financial viability of the DMMC, the SAC noted that this is dependent on a continued demonstration of added value to the constituent institutions. The SAC saw the contracted provision and coordination of high quality postgraduate training in biomedicine, in a manner that would be more efficient and cost-effective than providing it at the individual institutional level, as a very powerful driver for the future success of the DMMC.

The SAC comprises:

Prof Martin Carey (Professor of Medicine and Professor of Health Sciences & Technology, Brigham and Women's Hospital & Harvard Medical School, Boston, USA)
Prof Gordon Duff (Florey Professor of Molecular Medicine, University of Sheffield, England)
Prof Garrett FitzGerald (Professor of Cardiovascular Medicine & Professor of Pharmacology, School of Medicine, University of Pennsylvania, USA)
Dr Peter Ghazal (Director, Scottish Centre for Genomic Technology & Informatics, University of Edinburgh, Scotland)
Prof Stephen O'Rahilly (Department of Medicine & Clinical Biochemistry, Addenbrooke's Hospital, Cambridge, England)
Dr John Sims (Senior Scientific Director, Molecular Immunology, Amgen Corporation, Seattle, Washington, USA)
Dr Hugh Brady (President, University College Dublin, Ireland)

New DMMC Ownership Agreement

Below: introductory speeches from DMMC Chief Executive Officer Dr Pierre Meulien (*left*) and Dr Michael Kamarck, Chair of DMMC Board & Senior VP, Wyeth Biopharma (*right*).

The Minister for Education and Science, Ms Mary Hanafin TD, attended the signing of a new agreement between the three leading medical schools in Ireland which forms a single entity, the Dublin Molecular Medicine Centre, for high level medical research and teaching in Dublin. The agreement, signed on 25 April 2005, extends the ownership of the DMMC from its founding universities, Trinity College Dublin and University College Dublin, to include The Royal College of Surgeons in Ireland as an equal partner. The DMMC was formed with funding from the Higher Education Authority through the Programme for Research in Third Level Institutions (PRTLI) cycle 2 and further developed in cycle 3 through The Programme for Human Genomics in partnership with RCSI.

Below, sitting from left: Dr John Hegarty (Provost, TCD), Mr Michael Horgan (CEO & Registrar, RCSI), Dr Michael Kamarck, Dr Hugh Brady (President, UCD). *Standing from left:* Prof Niall O'Higgins (UCD & President of RCSI), Ms Mary Hanafin, TD (Minister for Education & Science), Dr Pierre Meulien.

The RCSI brings excellent research capabilities, complementing those of UCD and TCD and, through their affiliation with Beaumont hospital, the DMMC can now build real critical mass in clinical research in specific disease areas. RCSI's established expertise in cardiovascular disease, inflammation, neuro-psychiatric disorders and certain cancers, is already being integrated and developed within the Programme for Human Genomics, the first ever programme involving all three institutions.

Left: Minister Mary Hanafin at the podium. *Below, from left*: Prof Brian Harvey (Director, RCSI Research Institute), Prof Ian Robertson (Dean of Research, TCD), and Prof John Hegarty in discussion. *Bottom*: the audience after the signing.

The gap between the recent massive increase in scientific knowledge and our ability to translate that knowledge into patient benefit has never been wider and the DMMC gives us an opportunity to address this promptly and collectively. Indeed, the DMMC provides the perfect neutral platform on which cross-institutional multi-disciplinary research, education and training programmes can be built. The success of these initiatives will be key in bringing new technology, knowledge and treatments to the clinic. The creation of this single community facilitates collaborations with like-minded centres in Europe and in North America. As a small country, Ireland's contributions to biomedical breakthroughs will be most effective through collaborative efforts.

The DMMC has already been a catalyst for ambitious programmes in several areas and in the process has contributed to the breaking down of institutional barriers. We now look forward to operating at an even higher level, building more disease specific consortia where research and education are developed in parallel.

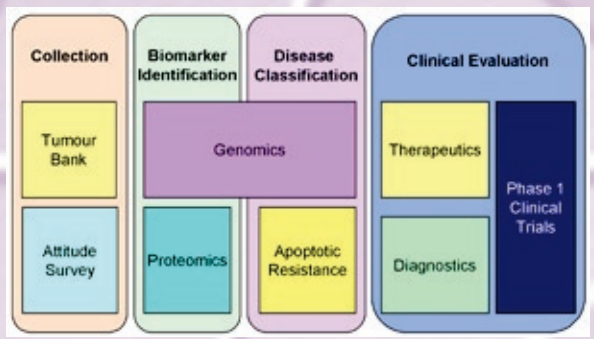
Research: Cancer

PROSTATE CANCER RESEARCH CONSORTIUM

Over 35 fundamental and clinical scientists from two universities and five hospitals

Created in 2003, the Prostate Cancer Research Consortium comprises investigators from TCD, UCD, and five hospitals (Adelaide & Meath, Mater Misericordiae, St. Vincent's, St. James's and St. Luke's). The collaboration represents a unique combination of surgeons, pathologists, research nurses and research scientists. The consortium was seeded through a research grant from the Irish Cancer Society and assembles resources worth over €7.5 million in a focused effort to improve detection and treatment of prostate cancer. The research programme aims to:

1. Establish a prostate cancer tumour bank and evaluate patient attitudes to tumour banking.
2. Examine novel biomarkers in early detection and prognosis of prostate cancer.
3. Classify disease stage and disease progression phenotypes.
4. Evaluate targeted therapy in pre-clinical and potential Phase I/II studies.



Objective 1. The consortium is collecting blood and urine from patients with early stage, locally advanced and metastatic disease. Tissue is also being collected from patients who are undergoing radical prostatectomy or transurethral resection. Ethical approval has been secured at all four hospitals, a common collection protocol agreed, and sampling has commenced at the Mater & St James's Hospitals. The collection is held within the DMMC Genome Resource Units and once the collection system has been validated it will be extended to include other surgical centres throughout Ireland. A patient survey is being undertaken to assess attitudes to tumour banking and gene profiling.

Objective 2. Using the biocollection to evaluate existing biomarkers of prostate cancer and identify & validate novel markers. Gene-specific DNA hypermethylation may be a characteristic signature of early stage and more aggressive later stage prostate cancer. The consortium has developed *in silico* methods to identify novel targets of DNA hypermethylation, which are being tested as potential biomarkers in collaboration with the NCI. 2-D gel electrophoresis and quantitative analysis are being applied to the serum and urine of a selected patient cohort with a view to identifying distinctive protein signatures. Signatures identified and validated will also be used to assess treatment response in prostate cancer clinical trials.

From left: Dr William Watson (UCD Conway Institute) and Prof Mark Lawler (Institute of Molecular Medicine, TCD & St James's Hospital).

Objective 3. Others have successfully used gene chip analysis to implicate candidate genes in the progression of prostate cancer in small groups of genetically diverse patients using heterogeneous tissue samples. The Consortium has developed cell culture techniques with no contaminating normal basal epithelial or stromal cells. Given this expertise and the relatively tight genetic pool of the Irish population, the consortium believes that it can develop a molecular classification of disease stage and progression. Bioinformatic analysis is being undertaken on a number of recently published gene datasets, including the Inhibitors of Apoptosis Proteins (IAP's) gene class.

Objective 4. Development of novel therapies for treating prostate cancer has to date been largely unsuccessful due to the limited understanding of disease progression/treatment failure and the lack of suitable cell lines. Primary cell lines representing different disease stages isolated by the consortium are being used to test several novel therapeutic approaches.

(a) RNA interference for the inhibition of specific gene products.

(b) Delivery of specific genes to increase susceptibility to existing therapies. Vectors expressing the cytosine deaminase gene under the control of a tissue-specific promoter that is selectively upregulated in prostate cancer have been generated, introduced into prostate cancer cell lines and specific killing induced by the action of 5-fluorocytosine.

(c) Small molecule agents that Interfere with Cell Death Pathways. A novel series of pyrrolo-1,5-benzoxazepine compounds that induce apoptotic cell death in a variety of human cancer lines appear to bypass the Bcl-2-mediated resistance to apoptosis that is associated with prostate cancer by phosphorylating and thus inactivating anti-apoptotic proteins. This hypothesis will be tested in a panel of prostate cancer lines. Also, the consortium has demonstrated that Diethylmaleate plays a crucial role in the regulation of pro-apoptotic caspases. In a strategy to develop agents that increase sensitivity to chemotherapy and radiotherapy, a series of DEM analogues have been synthesised and are being tested for their ability to induce apoptosis.

IRISH CERVICAL SCREENING RESEARCH CONSORTIUM

Investigators from seven academic institutions and eight hospitals, in partnership with eight biotechnology companies

Below: Prof John O'Leary (Coombe & St James's Hospitals).

Approximately 85 Irish women die each year from cervical cancer – almost twice the EU average. This high mortality rate is almost certainly due to the absence of a national cervical screening programme and poor awareness among women of the disease. Perhaps the greatest tragedy is that the disease is entirely preventable and that screening strategies have been shown to work in other countries. Many groups are lobbying for the establishment of a screening programme in Ireland and the biomedical research community is also keen to play its part in the fight against cervical cancer.

The *Irish Cervical Screening Research Consortium* aims to advance high quality peer-reviewed research programmes that provide the best possible information and guidance on the delivery of cervical screening services to Irish women. The consortium has secured a research grant from the Health Research Board under its Health Services Research & Development Awards 2005 for a 5 year programme. Led by Prof John O'Leary (Coombe & St James's Hospitals), the consortium members share the following strategic objectives:

Advance high quality peer-reviewed research programmes that provide the best possible information and guidance on the delivery of cervical screening services to Irish women.

- Critically assess the economic and scientific effectiveness of manual and automated cytoscreening regimes to ensure that the optimum screening test procedures are deployed across Irish cytology laboratories.
- Create a reference bank of digitised images such that virtual slides can be employed by Irish laboratories to establish the highest quality assurance standards and achieve internationally recognised laboratory accreditation.
- Undertake detailed surveys among Irish women to provide knowledge of attitudes towards cervical screening and Human Papilloma Virus oncogenic viral testing.
- Evaluate in controlled clinical studies alternative disease management algorithms and regimes to ensure that the most appropriate intervention is made for specific patient sub-populations.
- Examine the effectiveness of HPV vaccination programmes with respect to differences in immune response by individual patients.
- Advance the development of a biochip diagnostic device that can be deployed across Ireland to ensure more effective screening of Irish woman leading to earlier detection and improved management of disease.
- Act as a constructive lobby group to ensure continued support for research into diseases of the cervix and the effective deployment of resources leading to the best possible treatment of patients with cervical cancer.

This grant will allow the appointment of a programme manager to coordinate across 8 individual research programmes as well as a health economist, an epidemiology researcher, a part-time administrator and a part-time co-facilitator. The latter three positions will be appointed at the National Cancer Registry Ireland in Cork and will be essential to addressing lack of public awareness of cervical screening strategies.

Research: Infection, Immunity & Inflammation

The underlying mechanisms of inflammation and their involvement in host-pathogen relationships is the focus of many city-wide programmes that demonstrate how resources are being mobilised across the DMMC and beyond. Chronic infectious diseases such as Tuberculosis and Hepatitis C are the subjects of programmes part-funded through the PHG.

A large consortium involving investigators from UCD/St Vincent's University Hospital, TCD/St James's Hospital and NUI Maynooth under the coordination of Professor Cliona O'Farrelly are studying the mechanisms of immune evasion used by the Hepatitis C virus. These investigators have access to a unique resource; the so-called anti-D cohort of female patients who were exposed to the virus in the 1970's. This cohort has been followed for over 30 years and has resulted in great insights as to the mechanisms underlying chronicity and the host immune response to this infection. Using the technology platforms set up under PRTLI, protein and gene expression signatures of patients undergoing treatment are being obtained in order to understand which molecules are involved in this response. This strategy could lead to the discovery of new prognostic markers of response to therapy. Researchers at the TCD Institute of Molecular Medicine have identified and published in Gastroenterology a new mechanism whereby the Hepatitis C virus interferes with the immune system by paralysing lymphocyte migration.

Dr Joe Keane (a consultant in respiratory medicine at St. James's Hospital, and Principal Investigator at the IMM, TCD) is studying host responses to infection of *Mycobacterium tuberculosis,* the causative agent of TB. When this pathogen enters the host it invades macrophages in the peripheral blood stream. Usually, infected cells respond by undergoing programmed cell death or apoptosis but *M. tuberculosis* has developed strategies to prevent this occurring, thus prolonging the life of its host cell to its own advantage. Dr Keane is collaborating with UCD Conway Institute researcher Dr Paul Moynagh, an expert in inflammatory mechanisms, with the goal of understanding which pathways are activated by virulent *M. tuberculosis* to prevent apoptosis. This year Dr Keane received one of the first *Clinician Scientists Awards* from the Health Research Board, a new grant to support medical consultants to focus on world-class research in areas that will have direct benefits for patient care.

Research on chronic infectious diseases such as TB and Hepatitis C is part-funded through the Programme for Human Genomics

Inflammation also plays a key role in some non-infectious multifactorial diseases that result from an interplay of genetic and environmental factors. Dr Ross McManus, Prof Dermot Kelleher and their research teams based at the TCD Institute of Molecular Medicine have been investigating the genetic basis of two diseases of particular relevance to the Irish population: Inflammatory Bowel Disease (IBD; characterised by a chronic relapsing intestinal inflammation) and Coeliac Disease (an intestinal inflammatory response triggered in susceptible individuals by ingestion of gluten). These investigators have access to one of the largest cohorts of Coeliac Disease patients, allowing powerful study design to identify genes with a role in this immune-mediated disease. The links between mutations in genes responsible for the metabolism of xenobiotic compounds and inflammatory bowel disease are also being investigated. Researchers at IMM led by Ross McManus have identified a disease susceptibility gene PXR for IBD (published in Gastroenterology 2006). This gene is involved in the processing of external toxins by the colonic epithelium. Once again an important gene bank of 422 patients and 350 controls has been the cornerstone of this project. These collections are managed by the TCD component of the DMMC Biobank.

Research: Neuroscience

Work across the city is building biocollections for the neuroscience research community and helping to identify the genes involved in various psychiatric disorders, and in epilepsy.

The Neuropsychiatric Genetics laboratory at the TCD Institute of Molecular Medicine, headed by Prof Michael Gill and led by Dr Aiden Corvin, is the molecular genetics arm of the Neuropsychiatric Genetics Group in TCD that comprises psychiatrists, psychologists, molecular biologists, nurses and statisticians. The goal is to identify genes that cause psychiatric disorders such as schizophrenia, bipolar disorder, attention deficient hyperactivity disorder (ADHD), autism, Alzheimer's disease and depression. The rationale is to gain a better understanding of underlying biological abnormalities that interact with psychosocial and environmental factors in the development and characteristics of these conditions.

Below: Prof Michael Gill (TCD).

Gain a better understanding of the underlying biological abnormalities that interact with psychosocial and environmental factors in the development and characteristics of psychiatric disorders

Funded by the Wellcome Trust, the *Resource for Psychoses Genomics, Ireland* (RPGI) will establish detailed phenotypic information, environmental/demographic information, DNA and cell lines from over 1,200 subjects from the island of Ireland with a major psychotic disorder (principally Schizophrenia or Bipolar Disorder). These conditions have been targeted because, they affect ~2% of the population, have a chronic course, and cause significant morbidity and mortality. Research has identified chromosomal regions containing susceptibility genes for schizophrenia, bipolar disorder, or common to both. Individual gene effects are small and many risk genes combined with environmental risk factors lead to illness. Recently the first few genes have been identified, promising a major step forward in understanding. Investigators at the Neuropsychiatric Genetics Research Group (TCD), and others, have previously demonstrated that many of these genes contribute to schizophrenia susceptibility in the Irish population. This study will allow the collection of significant amounts of data on a large population of patients with psychotic disorders. As the RPGI is a resource this data will be available to local or international researchers who apply to the scientific committee of the RPGI with appropriate ethics approval.

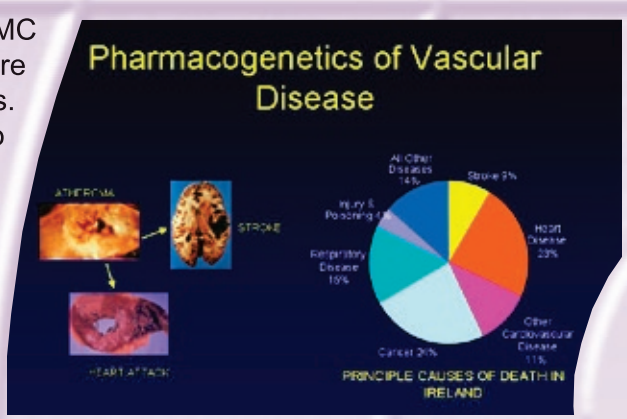
A PHG-funded demonstration project, *Cognitive Genomics of Psychosis*, (Principal Investigator Dr Gary Donohoe (TCD), collaborating with Prof Michael Gill), investigates the potential relationships between candidate genes for schizophrenia and cognitive function. Core features of schizophrenia are deficits in attention and memory. This study is investigating whether genes already associated with schizophrenia and with deficits in memory and cognition similarly influence cognitive function in the normal population. In terms of the over-riding goal of the PHG to apply human genomics and proteomics to the study of the pathogenesis, diagnosis and treatment of human disease, this project seeks to elucidate the function of candidate genes in the pathogenesis of schizophrenia and related psychosis at the level of brain function.

The *Epilepsy Pharmacogenomics Programme*, headed by Dr Norman Delanty (RCSI/Beaumont Hospital), aims to identify polymorphisms in key genes which may be involved in: 1) the predisposition to common forms of epilepsy; 2) the response to various types of pharmacological treatments; and 3) the development of important therapy-limiting adverse effects. Within the PHG, the aim of the epilepsy research theme is to use the infrastructure and funding provided to collect comprehensive clinical (phenotypic) and biologic (genotypic) information from patients with common, genetically complex, epilepsy, and to draw associations between single nucleotide polymorphisms in biologically plausible candidate genes and well characterised clinical and radiological endophenotypes.

Research: Cardiovascular

Several trans-institutional projects in cardiovascular diseases are being funded through the Program for Human Genomics and are leading to proposals for incremental funding from other sources. Many of these projects are led by investigators at RCSI/Beaumont Hospital and this reflects both the expertise and a clear priority area for that institution.

Dr Alice Stanton leads one group working on the pharmacogenomics of atherosclerosis. Given the complexity of the interplay between genetic and environmental factors in atherogenesis, the dangers of small studies of the associations of single variables with cardiovascular morbid events are now well recognised. Hence the team has adopted a number of key strategies for probing the pharmacogenetics of atherosclerosis *in vivo* in humans.



As with many of the projects involving DMMC investigators, the success of the studies are dependent on a collection of human samples. The initial focus of the project was thus to secure access to well phenotyped collections containing several thousand samples. Clinical trial populations are of particular interest in this regard because of the amount and quality of the data collected. Dr Stanton's group have subsequently added further characterisation details of these samples including biochemical measurements of vascular function. The group has collected or has access to DNA samples from in excess of 3,000 patients with symptomatic coronary heart disease, 10,000 hypertensive patients, 10,000 patients with diabetes, and 1,000 controls. A series of candidate gene studies are ongoing – testing whether genetic variants of the renin angiotensin system, pro-oxidant proteins, and/or enzymes involved in eicosinoid formation, influence response to the various currently used therapies. Recent novel findings concern significant associations between an ACE2 genetic variant and both blood pressure level and response to a renin angiotensin system blockade.

Dr Stanton has assembled a truly multidisciplinary group which taps into many aspects of the city-wide infrastructure that has been developed through the DMMC. Strong collaborative links have been formed between Dr Stanton's group and the Genetic Epidemiology platform (Profs Paul McKeigue and Helen Colhoun) and the Bioinformatics group (Prof Denis Shields), both in the UCD Conway Institute.

Other Cardiovascular themes include platelet biology where the group of Dr Niamh Moran, working on integrin signaling pathways, has identified a novel integrin-interacting protein, a chloride channel regulator ICln, that regulates integrin activation in the human platelet (Larkin *et al*, 2004). Dr Moran is collaborating with Prof David Foley in Beaumont Hospital to examine altered platelet function in ageing cardiovascular patients and to determine the comparative platelet proteome. Collaborations with Drs Helen Enright and Niamh O'Connell in AMNCH Tallaght Hospital, and with Dr Barry White of the National Centre for Inherited Coagulation Disorders at St James's Hospital to examine genetic disorders of platelet function are in development.

In parallel to these studies Professor Dermot Kenny (Director, Clinical Research Centre, Beaumont Hospital/RCSI) is developing technologies that will be critical in determining modulators of platelet aggregation. Conventional platelet function assays are generally *in vitro* static or aggregation assays using supraphysiological concentrations of platelet agonists and do not take into account the more physiological stimulus of fluid shear present in the vasculature. To address this problem the group has acquired a cone and plate viscometer (RheoStress 600, ThermoHaake, Germany) designed specifically to create physiological shear stresses on fluids (similar to that which platelets are exposed to in the vasculature). This is being used as a tool to study the effect of shear on platelets and its effect on signalling in the platelet.

Technologies

The following technology platforms have matured and developed further in 2005. Most use a collaborative model for access and are the source of many research collaborations across the city. DMMC Courses and various workshops introduce and promote use of these technologies.

RCSI Mass Spectrometry Core

Provides: trace analysis of drugs, drug metabolites and messenger molecules in clinical samples (blood, urine, tissue samples); peptide mapping and tandem-MS (MSMS) peptide sequencing to identify, quantify and characterise individual proteins and proteins in complex mixtures.

Contact: Dr Achim Treumann (atreumann@rcsi.ie)

RCSI Organic Synthesis Core

Equipped to carry out the automated synthesis, isolation and purification of peptides and biologically active compounds.

Contact: Dr Marc Devocelle (mdevocelle@rcsi.ie)

RCSI Centre for Human Proteomics

Application of proteomics technologies to identify proteins, their modifications and their role in disease.

Contact: Prof Jochen Prehn (jprehn@rcsi.ie)

UCD Conway Institute Bioinformatics Laboratory

Projects are in the areas of multiple sequence alignment, analysis of microarray data, identification of human gene promoters, and investigation of the molecular evolution of eukaryotic genomes.

Contact: Prof Des Higgins (des.higgins@ucd.ie)

UCD Conway Institute Histology Core

The Ariol imaging system has specific applications to automatically quantify membraneous, cytoplasmic, and nuclear staining patterns in tissue microarrays and full face sections.

Contact: Dr William Gallagher (william.gallagher@ucd.ie)

UCD Conway Institute Proteome Research Centre

The Proteome Research Centre (PRC) is equipped with state-of-the-art instrumentation and software to support a number of complementary proteomics workflows. Projects include a collaboration with the Prostate Cancer Research Consortium (see page 13).

Contact: Prof Stephen Pennington (stephen.pennington@ucd.ie)

UCD Conway Institute Transcriptomics Core

The facility provides access to core equipment, including Affymetrix GeneChip® technology, spotted microarrays, real time and high-throughput PCR, and automated liquid handling.

Contact: Ms Alison Murphy (alison.murphy@ucd.ie)

TCD IMM High Content Screening & Analysis Core

The Cellomics® KineticScan and the GE INcell analyser system are utilised in defining the function of genes, proteins and other bio-molecules in normal and abnormal cells. This technology is becoming key in many large-scale medical and drug discovery studies.

Contact: Dr Anthony Davies (anthony.davies@tcd.ie)

TCD Transgenic Facility

The small animal specific pathogen-free unit at Trinity College Dublin provides a number of central facilities to the research community for quarantine, re-derivation, micro-injection, and use of embryonic stem cell technology.

Contact: Prof Pete Humphries (pete.humphries@tcd.ie)

Translational Research: Infrastructure

This year, two new Genome Resource Units (GRU's) were completed, joining the RCSI/Beaumont Clinical Research Centre and the IMM Biobanking Facility (TCD) in the rapidly developing city-wide infrastructure for facilitating translational research.

Above, from top: Dr Peter Doran and Dr Seamas Donnelly, GRU Directors.

MATER MISERICORDIAE HOSPITAL GENOME RESOURCE UNIT

Director: Dr Peter Doran

The GRU at the Mater Misericordiae Hospital encompasses a state-of-the-art facility for translational research in molecular medicine. The GRU's goal is to further develop translational medicine infrastructure and expertise.

The key areas in which the GRU operates include:

- Creation of phenotypically well defined bioresources for human genomics research.
- Support and development of molecular research programmes at the hospital.
- Establishment of state-of-the-art infrastructure and facilities for clinical trials and investigations.

The GRU is composed of both a laboratory and a clinical component. The laboratory space, as well as having a fully equipped, operational molecular research facility is also home to the biological material storage facility comprising six –80 ºC freezers. The clinical facility provides interview and procedure rooms for patient contact as part of ongoing research activities.

These infrastructural developments are complemented by a research information management system aimed at the collection and storage, in a rational manner, of both clinical and molecular data pertaining to patients of interest. The aim is to ensure that the highest quality information on patient populations is available for research investigations.

ST VINCENT'S UNIVERSITY HOSPITAL GENOME RESOURCE UNIT

Director: Dr Seamas Donnelly

The GRU at St Vincent's University Hospital provides a 750 m^2 ambulatory care research facility. The facility is physically linked to the existing Education & Research Centre at the hospital to maximise the synergy between clinical scientists on the SVUH campus and bench-based scientists within UCD. In addition, this GRU will form part of a city-wide network of clinical research facilities under the auspices of the DMMC.

The GRU contains clinical investigator suites, an advanced procedure room, a bioinformatics suite, significant laboratory processing space, and a biorepository storage area. The research outpatient facility is expected to be operational by early 2006. Anticipated principal activities include bronchoscopy (plus biopsy, bronchoalveolar lavage), gastroscopy (plus biopsy), colonoscopy (plus biopsy), arthroscopy, bone marrow aspiration (plus biopsy), pulmonary function test (including reversibility, DLCO), blood sampling & collection (including processing of plasma/serum, RNA isolation, DNA isolation), cell & tissue processing, and standard histopathology blocks.

Translational Research: Moving Forward

HRB & DMMC TRANSLATIONAL WORKSHOP

The DMMC in conjunction with the Health Research Board held a highly successful workshop on Translational Research on 13 December 2005. Attended by over 60 delegates, the audience included representatives of many stakeholder groups including patient advocates, clinician scientists, nurses, academic institutions, hospital managers, funding agencies, clinical research organisations, pharmaceutical and informatics companies. The meeting was designed to explore Ireland's position in this emerging field and identify obstacles to further development. A series of short presentations highlighted recent initiatives that have the potential to position Ireland at the forefront of translational research. Breakout discussion groups explored urgent gaps which need to be filled and explored strategies for addressing these deficiencies.

The absence of a large cohort of Research Nurse Specialists was consistently identified as a major obstacle to translational research. Where research nurses exist, patient enrolment and liaison is much improved. The deficiency in this vital resource was traced to the absence of a career track, and insecurity stemming from relatively short term research projects. The small number of Clinician Scientists and their heavy caseloads also militates against participation in research programmes.

The volume of clinical information and characterisation data generated in translational research programmes requires the appointment of data managers and bioinformaticians, together with biostatisticians and epidemiologists. With formal research career structures an issue for all staff types, it was recommended that future government investment include fourth level education initiatives. In addition to the human capital, several infrastructure bottlenecks were identified including pre-clinical resources and dedicated clinical research centres. In Dublin, the Clinical Research Centre at Beaumont Hospital has been complemented with two new ambulatory care research facilities at Mater Misericordiae and St Vincent's University Hospitals (see page 19).

Despite the provisions of the EU Clinical Trials Directive, considerable delays in securing Research Ethics Approval and hence delays in the initiation of clinical trials are being experienced. It was recognised that a research culture needs to be established within the Irish healthcare system to ensure the competent collection and archival of human biological materials consistent with the recent Irish Council for Bioethics guidelines. Proactive communication and increased public awareness are essential if support for clinical research is to be fostered.

Much discussion was given to how the compelling case could be advanced to ensure continued government support for a translational medicine initiative. Several themes were articulated including "*building on NDP investment", "transforming healthcare", "essential for modern medicine",* and *"attracting R&D activity"*. It is hoped that additional workshops will be held in 2006 to build support for a significant government investment in the area of translational medicine. Local support is essential if Ireland is to compete within the forthcoming EU FP7 Innovative Medicines initiative.

This HRB and DMMC Workshop was supported by sponsorship from Hewlett-Packard and Enterprise Ireland Biotechnology Directorate.

DMMC Education & Training

The DMMC Education & Training Programme capitalises on the research and teaching strengths of TCD, UCD, RCSI, and the clinical expertise in the Dublin teaching hospitals to deliver an easily accessible means for researchers to develop their skills and broaden their training in the biosciences with a major emphasis on translational research.

The DMMC Programme is distinct from single institution teaching and learning activities: DMMC offerings are developed as cross-institutional in terms of curriculum and teaching staff, and are freely available to all those with an interest in molecular medicine in all the DMMC partner institutions. The programme is coordinated by DMMC Directorate staff, with advisory input from an Education Group comprising multi-institution representation. Scientific Coordinators are appointed for each course to facilitate programme development.

Short taught *DMMC Courses* (6-35 hours), both lecture-based and practical, supplement postgraduate research degrees in the biosciences and offer career-long training by enabling individuals to take time out from their laboratory research and enter a cross-institutional learning community. Workshops stimulate interaction between disciplines in targeted areas and promote the development and use of shared resources. They take place at various locations in the DMMC parent academic institutions and their affiliated teaching hospitals.

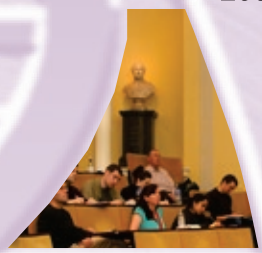
Up-to-date information, including detailed course contents and online application, is available to all via the DMMC website:
www.dmmc.ie/courses

DMMC Courses and Workshops running during the 2005 calendar year ranged from introductory to specialised; technology oriented to disease focussed; with the clear emphasis to provide background knowledge and specific skill-sets for translational research:

Course / Workshop Title	Dates	Venue
Molecular Cell Biology in Action	10 Jan – 21 Feb	UCD Conway Institute
Translational Workshop: Immunity & Lung Disease	28 Jan	UCD Conway Institute
Immunobiology	2 Feb – 23 Mar	Education & Research Centre, St Vincent's University Hospital
Thermodynamics of Membrane Transport Physiology	21 – 25 Feb	RCSI Education & Research Centre, Beaumont Hospital
Microarray Analysis	15 Mar	UCD Conway Institute
Translational Workshop: Breast Cancer	19 May	DMMC Directorate Offices, Newman House
Cancer Biology to Cancer Medicine I	26 – 27 May	Institute of Molecular Medicine, TCD, St James's Hospital
Proteomics: Methods & Applications	2 – 16 Jun	RCSI
Cancer Biology to Cancer Medicine II	7 – 8 Jul	Institute of Molecular Medicine, TCD, St James's Hospital
Molecular Cell Biology in Action	2 Nov – 14 Dec	UCD Conway Institute
Techniques & Strategies in Molecular Medicine	12-15 Dec	RCSI

DMMC Education & Training

At the beginning of 2005, the number of individuals applying for one or more DMMC Courses and Workshops since their inception (in December 2003) stood at 470. During the year this number grew to 879, an increase of 409 new users during 2005. The total of 879 individuals who applied for DMMC Courses and Workshops up to the end of 2005 comprises:



410 from UCD and affiliated hospitals
234 from TCD and affiliated hospitals
161 from RCSI and affiliated hospitals

With the remainder coming from other Dublin institutions and further afield.

The total of 879 includes:

407 PhD Students (basic science and medical backgrounds)
137 Postdoctoral Staff
62 Principal Investigators and Lecturers
48 Clinical Staff & Clinical Research Fellows
38 MSc Students
35 Technicians

Various new DMMC Courses were in development during 2005 (scheduled to run in 2006 and 2007). New features include the opening of selected courses to an international audience, the inclusion of keynote lecturers from outside Ireland, and obtaining sponsorship from relevant companies. The first course to incorporate these elements is *Unravelling Chromatin & the Role of Epigenetics in Disease*, running in April 2006.

Also at the planning stage is a DMMC/Wyeth Pharmaceuticals collaboration *Molecules to Medicines: How Biopharma Delivers* comprising a 1-day lecture course providing an overview from biopharmaceutical drug discovery to commercialisation, followed by a 1-day workshop that probes key issues arising during biopharmaceutical research, development, and manufacturing; all delivered by key Wyeth personnel based in the USA and Ireland.

The value and importance of cross-institutional coordination of elements in postgraduate education was highlighted by various developments throughout 2005. There was mention of DMMC Courses at the Irish Research Council for Science, Engineering and Technology (IRCSET) *Developing Graduate Schools in Ireland Conference* held on 27 September 2005. The conference summary paper (available from www.ircset.ie), discussing 'course-based research education', concluded "It is most unlikely that any one higher education institution would have the trainee numbers or teaching resources to make a suite of such courses viable."

Discussions were initiated at high level with the DMMC parent institutions on the subject of how we integrate DMMC Courses into the developing institutional Graduate Schools and Graduate Programmes. Such programmes require a significant taught course component, and it makes good sense to provide some elements in collaboration via organisations like the DMMC.

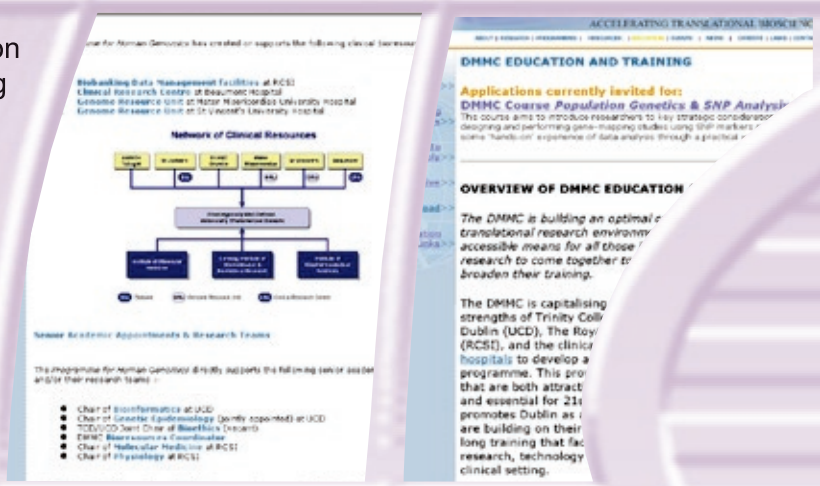
Our international Scientific Advisory Committee (SAC) reported that "the DMMC has had great success in developing educational programmes for postgraduate research in biomedical and translational medicine" and that there was "very strong support from the SAC for the notion that the DMMC could become an increasingly important vehicle for postgraduate education in biomedical science."

Communication: DMMC Website

The DMMC website *www.dmmc.ie* is an interactive means of representing researchers spread across multiple universities and hospitals, and providing them with the latest news, events, education and career opportunities in the field of molecular medicine. It also acts as a worldwide showcase for our efforts in building a broad molecular medicine research community with strategic coordination of collaborative research programmes, technologies and education activities.

Education

These pages allow easy access to details on all DMMC Courses and Workshops, including schedules, abstracts and other course materials (see page 21 for more information). Application to attend courses and workshops is via an easy on-line procedure.



News & Calendar

These pages list news items of relevance to the entire molecular medicine community, and forthcoming events at each of the participant institutions. News items of particular interest and impending events are regularly highlighted on the home page of the DMMC website.

Research

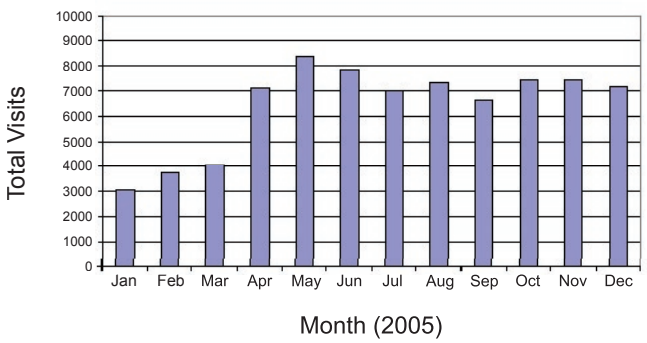
These pages allow users to explore the breadth and depth of research ongoing throughout the DMMC, including contact details and publications of researchers.

Careers

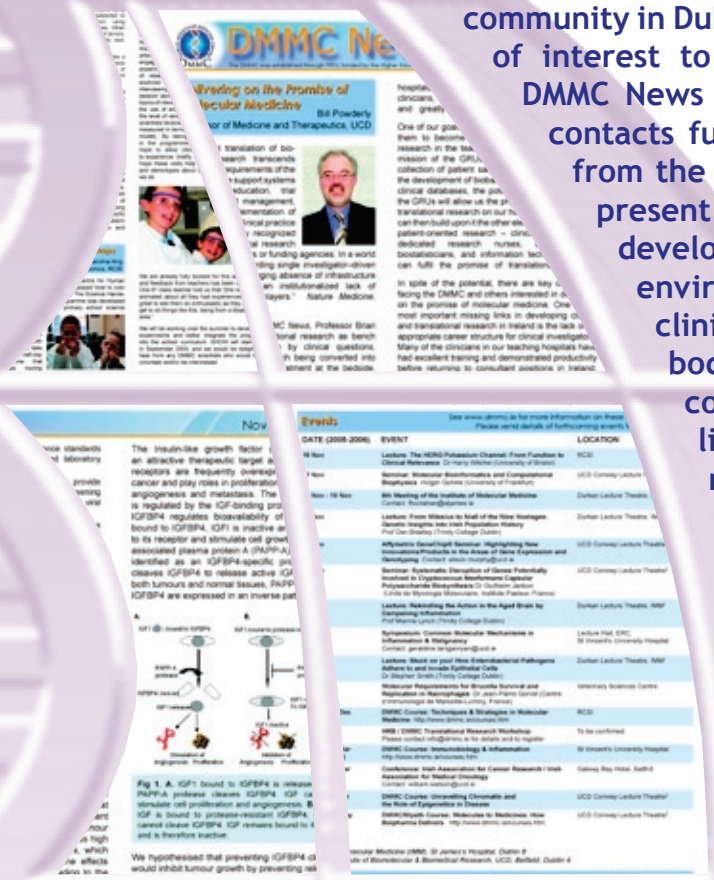
Information on vacancies for a variety of positions within each of the participant institutions are advertised on this page.

Traffic on the DMMC Website

In 2005 traffic on the DMMC website has steadily increased to an average in excess of 7,000 visits per month (7,167 visits / 255,745 hits during December 2005.



Communication: DMMC News



DMMC News is a forum for the molecular medicine research community in Dublin to present the latest developments of interest to a local and international audience. DMMC News is circulated widely in Dublin and to contacts further afield; it is also available to all from the DMMC website. It is an opportunity to present research news, in the context of the developing cross-institutional collaborative environment, to fellow scientists and clinicians, funding agencies, government bodies, and the public. DMMC News also contains reviews of past events and listings of forthcoming events (seminars, meetings, courses and workshops).

The DMMC Directorate published three issues of DMMC News in 2005, (in February, June and November). Articles and reports included:

- Collaborative Research into Hepatitis C
- World Congress on Psychiatric Genetics
- Metabolomics in Nutrition Workshop
- St Vincent's University Hospital Research Symposium
- Delivering on the Promise of Molecular Medicine
- Cancer 2005 & Irish Association for Cancer Research Meetings
- DMMC Translational Workshop: Immunity & Lung Disease
- Research Update on Oesophageal Cancer
- Transforming Translational Research in Ireland
- UCD Conway Institute Festival of Research
- New Trans-Institutional Collaborations
- *Research Update*: Development of Protease-Resistant IGFBP4 as Therapy for Breast Cancer
- Collaborative Biobanking & Translational Research
- UCD Conway Institute at the BA Festival of Science

Financial Report

OPERATING BUDGET

Table 1 ***Recurrent & Capital Budget by Institution*** (€,000)

	OPERATING BUDGETS (€ '000)			
Recurrent Budget	**RCSI**	**TCD**	**UCD**	**Total**
Dublin Molecular Medicine Centre (PRTLI Cycle 2)		3,333	2,748	6,081
Programme for Human Genomics (PRTLI Cycle 3)	12,038	8,328	5,918	26,284
Total Recurrent Budget	***12,038***	***11,661***	***8,666***	***32,365***
Capital Budget				
Dublin Molecular Medicine Centre (PRTLI Cycle 2)		12,139	8,666	20,805
Programme for Human Genomics (PRTLI Cycle 3)	8,569	2,448	7,522	18,539
Total Capital Budget	***8,569***	***14,587***	***16,188***	***39,344***
Total Operating Budget				
Dublin Molecular Medicine Centre (PRTLI Cycle 2)		15,472	11,414	26,886
Programme for Human Genomics (PRTLI Cycle 3)	20,607	10,776	13,440	44,823
Total Operating Budget	***20,607***	***26,248***	***24,854***	***71,709***

EXPENDITURE TO DATE

Table 2 ***Actual Expenditure to December 2005*** (€, 000)

	Actual Expenditure to December 2005 (€ '000)			
Total Expenditure	**RCSI**	**TCD**	**UCD**	**Total**
Recurrent Spend	8,745	7,072	4,603	20,420
Capital Spend	4,671	12,549	15,096	32,316
Total Spend	***13,416***	***19,621***	***19,699***	***52,736***

Table 3 ***Actual Expenditure to December 2005*** (% of Budget)

	Actual Expenditure to December 2005 (% of Budget)			
Total Expenditure %	**RCSI**	**TCD**	**UCD**	**Total**
Recurrent Spend	72.6%	60.6%	53.1%	63.1%
Capital Spend	54.5%	86.0%	93.3%	82.1%
Total Spend %	***65.1%***	***74.8%***	***79.3%***	***73.5%***

Contact Information

DMMC DIRECTORATE

Dublin Molecular Medicine Centre
Newman House
85A St. Stephen's Green
Dublin 2, Ireland

Tel: (+353 1) 716 5560
Fax: (+353 1) 716 7298
Email: info@dmmc.ie
Web: www.dmmc.ie

DMMC Directorate	Staff Name	Telephone	Email Address
Chief Executive	Dr Pierre Meulien	(+353 1) 716 7228	pierre.meulien@dmmc.ie
PA to Chief Executive	Ms Carmel Ni Luanai	(+353 1) 716 5560	carmel.niluanai@dmmc.ie
Programme Manager	Mr Paul Harkin		research@dmmc.ie
Financial Controller	Mr Peter O'Hara	(+353 1) 716 7216	peter.ohara@dmmc.ie
Education & Information Coordinator	Dr Mark Watson	(+353 1) 716 7396	mark.watson@dmmc.ie
DMMC Administrator	Ms Katherine Lacey	(+353 1) 716 5584	katherine.lacey@dmmc.ie

UCD CONWAY INSTITUTE OF BIOMOLECULAR & BIOMEDICAL RESEARCH

University College Dublin
Belfield
Dublin 4

Web: www.ucd.ie/conway

UCD Conway Institute Directorate	Staff Name	Telephone	Email Address
Director	Prof Janet Allen	(+353 1) 716 6782	conway.director@ucd.ie
PA to Director	Ms Bairbre Byrne	(+353 1) 716 6708	bairbre.byrne@ucd.ie
Assistant Director, Building & Technical Services	Mr Michael O'Sullivan	(+353 1) 716 6705	michael.t.osullivan@ucd.ie
Facilities Manager	Mr Eric Leonard	(+353 1) 716 6721	eric.leonard@ucd.ie
Business & Finance Manager	Mr Peter Mangan	(+353 1) 716 6704	peter.mangan@ucd.ie
Communications & Education Officer	Ms Elaine Quinn	(+353 1) 716 6706	elaine.quinn@ucd.ie
Assistant Communications & Education Officer	Ms Grace Sexton	(+353 1) 716 6922	grace.sexton@ucd.ie
Executive Assistant, Communications & Education	Ms Ciara O'Hanlon	(+353 1) 716 6720	ciara.ohanlon@ucd.ie
Information Technology Officer	Mr Paul O'Reilly	(+353 1) 716 6722	paul.oreilly@ucd.ie
Receptionist/Administrative Assistant	Ms Verona Patchell	(+353 1) 716 6700	verona.patchell@ucd.ie

Contact Information

RCSI RESEARCH INSTITUTE

The Royal College of Surgeons in Ireland
123 St Stephen's Green
Dublin 2

Email: resofficeadmin@rcsi.ie
Web: www.rcsi.ie/research2/index.htm

Directorate	Staff Name	Telephone	Email Address
Director	Prof Brian Harvey	(+353 1) 809 3817	bjpharvey@rcsi.ie
Research Programmes Manager	Dr Paola Della Porta	(+353 1) 402 2393	pdellaporta@rcsi.ie
Research Programmes Administrator	Ms Suzanne Sullivan	(+353 1) 402 8605	ssullivan2@rcsi.ie
Business and Finance Manager	Mr Barry McGowan	(+353 1) 402 2478	bmcgowan@rcsi.ie
Education & Outreach Officer	Dr Helen McVeigh	(+353 1) 402 8614	hmcveigh@rcsi.ie

TCD INSTITUTE OF MOLECULAR MEDICINE

Trinity Centre for Health Sciences
St James's Hospital
Dublin 8

Web: www.tcd.ie/IMM

Directorate	Staff Name	Telephone	Email Address
Director	Prof Dermot Kelleher	(+353 1) 608 2100	dermot.kelleher@tcd.ie
PA to Director	Ms Mary Kavanagh	(+353 1) 608 2100	mkvanagh@tcd.ie
Operations & Administration Manager	Ms Tharmarani Raja Thurai	(+353 1) 608 3295	thurait@tcd.ie
Technical Manager	Dr Anne Murphy	(+353 1) 608 3268	amurphy@tcd.ie

Abbreviations & Acronyms

AMNCH	Adelaide & Meath *incorporating the* National Children's Hospital
Beaumont	Beaumont Hospital
Conway	UCD Conway Institute of Biomolecular & Biomedical Research
CRC	Clinical Research Centre
CSCB	Centre for Synthesis and Chemical Biology
DMMC	Dublin Molecular Medicine Centre
EU FP	European Union Framework Plan
GRU	Genome Resource Unit
HEA	Higher Education Authority
HRB	Health Research Board
IMM	Institute of Molecular Medicine
Mater	Mater Misericordiae Hospital
NNN	National Neuroscience Network
NUI	National University of Ireland
OLHSC	Our Lady's Hospital for Sick Children
PCRC	Prostate Cancer Research Consortium
PHG	Programme for Human Genomics
PI	Principal Investigator
PRTLI	Programme for Research in Third Level Institutions
RCSI	Royal College of Surgeons in Ireland
RPGI	Resource for Psychoses Genomics, Ireland
SAC	Scientific Advisory Committee
St James's	St James's Hospital
St Vincent's	St Vincent's University Hospital
SFI	Science Foundation Ireland
TCD	Trinity College Dublin
UCD	University College Dublin

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HEA
Higher Education Authority
An tÚdarás um Ard-Oideachas

NDP
NATIONAL DEVELOPMENT PLAN