Accelerating Translational Biomedical Research

Annual Report 2004

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

Achievements for the Molecular Medicine Community in Dublin include :-

- The opening of over 18,000 m^2 of **New Research Laboratory Facilities** within

  - *Conway Institute of Biomolecular & Biomedical Research*, University College Dublin
  - *Institute of Molecular Medicine*, St James's Hospital & Trinity College Dublin
  - *Institute of Biopharmaceutical Sciences*, Royal College of Surgeons in Ireland.

  These facilities have been largely funded by the Higher Education Authority under its *Programme for Research in Third Level Institutions.*

- Construction has commenced on two **Genome Resource Units** at the Mater Misericordiae Hospital and at St Vincent's University Hospital. These clinician scientist-led facilities will provide an additional 2,500 m^2 of research space and when linked with other facilities around the city have the potential to create a highly specialised clinical research network.

- The establishment of a **Trans-Institutional Research Consortium** in Prostate Cancer that combines academic and clinician scientists from University College Dublin, Trinity College Dublin, Mater Misericordiae Hospital, St Vincent's University Hospital, St James's Hospital and St Luke's Hospital. The *Prostate Cancer Research Consortium* is funded by the Irish Cancer Society and is leveraging DMMC infrastructure to identify improved biomarkers for the disease and to evaluate novel therapeutic strategies.

- Wellcome Trust funding has been secured for a **National Biocollection Resource** for the study of psychoses in Ireland. Led by investigators within the *Institute of Molecular Medicine*, this programme draws on expertise from across the DMMC.

- An Education Strategy Group is developing a comprehensive and flexible **cross-institutional education and training programme** in Molecular Medicine. This curriculum combines the research and teaching strengths of our participant academic institutions and the clinical expertise within their affiliated teaching hospitals with a new administrative structure to ensure citywide dissemination of courses. The efforts of this group have been highly commended by various external review bodies.

HIGHLIGHTS

New technology cores have been developed within the participant institutions including :

- A **Transcriptomics** core at the *Conway Institute of Biomolecular & Biomedical Research* offering a fully integrated real time PCR system, RNA/DNA bioanalyser, gene expression profiling using Affymetrix GeneChip® technology, microarray spotters & readers and a robotic workstation that automates many liquid-handling tasks associated with molecular biology techniques.

- A **Proteomics** platform at the *Institute of Biopharmaceutical Science*s and at the *Conway Institute of Biomolecular & Biomedical Research* offering quantitative and qualitative analysis using SELDI-TOF mass spectrometry & protein chip technology. This platform offers large-scale screening of the proteins of a cell, organism or biological fluid to examine the entire protein complement expressed by a genome.

- The first of its kind in any European research centre, the installation of the Cellomics® **Cell Imaging system** (Cellomics® workstation) at the *Institute of Molecular Medicine* allows our researchers to undertake high throughput high-content cell screening. This resource enables exploration of molecular interactions in living cells under a range of physiological conditions.

- A dedicated **Transgenic** facility enabling the creation of sophisticated disease models using transgene, single cell microinjection and knockout technologies.

- A **Bioinformatics** core with expertise in multiple sequence alignment, the use of multivariate statistical methods for analysis of microarray data sets and molecular evolution (e.g. evolution of promoters, of introns and of noncoding RNA genes).

Several **Senior Academic Appointments** have been made across the participant institutions including :-

- a Chair of Proteomics, a jointly held Chair of Genetic Epidemiology, a Chair of Bioinformatics, a Chair of Molecular Medicine and a Chair of Physiology. Senior consultant staff appointments have been made across the participant institutions.

- A **Bioresource Co-ordination Group** has been constituted with participants representing all the major components within the combined DMMC clinical infrastructure. This group is developing common protocols and establishing core resources that will support the establishment of disease-specific collections across multiple centres.

- As part of a strategy of developing **collaborations with international research groups**, a very successful meeting was held between senior investigators from the *Institut Pasteur*, Paris and from participant groups within the DMMC. Scientists exchanged details of complementary research interests in various areas of immunology & infectious disease. Several follow-up collaborations between investigators have been seeded.

- Under the auspices of the DMMC, the participant institutions have hosted a series of **research symposia and scientific meetings** that have been accessible to the entire DMMC community. These events have raised awareness of the depth and breadth of molecular medicine research across Dublin and help to raise international awareness.

Further momentum has been added to the DMMC vision through the establishment of a 6-person **Central Directorate** under the leadership of Dr Pierre Meulien (Chief Executive, DMMC). Charged with advancing trans-institutional initiatives, this group has :-

- Developed a **Strategic Plan** for the DMMC following wide-ranging consultation with internal and external stakeholders. This document articulates a shared vision of a centre of excellence in molecular medicine in Dublin and establishes agreed objectives designed to build trans-institutional collaboration, advance translational medicine and leverage the combined infrastructure to secure additional funding for research.

- Brokered a **Tripartite Agreement** between our parent academic institutions on the treatment of intellectual property arising from collaborative research.

- Designed and implemented a **DMMC Website** which acts as a central information portal for all molecular medicine activities within the participant institutions.

- Created a **Research Database** to manage contact, research, publication, collaboration details and other professional information on Principal Investigators, Clinicians, Post-Doctoral Fellows, Doctoral students and DMMC Associates. The database provides the Directorate with a practical tool to manage contact with, and direct information to over 400 investigators across 9 different locations. The database also populates research information on the DMMC website.

- Built a cross-institutional education resource, including online application for DMMC Courses and Workshops, accessible to all those in DMMC partner institutions with an interest in molecular medicine research.

TABLE OF CONTENTS

CHAIRMAN'S STATEMENT

The three groups at the heart of modern medicine – academia, the healthcare sector and the biopharmaceutical industry – are facing unprecedented challenges. The human genome revolution presents vast quantities of new molecular information and has spawned impressive high-throughput screening technologies. This knowledge provides new research tools and raises the possibility of developing novel therapeutics and disease biomarkers that treat each patient as an individual. Such opportunity has profound implications for those who develop new therapeutic strategies and for those charged with delivering them in a clinical setting. In parallel, unprecedented demands are being made on each of the three sectors for improved productivity and value for money. It is evident that a new paradigm is urgently required that supports a breadth of research whilst simultaneously improving our ability to translate this new knowledge into tangible medical benefits. As I begin my term as Chairman of the Board of Directors, I am struck by the potential that the *Dublin Molecular Medicine Centre* model offers to academia, to clinical research and to the biopharmaceutical industry.

"The DMMC has the potential to establish international leadership in translational research"

Dr Michael Kamarck
Chairman, DMMC

The Higher Education Authority and the three academic institutions, Trinity College Dublin, University College Dublin and the Royal College of Surgeons in Ireland have created a vehicle that will transform the way translational research is performed in Ireland. At the same time, it offers the critical mass in terms of breadth and depth to allow Ireland to be truly competitive in this post-genomic era. The architects of the DMMC should be commended for their vision of what can and what needs to be done in molecular medicine. Indeed, the DMMC model, enabling strategic alignment of individual strengths, lends itself to many other areas of scientific research and commercial exploitation.

I believe that the DMMC has the potential to establish international leadership in translational research in niche areas where Ireland has both academic research and clinical expertise. To achieve this, Ireland needs to resource academic researchers with the sort of sophisticated new technologies that are now becoming available. These tools will not only advance their

own competitive research but will also allow clinician scientists to define disease relevant molecular phenotypes. As pharmaceutical companies begin exploiting the data arising from the human genome project, biomedical research will move towards more targeted therapeutic intervention. New products will be developed clinically using cohorts of molecularly defined patients stratified into different disease subtypes. Drug trials will be more numerous and in the early stages will require smaller numbers of better-characterised patients. This will necessitate a strong partnership between fundamental researcher, clinician scientist and the pharmaceutical industry.

In short, success in molecular medicine will depend on bringing together many component parts into a single body united by a common strategic vision. The funding agencies, universities and hospitals are building the resources, the challenge of the DMMC is to put these pieces together in a way that is internationally competitive. The network of clinical sites within the DMMC strongly linked to high performance technologies will provide the essential platform to compete in modern medicine research, education and training. It will act as a magnet for industry to interact at the science/clinical interface.

Dr Michael Kamarck
Chairman, DMMC

MESSAGE FROM THE CHIEF EXECUTIVE

Investments of the order of €100 million have allowed the creation of a unique research platform involving three of Ireland's premier medical schools and their affiliated teaching hospitals. This entity is known as the *Dublin Molecular Medicine Centre*.

This investment has already provided in excess of 18,000 M^2 of state-of-the-art laboratory space dedicated to the advancement of molecular medicine in Dublin. It has acted as a magnet in attracting many senior academics and clinician scientists to what amounts to the first attempt to build critical mass in this area in Ireland.

The first two years of activities have seen the building blocks emerge. As we write this first formal annual report, the second phase of development is breaking ground at the Mater Misericordiae Hospital and at St Vincent's University Hospital where two of the DMMC's Genome Resource Units will be located. These facilities will considerably enhance the modern clinical research infrastructure emerging across Dublin.

"The basic building blocks are now in place but we need to move up a gear in order to be internationally competitive."

Dr Pierre Meulien
Chief Executive, DMMC

The *Programme for Human Genomics* (PHG), which has financed these developments, is also funding important cross-institutional collaboration that will over time create the boundary-less operations envisaged by the DMMC's founders. Several enablers have been put in place by the DMMC to facilitate this new way of working, not the least the tri-institutional intellectual property agreement, a web-enabled research database featuring investigators across all participant institutions and the DMMC education programme. The latter mobilises educational resources across the city providing wide access to career-long learning opportunities. Through these initiatives, the DMMC strives to build the community from the bottom up to complement the emerging physical infrastructure.

MESSAGE FROM CEO

The DMMC is currently driving the establishment of a citywide clinical research infrastructure. Disease-specific biocollections created within these facilities will be the cornerstone of our genetic epidemiology programmes. These will provide many scientists with access to tissue collections, a fundamental resource required in the elucidation of molecules involved in disease pathogenesis.

The overall DMMC infrastructure has assisted individual scientists and trans-institutional groups to obtain extramural funding to a level rarely seen in Ireland. Many examples already exist of proposals that have secured research grants from SFI, HRB, EU and Wellcome Trust. We hope that in the future trans-institutional consortia will be formed in specific areas and will use the DMMC platform to build multi-investigator programmes.

2004 also saw the first review by our international Scientific Advisory Committee. The SAC strongly support the DMMC model and were greatly impressed at the level of collaboration being demonstrated amongst the institutions, particularly with the excellent tri-institutional education programme. The SAC highlighted our need to get to another level of operations in order to be internationally competitive ; building on our strengths and focusing on the translational aspects of our work.

The basic building blocks are now in place but we need to move up a gear in order to be internationally competitive. This will entail collaborating at a level never before seen in Ireland. The road will be full of new challenges that we must face together. Our competitive edge is in our ability to network, to break down silos and to synergise in a multidisciplinary fashion that other countries may have difficulty in achieving. We cannot predict the future but we can position ourselves in a way that will maximise our chances of exploiting the opportunities that will come our way. In the words of Arthur Kornberg, winner of the Nobel Prize for Medicine in 1959,

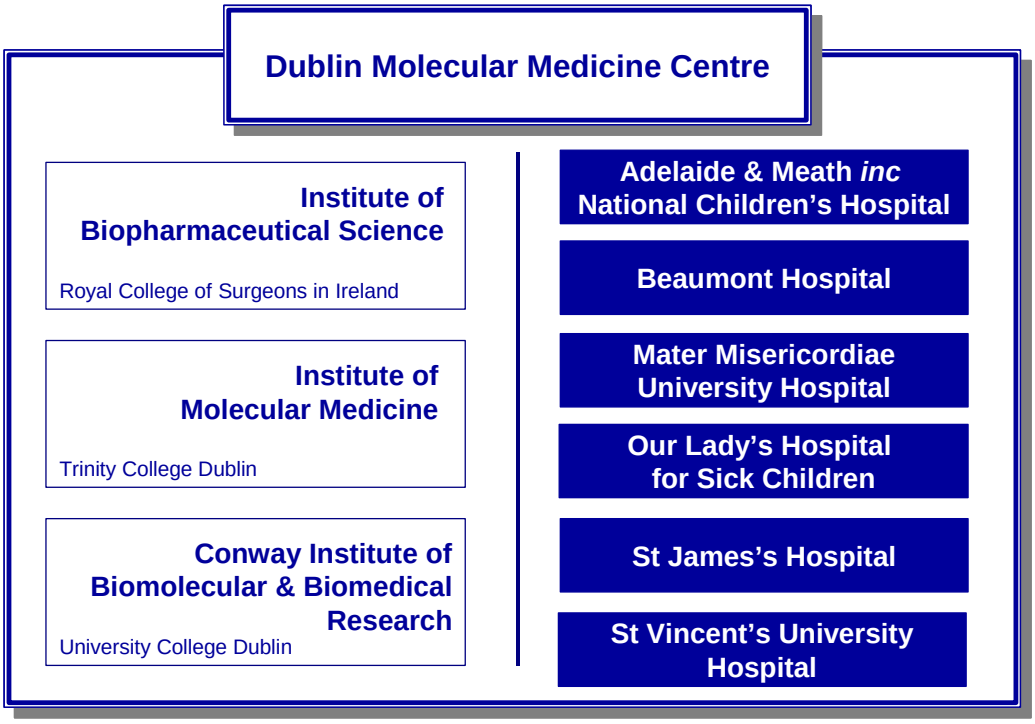
“The future is invented, not predicted.”

Dr Pierre Meulien
Chief Executive, DMMC

OVERVIEW

The *Dublin Molecular Medicine Centre* was established through funding from the Higher Education Authority as a biomedical research partnership between the *Institute of Molecular Medicine* (Trinity College Dublin) and the *Conway Institute of Biomolecular & Biomedical Research* (University College Dublin). The activities of the DMMC are being integrated with complementary research at the Royal College of Surgeons in Ireland.

The DMMC was established to create a critical mass in molecular medicine research in the post genomic era. Recognising that no single institution alone can assemble the necessary resources, the participants elected to enter into a collaborative partnership with the common goal of creating a centre of excellence in molecular medicine in Dublin.



As a result of this trans-institutional partnership, the activities of Dublin's three premier biomedical research institutions and their six affiliated teaching hospitals are being aligned under a common framework designed to facilitate cross-institution collaboration and enhance translational science capability. The DMMC aims to defragment the research community and enable fundamental academic investigators and clinician scientists to collaborate on research programmes regardless of their institutional affiliation.

GOVERNANCE

The *Dublin Molecular Medicine Centre* is a joint venture company created by the Trinity College Dublin and University College Dublin with funding from the Higher Education Authority. Formally incorporated in March 2002, the 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.

Organisational Structure

The DMMC is in essence a virtual organisation since, with the exception of the 6-person Directorate, all staff are employed by the parent academic institutions or teaching hospitals.

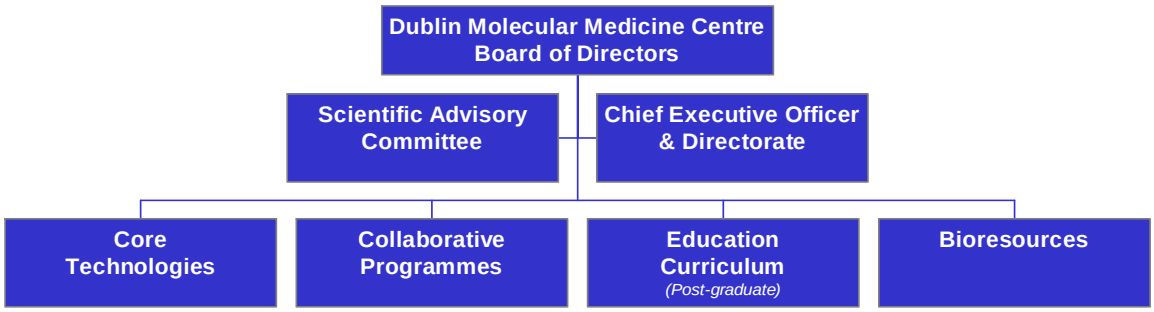


Figure 1 ***Overview of DMMC Governance Structures***

DMMC Board of Directors

A Board of Directors was initially appointed with representation from both parent universities and with independent directors. The membership has evolved to reflect personnel changes within the universities and the integration of RCSI. The current membership of the Board of Directors is detailed in Figure 2.

Scientific Advisory Committee

A *Scientific Advisory Committee* has been created to provide independent and objective critique of the strategic direction and the scientific excellence of the DMMC and its constituent research institutions. The current composition of the *Scientific Advisory Committee* is summarised on Page 14.

Executive Function

The Board has appointed Mr John Coman, Corporate & Legal Affairs Secretary, UCD as Company Secretary and Dr Pierre Meulien as Chief Executive Officer. Dr Meulien has recruited a 6-person Directorate team that includes a Senior Executive Assistant, a Financial Controller, a Programme Manager, an Education & Information Co-ordinator and an Education Administration Assistant. The Directorate provides a focal point for trans-institutional activities and works in close co-operation 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 trans-institutional educational resources.

BOARD OF DIRECTORS

as at 31st December 2004

Chairman

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

Directors

Prof Brian Harvey
Professor of Molecular Medicine
Director, Institute of Biopharmaceutical Sciences,
Royal College of Surgeons in Ireland

Mr Michael Gleeson
Secretary to the College
Trinity College Dublin

Prof Dermot Kelleher
Professor of Clinical Medicine
Director, Institute of Molecular Medicine
Trinity College Dublin

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

Prof Muiris FitzGerald
Dean of Faculty of Medicine
University College Dublin

BOARD OF DIRECTORS

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

Mr Frank Kenny
Founding Partner
Delta Partners

Mr Ronan O'Caoimh
Chief Executive Officer
Trinity Biotech

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

Prof Ian Robertson
Dean of Research
Director, Trinity College Institute of Neuroscience
Trinity College Dublin

Company Secretary
Mr John Coman
Corporate & Legal Affairs Secretary
University College Dublin

SCIENTIFIC ADVISORY COMMITTEE

Professor Martin Carey
Professor of Medicine and Professor of Health Sciences & Technology
Brigham and Women's Hospital and Harvard Medical School, Boston, USA

Professor Gordon Duff
Professor of Molecular Medicine
University of Sheffield, England

Professor Garret 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

Professor Stephen O'Rahilly
Professor of Clinical Biochemistry,
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, Dublin, Ireland

(Left to Right) : Dr Hugh Brady, Dr John Sims, Prof Gordon Duff, Prof Garret FitzGerald, Dr Peter Ghazal, Prof Stephen O'Rahilly, Prof Martin Carey

STRATEGIC PLAN

Abstracted from DMMC Strategic Plan in October 2003.

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 focused research partnership that respects the diversity & tradition of its constituent institutions while embracing their unique strengths & capabilities. The DMMC will embrace new developments and will position Dublin as an internationally recognised centre of excellence in molecular medicine by 2010.

Mission Statement

DMMC will accelerate translational bioscience by:

1. Creating trans-institutional research clusters with focused 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 bio-pharmaceutical 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

DMMC believes that achievement of these objectives will result in :-

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

RESEARCH INSTITUTIONS

Conway Institute of Biomolecular & Biomedical Research, University College Dublin

Located at University College Dublin, the *Conway Institute of Biomolecular and Biomedical Research* is one of Ireland's premier biomedical research facilities. The institute focuses on how individual biological molecules contribute to the normal operation of our cells and organs, and how these are disrupted by disease. This knowledge contributes to a detailed understanding of the causes and effects of disease, leading to simpler and more reliable diagnostic tests, and more effective treatments for human and animal disorders.

Funded under the *Programme for Research in Third-Level Institutions,* this €90 million Institute has created a critical mass of researchers collaborating across traditional faculty and departmental boundaries. Initially created to mobilise multi-disciplinary biomolecular and biomedical research at UCD, the *Conway Institute of Biomolecular & Biomedical Research* has developed in partnership with Trinity College Dublin and the Royal College of Surgeons in Ireland to create two trans-institutional multi-disciplinary research collaborations in the *Dublin Molecular Medicine Centre* and the *Centre for Synthesis and Chemical Biology*.

Officially opened in September 2003 by An Tánaiste, Mary Harney, recent developments at the 11,300 m^2 institute include the establishment of a bioinformatics core led by Prof. Des Higgins and the launch of the *Conway Proteome Research Centre* under the stewardship of Prof. Stephen Pennington. This centre facilitates the study of the range of proteins coded by the human genome and investigates how they operate in health and disease. Science Foundation Ireland awarded €7.7 million to the Applied Neurotherapeutics Research Group led by Prof. Ciaran Regan and including other researchers from the Conway Institute, Trinity College Dublin and the Neuroscience Discovery Group of Wyeth Research. In what is the most comprehensive study of it's kind in the state, this cluster of scientists from academia and industry are investigating treatments of neurological disorders such as Alzheimer's disease, schizophrenia, and depression. The Conway Institute is also a partner in the inter-institutional *National Neuroscience Networ*k, funded under PRTLI.

There are currently 128 Conway investigators and their research teams working within the Institute and in affiliated centres and hospital sites. Research at the Conway Institute is organised into three interactive multi-disciplinary centres; Conway Synthesis & Chemical Biology, Conway Integrative Biology, Conway Molecular Medicine. Collaborative research

across the 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.

Conway Institute of Biomolecular & Biomedical Research

The innovative design of the Conway Institute building contributes to promoting interaction between research groups by virtue of its large, open-plan research laboratories with shared support facilities. Conway investigators and their staff have access to high value, specialised equipment through the core technology programme. A number of technologies are centrally located, properly maintained and managed by a cohort of technical staff who provide support to Conway researchers. The building houses a 128-person conference theatre and specialist research laboratories including transgenic and high-field Nuclear Magnetic Resonance facilities. Undergraduate teaching facilities, incorporating laboratories and classrooms, form an integral part of the new building ensuring that students are embedded in the research environment from a very early stage and that Conway Institute graduates are well equipped for careers in the expanding knowledge-based bioindustry and healthcare sectors.

Institute of Biopharmaceutical Science, Royal College of Surgeons in Ireland

The *Institute of Biopharmaceutical Sciences* (IBS) at the Royal College of Surgeons in Ireland was created in 1999 with funding from the Higher Education Authority under Cycle 1 of its PRTLI programme. This institute has developed from long-standing research interest in pharmacogenetics within the RCSI.

Research Strategy

While therapeutics today is based on a very few drugs directed at just 300-400 targets, the sequencing of the human genome has revealed 30,000-40,000 human genes, encoding up to a quarter of a million potential drug targets. This opens the potential for an era of directed drug discovery that will see thousands of new compounds developed annually. Common genetic variations in genes may predict patients who will develop an end-point in a clinical trial or who cannot respond to a drug, perhaps due to a defect in the drug target. Knowledge of such genetic polymorphisms may also help exclude patients likely to develop a side effect of a drug. Clinical trials represent the main factor adding to the cost and time involved in bringing a new drug to market. Hence pharmacogenetic studies will be vital to allow the full benefit of advances in molecular medicine to be harnessed. Prior identification of patients likely to suffer an end-point would not only allow the size and cost of studies to be greatly reduced, but also only expose to the drug those patients most likely to benefit.

The research strategy of the IBS is encompassed in its stated mission that directs towards the 'integration of basic and clinical sciences towards a better understanding of how drugs work in man'. To deliver on this objective, the Institute of Biopharmaceutical Science is

- Building core technology facilities in support of research programmes
- Fostering research programmes that integrate technology and biology

Research Infrastructure

Key research infrastructure at the *RCSI* developed or supported by the IBS includes :-

- Biomedical research facilities housing bioinformatics, mass spectrometry & proteomics
- Centre for Advanced Drug Delivery
- Centre for Human Proteomics
- School of Pharmacy
- Clinical Research Centre at Beaumont Hospital

The IBS has developed a Strategic Plan to foster translational research through PHG-DMMC activity and to align future research programmes with the RCSI Strategic Plan 2004-2009.

Clinical Research Centre

The Clinical Research Centre (CRC) at Beaumont Hospital uniquely combines dedicated research beds with laboratories equipped for cell and molecular biology, allowing a vertically integrated bench-to-bedside approach, in line with the mission of the IBS. The CRC is committed to bringing together academic scientists, clinical researchers, and the commercial sector, in order to better understand how drugs work in man, and to develop life-enhancing therapies through clinical trials and basic research.

The CRC, for the first time in Ireland, provides the resources to perform complex clinical investigations. Included in the CRC's 15,000 sq ft of research space are overnight and day beds, out-patient suites and a state-of-the-art procedure room. A computerised clinical research management system allows the generation of electronic databases and the direct entry of biometric and laboratory information. The laboratories include facilities for viral vector development designed to support Gene Therapy Programmes in two areas, cystic fibrosis and cardiovascular disease. Since opening in July 2000, over 2,600 patients have been involved in studies at the CRC, including investigations of lung and colon cancer, epilepsy, Parkinson's Disease and Motor Neurone Disease.

Institute of Biopharmaceutical Science, RCSI

Institute of Molecular Medicine, Trinity College Dublin

The *Institute of Molecular Medicine* (IMM) is situated within a modern health research centre, the *Trinity College Centre for Health Sciences* on the St James's Hospital campus. Opened in November 2003, the IMM building comprises approximately 4,500m^2 floor space and is currently home to 130 investigators focused on multidisciplinary research into the molecular basis of human disease.

Principal research within the IMM includes :-

- Cancer
- Immunology & Infection
- Cell Signalling & Migration
- Thrombosis & Haemostasis
- Nutrigenomics
- Vitamin Research
- Neuropsychiatric Genetics

The *Institute of Molecular Medicine* is funded by the *Programme for Research in Third Level Institutions* programme as a centre for collaborative molecular medicine research and provides a major contribution to graduate education in the life sciences.

The *Institute of Molecular Medicine* contains several technology resources including dedicated biobank, proteomics, imaging and molecular histopathology facilities. The Biobank has established best practice procedures for collection, extraction, storage and distribution of biological material from 'normal donors' for use in case-control studies. The Biobank will serve as the main processing and extraction terminus for a number of biological research collections including the *Resource for Psychoses Genomics Ireland*.

The IMM in collaboration with the DMMC aims to fuel Irish drug discovery and biotechnology ventures, and attract pharmaceutical contract R & D research to Ireland. An Enterprise Ireland grant has been awarded to develop a bio-incubator facility on this site, which will permit rapid translation of the results of bench science to development of products for use in the diagnosis and treatment of disease.

Through the *Institute of Molecular Medicine,* the DMMC also supports the maintenance of the National Transgene Unit situated on the main Trinity College Dublin campus. This facility, run by Professor Peter Humphries, provides transgenic and knockout models necessary for the validation of gene association findings.

CLINICAL RESEARCH FACILITIES

Dublin's six teaching hospitals are geographically distributed around the city with two facilities each on the north, south and west sides of the city. These hospitals provide combined Accident & Emergency coverage for the metropolis. In addition to providing healthcare services to the 1.3 million people within the eastern regional area, they provide Regional and National specialities for patients suffering from certain serious diseases. Each of the hospitals are affiliated to participant academic institutions within the DMMC.

Adelaide & Meath *incorporating the* National Children's Hospital, Tallaght

Location :	South-West Dublin
Academic Affiliation :	Trinity College Dublin
Brief History :	The £140 million acute hospital was opened in June 1998 on a 35-acre greenfield site following amalgamation and closure of existing city centre hospitals.
Catchment Area :	South Dublin, West Wicklow and parts of Co. Kildare.
Specialisms :	National Urology Centre Regional Dialysis Centre Regional Orthopaedic Trauma Centre
No. of Beds :	600 beds

Beaumont Hospital

Location :	North Dublin
Academic Affiliation :	Royal College of Surgeons in Ireland
Brief History :	This major acute hospital was opened in November 1987 following the amalgamation of two older Dublin hospitals.
Catchment Area :	Approximately 250,000 people in North Dublin
Specialisms :	Cardiology, Gastroenterology, Respiratory Medicine Endocrinology, Vascular and Thoracic Surgery, Ear Nose and Throat Surgery, Ophthalmology, Ano-Rectal Surgery, Orthopaedics, Gynaecology and Cochlear Implantation
No. of Beds :	620
Research Centres :	Clinical Research Centre

Our Lady's Hospital for Sick Children, Crumlin

Location :	South Dublin
Academic Affiliations :	Royal College of Surgeons in Ireland Trinity College Dublin University College Dublin
Brief Description :	Ireland's largest paediatric hospital was built on its 15-acre site in 1956. It has national responsibility for the majority of paediatric tertiary care services and medical research into childhood illnesses.
Catchment Area :	National
Specialisms :	Accident & Emergency including a Burns Unit, Dermatology, Gastroenterology, Haematology, Radiology and Oncology, Infectious Diseases, Intensive Care, Neurology, Respirology & Cystic Fibrosis.
No. of Beds :	250 beds
Research Centres :	National Centre for Medical Genetics

Mater Misericordiae University Hospital

Location :	North Dublin
Academic Affiliations :	University College Dublin
Brief Description :	Founded in 1861 by the Sisters of Mercy on a 15-acre site, this tertiary acute hospital is the national referral centre for cardiothoracic surgery and spinal injuries. Ireland's first heart/lung transplant unit was opened in March 2004. It is the location of one of two National Breast Cancer Screening centres. Significant campus redevelopment will see it incorporate the Children's Hospital at Temple Street.
Catchment Area :	North inner city of Dublin ; National referrals
Specialisms :	Accident & Emergency, Cardiothoracic, Orthopaedic/ Spinal, Vascular plastic, ENT and Maxillo Facial surgeries, Endocrinology and Diabetes, Infectious Diseases, Ophthalmology, Orthopaedics, Gastro-Enterology, Gynaecology and Child Psychiatry.
No. of Beds :	> 500 beds
Research Centres :	A 1,000m^2 Genome Resource Unit being built by the DMMC is due for completion in September 2005.

St James's Hospital

Location :	West inner city
Academic Affiliations :	Trinity College Dublin
Brief Description :	Established in 1971, St James's Hospital is the largest acute general hospital in Ireland. It is home to the National Centre for Adult Bone Marrow Transplantation and the National Centre for Hereditary Coagulation Disorders.
Catchment Area :	Dublin inner city ; National referral
Specialisms :	Accident & emergency, cardiovascular & respiratory, diagnostic imaging, gastro-intestinal, gerontology, haematology, general, plastic & reconstructive surgery, burns unit, maxillofacial, orthodontic & orthopaedic surgery, dermatology, endocrinology, genito-urinary medicine, infectious diseases, gynaecology, neurology, ophthalmology, rheumatology, clinical neurophysiology and ENT.
No. of Beds :	> 780 beds
Research Centres :	Institute of Molecular Medicine Trinity College Centre for Health Sciences

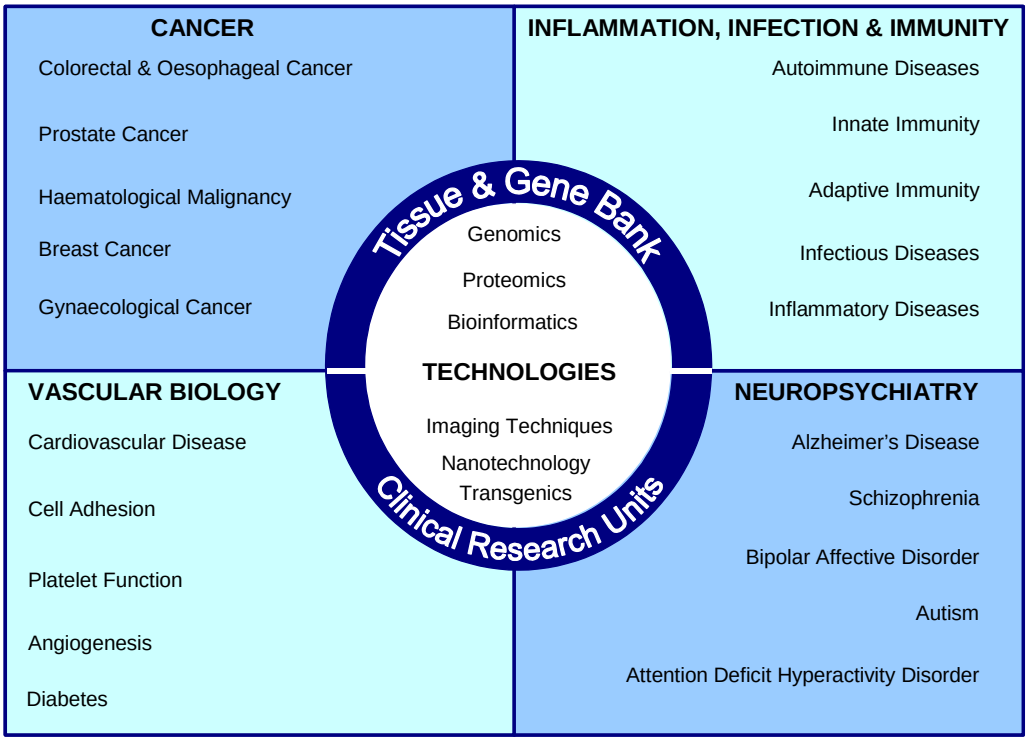
St Vincent's University Hospital

Location :	South Dublin
Academic Affiliations :	University College Dublin
Brief Description :	Founded in 1834 by the Sisters of Charity, the hospital opened at its present location in 1970 and provides local, national and regional inpatient and outpatient care.
Catchment Area :	South Dublin ; National Referral
Specialisms :	Accident & emergency, chronic inflammatory diseases, cancer National referral centre for cystic fibrosis, lung fibrosis, cancer, liver transplantation and inflammatory bowel disease. National Liver Transplant Programme, National Early Arthritis Clinic, Hepatitis C and Endocrinology. One of two permanent screening units in the National Breast Screening Programme
No. of Beds :	480 in-patient beds
Research Centres :	Education & Research Centre DMMC Genome Resource Unit (*Due to open in November 2005)* Centre for Colorectal Cancer Research

RESEARCH PORTFOLIO

The DMMC research portfolio comprises a broad range of genomic, proteomic and transcriptomic investigations conducted within the constituent institutions. These investigations are not static hypotheses but rather are continuously evolving. In the same way, the extent to which they are executed by individual investigator or institution or by trans-institutional collaboration is continuously changing.

The DMMC research portfolio can be summarised as investigations into four principal disease areas and the development of enabling resources and technologies.



This report concentrates on the collaborative actions associated with the combined molecular medicine research portfolio. A detailed description of individual research hypotheses or expertise is beyond the scope of this document. Further information on individual investigators can be found at www.dmmc.ie.

SELECTED COLLABORATIVE PROGRAMMES

PROGRAMME FOR HUMAN GENOMICS

The *Programme for Human Genomics* (PHG) is a multi-component trans-institutional programme led by the Royal College of Surgeons in Ireland in collaboration with the DMMC. A total budget of €45 million was awarded over 5 years by the Higher Education Authority (HEA) to develop a citywide infrastructure platform. This grant represents the largest single award ever made by the HEA to the third level sector. It aims to resource the participant institutions such that they can capitalise on recent advances in proteomic and genomic technologies with component resources each directed towards specific disease areas.

Component Elements	Disease Areas
o Research Programmes	o Cancer
o Core Technologies	o Cardio/Renal Inflammation
o Bioresources	o Host Defence & Immunity
o Senior Staff Appointments	o Neuropsychiatric Disorders
o Education Curriculum	

These activities are being undertaken within RCSI, TCD, UCD and their affiliated hospitals. The *Programme for Human Genomics* aims to establish Dublin as a Centre of Excellence in human genomic and proteomic research through a collaborative partnership of the *Dublin Molecular Medicine Centre* and the *Biopharmaceutical Science Network.*

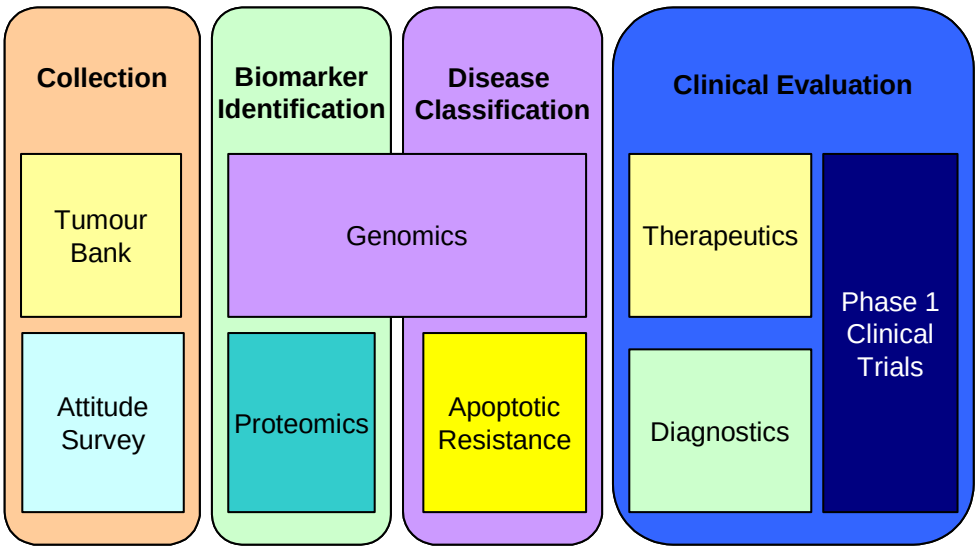
The *Programme for Human Genomics* will apply human genomic & proteomic expertise to advance our understanding of the aetiology, pathogenesis & treatment of commonly acquired human disease. The PHG will seek to characterise the genetics of common Irish diseases, to transfer this knowledge rapidly to the research community and to develop a new generation of scientific leaders in biomedical research & technology. This will be achieved by:

- Integrating our leading researchers into specific **research programmes** focusing on common and relevant areas of human diseases and therapeutic challenges
- Building a **portfolio of enabling technologies** that are state-of-the-art, accessible to all researchers and which support strategically important research
- Establishing a **targeted bioresource** of genes & phenotypic information, supported by data management & genetic epidemiology that allows the evaluation of specific research hypotheses.
- Developing innovative & collaborative educational initiatives in molecular medicine at both undergraduate & postgraduate levels.

PROSTATE CANCER RESEARCH CONSORTIUM

Created in October 2003, the Prostate Cancer Research Consortium comprises 22 principal investigators from two universities (TCD & UCD) and four hospitals (Mater Misericordiae, St Vincent's, St James's and St Luke's) with three year funding from the Irish Cancer Society. The research programme aims to :-

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



Tumour Bank

The consortium is collecting blood and urine from patients with early stage, locally advanced & metastatic disease and tissue from patients who are undergoing radical prostatectomy or transurethral resection. Tumour classification by local pathologists is confirmed by a review panel of three consultant pathologists. A technique has been developed to securely separate malignant cells from surrounding benign material.

Patient Attitudes

A survey to assess patient attitudes to tumour banking and gene profiling will help inform the clinical research community about attitudes and extent of participation amongst Irish males.

Biomarker Identification

It may be possible to use genomic and proteomic analyses to identify characteristic disease signatures. For example, the consortium is examining gene-specific DNA hypermethylation that may be a characteristic signature of early stage and more aggressive later stage prostate cancer. Novel candidate genes are being investigated in collaboration with the National Cancer Institute (US). Surface-enhanced laser desorption ionization time-of-flight mass spectrometry (SELDI-TOF) will be applied to the serum and urine of a selected patient cohort with a view to identifying distinctive protein signatures. The resulting signatures will then be tested in the remaining collections as a marker of early disease, disease progression and to assess treatment response in prostate cancer clinical trials.

Disease Classification

Given 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. Real time PCR on RNA isolated from primary cultures demonstrates increased IAP expression in the diseased state. The androgen receptor represents an important target in Prostate Cancer. Differences have been observed in CAG repeat length number in the androgen receptor (AR) gene in matched androgen dependent and independent cell lines. The consortium will next evaluate repeat length number variation in retrospective material from patients who have shown evidence of progression.

Novel Therapeutic Strategies

The primary cell lines representing different disease stages isolated by the consortium will be used to test three novel therapeutic approaches.

- RNA Interference for the Inhibition of Specific Gene Products
- Gene Delivery of Specific Genes to Increase Susceptibility to Existing Therapies
- Small molecule agents that Interfere with Cell Death Pathways

RESOURCE FOR PSYCHOSES GENOMICS, IRELAND

Funded by the Wellcome Trust, the *Resource for Psychoses Genomics, Ireland* (RPGI) will establish a resource for the scientific community comprising 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. The underlying biology of psychotic disorders is thought to overlap, but the pathways involved are unknown, existing treatments are only partially effective, and they do not appear to be significantly amenable to environmental modification.

To date, linkage 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 collect detailed clinical information from over 1,200 subjects with psychotic disorders and have access to control DNA samples from 2,000 members of the general population. The investigators envisage that the resource will be used for the following study designs:

- To confirm genetic associations detected in other samples.
- To investigate the relationships between susceptibility genes and their relative contributions to expression of the psychoses phenotype(s).
- Targeted functional candidate gene or pharmacogenetic studies.
- To screen select regions of the genome in high-density linkage disequilibrium (LD) studies. As genotypic data will be returned to the RPGI database, this in turn will become a genotypic resource eventually covering the whole genome.

- To explore the relationship between genotype and specific aspects of phenotype (e.g. course of illness, clinical, neuropsychological or neuropharmacological indices, or treatment response).

- Statistical genetic/bioinformatic studies of the relationships between genes and between genotype and known or suspected environmental indices.

- Genetic studies relating to patterns of LD in comparison to other population samples.

- Functional investigations of genetic associations. Specific variants or combinations of variants identified in silico could be investigated using in vitro cellular assays.

- Epidemiological, clinical, psychological or neuropharmacological studies.

- Prospective studies using this baseline data on illness course, psychological performance, treatment response etc. This will allow prospective analyses on gene: environment and gene: phenotype relationships.

- Subgroup analyses (e.g. first episode studies) allowing subjects with specific genotypes to be targeted (e.g. for neuroendocrinology, imaging or pharmacological studies).

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 to conduct studies such as those listed above.

NUTRIGENOMICS RESEARCH COLLABORATIONS

The Molecular Nutrition Research Group at the *Institute of Molecular Medicine* investigates the interaction between Nutrition and the Human Genome. Whilst it is known that nutrition plays an important role in health and disease, often the cellular and molecular effects of nutrients are not fully understood. In light of the Human Genome Project and the rapid advances in molecular biology, it is essential that these opportunities be applied to nutrition research to progress our understanding of the role of nutrition in health and disease.

The potential scope of research within the context of Nutrigenomics / Molecular Nutrition is enormous and could include

- Genetic determinants of nutrient status, metabolic response and predisposition to diet related diseases (CVD, diabetes, cancer, etc)
- Nutrient regulation of gene expression, genetic determinant of responsiveness to nutritional therapy and/or diet-related disease progression.

Dr Helen Roche and Prof Michael Gibney are co-ordinating a €12.5m EU Sixth Framework Programme Integrated Project (2004-2009), entitled *LIPGEN*, dedicated to investigating the interactions between dietary fat composition, genotype and the metabolic syndrome. A consortium of 25 research laboratories across Europe, *LIPGEN* sets out to provide a truly integrated examination of the interaction of food supply and genes in the metabolic syndrome. In the course of this 5-year project the consortium will seek to :

- Understand how differences in the composition of dietary fat interacts with natural human genetic variation to influence the development of the metabolic syndrome
- Create, using marine algae genes, a seed-oil rich in long chain n-3 polyunsaturated fatty acids (LC n-3 PUFA) known to protect against the metabolic syndrome
- Demonstrate the principles of animal nutrition, by changing the composition of cow milk fat to contain less saturates, less trans fats and more monounsaturated fats.
- Ascertain consumer attitudes to the risks arising from the metabolic syndrome and benefits of introducing new agro-food technologies to combat the disorder
- Examine the economic barriers to introducing new agro-food technologies and the cost of the management of the metabolic syndrome by diet versus by pharmaceutics

- Complete a wide-ranging dissemination programme to: (i) create awareness of the need to integrate diet and genetics in addressing the metabolic syndrome, (ii) create awareness of the potential of new agro-food technologies to help combat the disease and (iii) improve our understanding of the economics and consumer science perspectives linked to both the problem and possible solutions

This group is also a founding member of The European Nutrigenomics Organisation, an EU Framework 6 Network of Excellence that received funding of €17.2m to research links between genomics, nutrition and health research.

IRISH AUTISM GENETICS COLLABORATION

Autism is a complex neurodevelopmental spectrum disorder that affects 1 in 1000 births with devastating social, behavioural and communication consequences. While the causes of autism are not yet understood, it is clear that there is a strong genetic component with the possibility of predisposition and heritability.

Established in 1994, the *National Alliance for Autism Research* is a US parent-led organisation funding strategic research into autism and in the process attracting more than $37 million of additional funds. NAAR in partnership with four US National Institutes has created a large scale genetics collaboration (*Autism Genome Project*) designed to interrogate the human genome for susceptibility genes. This global initiative with over 50 participating academic and research institutes focuses on a collection of approximately 1,200 multiplex families (*i.e. families containing two or more affected children).*

Autism research within the DMMC includes collaborative investigations by scientists from both TCD's Department of Genetics and UCD's Department of Medical Genetics at Our Lady's Hospital for Sick Children, Crumlin. Principal investigators within this *Irish Autism Genetics Collaboration (IAGC)* are Prof Michael Gill & Dr Louise Gallagher (TCD) and Prof Andrew Green & Dr Sean Ennis (UCD, Crumlin). It is a testament to their growing reputation in the field that IAGC have been invited to participate in NAAR's *Autism Genome Project*. The Minister for Health and Children, Mr Micheál Martin formally launched this participation on the 14th June 2004 at the National Centre for Medical Genetics, Crumlin. Recognising the importance of continued funding for both research and support services, the minister pledged his department's support for this initiative.

Minister for Health & Children, Mr Micheál Martin T.D. meets researchers at the National Centre for Medical Genetics, Crumlin.

EMERGING COLLABORATIONS

In addition to the successfully funded collaborations, various combinations of DMMC investigators have combined over the past two years to build a series of research collaboration proposals. These, including initiatives under development, combine researchers and resources from across a variety of participant institutions. While funding has not yet been secured for these initiatives, they represent areas where we believe that the DMMC can bring a collective expertise and include :-

- Breast Cancer
- Colorectal Cancer
- Computational Biology
- Diabetes, Obesity & Metabolic Syndrome
- Epilepsy
- Gastro-Intestinal Cancer
- Hepatitis C
- Inflammation & Host Defense
- Molecular & Biomedical Imaging
- Rheumatoid Arthritis

EDUCATION & TRAINING

The DMMC has created an Education Strategy Group comprising representatives from its participant institutions.

DMMC EDUCATION STRATEGY GROUP

Dr Mark Watson, *DMMC Education & Information Coordinator* (Chair)

Dr Helen McVeigh, *Education & Outreach Officer, Royal College of Surgeons in Ireland*

Dr Niamh Moran, *Senior Lecturer, Royal College of Surgeons in Ireland*

Prof Cliona O'Farrelly, *Director, Education & Research Centre, St Vincent's University Hospital*

Dr Ross McManus, *Senior Lecturer, Institute of Molecular Medicine, TCD*

Ms Elaine Quinn, *Communications & Education Officer, Conway Institute, UCD*

Dr Clare O'Connor, *Postgraduate Education Committee Chair, Conway Institute, UCD*

STRATEGY

The DMMC is developing a comprehensive and flexible cross-institutional education and training programme in Molecular Medicine. This capitalises on the research and teaching strengths of Trinity College Dublin, University College Dublin, The Royal College of Surgeons in Ireland, and the clinical expertise in the affiliated teaching hospitals. This will provide postgraduate students with skills that are both attractive to the biopharmaceutical industry and essential for 21st century academic research. It will promote Dublin as a location where academic institutions are building on their traditional strengths to provide career-long training that facilitates collaborative molecular medicine research, technology development and their translation to a clinical setting.

Programme aims :-

- Offer cross-institutional courses in important areas of molecular medicine that provide participants with experience of state-of-the-art technologies and their applications.

- Develop courses in research management and business skills to foster entrepreneurship.

- Work with biopharmaceutical and biotechnology companies to bring an industry perspective to education and training.

- Pursue funding for postgraduate studentships and postdoctoral fellowships.

- Organise workshops, bringing together workers in key areas to develop research strategies, review progress, and promote consistency in use of technology platforms and data analysis.

- Make selected courses available to academic researchers outside Dublin and Ireland and to biopharmaceutical industry staff.

DMMC COURSES AND WORKSHOPS

A primary vehicle for achieving these aims is a growing series of short courses and workshops that are available to all those interested in molecular medicine in TCD, UCD, RCSI, and affiliated teaching hospitals. They are developed for the DMMC Education & Training Programme and are administered by the DMMC directorate, with assistance.

DMMC courses and workshops enable molecular medicine postgraduate students in each institution to tailor their own education in response to developing needs (e.g. postdoctoral research plans or a career in the biopharmaceutical industry). Each institution stipulates the number of DMMC courses that their own postgraduate students are required to complete.

DMMC courses and workshops also provide career-long training opportunities for postdoctoral workers, technical staff, academic staff and clinicians at the institutions and affiliated teaching hospitals. These groups are free to use DMMC courses in a flexible way, attending individual sessions of interest.

The DMMC Directorate coordinates and administers the programme: developing existing and new courses and workshops, advertising, maintaining a website that includes online application and course material available for download, registration, feedback questionnaires, certificates of attendance, attendance reports for each institution.

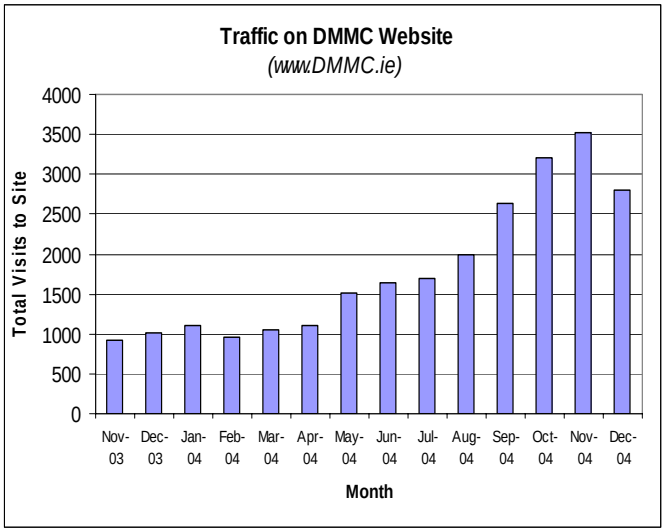
We are currently meeting with industry representatives to discuss their role in DMMC Education & Training. Areas discussed include the skills required by industry, and how we enlarge the DMMC community in molecular medicine by bringing industry employees in as course givers and attendees. Plans for courses include an overview of various areas in industry research, development, and manufacturing (with input from a number of companies; designed to give academic scientists a realistic view of how science is done in industry), as well as more specialised courses.

COMMUNICATION

WEB SITE

The DMMC website has developed as an informative and interactive means of representing institutions spread across Dublin and the researchers within them (a 'virtual centre' of molecular medicine expertise), and as a means of providing the latest news, events, and education opportunities.

- The **Education** pages lists details of forthcoming and previous training courses. These pages allow access to course materials and facilitate easy on-line registration. Information capture through this on-line registration drives an Education Resource Database that enables the Directorate manage information on course attendance, etc.
- The "**News & Calendar**" pages list news items of relevance to the entire molecular medicine community and forthcoming events at each of the participant institutions. Where appropriate, entries are categorised by disease area or technology to allow the user to display a filtered list. Items are ranked both in priority and in chronological order. Items of particular interest are regularly highlighted on the "**Home**" page of the website. This page is updated on a daily basis to ensure that the DMMC website maintains a contemporary impression.
- The "**Research**" pages allow users to explore the breadth and depth of research ongoing throughout the DMMC and to interrogate by disease area, investigator name or keyword. Such searches provide detail of specific research topics, lists of investigators and their publication records. The next phase of development will see the emergence of more detailed information on **Programmes** (Projects) and **Technologies**.



Despite no formal promotion of the portal, traffic on the DMMC website has steadily increased to the current average of 100,000 hits and 2,000 visits per month.

E-MAIL ALERTS

The DMMC Directorate generally refrains from indiscriminately e-mailing investigators. We prefer instead to cascade information through established communication channels at each institution and by directing information to those individuals who have sought particular updates. The Directorate has made e-mail alerts at most once per quarter to capture important items that fall between publications of the *DMMC News*.

DMMC NEWSLETTERS

The Directorate Office has initiated a quarterly newsletter (*DMMC News)* aimed at raising the awareness of DMMC activities to a wide constituency of interested parties both internally and externally.

April 2004

August 2004

November 2004

DMMC Newsletters raise awareness of current activities across the city.

OPERATING BUDGET

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

	OPERATING BUDGETS *(€, 000)*			
	RCSI	**TCD**	**UCD**	**Total**
Recurrent Budget				
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				
Recurrent Budget	12,038	11,661	8,666	**32,365**
Capital Budget	8,569	14,587	16,188	**39,344**
Total Operating Budget	***20,607***	***26,247***	***24,854***	***71,708***

EXPENDITURE TO DATE

Table 2 ***Actual Expenditure to December 2004*** (€, 000)

	Actual Expenditure to December 2004 *(€, 000)*			
Total Expenditure	**RCSI**	**TCD**	**UCD**	**Total**
Recurrent Spend	6,115	5,409	3,714	**15,238**
Capital Spend	3,778	12,511	9,605	**25,894**
Total Spend	***9,893***	***17,920***	***13,319***	***41,132***

Table 3 ***Actual Expenditure to December 2004*** (% of Budget)

	Actual Expenditure to December 2004 *(% of Budget)*			
Total Expenditure	**RCSI**	**TCD**	**UCD**	**Total**
Recurrent Spend	50.8%	46.4%	42.9%	47.1%
Capital Spend	44.1%	85.8%	59.3%	65.8%
Total Spend	**48.0%**	**68.3%**	**53.6%**	**57.4%**

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ABBREVIATIONS & ACRONYMS

AMNCH	Adelaide & Meath *incorporating the* National Children's Hospital
Beaumont	Beaumont Hospital
Conway	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 Programme
GRU	Genome Resource Unit
HEA	Higher Education Authority
IDA	Industrial Development Authority (*IDA Ireland)*
IBS	Institute of Biopharmaceutical Sciences
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, Crumlin
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