

The Dublin Molecular Medicine Landscape

Pierre Meulien
Chief Executive of the DMMC

Almost two years have passed since the official creation of the DMMC: the agreement between UCD and TCD was signed on 21 April 2002, and the directorate was established in September 2002. Our environment has changed radically in that time and we find ourselves today in a more scientifically mature and confident context. The spirit of collaboration cannot be compared with what existed before. Modern infrastructure, whether at the Conway Institute, The Institute of Molecular Medicine, or The Institute of Biopharmaceutical Sciences, has allowed Dublin-based investigators to leverage unparalleled funding from HRB, SFI, the Wellcome Trust and the European Commission.



The next phase of our development is to build on the spirit of cooperation, and drive more cross-institutional and translational programmes. This will ►

Welcome to DMMC News

DMMC News is a forum for the molecular medicine community in Dublin to present the latest developments of interest to a local and international audience. *DMMC News* will be circulated widely in Dublin and to contacts further afield; it will also be available to all from the DMMC website (www.dmmc.ie). It is an opportunity to present your work, in the context of the developing cross-institutional collaborative environment, to fellow scientists and clinicians, funding agencies, government bodies, and the public who want to know more about what you do. *DMMC News* will contain listings of events (seminars, meetings, courses and workshops), and details of new arrivals. Please contribute to future issues with news items and information on upcoming events (contact info@dmmc.ie).

be achieved through the Programme for Human Genomics, which brings UCD, TCD and RCSI together on a scale never seen previously. This €45 million programme is one of the largest of its kind in Europe; highlights of the deliverables, for which the capital has now been 'unfrozen', appear in this and forthcoming issues of *DMMC News*.

The DMMC model of cross-institutional collaboration and translational research is also making its mark internationally. I was asked to present the model at the CHI Molecular Medicine conference in San Francisco in March, and at the associated US-Ireland Biolink meeting. This CHI meeting attracted around 1500 delegates from the biotech and pharmaceutical sector and it was a great forum for presenting a coherent picture of what is happening in Dublin. Attracting the best scientists to Ireland is of primary importance for us, and the changing scene is exciting for young post-docs eager to return or non-Irish scientists hungry for adventure.

We now need to accelerate the pace, and avoid the traps associated with too much introspection. Building collaborative research and education programmes, breaking down traditional barriers, and seeking to attract and retain the best people remain our first priorities. These objectives will, I am sure, lead to an internationally renowned community in Molecular Medicine that will more than justify the important investment made and realise the vision of the originators.

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Proteomics in Dublin

With the arrival of Dolores Cahill and Stephen Pennington, and the development of new facilities at RCSI and at the Conway Institute UCD, Dublin is well placed to take a lead in applying proteomics to molecular medicine.



Centre for Human Proteomics
Royal College of Surgeons in Ireland
St Stephens Green, Dublin 2, Ireland
<http://chp.rcsi.ie>

The Centre for Human Proteomics (CHP) provides a comprehensive proteomics facility that includes protein and antibody arrays and protein separation. Applying these technologies towards the diagnosis and treatment of human diseases are the prime goals of the Centre's research programmes. The CHP has the following aims: (i) develop comprehensive proteomics resources and expertise at the international forefront; (ii) recombinantly express the human proteome; (iii) apply protein and antibody array and microfluidic chip technologies to medical and diagnostic applications; (iv) educate and train academic and industrial scientists, technicians and engineers from Ireland and abroad in all aspects of proteomics technology; (v) advance the understanding, relevance and impact of science in Ireland. The potential commercial applications of our work have already been recognised by industrial partners such as Les Laboratoires Servier and Allegro Technologies.

The Director of the CHP, Prof. Dolores Cahill, has been at the forefront of protein expression/cDNA library technology and its application to proteomics, cell biology and biomedical applications. She has been instrumental in developing and applying high density arraying technologies and automation to generate high content, high-density protein arrays and antibody arrays of target human tissue. ▶

These arrays could potentially be used as a diagnostic tool for patients with various conditions such as auto-immune diseases.

Further information can be found at <http://chp.rcsi.ie>

The Conway Institute Proteome Research Centre

The Proteome Research Centre in the Conway Institute, University College Dublin is now being equipped with state-of-the-art proteomics instrumentation and software. The Centre is also in the process of recruiting staff (if you are interested, please contact stephen.pennington@ucd.ie).

The equipment that is arriving includes:

- Rigs for IEF and SDS-PAGE (Multiphor, IPGPhor, EttanDalt 6, EttanDalt 12).
- Gel scanner + software for image analysis (Imagemaster).
- A three colour laser scanner (Typhoon 7410 - obtained in conjunction with the transcriptomics group) and Decyder software for analysis of fluorescent dye labelled 2-D gels.
- Equipment to support liquid chromatography including a nano liquid chromatography system, and two multi-dimensional HPLC systems (Vision, Integral).
- A MALDI target loading robot (PROBOT).

Together with a suite of mass spectrometers:

- A 4700 Proteomics Discovery System - MALDI-Tof./Tof.
- A linear ion trap ESI MS instrument for MS_n (Thermo LTQ).
- A linear ion trap ESI coupled to a Fourier Transform Ion Cyclotron Resonance detector for ultra high mass accuracy and resolution (Thermo LTQ-FT).

The facility also includes:

- Biacore instrument for monitoring protein-protein interactions.
- SELDI protein chip system (obtained on an HRB grant by Dr William Gallagher).

The Centre has a launch event on the 3rd and 4th of June 2004 – participation is by registration only. If you are interested in attending please contact ashling.gantly@ucd.ie

DMMC Strategic Plan

After consultation with stakeholders inside and outside of the DMMC, the *Directorate Office* has prepared a strategic plan that attempts to articulate the vision of creating in Dublin an internationally recognised centre of excellence in molecular medicine. This Strategic Plan, ratified by the DMMC Board Meeting in December 2003, is available on the DMMC website. Copies can be obtained by request from the Directorate Office. Key elements of the DMMC strategy include:

1. Create trans-institutional **research clusters** with focused programmes that exploit state-of-the-art technologies.
2. Generate a **bioresource network** of tissue samples, genetic material, genotypic & phenotypic data that enable the evaluation of clinical hypotheses.
3. Retain & attract **world-class scientists** and build a multi-disciplinary **education curriculum** that is informed by the biopharmaceutical industry and which enables career-long learning.
4. Secure **finance** for competitive multi-investigator research proposals and make our combined resources available to better enable individual researchers to attract funds.
5. Build **strategic partnerships** with industry & international research centres.
6. Offer a **professional, accessible interface** that facilitates collaboration & the exploitation of knowledge & resources on behalf of the participant institutions.

Interdisciplinary Research into Synaesthesia at TCD

Kevin Mitchell
Department of Genetics, TCD

Synaesthesia is an unusual condition involving a 'mixing of the senses'. It takes different forms, most often involving perception of colours in response to sounds, words, letters or digits (and commonly days of the week or months of the year). Less common forms involve other sensory modalities including taste, smell, touch or pain. The particular synaesthetic perceptions experienced are highly specific to each individual, stable over their lifetime ►

and usually described as having always been there. Remarkably, synaesthesia shows a very high degree of heritability, consistent with a simple Mendelian trait. These facts suggest that synaesthesia could be caused by mutations in genes that specify the wiring of the brain during development.

We have identified over fifty synaesthetic individuals in Ireland to date, many of whom report at least one synaesthetic relative. We are planning a detailed study to objectively measure synaesthetic experiences using psychophysical tests and functional neuroimaging and to map and identify the gene(s) affected in these families as a first step towards understanding the underlying developmental mechanisms.

The Synaesthesia Research Group includes Dr Kevin Mitchell, developmental neurogenetics, Dr Aiden Corvin, psychiatric genetics, Dr Fiona Newell and Ms Ciara Finucane, cognitive neuroscience. For more information, please contact the Synaesthesia Research Group, Department of Psychology, Trinity College, Dublin 2. Email: synres@tcd.ie; Tel: 086 076 7753. Website: www.tcd.ie/Psychology/synres/

DMMC & Institut Pasteur Meeting 25-26 November 2003



We are pleased to report on the first formal bilateral meeting between the Institut Pasteur, Paris and the *Dublin Molecular Medicine Centre*, in Dublin during November 2003. This meeting brought together senior scientists from one of the world's most successful research centres with Principal Investigators from Dublin's leading medical research ►

institutes (the Conway Institute of Biomolecular & Biomedical Research, the Institute of Molecular Medicine and the Institute of Biopharmaceutical Science).

25 scientists presented their work. Smaller groups then formed, with individuals exploring the potential for collaborative research and staff exchange. Several complementary areas were identified. For example, within the Institut Pasteur, there is a 7-laboratory research network focusing on mediators of inflammation. It was agreed that this group could interact strongly with DMMC researchers with interests in toll-like receptors and transcription factors such as NFkappaB. Also there is a commonality of interest in both institutions on investigation of mechanisms around cell differentiation and on immune evasion strategies. DMMC investigators displayed an array of characterisation technologies with application to exploring the fundamentals of cell migration and platelet adhesion.



From left: Elisabeth Labreyere (Institut Pasteur), Yuri Volkov (TCD), Aideen Long (RCSI), Dermot Kenny (RCSI), Niamh Moran (RCSI), Jean-Louis Virelizier (Institut Pasteur), Brian Harvey (RCSI).

This was a highly successful first formal meeting between the Institut Pasteur and the DMMC. We are left with a tangible sense of collaborative potential on both sides; a series of investigator-led follow-up meetings are expected during 2004. We wish to thank and acknowledge the support of the principal sponsors of this meeting, Science Foundation Ireland and the French Embassy in Ireland.

DMMC Education & Training

The DMMC is capitalising 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 to develop a collaborative education and training programme. An Education Consultation Group with members from each institution meets to discuss and implement cross-institutional education and training. We are currently putting together an advisory panel comprising representatives from the biopharmaceutical industry.

DMMC courses are part of molecular medicine postgraduate training and are also available to all those with an interest in molecular medicine in TCD, UCD, RCSI, and affiliated teaching hospitals (postdoctoral staff, academic staff, technical staff, clinical staff). Seven DMMC courses are running in 2003/2004:

- Techniques & Strategies in Molecular Medicine
- Advanced Proteomics
- Molecular Cell Biology
- Neurobiology
- Immunology & Inflammation
- Molecular Haematology & Oncology
- Coronary Artery Disease

Other courses and workshops are also available cross-institutionally: *Intellectual Property for Biotechnology & Life Sciences* and *An Introduction to Postdoctoral Research* are among those completed so far. We are now working to put together a programme of introductory and advanced bioinformatics training.

Currently under development is short duration in-lab training: labs with expertise in particular techniques will be listed on the DMMC website. Those needing to learn a technique or obtain advice will, with the support of their supervisor, apply for training. The head of the lab offering training will decide whether to accept an applicant and any recompense required. A cross-institutional portfolio of accessible expertise will be valuable to anyone needing to identify an alternative approach in their research or get up to speed with a different technique.

More information: www.dmmc.ie/education.htm

DMMC Focus Group Meetings

One of our objectives is to create new trans-institutional clusters of researchers around common themes. By bringing together scientists with complementary research interests, we hope to spark new collaborations, improve communication and continuously challenge our assumptions. The DMMC is delighted to provide support to the many existing trans initiatives, which are consistent with our goal of establishing Dublin as an internationally recognised centre of excellence in molecular medicine.

17 investigators from our constituent institutions attended a focus group meeting on Diabetes, Obesity & Metabolic Health (25 March 2004, Newman House). This meeting was chaired by Professor Stephen O’Rahilly (University of Cambridge), with Professor Tim O’Brien (NUI, Galway) and Professor Kevin Collins (University College Cork) in attendance. Investigators outlined their current research interests and the concept of an Irish Diabetes Research Consortium was discussed. The meeting was most timely, coming as it did in the same week that Science Foundation Ireland launched a call for proposals on a diabetes-specific centre of excellence.

The DMMC Directorate is hosting a series of focus group meetings during 2004 on specific themes (see www.dmmc.ie for details), and is keen to ensure that all the appropriate investigators are afforded the opportunity to participate. We invite nominations for topics where molecular medicine-related research, enabling technologies or clinical application can be enhanced through trans-institutional collaboration.

Nutrigenomics

Helen Roche
Institute of Molecular Medicine, TCD

The Nutrigenomics / Molecular Nutrition Research Group, within the Department of Clinical Medicine, Trinity College Dublin and 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, the cellular and molecular effects of ▶

nutrients are often not fully understood. Dr Helen Roche established the group within the remit of the New Blood Fellowship Programme of The Wellcome Trust. Through the European Framework 6, the team is co-ordinating a €12.5m Integrated Project, entitled LIPGENE, dedicated to investigating the interactions between dietary fat composition, genotype and the metabolic syndrome (www.lipgene.tcd.ie). The Nutrigenomics group is also a founding member of The European Nutrigenomics Organisation – linking genomics, nutrition and health research, which received €17.2m from the European Framework 6 grant programme to establish a European Nutrigenomic Network of Excellence.

The group has a particular interest in nutrient regulation of gene expression and is investigating the effects of dietary fatty acids on the expression of the genes involved in metabolic health (diabetes), cardiovascular disease, inflammation and colon cancer. We are also determining the interactions between common polymorphisms, metabolic responses, and dietary intervention/responsiveness. The Nutrigenomics Research group is open to developing all research technologies (such as DNA chip array technology, proteomics, bioinformatics and systems biology) within the context of Molecular Nutrition.

For further information, please contact Dr Helen Roche, e-mail: hmroche@tcd.ie

DMMC Website Research Database Launch

If you are a periodic visitor to the DMMC website recent developments may have passed you by. Our News and Events pages now provide a comprehensive chronological listing of items of interest with events colour coded by thematic area. Our Education pages detail various courses and workshops available across Dublin, and application for the *DMMC courses* is now a fully online process.

The launch of an online Research Database marks the next phase of our website development. This is a comprehensive mapping of the activities of all molecular medicine researchers and is constructed to show the overall breadth, scale and connectivity ▶

of DMMC associated research. It illustrates at a macro level both the areas of research focus and the personnel involved while at a micro level makes linkages between multi-disciplinary themes that may not otherwise be immediately evident. At all levels the teams of researchers involved in a strand of research can be listed, as can additional details on research topics. At the individual level all research interests together with a listing of publications provides a comprehensive picture of an Investigator's research portfolio and allows potential collaborators to assess who's who in their chosen field and to make email contact. Publications are web-linked to PubMed.

molecule, environmental factor, etc. This allows extensive linkages between topics and between researchers working on those topics.

It is hoped that the Research Database will enhance the profile of the research and of the Investigators in the broad DMMC family. This section of the site will go live to the general public on 1 May at www.dmmc.ie/research. We are presently confirming details with Investigators (if you have not yet been contacted, please email research@dmmc.ie and we will send you the web-link to the test version of the site where you can review your details). The Research Database will be on display at the DMMC symposium (21–22 April 2004 at the Conway Institute, UCD). You are welcome to drop by to see how it works and check that your details are correct.

ACCELERATING TRANSLATIONAL BIOSCIENCE

ABOUT | RESEARCH | PROGRAMMES | BIOSOURCES | EDUCATION | EVENTS | NEWS | LINKS | CONTACT

SEARCH PERSPECTIVES >>

This page allows you to take different routes through the DMMC research map depending on their particular perspective. Each perspective (e.g. By Disease) allows you to access a range of different themes (e.g. Cancer) which in turn are subdivided into specific programmes (e.g. Breast Cancer). Programmes are comprised of collections of research topics being pursued by investigators. Investigators involved at each level are detailed. Many topics are multi-disciplinary and fall into more than one programme so they become connected to like topics in a number of ways. This top down approach will bring you to related topics, which may link to related programmes, themes and perspectives. Likewise topics connect investigators who are grouped together in by topic.

- Disease**
 - Cancer
 - Inflammatory Disease
 - Neurological Disorders
 - Cardiovascular Disease
- Biological System**
 - Central Nervous
 - Circulatory
 - Digestive
 - Endocrine
 - Lymphatic
 - Reproductive
 - Respiratory
 - Skeleton & Muscle
 - Urinary
- Technology**
 - Computational Biology
 - Genomics
 - Imaging
 - Bio-Collection
 - Proteomics
 - Transgenic & Animal Models
 - Enabling Technology
- Environmental**
 - Nutrition
 - Chemical
 - Oxidation
 - Radiation

Cancer 2004 Meeting

Mark Lawler
St James's Hospital and TCD

Cancer 2004 was held in St James's Hospital in the Institute of Molecular Medicine, 11-12 March 2004. This conference is now in its second year and has attracted significant interest in the Irish Cancer Community. The theme of the conference this year was collaboration and co-operation. Over 230 delegates attended this 2-day conference to hear lectures on topics such as *Cancer Strategy*, *Cancer Care*, *Frontiers in Cancer Research* and *Technology and its role in Cancer Research and Cancer Practice*.

Speakers from Ireland, Europe and United States were present at the conference, including a significant number of speakers and attendees from the National Cancer Institute. Professor Donal Hollywood (Academic Unit of Clinical and Molecular Oncology, St James's Hospital and TCD) outlined the plans for Radiation Therapy in Ireland over the next number of years and Professor Paddy Johnston (Belfast City Hospital) looked at the role of the Comprehensive Cancer Centre and how cancer research will fit into that role. This is the model that we aspire to in relation to linking the researcher, the clinician and the patient so that we can provide the best possible service for cancer patients in this country. ▶

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Welcome to the DMMC Research Map.

This Map is constructed to show the overall breadth of research and to navigate you to groups of investigators who are described by their key interests (*Research Interests*). As we continue to detail the DMMC landscape, brief synopses of each research topic will be added.

Like any map, it can be used in a number of ways to view the scale and connectivity of DMMC research. For example, you can follow a pre-defined route via page links or you can explore particular regions in more detail by direct search.

- Page driven Navigation (where Research Topics are grouped by specific categories). This approach allows you to follow a particular route through the research landscape. e.g. Perspective: Disease > Theme: Cancer > Programme: Breast Cancer > Topic: Biomarkers in Breast Cancer
- Biological System > Central Nervous > Brain > Alzheimer's Disease
- Search for specific Investigator
- Search for Research Topics by their Component Elements

SEARCH PERSPECTIVES >>

- Disease
- Biological System
- Technology
- Environmental

SEARCH STAFF >>

a b c d e f g h i j
k l m n o p q r s t
u v x y z

SEARCH ELEMENTS >>

- Cell:
- EnvironmentalFactor:
- InfectiousAgent:
- Molecule:
- Organ:
- Process:
- Tissue:
- Tools:

Select Types

The taxonomy used to establish connectivity in research has been arrived at by thoroughly detailing all component factors involved in a research topic: i.e. disease areas, biological system, cell type, ▶

In relation to the Dublin Molecular Medicine Centre, a number of talks reflected the cooperation that we have seen in the DMMC. This was particularly evident in the talk given by Dr Bill Watson on prostate cancer, highlighting the new Prostate Cancer Research Consortium, a linkage between TCD and UCD and many of the Academic Teaching Hospitals in Dublin.

Professor Norman Coleman, Deputy Director NCI, gave a State of the Art talk on radiation research and how it will impact on cancer research and cancer care in coming years. We also heard from Prof Don Coffey, from Johns Hopkins University School of Medicine in the US, who gave a State of the Art Lecture on the future of Cancer Research. The large audience appreciated his excellent presentation.



From left: Mark Lawler (St James's Hospital and TCD), Micheál Martin TD. (Minister for Health and Children), Donal Hollywood (St James's Hospital and TCD).

Cancer survivorship is an important part of Cancer Care. Vickie Maye, a Cancer Survivor, gave a superb talk on her experiences both positive and negative. In addition, we heard talks on many aspects of cancer research including Professor Noel Lowndes (NUIG) on the role of the cell cycle and genome instability in cancer. The role of cancer care and cancer research in childhood leukaemia was highlighted by both Professor Owen Smith and Dr Fin Breatnach from Our Lady's Hospital for Sick Children in Crumlin.

Overall, Cancer 2004 was a huge success attracting a significant audience and it showed the wealth of knowledge and research that is going on in this country and also the potential links that have been developed with institutes such as the National Cancer Institute in the United States.

DMMC Spring Symposium

We are pleased to announce that the next DMMC Research Symposium will be held on the 21 and 22 April 2004 at the Conway Institute of Biomolecular and Biomedical Research, University College Dublin. DMMC Symposia are held every six months in alternate venues around the city to showcase the breadth of molecular medicine research in Dublin and advance opportunities for further trans-institutional collaboration.

The programme for the April 2004 meeting can be found on the DMMC website and includes presentations in the areas of Apoptosis & Cell Cycle, Angiogenesis & Hypoxia, CNS Development & Disease, and Resolution of Inflammation. The speakers include Principal Investigators from each of our constituent institutions, and from other Irish universities. We are particularly pleased to welcome as plenary speakers Dr Kari Stefansson (President & CEO, DeCode), Prof Alan Hall (University College London), Dr Ciaran Morrison (NUI, Galway) and Dr Bruno Morgan (University of Leicester).

In addition to the formal lecture presentations over the two-day meeting, we will also be hosting informal workshops designed to allow more detailed exchanges among specialist groups and presentations by emerging younger scientists.

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Events

Please send details of forthcoming events to info@dmmc.ie

DATE & TIME	EVENT	LOCATION
19 April - 13.00 (Lunch - 12.30)	Poxvirus genome evolution Dr Aoife McLysaght (Dept. Genetics, TCD)	Durkan Theatre, IMM ²
21 April - 10.00 22 April - 10.00	DMMC Spring Symposium Programme & registration details on: www.dmmc.ie	Conway Institute ¹ ,
21 April 0930-1600	Recombinant Protein Purification Workshop Programme & registration details on: www.dmmc.ie	Durkan Theatre, IMM ²
26 April - 13.00 (Lunch - 12.30)	Barrett's Oesophagus and Barrett's Associated Neoplasia: Pathology & Molecular Biology Dr Ali Raouf (Dept. Surgery, TCD)	Durkan Theatre, IMM ²
10 May - 13.00 (Lunch - 12.30)	The Biology of Malignant Pleural Mesothelioma Dr Ken O'Byrne (HOPE, St. James's Hospital)	Durkan Theatre, IMM ²
13 May - 16.00	The Neutrophil annexin-1 system Professor Mauro Perretti (Kennedy Institute, UK) Further details from: seamas.donnelly@ucd.ie	Lecture Theatre, Conway Institute ¹
17 May - 13.00 (Lunch - 12.30)	Antibodies to alpha-actin – a skeleton in the cupboard of coeliac disease diagnosis Dr Jean Dunne (Dept. Immunology, IMM, TCD)	Durkan Theatre, IMM ²
24 May - 13.00 (Lunch - 12.30)	BH3 only proteins: a deadly family Professor Jochen Prehn (Dept. Physiology, RCSI)	Durkan Theatre, IMM ²
31 May - 13.00 (Lunch - 12.30)	Title to be announced Professor Alex Whelan (Dept. Immunology, IMM, TCD)	Durkan Theatre, IMM ²
10 June - 16.00	Neutrophil apoptosis, the innate immune response to bacterial pathogens Professor Moira Whyte (University of Sheffield, UK) Further details from: seamas.donnelly@ucd.ie	Lecture Theatre, Conway Institute ¹
14 June - 13.00 (Lunch - 12.30)	Characterization of Cinnamyl Alcohol Dehydrogenase in <i>H. Pylori</i> Ms Blanaid Mee (Infection and Immunity Group, IMM, TCD)	Durkan Theatre, IMM ²
24 June - 13.00 (Lunch -12.30)	Title to be announced Dr Orla Sheils (Student Histopathology, IMM, TCD)	Durkan Theatre, IMM ²
28 June - 13.00 (Lunch -12.30)	Low pH Results in Co-ordinate Regulation of Gene Expression in Oesophageal Cells Mr Shane Duggan (IMM, TCD)	Durkan Theatre, IMM ²

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