

Atomic Force Microscopy (AFM) Forum at UCD Conway Institute



Delegate Dr. Cristiano Giordani, UCD attending the AFM Forum

Nearly 100 international researchers attended the AFM Forum on November 20th & 21st 2008, jointly hosted by Asylum Research and Professor Suzi Jarvis, UCD Conway nanoscale function group.

Highlights of the conference included seminars by Dr. Phillip Thurner (University of Southampton) and Dr. Colin Grant (University of Leeds) and an equipment workshop where participants could interact with a scientist while actually using AFM instrumentation to learn specific imaging tips and techniques.

Dr. Sonia Triqueros, University of Oxford won first prize for the best poster on *DNA conformation and biomolecular motors: new nanomedicine research targets* and Dr. Lyubov Belova, Royal Institute of Technology (KTH), Sweden won the image contest for her submission of the *Magnetic butterfly*.

Asylum Research also unveiled its new Cypher™ AFM; the first new small sample AFM in over a decade, featuring closed loop atomic resolution, automated laser and photodetector alignment and several other innovative capabilities.

'Science Alive'

UCD Conway Institute hosted four days of *Science Alive* seminars aimed at transition year students during October 2008. The talks were attended by over 400 students from fifteen secondary schools in Dublin, Wicklow and Meath.

For the first time, through collaboration between UCD Conway Institute and UCD Science Programme Office, the seminars were delivered by both Conway investigators and colleagues working in other areas of the life sciences. The aim of the series is to encourage students to study science subjects for their Leaving Certificate.

Podcasts of the seminars, which ranged from zebrafish and eye disease to cosmic explosions and the large hadron collider, are available on: <http://www.ucd.ie/conway/media/latest-news/title,21265,en.html>.

Our thanks to Conway fellows; Prof Brendan Loftus, Prof Helen Roche, Dr Keith Murphy, Dr Paul Evans and Dr Brendan Kennedy as well as College of Life Sciences colleagues, Dr Julian Menuge, Dr Peter Duffy and Dr Fred Cummins.



Loreto Foxrock pupils Rebecca Manning (left) and Sarah Geoghegan pictured at the 2008 Science Alive seminars with Dr Paul Evans, UCD Conway Institute & UCD School of Chemistry & Chemical Science.

New Irish Cancer Society fellowship grant for young Conway researcher

Dr Fiona Furlong was awarded a research fellowship grant by the Irish Cancer Society in November 2008. This new scheme is aimed at supporting career development in cancer research and cultivating the next generation of cancer researchers in Ireland.

One of only two recipients, Dr Furlong will receive €225,000 over the next three years to support her research into why some women suffering from ovarian cancer do not respond to the chemotherapeutic agent, paclitaxel.

Commenting on the award, Fiona said, "This fellowship will aid in my development into an independent scientist and allow me to pursue my own research ideas."

Recognition for Conway student at EU Carcinogenomics meeting



(L-R) Dr. Yvonne Staal (TNO Quality of Life), Mr. Robert Radford (UCD Conway Institute), Dr. Theo de Kok (Maastricht University), and Prof. Jos Kleinjans (Maastricht University).

Conway PhD student, Robert Radford won the best scientific presentation award at the 2nd annual EU Carcinogenomics Consortium meeting, held in Dublin on November 10th -12th 2008.

Part of the research group led by Professor Michael Ryan and Dr Tara McMorrow, Robert's presentation centred on kidney cells and novel approaches to identifying carcinogenic markers.

The EU Carcinogenomics project is an integrated project within the European 6th Framework Programme comprising twenty leading European research laboratories.



conway focus

Unprecedented innovation successes for Conway scientists

The generation, capture, protection and development of intellectual property is recognised as being central to any world-class research environment. The leadership shown by UCD Conway Institute on its innovation agenda has resulted in an unprecedented level of success in 2008¹. UCD Conway scientists signed nineteen invention disclosures, thirteen patent applications and four licensing agreements.

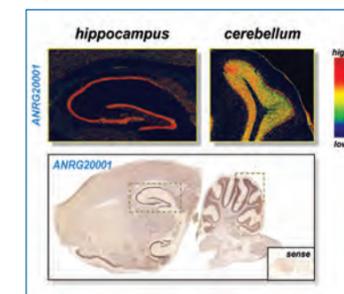
Working closely with NovaUCD and Enterprise Ireland Biotechnology Directorate, UCD Conway Institute has facilitated the development of a framework to enable researchers to access the support services necessary for intellectual property management. This framework assists scientists at all stages of the innovation spectrum from technology transfer advice to continuing professional development programmes to establishing incubation facilities. In 2008, there were many examples of the success of this proactive policy for the translation of research.

Professor Ciaran Regan and Dr Keith Murphy of the Applied Neurotherapeutics Research Group (ANRG) filed patents to protect two genetic databases; one describing the change in gene transcription that occurs during learning and the second describing genes that change their expression during the emergence of

schizophrenia-like symptoms in an animal model of the disease. Gene products that might serve as drug targets to treat the notoriously difficult cognitive deficits of schizophrenia were identified through the comparison of these two databases. Many of the campus companies involving Conway Fellows went from strength to strength during 2008. Celtic Catalysts, a campus company co-founded in 2000 by Professor Declan Gilheany won the NovaUCD 2008 Innovation Award. The company has developed 'P-chiral' technology, which enables global pharmaceutical companies manufacture drugs more cost effectively, particularly in anti-viral and anti-cancer therapeutic areas. Enzolve Technologies, which began commercial life in UCD Conway under Professor Paul Engel, moved to the incubation facilities in NovaUCD. The company produces genetically engineered enzymes and enzyme-based specialty products. Dr Kevin O'Connor completed the 2008 NovaUCD Campus Company Development Programme (CCDP). This support programme for academic entrepreneurs provides the skills necessary to transform ideas into commercially viable ventures. Dr O'Connor's research centres on recycling waste to bioplastics. Professor Dolores Cahill took part in the inaugural event by IBIA/BioConnect Ireland, to identify entrepreneurs interested in getting involved in start-ups arising from the third level sector.

During 2008, Conway Fellows secured funding for commercialisation through agencies such as Enterprise Ireland (EI). EI Commercialisation Fund supported eight projects in the life sciences and food category; six under the proof of concept scheme in areas such as preventing surgical adhesions, biocatalysis, and biomarkers as well as two technology development projects in the areas of cancer imaging and depression.

¹Commercialisation information for UCD Conway researchers in the academic year to the end of August 2008



Cognition target ANRG20001 mRNA expression is especially prevalent in the dentate granule and CA pyramidal cells of the hippocampus as well as with *in situ* hybridisation. There is also substantial expression in the cerebellum and olfactory bulb, regions that exhibit high neuroplastic potential, suggesting ANRG20001 may play an important role in cognition-associated synaptic reorganisation.

Director's Message

Happy New Year! I am delighted to welcome you to the first edition of 'Conway Focus' in 2009.

UCD Conway Institute is now at the mid-point of the 10-year roadmap formulated at its inception. Much has been achieved to date, but during the challenging times ahead we must redouble our efforts and heighten our ambition to be a leading institute in

biomedical and biomolecular sciences internationally.

This year, we will ensure the highest standards in postgraduate education and define development paths for our postdoctoral scientists. We will continue to strengthen existing relationships with academic and industrial partners and forge new ones. Above all, we will ensure that UCD Conway Institute is defined by

excellence in research and innovative thinking.

I believe the year ahead will be an exciting and successful one for the Institute and look forward to working with you all to realise this goal.

Professor Des Fitzgerald
Director



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Biochemical Society gold medal for Professor Kinsella

In December 2008, Professor Therese Kinsella was awarded the Biochemical Society Irish Area Section (IAS) medal in recognition of her outstanding contribution to Irish research over the past decade. She presented her medal lecture, entitled *Expression and intracellular signalling by the TP α and TP β isoforms of the human Thromboxane A $_2$ Receptor*, at the annual Biochemical Society Irish Area Section (IAS) meeting on held in NUI Galway.

One research focus of Professor Kinsella and her team centres on the prostanoid thromboxane (TX) A $_2$, a potent stimulator of platelet activation and aggregation as well as a mediator of smooth muscle contraction. TXA $_2$ contributes to a variety of pathologies within the vasculature including thrombosis, heart attack, stroke and various types of hypertension.

In humans but not in non-primates, TXA $_2$ actually signals through two distinct receptor isoforms referred to as TP α and TP β that differ exclusively within their intracellular carboxyl-terminal (C)-tail domains and were originally thought to

arise by differential splicing of the primary gene transcript.

Although the biologic significance for the existence of two receptors for TXA $_2$ in humans and primates is unknown, there is emerging and compelling evidence that they have distinct physiologic roles. Both receptors display critical differences in their intracellular signalling, modes of desensitisation and regulation, and patterns of expression in a range of cell and tissue types of vascular and non-vascular origin. Critically, researchers within the Kinsella group have discovered that expression of TP α and TP β is regulated at the transcriptional level by entirely distinct promoters within the single TP gene located on chromosome 19.

In her medal lecture, Professor Kinsella highlighted some of the key discoveries made by her team in this area and outlined her thoughts on why TP α and TP β are not just isoforms of the same receptor but are functionally and physiologically quite distinct.

Biochemical Society IAS representatives of Irish universities, north and south submit their nominations to acknowledge the work of an outstanding biochemist, cell or molecular biologist through this award. Previous winners have included Professor Peter Flatt (UU), Professor Kay Ohlendorf (NUIM) and Professor Rosemary O'Connor (UCC).



(L-R) Dr Michael Carty, NUIG; Professor Therese Kinsella, UCD; Dr David Timpson, Queen's University Belfast, chair of the Biochemical Society IAS committee

UCD Conway hosts international meeting of the Irish Cytometry Society

The 4th Irish Cytometry Society meeting, organised by Dr Alfonso Blanco, UCD Conway Institute took place on November 25th & 26th 2008. Nearly 200 international delegates attended seminars, tutorials and demonstrations on the applications of technology platforms such as flow cytometry, imaging and high content screening as well as insights into emerging technologies.

Seminars from Dr John F. Daley, Dana-Farber Cancer Institute, USA and Mr Andrew Riddell, EMBL, Germany charted the development of flow cytometry in their respective institutions while Professor Kingston Mills, Trinity College Dublin highlighted the use of flow cytometry in basic cellular immunology and the development of novel immunotherapeutics. Dr Spencer L. Shorte, Institute Pasteur, France outlined to delegates how cells in suspension can be seen 3-dimensionally using a new technology that is closing the gap between flow cytometry and confocal microscopy. Mr Ricardo Morilla, Royal Cancer Hospital, UK and Professor Jeremy Simpson, UCD presented on aspects of multicolour immunophenotyping assays

and genome-wide imaging approaches to study membrane traffic respectively.

Dr Fionnuala Hickey, UCD won the oral presentation category with her insight into *Characterisation of IHG-1 - a novel transcript increased in tubulointerstitial fibrosis*. Mr Nigel Rust, Oxford; *Isolating coccoliths from sediment for geochemical analysis* and Mr Navin Kumar Verma, TCD; *High content screening and analysis (HCS/A) for the identification of compounds regulating T-cell migration* were also recognised in this competition. Awards for best poster presentations went to Mr Nigel Rust, Oxford; Dr Lori Yang, NUIG; *Multiplexed Analysis of Influenza Virus Type, Sub-type, and Receptor Specificity* and Dr Fionnuala Hickey, UCD.

Delegates at the meeting found the tutorials on the applications of technologies such as flow cytometry (Dr Alfonso Blanco, UCD) and confocal microscopy (Dr Orla Hanrahan, TCD) and hands-on demonstrations on the analysis of cytometry data (Dr Helene Dujardin, Treestar) to be very beneficial.

There was also great interest in the mini-symposium on high content analysis, a UCD-wide imaging seminar series sponsored event, joint chaired by Professor Jeremy Simpson, Dr Peter O'Brien and Dr Dimitri Scholz. Main sponsors of the meeting were Beckman Coulter, Brennan & Company and Millipore.



Dr Fionnuala Hickey (left), winner of best oral presentation at the 4th meeting of the Irish Cytometry Society and Ms Jane Wood (Partec)

New research holds promise for urothelial carcinoma of the bladder

New research by Conway scientists and clinicians; Professor John Fitzpatrick, Mater Misericordiae University Hospital and Professor Elaine Kay, Beaumont Hospital and Royal College of Surgeons in Ireland, has identified a biomarker and potential therapeutic target for urothelial carcinoma of the bladder (UCB). The findings of the research group led by Dr Amanda McCann were published recently in *Clinical Cancer Research*.

The majority of bladder malignancies do not invade muscle at diagnosis. However, these tumours have a highly unpredictable potential for recurrence and progression into muscle invasive disease. High-grade UCB tumours with lamina propria invasion (pT1, grade 3) represent those at the greatest risk. There is much debate about the appropriate surgical management of these patients. Nearly one-third will ultimately require cystectomy as second-line treatment. By identifying these high-risk cases early, the appropriate radical treatment can be given from the outset.

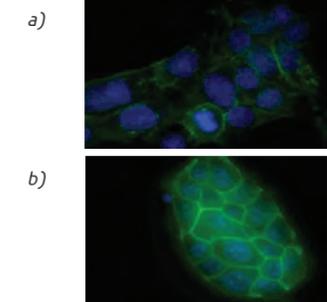
Post-doctoral researcher Dr. Emma Gallagher looked at loss of imprinting (LOI) of insulin-like growth factor-II (IGF-II) in relation to its association with cytoplasmic E-cadherin (CDH1) immunolocalisation. Moreover, on a UCB tissue microarray platform of 114 UCB cases, the group have shown that immunohistochemical assessment of CDH1 staining can independently predict time to recurrence in the non-muscle invasive pTa and pT1 tumours over and above stage and grade. In addition, CDH1 cytoplasmic staining is predictive of recurrence in the controversial pT1, grade 3 group.

IGF-II loss of imprinting (LOI) has already been identified as an epimarker of colorectal cancer development. This research suggests that the finding of LOI in the tumour associated normal of this UCB cohort points to it as a predictor of tumour development and playing a significant role in compromising cellular adherence through the internalisation of CDH1.

Dr Amanda McCann believes that specific assessment of cytoplasmic CDH1 staining

might be beneficial in the clinical setting in the future to determine whether the bladder should be conserved in high risk patients. Furthermore, the possibility of impeding tumour progression by restoring aberrant clinical levels of IGF-II to normal is an exciting one.

Clin Cancer Res. 2008 Nov 1;14(21):6829-38. PMID: 18980977



E-cadherin (CDH1) immunofluorescence within UCB cell lines: (a) CAL29 and (b) RT4 cells are stained with DAPI (blue) highlighting cell nuclei and FITC (green) highlighting CDH1 immunolocalisation. Cytoplasmic CDH1 staining is clearly evident in CAL29 cells compared to RT4 cells, which display crisp membranous staining.

CIBS produce first transgenic mouse model at UCD

UCD Conway Institute Biotechnical Services (CIBS) facility have successfully produced the first transgenic mouse model at UCD.

These models are produced by microinjection of DNA into the pronuclei of fertilised single-cell embryos, which are then transferred to pseudopregnant foster mothers. They facilitate the study of the

role of genes in development and disease and have become increasingly important in research.

Even though pronuclear injection and embryo transfer technologies are recent additions to the CIBS portfolio, two new model lines have already been successfully produced. They contain 'recombined' bacterial artificial chromosome (BAC)

created by a research team at the Institute, through funding from Science Foundation Ireland (SFI).

The successful creation of these models using a technically challenging construct is a welcome addition to the state-of-the-art services provided for researchers.

Unique platform for peptide quantification in UCD Conway

The installation of new equipment purchased through a Science Foundation Ireland grant by Professors Mike Dunn, Steve Pennington and a number of co-applicants began in September 2008. The process of installation, testing and training on Agilent 6520 Q-ToF and 6460 triple quadrupole mass spectrometers with nano-flow liquid chromatography and ChipCube and Rapid Resolution liquid chromatography and JetSpray is well underway.

These instruments form part of suite in the Conway Mass Spectrometry Resource, led by Professor Giuliano Elia, and will be used

for advanced proteomics discovery and peptide quantification. The latter is used to support both biomarker quantification and quantitative measurements for systems biology. The platform could enable drug target discovery work along with phase I clinical trials in the future.

The installation of this combination of instruments and accessories for peptide quantification is a first for Ireland, and possibly globally. The grant has also facilitated the recruitment of Cathy Rooney, a highly qualified technical expert in the area of triple quadrupole mass spectrometry.



Agilent engineer, Dr William EP Greenland leads a training session on the new mass spectrometry platform in UCD Conway Institute