All abroad for science!

Six primary and secondary school pupils will have their images of science displayed in DART trains and stations over the summer as part of *Science Track*, a joint initiative between UCD Conway Institute of Biomolecular & Biomedical Research and Iarnród Éireann.

The pupils are winners of UCD Conway Institute's AccesScience '09 poster competition, which was held earlier this year. They successfully rose to the challenge set to visually represent Science: *What's on the horizon?*

Members of the commuting public will be buoyed by the vivid imagery and intrigued by the concepts that these young people have captured in their posters.
Pupils from Gorey Educate Together National School swept the boards in the primary school category. Jamie Dixon, a 5th class pupil took first place with his poster, *You could be the next Albert Einstein.* Sophie Ryle (5th class) and Aine Dunne (6th class) were placed in second and third place respectively.

Sarah Dunne, a 4th year pupil at Loreto Abbey, Dalkey won the secondary school category with her poster, *Science; Broadening horizons.* Gabriela Duffy-Morales, also a 4th year pupil at Loreto Abbey, Dalkey took second place and Jasmine Talukder from the Dominican College, Sion Hill, Blackrock was placed third.

The competition is designed to encourage a positive attitude to scientific research among a diverse audience. MacLachan & Donaldson, Merck Sharpe & Dohme, the Environmental Protection Agency and The Irish Times sponsored the Science Track '09 initiative.

L-R: Jasmine Talukder (Dominican College, Sion Hill); Gabriela Duffy-Morales (Loreto Abbey, Dalkey); Sophie Ryle, Aine Dunne, & Jamie Dixon (Gorey Educate Together N.S) and Sarah Dunne (Loreto Abbey, Dalkey) pictured on the DART for the launch of Science Track

Recognition for graduate research

Graduate students Denise Lynch and John Synnott received prizes at the 3rd FEBS Advanced Lecture Course, Human Fungal Pathogens, which was held in La Colle sur Loup, France during May 2009.

In the Cell, Host and Microbe section, Denise was awarded best speaker for her presentation, *G+C variation in the Saccharomycotina.* John was awarded for the best poster in this section for his research on the *Analysis of the hypoxic response in Candida albicans.*

New look for Festival & CLASS in '09/'10

Autumn 2009 will bring a fresh format to both the annual Festival of Research and weekly seminar programme of UCD Conway Institute. With a firm focus on showcasing excellence in research, the Conway seminar committee, chaired by Dr Orina Belton believes that the new structures will create a vibrant scientific forum for the community of Conway researchers.

"We are returning to the original concept of the UCD Conway Festival of Research being a celebration of the outstanding achievements by Conway researchers in previous year; securing highly competitive grant funding, publishing in high quality, peer-reviewed journals, achieving innovation success, and guiding the next generation of scientists", commented Dr Belton. "And, it seems fitting to do this within the Institute".

So, we invite you to save the date for the 9th annual event, which will take place on Thursday, September 17th 2009 in UCD Conway Institute & Health Sciences Centre. This year there will be greater emphasis on moderated posters sessions based on their success last year and oral presentations will centre on recently published work. Keynote speakers will include UCD Conway Fellow, Professor Geraldine Butler who recently published genetic research on fungal pathogens in Nature. Nobel laureate, Professor Eric Kandel from Columbia University will present his Ulysses medal lecture at the final plenary session of the day.

The Conway Lecture & Seminar Series '09/'10 will continue to bring you the latest national and international research expertise in aligned thematic areas but, for the first time, this weekly seminar series will also provide a platform for graduate and postdoctoral Conway members to showcase their research. We hope you'll look forward to taking your seats for CLASS this autumn!

2008 UCD Conway Festival of Research medal winner Dr Lydia Lynch pictured with Roche representative Jenny Pearson. Lydia went on to win a 2009 L'Oreal-UNESCO International Fellowship to support a research internship in Harvard Medical School.

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conway focus

Fundamental insights to Candida species

Chinese military strategist, Sun Tzu famously wrote in the 6th Century BC about knowing your enemy. Research published recently in *Nature* by an international team coordinated by UCD Conway Fellow, Professor Geraldine Butler together with Dr Christina Cuomo and Dr Manolis Kellis from MIT, has described six new genome sequences and fundamental insights into *Candida* species, including the most common causes of opportunistic fungal infection worldwide. This should pave the way for scientists to develop treatment strategies to combat these pathogens.

Premature babies, neonates and transplant patients are most at risk from acquired blood borne infections and invasive disease when *Candida* forms a film that coats the inside of medical devices such as implants, catheters or feeding tubes. The fungi are drug resistant and, currently, the only effective treatment involves the removal of the medical device. However, up to 40% of patients who acquire blood borne infections with *Candida* die as a result.

The international collaboration involving scientists at twenty-one institutes including the genome sequencing centres in the Wellcome Trust Sanger Institute, UK and the Broad Institute at MIT and Harvard, USA have described how *Candida* strains have evolved and ensured their survival by adapting their genetic makeup to respond to changes in their environment.

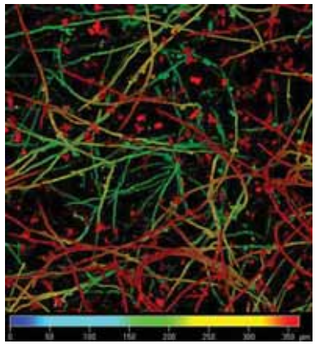
The UCD research team led by Professor Butler, the scientific coordinator on this project, looked at key components of mating and cell division in *Candida* species, shedding new light on how the fungi reproduce and survive.

They started work to sequence small parts of the *C. parapsilosis* genome in 2003 through an award from Science Foundation Ireland. This led to the collaboration with the Sanger Institute to sequence the entire genome, and finally to combining this genome with others sequenced by the Broad Institute.

Commenting on their findings, Professor Butler says, "*Candida* species were originally believed to be incapable of mating, and so may have difficulties in adapting to new environments or new hosts. As a result of our analysis, we now know a great deal more about the evolution of mating, and how some species recombine their genes. Interestingly, *C. parapsilosis* is probably the only species that cannot mate".

By comparing the genetic sequences in disease and non-disease causing fungi, the team found that in general, the disease causing *Candida* species have many more copies of genes involved in adhesion, and in the cell wall. The stickiness of the proteins in the cell wall makes it easier for the fungi to adhere to the human host. Further research on the regulation of these proteins may lead to developing treatment methods for infections caused by fungi in the future.

Ref: Evolution of pathogenicity and sexual reproduction in eight Candida genomes (2009). Butler, G et al. Nature 459, 657-662 I doi:10.1038/nature08064



Candida species growing as biofilms on catheter material

Director's Message

Welcome to the July edition of Conway Focus!

The last quarter has seen some outstanding research achievements by Conway Fellows. In particular, I extend congratulations to Prof. Geraldine Butler on her Nature publication and Prof. Catherine Godson on securing a SFI US-Ireland R&D programme award in diabetes. We are eagerly anticipating the arrival of Prof. Walter Kolch later in July to lead the Systems Biology initiative in conjunction with SFI Stokes Professor in Systems Biology, Prof. Boris Kholodenko, Prof. Des Higgins and Prof. Cormac Taylor. It is research of this calibre that will allow the Institute to achieve and sustain international recognition as a centre of excellence in cell and systems biology.

I would like to thank the various committees who have worked hard during the academic year on aspects of strategic importance to the Institute. Their input on behalf of colleagues has been invaluable and I look forward to bringing their recommendations to implementation phase in the coming months.

Professor Des Fitzgerald,
Director

conway focus

Discussion forum on biobanks at cancer proteomics conference

In June, UCD hosted Cancer Proteomics 2009; Mechanistic Insights, Technological Advances, and Molecular Medicine. This flagship event in the EMBO conference series programme was the first in a series of three events to be held over the next six years on the theme of cancer proteomics.

International experts met to discuss how the convergence of these research areas can improve the process of identifying new cancer biomarkers and therapeutic targets. This is considered important for disease diagnosis, personalising treatment regimes and monitoring therapy.

Plenary speakers included Ruedi Aebersold, Professor of Systems Biology at the Institute of Biotechnology, ETH-Zürich who is trying to detect protein biomarkers in blood plasma using a new, hypothesis driven, targeted quantitative proteomic strategy.

Members of the public were invited to join delegates to discuss biobanks, an invaluable research resource for those working in the area of biomarker discovery and validation. Professor Elaine Kay and Dr David Smith from Beaumont Hospital and the Royal College of Surgeons in Ireland led the discussion and outlined issues relating to the establishment, governance, management, and use of human biobanks for research purposes. UCD Conway Fellow, Professor William Watson chaired the discussion forum, which was timely given the recent publication of a Government report on the creation of a national biobank.

From the discussion, it seemed clear that a national repository of biological samples from particular diseases is critical to the ability of scientists and clinicians to deliver on translational research. While many factors contribute to the quality of biobanks, the issue of consent is pivotal.

There was general consensus that the process of obtaining consent from patients to use their biological samples should clearly indicate that they could be used for a number of future studies. This reflects the opinion of the expert group who compiled the *Recommendations for the Establishment of a National Cancer Biobank*. They advised that "consent should be given in the form of general consent or broad consent for 'unspecified future research use'" and that "a generic, national consent process must be enacted".

Cancer Proteomics 2009 was a Science Foundation Ireland designated tier 1 level conference organised by UCD Conway Fellows, Professors William Gallagher, Michael Dunn, Stephen Pennington, William Watson and Dolores Cahill in conjunction with collaborators from the United Kingdom and Sweden.

Plenary speakers at Cancer Proteomics 2009, Professor Ruedi Aebersold, Swiss Federal Institute of Technology; Professor Paul Tempst, Memorial Sloan-Kettering Cancer Center, USA; Professor Richard Simpson, Ludwig Institute for Cancer Research, Australia

Invited Material Research Society talk on Piezoresponse Force Microscopy (PFM)

Scholars of Greek know that *piezo* translates to pressure. The piezoelectric effect occurs in non-conductive materials when mechanical stress creates an electric charge in proportion to the stress applied. A typical example is the inflation of a passenger airbag in a car as a result of impact. The shock intensity of the impact in a collision creates an electronic signal that triggers the airbag to inflate.

Piezoresponse force microscopy (PFM) is an advanced imaging technique that measures electromechanical activity at the nanometre and molecular scale. Dr Brian Rodriguez, a lecturer in nanoscience and recent member of the atomic force microscopy (AFM) research group led by UCD Conway Fellow, Professor Suzi Jarvis, presented PFM research at the invitation of the Materials Research Society in San Francisco, California, USA in April.

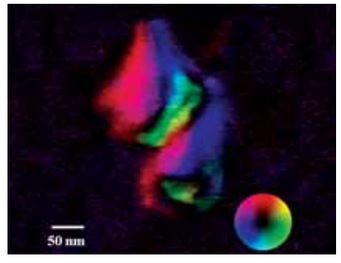
A problem associated with PFM is that it can cause damage to both the tip and sample due to the high indentation forces used to maximise the electromechanical contribution to the signal. In an effort to minimise the surface damage, research published recently in Nanotechnology by Dr Rodriguez and his collaborators examined the feasibility of carrying out PFM imaging using intermittent contact or 'tapping' in a liquid environment.

Coupling between electrical signals and mechanical motion in biological systems is essential to life and many biopolymers are piezoelectric. Little is known, however, about the effect of electrical stimuli on the chemistry and functionality of biological systems, particularly at the nanoscale.

Dr Rodriguez presented to delegates using examples of electromechanical imaging of cellular and biomolecular systems such as human teeth (dentin versus enamel), collagen as well as other tissues. Nanoscale piezoelectricity is ubiquitous in biosystems due to the combination of polar bonds and optical activity in biopolymers.

He also discussed PFM of cellular systems including red blood cells and yeast cells. He mentioned the use of liquid PFM of cells in solution. Work is currently ongoing to address separation of the electromechanical response from electrostatic, elastic and topographic contributions, and to relate the electromechanical response to biofunctionality.

Ref: Intermittent contact mode piezoresponse force microscopy in a liquid environment. Brian J Rodriguez, Stephen Jesse, Stefan Habelitz, Roger Proksch and Sergei V Kalinin (2009) Nanotechnology 20 195701 (6pp) doi: 10.1088/0957-4484/20/19/195701



Electromechanical map of embedded proteins in human milk tooth enamel. The color wheel shows the orientation and intensity of the electromechanical response.

New vessels for old lungs: reducing pulmonary hypertension through a novel mechanism

Supplementing dietary L-arginine may relieve pulmonary hypertension, a common and serious complication of lung diseases, by creating new blood vessels in the pulmonary circulation. The research, recently published in the American Journal of Physiology, was undertaken by Dr Katherine Howell as part of the Health Research Board funded programme of UCD Conway Fellow, Professor Paul McLoughlin.

Reduced oxygen levels in patients with lung diseases such as cystic fibrosis, emphysema and lung fibrosis lead to increased resistance to blood flow through the lungs and an abnormally high workload on the heart. This results in heart failure, increased breathlessness, further disability and ultimately reduces the life expectancy of patients with these conditions.

Scientists believed that the increased resistance to blood flow in pulmonary hypertension was predominantly caused by narrowing of the blood vessel lumen within the lung, and treatment strategies focused on reversing this. The McLoughlin group challenged this paradigm as a result of their work to examine the effects of dietary L-arginine on pulmonary vasoconstriction, vascular lumen diameter and vessel length.

They found that while this intervention effectively reduced pulmonary hypertension, it did not change the diameter of the blood vessel lumen but rather caused a significant increase in the length of blood vessels in the lung, demonstrating new vessel growth.

These findings suggest that dietary L-arginine reduces hypoxic pulmonary hypertension not, as previously thought, by an effect on the structurally determined lumen diameter of pulmonary blood vessels but rather by stimulating the formation of new vascular pathways through the lungs. It opens the possibility of a previously unrecognised approach to the treatment of lung diseases. Professor McLoughlin's group are currently examining the specific molecular mechanisms that produce this potentially beneficial response.

Ref: L-Arginine promotes angiogenesis in the chronically hypoxic lung: a novel mechanism ameliorating pulmonary hypertension (2009) K. Howell, C. M. Costello, M. Sands, I. Dooley, and P. McLoughlin. Am J Physiol Lung Cell Mol Physiol 296: L1042-L1050.

Generating precise spatial guidance for cellular processes

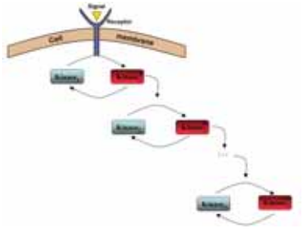
How do proteins know their position inside a cell? How does the cell obtain information about its own size? A simple pattern formation mechanism derived by UCD Conway Fellow, Professor Boris Kholodenko in collaboration with Dr Zoltan Neufeld, UCD School of Mathematical Sciences and Dr Javier Muñoz-García, published recently in *PLoS Computational Biology*, may provide an answer to these questions.

Living cells detect environmental cues through a variety of plasma membrane receptors. When activated by external signals, these receptors initiate signalling cascades. In this mechanism, digital positional information arises from cascades of protein modification cycles, in which a pair of opposing enzymes control the activation and deactivation of a protein.

The activated form of a protein arising from one cascade transmits a signal to the next cascade level and continues step-wise until it reaches the cell nucleus. Since only the activation of the first cascade level takes place near the cell membrane, the density of the activated form of these proteins diffusing in the cell decreases quickly towards the cell interior.

This spatially-distributed cascade creates step-like activation profiles, which decay at different distances from the cell membrane and assign digital positional information to different regions in the cell. The research team looked at conditions when signals either stall or robustly propagate through spatially distributed cascades. This allowed them to derive an analytical solution for activation profiles as a function of the cascade level, protein diffusivity, and the ratio of the opposing enzyme activities. Information from this research can now be exploited by other cellular processes, such as vesicle and molecule transport, cell growth and division.

Ref: Positional Information Generated by Spatially Distributed Signaling Cascades. (2009) Muñoz-Garcia J, Neufeld Z, Kholodenko BN. PLoS Comput Biol 5(3): e1000330.



Cascade signalling scheme of phosphorylated and unphosphorylated kinases activated at the membrane.

Collaborative research identifies protein expression alterations in the brain

Can changes at the level of individual proteins help us understand diseases of the brain such as schizophrenia and bipolar disorder? The results of research by scientists in RCSI and UCD published recently in *Molecular Psychiatry* have identified significantly increased protein expression in patients with these conditions.

This study, a collaboration between Professor David Cotter, Department of Psychiatry, RCSI and UCD Conway Fellows Professor Michael Dunn and Dr Gerard Cagney used advanced proteomics methods to analyse changes in prefrontal brain tissue of schizophrenia and bipolar disorder patients.

The research focused on the membrane microdomains in the dorsolateral prefrontal cortex of the brain tissue samples donated from two biobanks; the Stanley Medical Research Institute and the Harvard Tissue Resource Centre, USA.

Using two different proteomic methods, 2-dimensional difference gel electrophoresis (2D DIGE) and label-free quantitative proteomics, the expression of sixteen proteins was altered in one or both conditions. Interestingly, the up-regulated proteins tended to be involved in four main cellular functions: synaptic transmission, ion channel activity, signal transduction, and cytoskeletal activities.

Three proteins with important roles in synaptic transmission were then selected for further investigation in individual patient samples in the two brain series; limbic-system associated membrane protein (LAMP), brain abundant membrane-attached signal protein 1 (BASP1), and syntaxin-binding protein 1 (STXBP1). Changes were confirmed in one brain series of bipolar disorder and in both brain series of schizophrenia. The results support the view that the pathology of schizophrenia involves neuritic and synaptic dysfunction.

The proteomic analysis was carried out primarily by Dr Aine Behan with technical assistance from Dr Connie Byrne in the UCD Conway Institute Mass Spectrometry Resource, led by Professor Giuliano Elia. The Health Research Board, the Wellcome Trust, and Science Foundation Ireland supported the research.

Ref: Proteomic analysis of membrane microdomain-associated proteins in the dorsolateral prefrontal cortex in schizophrenia and bipolar disorder reveals alterations in LAMP, STXBP1 and BASP1 protein expression (2009). Behan AT,Byrne , Dunn MJ, Cagney G and Cotter DR. Molecular Psychiatry 14, 601–613