Recognising excellence in research

A number of Conway graduate and postdoctoral researchers have recently been recognised for outstanding research in national and international competitions.

Dr. Patricia McGowan won the 8th St Luke's Young Investigators Award for her presentation on 'ADAMs: new players in breast cancer progression'. A senior postdoctoral researcher working in the Education & Research Centre, St Vincent's University Hospital with Professor Joe Duffy, Dr McGowan received the Royal Academy of Medicine in Ireland bronze medal and €1000.

Brian Morrissey, PhD student with Professors Stephen Pennington and John Armstrong (St Luke's Hospital) won the Waters postgraduate symposium competition for demonstrating innovative, analytical ideas through his proteomic research.

As part of his €20,000 prize, Brian will spend a week in Waters laboratories in Manchester where their high value mass spectrometry equipment and specialist advice will be at his disposal.

Dr Judith Conroy, postgraduate researcher with Drs Sean Ennis and Sally Ann Lynch in UCD School of Medicine & Medical Science was one of three scientists awarded KnomeDISCOVERY™ exome sequencing and comparative analysis packages.

Judith will use KnomeDISCOVERY™ in her research on facio-audio-symphalangism (FAS), a rare developmental syndrome. Working with two Irish families each with a set of triplets where only two children are 'identical' twins and both have FAS, she hopes to identify distinctive spelling variants that could cause the disease and establish if there is any link to the process of twinning.

Back row (L-R): Dr John O'Connor, Gen Sec RAMI and UCD SBBS and Conway Institute; Dr Patrick Buckley, RCSI, finalist; Dr Patricia McGowan, UCD SBBS and Conway Institute, winner 8th St Luke's Young Investigators Award; Dr Antoinette Powell, TCD, finalist; Mr Tom Walsh, President RAMI. Front row (L-R): Prof Donal Hollywood, Professor Clinical Oncology TCD; Dr Catriona O'Sullivan, Medical Director St Luke's Hospital; Dr Claire Donohoe, TCD, finalist.

New 3-D visual of intestinal growth promoting peptide

PhD student, Kalyana Venneti and Conway Fellow, Dr Chandralal Hewage have determined the 3-dimensional solution structure of glucagon-like peptide-2 (GLP-2) for the first time using nuclear magnetic resonance and molecular modelling. This visual was selected as the cover image of the current issue of the biochemical journal, FEBS Letters.

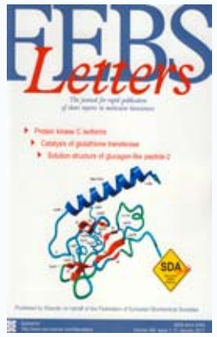
Acting as an intestinal growth promoting agent in the small and large bowel, GLP-2 promotes the expansion of the epithelial mucosa and, consequently, better absorption of nutrients. It does this by stimulating crypt cell proliferation and preventing cell death in the gut epithelium.

Glucagon-like peptide-2 (GLP-2) is a therapeutic target used in the treatment of short bowel syndrome, where nutrients are not being correctly absorbed either due to severe intestinal disease or surgical resection of a large portion of the intestine.

"These results provide a valuable insight into the structural and functional properties of GLP-2 and its receptor interactions, which could help in the design of novel therapeutic drugs that may be active at the GLP-2 receptor", says Dr Hewage.

Reference

Conformational and molecular interaction studies of glucagon-like peptide-2 with its N-terminal extracellular receptor domain. Kalyana C. Venneti, Chandralal Hewage. FEBS Letters volume 585 issue 2 21 January 2011



Solution structure of glucagon-like peptide-2 as the cover image of FEBS Letters, January 2011

New biochemistry applications for iTunes store

Conway Fellow, Professor J. Paul G. Malthouse has developed three iPhone applications intended as experimental planning aids for researchers and revision aids for undergraduate and postgraduate students. EnzymeQA, AminoAcidQA and NMRQA contain a series of questions and answers on the topics of enzymology, amino acid metabolism and 1- dimensional nuclear magnetic resonance (NMR).

Scientists using NMR in their research can avail of practical tips on setting up experiments such as parameters and signal processing, interacting with NMR operators and even basic NMR facts. Those researchers considering using single substrate enzyme catalysis can check on appropriate experimental conditions for determining catalytic constants using EnzymeQA. The applications can be found on http://itunes.apple.com/us/app/enzymeqa/id412649030?mt=8

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Investing in Your Future

March 2011 Issue 13

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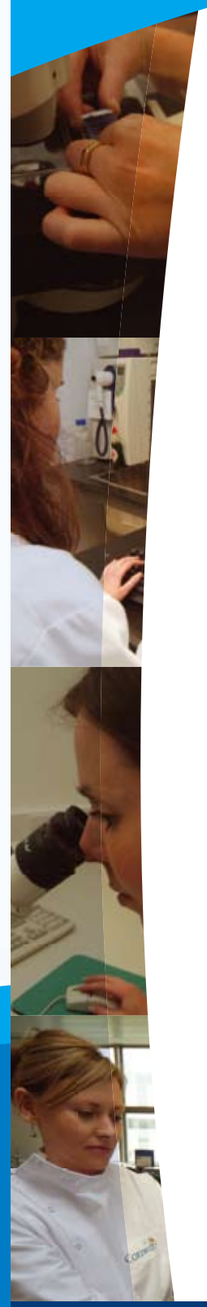


Towards personalised nutrition

As the latest addition to the 'omic' field of science, metabolomics shows potential in the area of nutrition research. New research led by Conway Fellow, Dr Lorraine Brennan is making strides in developing the use of metabolomics to discover potential dietary biomarkers and in identifying groups of people who respond to specific dietary interventions.

The link between diet, lifestyle, genetics and risk factors for chronic diseases is now a focus of international research. With diet being a major contributory factor to the increase in metabolic diseases such as obesity, diabetes and cardiovascular disease, a reliable dietary assessment method is crucial to understanding this link.

The small molecules or metabolites that result from complex processes within the cell are influenced both by endogenous factors (such as age, sex, genes and disease) and exogenous factors (such as diet and drugs). Using nuclear magnetic resonance (NMR) and mass spectrometry, multivariate analysis of metabolites can provide a chemical profile of activity within cells.

New findings by this team show that metabolic profiling of urine can reflect dietary patterns of individuals. The study, published recently in the American Journal Clinical Nutrition, identified two novel biomarkers for red meat and vegetable intake.

Using biofluids and food diaries from 160 individuals, researchers were able to identify metabolites associated with different dietary patterns from 33 different food groups. Several of the metabolites were linked to specific food groups. In particular, O-acetylcarnitine was associated with red meat intake and phenylacetylglutamine with vegetable intake.

Commenting on these findings, Dr Brennan says, "By identifying these biomarkers, we are taking a significant step forward in developing the novel concept of nutritype. The ability to produce a metabolic profile that reflects patterns of dietary intake could be extremely valuable as part of dietary assessment in the clinical setting".

As well as gaining insight into the habitual dietary patterns of individuals, this research group have also used metabolomic profiling to monitor specific dietary interventions.

There is evidence to suggest that vitamin D status may play a role in the development of diseases related to the metabolic syndrome. This syndrome is the collective name for a group of risk factors that occur together and increase risk of stroke, cardiovascular disease and type II diabetes. Research findings by groups working in this area suggest that low serum levels of vitamin D are associated with markers of disturbed glucose metabolism and cardiovascular disease.

"We have developed a method to identify people who respond to supplementation with vitamin D with respect to the markers of the metabolic syndrome. This new method is a move towards personalised nutrition and being in a position to advise specific groups of people based on their metabolic phenotype rather than more generic , 'one size fits all' approach."

Lorraine Brennan, and her colleagues in the UCD Institute of Food & Health and University College Cork, are now in the process of expanding both of these studies to assess applicability in larger cohorts and, in respect of the latter study, to other dietary interventions. This work has been funded by the Irish Department of Agriculture, Food and Fisheries.

Reference

O'Sullivan A, Gibney MJ, Brennan L. Dietary intake patterns are reflected in metabolomic profiles: potential role in dietary assessment studies. American Journal Clinical Nutrition 2011 93:314-321. In press

O'Sullivan A, Gibney MJ, O Connor A, Mion B, Kaluskar S, Cashman KD, Flynn A, Shanahan F, Brennan L. (2010) Biochemical and Metabolomic Phenotyping in the Identification of a Vitamin D Responsive Metabotype for Markers of the Metabolic Syndrome.Molecular Nutrition and Food Research.In press DOI 10.1002/mnfr.201000458

Director's Message

I am delighted to welcome Dr Ian Barwick, Business Development Manager for the Conway, Systems Biology Ireland & Charles Institute to the directorate team. Ian will be pivotal in driving our strategic innovation agenda and maximising the impact of our relationships with industrial partners. Specifically, he aims to attract new collaborative research funds and identify opportunities for new product/process development with industry partners.

With a background in chemistry and over 18 years experience in the pharmaceutical industry, Ian comes to UCD from Bangor University, Wales where he spent 4 years as Technical Director for Intellectual Property and Commercialisation.

Congratulations to Professors Geraldine Butler and Denis Shields as they launch the Wellcome Trust UCD PhD programme in Computational Infection Biology. Their success in securing such competitive funding is testament not only to the scientific credentials of the investigators involved but also to the collaborative strength that manifests with cross-institutional interactions.

Professor Walter Kolch
Director

conway focus

First Welcome Trust funding for Irish based PhD Programme

For the first time in its history, the Welcome Trust has awarded funding for an Irish based PhD programme. The UK charitable foundation will provide upwards of €3 million towards a four-year structured UCD PhD programme in Computational Infection Biology.

The UCD PhD Programme will contribute to one of the Wellcome Trust's major research challenges, namely to understand the emergence, transmission, pathogenesis and control of acute and chronic infectious diseases at the global level.

"The research programme will investigate the basis of pathogenicity and virulence in infectious organisms ranging from viruses (such as human immunodeficiency virus (HIV), hepatitis B, and influenza) to bacteria causing malaria, TB and other major diseases, and fungi, which grow on indwelling medical devices," says programme director, Professor Geraldine Butler, UCD School of Biomolecular & Biomedical Science and UCD Conway Institute.

"The areas of investigation will include the host response to infection, identifying therapeutic targets and developing novel drugs. One aspect unique to University College Dublin is that the programme will investigate pathogenesis in both animals and man, addressing the 'One World, One Health' initiative, linking human, animal and environmental health."

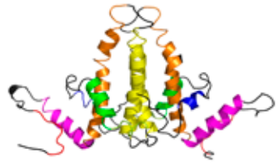
Advances in the development of new high-throughput scientific techniques have generated enormous amounts of data relevant to infectious disease research that is currently under-utilised, due to a lack of methodologies and suitably trained scientists.

The new UCD PhD programme aims to address this by equipping students with the skills necessary to negotiate the cultural and linguistic barriers that currently separate biological and computational research disciplines.

The PhD programme will draw on expertise from across five UCD Schools, the UCD Conway Institute, and the UCD Complex and Adaptive Systems Laboratory (CASL) and will train scientists to integrate computational methods with biological research focused on infectious diseases.

It will build on the success of the UCD PhD programme in Bioinformatics and Systems Biology funded by the Irish Research Council for Science, Engineering & Technology (IRCSET) since 2007, and also on individual research projects on infectious disease and bioinformatics funded by Science Foundation Ireland grants to participating investigators.

Professor Denis Shields, UCD School of Medicine & Medical Science, UCD Conway Institute & UCD CASL is the deputy director of the programme and many Conway Fellows will be involved in aspects of delivery. More details on the programme and application process are available on: http://bioinfo-casl.ucd.ie/cib. The deadline for the 2011/2012 academic year is 18th March 2011.



Ribbon representation of human hepatitis B virus core protein (HBc) dimers as found within recombinant capsids

Proteomics underpinning research across diverse disciplines

The UCD Conway Mass Spectrometry Resource (MSR) instrumentation and expertise are being utilised in a diverse range of projects that aim to identify proteins and their modifications implicated in fundamental biology in health and disease.

Two recent examples of publications involving the MSR highlight the fact that proteomics as a core technology platform is underpinning research across scientific disciplines from agriculture to nanotechnology.

Currently, a major challenge for the swine industry is to improve the water holding capacity (WHC) of pork and reduce the incidence of meat with poor appearance, texture and a reduced shelf life.

Dr Giuliano Elia, MSR Director worked with collaborators in Teagasc Food Research Centre and NUI Galway to identify potential biomarkers for the early prediction of meat quality in an industrial setting.

The study detailed 44 proteins recovered in exudates from muscle tissue. There were several significant associations between the protein fragment band volumes that can be related to WHC or post mortem degradation.

A number of peptides from the heat shock protein (HSP) family involved in protecting cells from stress were identified. HSP interact with damaged proteins in an effort to restore function. The team believe that HSP70 may have potential as a biomarker for moderate to good WHC.

Working with Professor Kenneth Dawson, Centre for Bio-Nano Interactions (CBNI), the MSR were involved in a project to initiate a framework for the study of the protein corona surrounding nanoparticles in biological media.

This durable, stabilising protein coating on the bare surface of nanoparticle (NP) monomers is now thought to be a primary defining element of nanoscale objects in biological media. The extent of screening of the NP surface by the corona may impact on cell-particle interactions.

Taking two compositionally different nanoparticles, polystyrene and silica, in different plasma concentrations, protein adsorption studies showed that the hard corona can evolve quite significantly in different plasma concentrations.

The findings have implications for experimental design and in vitro – in vivo extrapolations given the varying protein concentrations in each type of study.

Reference :
Physical-Chemical Aspects of Protein Corona: Relevance to in Vitro and in Vivo Biological Impacts of Nanoparticles. Marco P. Monopoli, Dorota Walczyk,Abigail Campbell,Giuliano Elia,Iseult Lynch, Francesca Baldelli Bombelli, and Kenneth A. Dawson. J. Am. Chem. Soc. 2011 In press dx.doi.org/10.1021/ja107583h

Centrifugal drip is an accessible source for protein indicators of pork ageing and water-holding capacity. Alessio Di Luca, Anne Maria Mullen, Giuliano Elia, Grace Davey, Ruth M. Hamill. Meat Science 2010 doi:10.1016/j.meatsci.2010.12.033

Novel regulator of photoreceptor gene expression

Conway Fellow, Dr Breandan Kennedy and his team, in collaboration with scientists in the University of Washington, Seattle, have identified a transcriptional regulator that is sufficient to enhance the initiation of photoreceptor specific gene expression.

Photoreceptors are the sensory neurons that capture images of the world around us. Although the two types of photoreceptor appear structurally similar grossly, they are functionally distinct with cone photoreceptors enabling colour vision and rods adapted to function in low light.

The morphological and functional development of photoreceptors depends on regulated gene transcription but very few cis-regulatory elements have been identified to date.

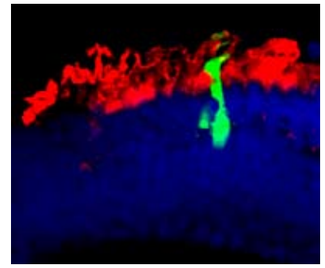
Using a zebrafish model, this study focused on expression in the cone transducin gene (TαC), which is required for colour vision. Mutations in this gene in humans cause total colour blindness and cone-based blindness in zebrafish.

The team identified photoreceptor regulatory element 1 (PRE-1), a 41 base pair sequence that specifically binds eye nuclear protein. It has a number of unique characteristics when compared to other cis-regulators of photoreceptor expression.

Commenting on the recent publication of this research in BMC Developmental Biology, Dr Breandan Kennedy said, "It is only by deciphering the molecular mechanisms responsible for development and functionality in such complex systems that we can hope to engineer appropriate gene expression responses in the future".

Science Foundation Ireland funded this research. The Kennedy group hope to further expand this study to identify elements acting with PRE-1 to regulate cone-specific expression.

Reference
PRE-1, a cis element sufficient to enhance cone- and rod- specific expression in differentiating zebrafish photoreceptors. Maria E. Morrissey, Sara Shelton, Susan E. Brockerhoff, James B. Hurley and Breandán N. Kennedy. BMC Developmental Biology 2011, 11:3 doi:10.1186/1471-213X-11-3



Highlighted for mention by BMC Developmental Biology. Confocal micrographs of retinal sections from 5 dpf zebrafish embryos injected with the (3x PRE-1)-1.2 kb ZOP-EGFP construct shows co-localisation with a marker for rod photoreceptors. Staining shows enhanced green fluorescent protein EGFP (green), rod photoreceptors (4C12; red) and nuclei (DAPI; blue)

Specific effect of cigarette smoke on innate immune cells

UCD researchers in the obesity immunology research group led by Conway Fellow, Professor Donal O'Shea have demonstrated for the first time that cigarette smoke extract (CSE) has a specific effect on a minor subset of immune cells and this may contribute to the role of cigarette smoke in the development of cancer.

Carginogens in cigarette smoke can lead directly to lung cancer and have been implicated in several other malignancies. In addition, cigarette smokers have an increased susceptibility to type II diabetes, infections and autoimmune disorders such as rheumatoid arthritis.

Invariant natural killer T (iNKT) cells are immune regulators that play an important role in mounting anti-tumour responses with the early production of potent cytokines. Many studies have already shown that iNKT cells are defective in certain cancers.

This study compared the number and function of iNKT cells in a group of healthy individuals who smoke 20 cigarettes each day to those in non-smoking individuals of the same age group.

The recently published findings showed reduced iNKT cell numbers in cigarette smokers and also significant defects in the ability of iNKT cells to produce cytokines and kill target cells.

Commenting on the work, postdoctoral researcher and first author on this publication, Dr Andrew Hogan said, "It would seem that cigarette smoke has multiple negative effects on innate immune cells that are important in tumour surveillance and protection against infection. In addition to increasing your risk of developing cancer, it appears that smoking also impairs your body's ability to fight the disease effectively". This research was funded through a Sanofi Aventis Newman scholarship to Dr Hogan.

Reference
Andrew. E. Hogan, Michelle. A. Corrigan, Vincent O'Reilly, Gadintshware Gaoatswe, Jean O'Connell, Derek. G. Doherty, Lydia Lynch, Donal O'Shea, Cigarette smoke alters invariant natural killer T cell function and may inhibit anti-tumour responses, Clinical Immunology (2011), doi:10.1016/j.clim.2011.01.011

IDDN announce new industrial partnership with Arch Therapeutics

The Irish Drug Delivery Network (IDDN), a strategic research cluster funded by Science Foundation Ireland, has announced that it will collaborate with Boston-based Arch Therapeutics to optimise the development of novel products for surgery and trauma.

Arch Therapeutics has developed a clear liquid that forms a barrier when topically applied to a wound. The barrier promptly stops bleeding and seals leaking. The material has no effect on the coagulation process and is biocompatible. The underlying technology platform was licensed from the Massachusetts Institute of Technology.

Welcoming the announcement, Professor David Brayden, IDDN Director and Conway Fellow, said, "We look forward to working with Dr Terence Norchi, CEO Arch Therapeutics to help optimise the polymer formulation process and characterise the material at all stages of the synthetic process for this product. Our aim is to ensure a reproducible process for effective application of the product in surgery. "

IDDN scientists are based in four academic centres; UCD, TCD, RCSI and UCC. This project will involve Prof. David Brayden, Dr Marc Devocelle (RCSI) and postdoctoral scientists based at Centre for Synthesis & Chemical Biology (UCD) and the Peptide Synthesis Laboratory (RCSI). Dr Abina Crean (UCC) will work to optimise certain aspects of the manufacturing process and look at peptide secondary structure.

Arch Therapeutics was co-founded by a group of Irish-Americans in Massachusetts, USA and named after the iconic Spanish Arch in Galway.