

## New horizons for neglected diseases

Dr Patrick Brennan was recently honoured with an Alumnus Award by Trinity College Dublin in recognition of his internationally acclaimed work on the twin scourges of tuberculosis and leprosy. Dr Brennan carried out his PhD in the Department of Biochemistry (1962–1965). Recognition of his work is a reminder of the strong tradition in this area established by Dr Vincent Barry and his team at the Medical Research Council laboratory at TCD. That work culminated in the discovery of Clofazimine which is still a first line drug in the treatment of leprosy. In celebration of his award, Dr Derek Nolan of the School's Molecular Parasitology group organised a symposium on neglected diseases which was addressed by Professor Brennan and by a new generation of researchers who described their research and its implications for diseases of developing countries.



Professor Patrick Brennan  
and his wife Professor Carol Blair

## Keystone conference in Trinity College Dublin

A major Science Foundation Ireland-sponsored global conference examining the role that the immune system plays in disease took place in Trinity in June 2010. Many of the world's leading immunologists and influential industry figures participated in the conference - 'Innate Immunity: Mechanisms Linking with Adaptive Immunity': a Keystone Symposium on Molecular and Cellular Biology. "With remarkable recent advances in immunology, there is now tremendous excitement internationally around the prospect of new treatments for diseases such as cancer, arthritis, MS, asthma and infections. With Ireland now ranked third in the world in immunology research, this conference is particularly timely," according to Professor Luke O'Neill, conference organiser and multi award-winning researcher from the School of Biochemistry and Immunology.



Phagocyte ingesting bacteria

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## School of Biochemistry and Immunology moves to Biomedical Sciences Development

The School of Biochemistry and Immunology arose from the original Department of Biochemistry established in 1960 and the emerging discipline of immunology. The School already has a world-renowned reputation for research and teaching. The school will move out of the old Wellcome and Biotechnology buildings to state-of-the-art facilities in The Biomedical Sciences Development on Pearse Street in July.



Biomedical Sciences Building, Trinity College Dublin

We offer 4 undergraduate degree courses, with over 50 Sophister students per year. We have 76 PhD students and 61 Postdoctoral Fellows involved in cutting edge research across the disciplines of biochemistry and immunology, including the development of therapies for diseases with unmet needs, such as cancer and infectious diseases. Six PIs from the School of Biochemistry and Immunology have helped to establish The Immunology Research Centre (IRC), a strategic research cluster funded by Science Foundation Ireland and Industry. The IRC is directed by Head of School Professor Kingston Mills, and focuses on the identification of novel modulators of innate immunity. Thomson Reuters Essential Indicator Database ranked Ireland third in the world in immunology in 2009 and researchers from our school were primarily responsible for this achievement.

## Public promotion of science

The School engages with the public through its involvement with the Science Gallery, an innovative TCD enterprise whose mission is to engage 15-25 year olds with science and innovation. One of the most successful Science Gallery exhibitions "INFECTIOUS: Stay Away", curated by Professor Luke O'Neill and Professor Cliona O'Farrelly of the School explored contagion through science and art. It included a public lecture on pandemic influenza by Professor Kingston Mills and Professor Luke O'Neill and the world's first live epidemic simulation. It allowed visitors to have their DNA analysed for variations in Mal, a protein discovered in Professor O'Neill's lab, which explains differences in people's immune response to certain diseases. The exhibition had over 45,000 visitors and received widespread international coverage, including articles in Science and Nature Immunology. The success of the Science Gallery shows the huge public interest in science as Dublin prepares to be the European City of Science in 2012.



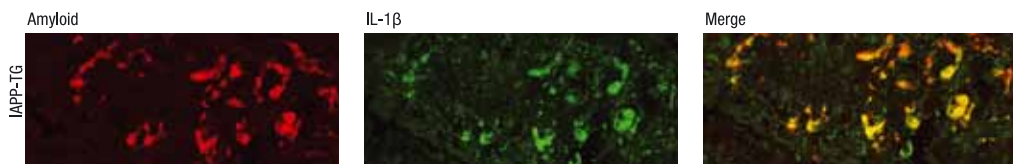
Professor Luke O'Neill, Professor Cliona O'Farrelly, Professor Kingston Mills

# Research

## Breakthrough in diabetes research

A team from Professor Luke O'Neill's group has discovered what could be the underlying basis for Type 2 Diabetes. They found that the peptide hormone, Islet Amyloid Polypeptide (IAPP), which is deposited in the pancreas in Type 2 Diabetes, is the trigger for a protein complex called the NLRP3-inflammasome leading to the over-production of the pro-inflammatory agent IL-1beta. Dr Seth Masters, lead author of the work which was

published in Nature Immunology, says "IL-1beta is known to be important in diabetes and we have found what might be the key mechanism leading to its over-production." IL-1beta is being explored by several drug companies and results are promising. This work confirms the importance of IL-1beta in diabetes, points to NLRP3 as a new drug target and provides real hope that much better treatments for Type 2 diabetes will emerge in the near future.



Overexpression of the amyloid protein (red) and the inflammatory molecule IL-1β (green) in Type 2 diabetes

## Folate, vitamin B12 and neural tube defects

Professor John Scott and Dr Anne Molloy have been studying the genetics and biochemistry of neural tube defects in relation to folate and vitamin B12 for many years. The group was first to demonstrate that low or inadequate maternal folate status is an important risk factor for neural tube defects. Their follow-on studies established appropriate folate intakes that would be protective against these birth defects and provided crucial information for public health strategy in the USA and other countries to fortify foods with folic acid, an intervention that has resulted in a significant decrease in the incidence of neural tube defects. Their ongoing work to determine the folate and vitamin B12 related genetic factors that confer risk of birth defects such as neural tube defects and orofacial clefts has been funded for many years by the US National Institutes for Health.

## Membrane Structural and Functional Biology Group



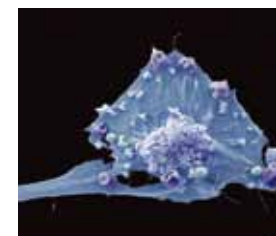
Schematic representation of the events proposed to take place during the crystallization of an integral membrane protein from the lipidic cubic mesophase.

The fundamental unit of life is the cell. A healthy cell requires an intact, enveloping membrane across and along which material and information flows. The Membrane Structural and Functional Biology Group led by Professor Martin Caffrey seeks to establish how membranes work at a structural level and in molecular detail. Professor Caffrey's group has designed and built robots that can accurately and reproducibly dispense nanolitre volumes for controlled crystallization and structure determination of membrane proteins and for the creation of microarray sensors. This will enhance our understanding of and control over some of the most fundamental processes underlying cellular function that are integral to human health.

# Research

## Cancer Vaccines and Immunotherapeutics

The Trinity Office of Research and Innovation recently showcased a selection of the latest exciting advances by TCD researchers in technologies which offer significant commercial, economic and societal value. Among the work highlighted was the research led by Professor Kingston Mills on the development of a novel and highly effective immunotherapeutic approach for the treatment of cancer. Currently, many cancer vaccines and immunotherapeutics suppress protective tumour-eradicating T-cells. Professor Mills's group has developed an immunotherapy which results in the activation and expansion of these protective T-cells thus destroying tumours. This technique has shown considerable efficacy in pre-clinical models of cancer and is now ready for translation to clinical trial. Opsona Therapeutics, a Trinity College campus biotechnology company, has exclusively licensed the technology from TCD and is exploring a variety of partnering and licensing opportunities.



Breast Cancer Cell.

Image: Anne Weston, Wellcome Images

## Roche Researcher of the year

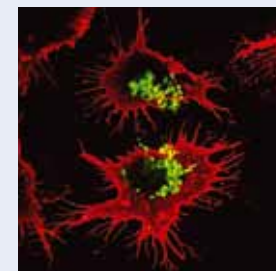


Professor Frank Gannon, SFI,  
Dr Susan Carpenter, TCD,  
Dr Finbar Kenny, Roche Diagnostics

Dr Susan Carpenter of Trinity's School of Biochemistry and Immunology was awarded the Roche Researcher of the Year Award 2009 for her PhD work on a new protein named TRIL which may play a role in alleviating central nervous system related disorders such as multiple sclerosis and Alzheimer's disease. In her presentation to the judging panel Dr Carpenter described how the protein has a key role in the inflammatory pathway of the innate immune system. She described the practical application her research has generated to date and the international attention it has received since its publication in the Journal of Immunology.

## Adjuvant research

The adjuvant research group led by Dr Ed Lavelle is investigating how adjuvants, which are essential immunostimulatory components of vaccines can activate the immune system. The work is of key importance as improved adjuvants are required to advance the development of vaccines for a number of globally important diseases. In collaboration with industrial partners, the group is developing novel strategies involving particulate adjuvants to promote protective immunity against mucosal infections, including influenza, pneumococcal infection, cholera and traveller's diarrhoea. The group has recently shown that the adjuvants activate inflammasomes, which play a role in protection against respiratory pneumococcal infection and thus provide an important target in the development of new and improved vaccines.



A dendritic cell infected with Streptococcus pneumoniae