

Trinity Research & Innovation is the first point of contact for companies seeking to find opportunities to collaborate with leading research groups in Trinity College Dublin

Trinity Research & Innovation promote and manage the interaction between TCD researchers, funding agencies and industry. It is also responsible for managing TCD's Intellectual Property, Technology Transfer and Innovation, Commercialisation and Entrepreneurship.



On the evening of Thursday March 12th, Trinity College Dublin (TCD) will be showcasing a selection of the latest exciting Bioscience technologies developed by TCD researchers. The technologies encompass the areas of biopharmaceuticals, drug development and medical devices. The format will be open demos, animations and displays, all available for viewing in the cool and funky Science Gallery with refreshments served to fuel the interaction.

Where?

Science Gallery
Trinity College
Pearse Street
Dublin 2.
(see below)

When?

March 12th 2009

What time?

6:30pm – 9:30pm

Contact details:

Trinity Research & Innovation
O'Reilly Institute,
Trinity College,
Dublin 2

Audrie Crosbie
Industrial Liaison Manager
acrosbie@tcd.ie
01-896 3839

Gordon Elliott
Technology Transfer
Translational Science
Case Manager
gordon.elliott@tcd.ie
01-896 4151

Emily Vereker
Technology Transfer
Life-Science Case Manager
emily.vereker@tcd.ie
01-896 4152



Trinity Research & Innovation
Bioscience Open Demonstration

- Biopharmaceuticals
- Medical Devices
- Drug Development

March 12th 2009
6:30pm – 9:30pm

Science Gallery at Trinity College Dublin

BIO/PHARMACEUTICALS

1 Inhibiting Tumors

Dr. John Walsh

Novel inhibitors of tumor angiogenesis and vasculature with a dual mechanism of action

Tumor angiogenesis (blood vessel formation) and vasculature have recently emerged as important targets in cancer treatment, applicable to multiple tumor types. Enzymes, specifically expressed in endothelial cells during tumor angiogenesis but not normal vasculature represent an important target for inhibiting tumor growth and metastasis. The recent advance in identifying the role played by tubulin inhibitors in causing tumor vasculature shutdown also represents an attractive target for inhibiting tumor angiogenesis/vasculature. Researchers at TCD have developed novel hybrid inhibitors of tumor angiogenesis and vasculature with a dual mechanism of action, namely prevention of tubulin polymerization and enzyme inhibition.

2 Safepirin (Aspirin Prodrug Technology)

Dr. John Gilmer

A safer form of aspirin

Aspirin is one of the most widely used drugs in the treatment of inflammation, pain and fever. Recently it has found application in the prevention of heart attacks and stroke and is being studied as a cancer chemopreventative agent. Despite its value aspirin continues to be under-utilised as a long-term preventative in a range of common indications because it causes gastric bleeding and is associated with a low but significant risk of ulceration and haemorrhage. Safepirin, developed at the TCD School of Pharmacy and Pharmaceutical Sciences, is designed to reduce contact between the drug and the intestinal lining. Aspirin toxicity in the

intestine is blocked by the attachment of a protecting agent which is automatically removed once the prodrug enters the bloodstream, releasing active aspirin to the circulation in a safe way. Uniquely, the technology can be adapted to release nitric oxide as well. This small gaseous molecule protects the gut from aspirin induced erosion and has other effects of its own that are synergistic with aspirin in cancer and heart attack prevention and treatment.

3 Novel compound (JAK4D) to enhance thyrotropin-releasing hormone (TRH) actions in the treatment of neurological disorders

Dr. Julie Kelly

Thyrotropin-releasing hormone (TRH)-based neurotherapeutics

Glp-Asn-Pro-d-Tyr-d-TrpNH₂ (JAK4D) is the lead compound of a set of novel, dual action, degradation-stabilised neuroactive peptides developed in TCD School of Biochemistry and Immunology and Trinity College Institute of Neuroscience (TCIN) through research funded by the Wellcome Trust. Due to its ability to mimic and potentiate central actions of thyrotropin-releasing hormone (TRH), JAK4D has potential to provide an innovative therapeutic strategy for a broad platform of neurological disorders with unmet clinical need, including chronic and acute neurodegenerative conditions, and it is an attractive candidate for clinical development. TRH is a natural neuropeptide that displays multiple actions in the central nervous system (CNS), which are recognised to have beneficial use in a wide range of CNS disorders, such as trauma, epilepsy, depression, stroke and spinocerebellar degeneration (SCD). Critically, however, the use of TRH in therapy is currently limited because of its short half-life due to rapid degradation by TRH-degrading ectoenzyme (TRH-DE), as well as potential endocrine side

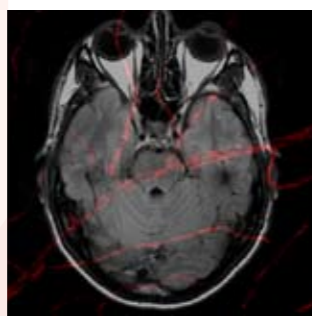
effects. JAK4D combines potent inhibition of TRH-DE with high affinity binding to central TRH receptors and both mimics and potentiates TRH actions in vivo without evoking endocrine effects. Thus, the discovery of this molecule realises longstanding efforts to overcome the restrictions of the short-half life and endocrine effects of TRH in relation to treating neurological disorders. JAK4D is now in preclinical development funded by Enterprise Ireland.

4 Breaking Barriers With RNAi

Prof. Pete Humphries, Dr. Matthew Campbell and Dr. Anna-Sophia Kiang

RNAi-mediated Blood Brain and Blood retina Barrier modulation

Many attempts have been made to disrupt the blood-brain barrier (BBB) and the inner blood-retina barrier (iBRB) to enable pharmacological agents to traverse the endothelial cells of brain and retinal capillaries. This technology manipulates tight junctions (TJs), reducing the space between the plasma membranes of contacting endothelial cells to form a selective and highly regulatable barrier. This novel platform technology employs the use of small interfering RNA (siRNA) to target TJ proteins that are present at the BBB and iBRB. Targeting TJ proteins induces both a transient and size-selective increase in permeability of the BBB and iBRB, thus allowing for the delivery of small therapeutic molecules.



5 Spinning out of Trinity



About

Opsona Ltd. is a successful biotechnology company focused on novel therapeutic and preventative approaches to autoimmune and inflammatory diseases. Founded in 2004 by Dr. Mark Heffernan together with three world renowned immunologists from TCD; Professors Kingston Mills, Luke O'Neill and Dermot Kelleher. Opsona is developing various technologies in its pipeline of immunomodulators, one of which relates to Toll-like receptors (TLR) and has been licensed from the laboratory of Prof. Luke O'Neill and forms part of a major collaboration with Wyeth Pharmaceuticals (USA). Opsona continues to enjoy a high level of fruitful collaborations with TCD; having further announced two Enterprise Ireland-funded Innovation Partnerships and its participation in a €7.5million Science Foundation Ireland-funded Strategic Research Cluster (SRC) programme, which also includes NUI Maynooth and Schering-Plough.

OpsoVac™ – Increased Efficacy and Antigen Sparing of Vaccines & Immunotherapeutics

Toll like Receptor (TLR) agonists are highly potent adjuvants in clinical development as immunotherapies for cancer, vaccines against infectious disease and therapies for asthma/allergy. They act by promoting innate inflammatory responses and Th1 responses to co-administered antigens. Significantly, a number of these potential treatments have met with limited success through lack of clinical outcome. TCD and Opsona scientists have discovered that contrary to current dogma, TLR ligands additionally promote the induction of anti-inflammatory

mediators and regulatory T cells such that immunosuppressive conditions in patients with cancer or chronic infections are exacerbated. Proof-of-principle has been demonstrated in pre-clinical models using TLR-immunotherapy against certain resistant cancers and also protective immunity induced with a vaccine against Bordetella pertussis, the causal agent of whooping cough. Opsona has exclusively licensed the technology from TCD and is seeking to develop OpsoVac through high-profile collaboration with specialist vaccine and immunotherapy companies.

6 Modulating Immunity

Prof. Kingston Mills & Dr. Sarah Higgins

A Therapeutic For Inflammatory & Autoimmune Diseases

With nearly 20% of the developed world suffering or developing autoimmune and inflammatory related diseases, there is a growing and urgent need for more specific and effective therapeutics. This technology is a novel method of suppressing the induction of specific subtypes of T cell responses in vivo, which are fundamental players in autoimmune and inflammatory related diseases, such as multiple sclerosis (MS), Graft Versus Host Disease (GVHD), rheumatoid arthritis (RA), ulcerative colitis and allergies. The Researchers have shown that a novel low molecular weight molecule can attenuate the onset and clinical signs of experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis.

Fig. 1



MEDICAL DEVICES

7 Arti-Stent

Dr. Daniel Kelly

Flexible Stents for Peripheral Arteries - Reducing post-operative complications for increased market utilisation

Peripheral Arterial Disease (PAD) is a term referring to a number of conditions that affect the larger peripheral arteries. It can result from atherosclerosis and inflammatory processes, leading to stenosis, an embolism or thrombus formation. Peripheral arteries are, generally, highly flexible vessels which undergo various bending, twisting and torsion modes in multiple planes. Hence, it is essential for peripheral stents to allow maximum flexibility, whilst providing good support of the vessel wall and resisting radial forces (see Figure 1). In terms of contemporary stent designs, this has proven difficult to achieve, requiring a trade-off between stent flexibility and wall support. The novel stent developed at the Trinity Centre for Bioengineering (TCBE) consists of multiple stent segments that interlock once crimped onto a single balloon, but that completely disengage from each other during balloon expansion so that each stent segment can articulate independently within the vessel.

8 PreSepsis

Dr. Thomas Ryan

Predicting patient response to infection

Pneumonia, urinary infection, and skin or wound infections are frequently seen in hospitalised patients. A minority of infected patients develop an overwhelming illness, termed "Sepsis", require admission to an intensive care unit, and these patients have a mortality rate of 20-30%. Importantly, there is currently no way of predicting which patients are at risk of developing sepsis from infection. Sepsis is a common disease in western society, with 750,000 episodes annually in the US, and a similar number in Europe, and with individual medical bills of c. €30,000 per patient, sepsis represents an annual cost to Western economies of the order of €45 billion. Researchers at TCD's Institute for Molecular Medicine at St. James Hospital Dublin have developed PreSepsis, a test based on Cytokine expression profiling (mRNA/cDNA) patient blood samples. PreSepsis can be implemented using standard nucleic acid diagnostic platforms at relatively low cost. PreSepsis is a unique and pioneering method of predicting which infected patients will develop sepsis, enabling cost effective pre-emptive therapies to be targeted at these individuals, thereby reducing the burden of sepsis overall.

9 Cartilage transplantation technology

Dr. Daniel Kelly

A device for transplantation of cartilage forming cells

Articular cartilage has a poor intrinsic capacity for repair. Even a small defect caused by mechanical damage (see Figure) may fail to heal and can degenerate over time, progressing to the debilitating condition of osteoarthritis (OA). Various surgical techniques and strategies

for cartilage repair, such as abrasion arthroplasty, osteochondral drilling, microfracture and mosaicplasty have been attempted, however these techniques have had limited success. Transplantation of isolated chondrocytes (live cartilage forming cells) such as the autologous chondrocyte implantation (ACI) represents the first generation tissue engineering strategy for cartilage repair, and is now in widespread clinical use. However its efficacy is constrained by the need to deliver the cells on a preformed solid matrix. The novel delivery device developed at the Trinity Centre for Bioengineering (TCBE) allows the delivery of the cells as a liquid suspension to the damaged area thus forming a semi-solid gel scaffold of precisely the correct shape.

Fig. 2 Arthroscopic image of cartilage damage



10 ROSIS

Ms. Mary Coffey & Dr. Siobhán Ni Chiuinneagáin

Radiation Oncology Safety Information System

Radiation Oncology (RO) involves the therapeutic delivery of radiation to cancer patients. ROSIS is a web-based safety information database for RO. Professional front-line staff in de-identified radiotherapy clinics report incidents, near-incidents and corrective actions, which are shared with the RO Community via a web-platform. **ROSI**s aims:

- To establish an international reporting system in radiation oncology, and
- To use this system to reduce the occurrence of incidents in RO

By enabling RO departments to share and view reports on incidents; By collecting and analysing information on the occurrence, detection, severity and correction of RO incidents; By disseminating the results an promoting awareness of incidents and a culture of safety an openness in RO

ROSIs is designed for safer health-care delivery by minimising the impact of incidents in radiotherapy

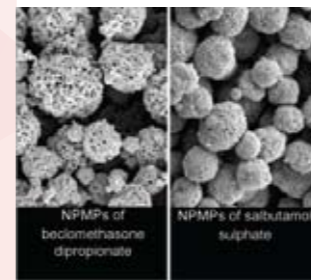
DRUG DEVELOPMENT

11 Nanoporous Microparticles (NPMs)

Dr. Anne Marie Healy

A novel spray-drying process

Porous particles are beneficial for drug delivery to the respiratory tract by oral inhalation and offer improved dissolution rates for oral routes. This proprietary process developed at TCD School of Pharmacy and Pharmaceutical Sciences, results in homogenous excipient-free porous microparticle powder



- The **NPM** method results in all the benefits of an excipient-free product

- More stable in suspension
- Improved dissolution
- **NPMs** have reduced interparticle attractive forces and improved flow characteristics relative to micronized drug materials
- Reduced aerodynamic diameters this technology offers a simplified production process (reduced production time and material costs)
- Flexible platform – to date **NPMs** have been prepared from over 40 common drug substances

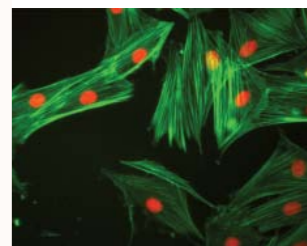
12 CardioMim

Dr. Adriele Prina-Mello

A technology for applying stretch-stimuli to cardiovascular cells

In vitro screening of large chemical libraries is an important process in the identification and development of novel therapeutics agents against cardiovascular disease. Current methodologies are limited to static or non-contracting cells which limit their applicability. CardioMim was developed by TCD School of Physics researchers based at CRANN in the Naughton Institute. CardioMim is an automated device for mimicking the biological cardiac cycle strain stimulation to which cardiomyocytes are exposed in their physiological environment. CardioMim is designed to offer a modular solution to cardiomyocyte culture applications in the high content analysis drug development environment.

parameters in a single assay. The Trinity HCA facility supports a wide range of bioscience research projects and is now planning on growing its activities to a commercial level through the formation of a spin-out High Content Research (HCR); offering services to the international commercial drug development market. HCR is in a position to offer unique capabilities in cardiomyocyte based assays for cardiac drug screening as well as generic HCA programmes. Trinity HCA researchers at the Institute for Molecular Medicine at St. James Hospital Dublin have developed Plate-Minder a novel technology (patent pending) which stabilises microwell cell cultures in the HCA environment. Plate-Minder protects cultures from the problems of edge-effects, shifts in temperature, pH and other environmental parameters in the HCA environment.



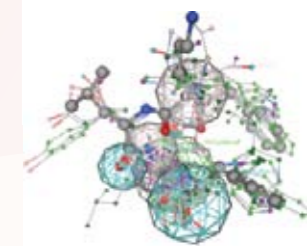
13 Designer Molecules

Prof. David Lloyd & Dr. Darren Fayne

An integrated in silico/in vitro drug discovery platform - CodeX

The Molecular Design Group (MDG), founded in January 2004 by Dr David Lloyd has developed an integrated in silico in vitro drug discovery platform called CodeX. This platform technology combines computational efforts in the areas of virtual high-throughput screening (VS) in conjunction with structure-based drug design (SBDD) and ligand-based drug design (LBDD) approaches, in addition to measures of Absorption, Distribution, Metabolism, Elimination and Toxicity

(ADMET). CodeX will shorten lead-to-drug timelines and reduce compound attrition rates. This will result in reduced costs, improved industry productivity and increased number of New Chemical Entities for progression through clinical trials.



15 Learning How To Behave

Prof. Shane O'Mara

Electrophysiological and behavioral analysis of brain function

How changes arising from experience (learning and memory) become functional and structural alterations in the brain and how these changes are affected by a common neuropsychiatric disease (depression) are the focus of this research. A combination of in vivo multi-electrode neurophysiology, behavioral analysis, molecular biology and pharmacological intervention are employed to investigate the function of brain systems implicated in memory function, dysfunction and in psychiatric diseases. These research endeavors are part of a major research consortium funded by GlaxoSmithKline (GSK). This is a large scale collaboration between Trinity College Institute of Neuroscience. The collaboration aims to rapidly advance therapies for Alzheimer's disease and other age-related cognitive diseases.