The research commercialisation office of the University of Oxford, previously called **Isis Innovation**, has been renamed **Oxford University Innovation**

All documents and other materials will be updated accordingly. In the meantime the remaining content of this Isis Innovation document is still valid.

URLs beginning www.isis-innovation.com/... are automatically redirected to our new domain, www.innovation.ox.ac.uk/...

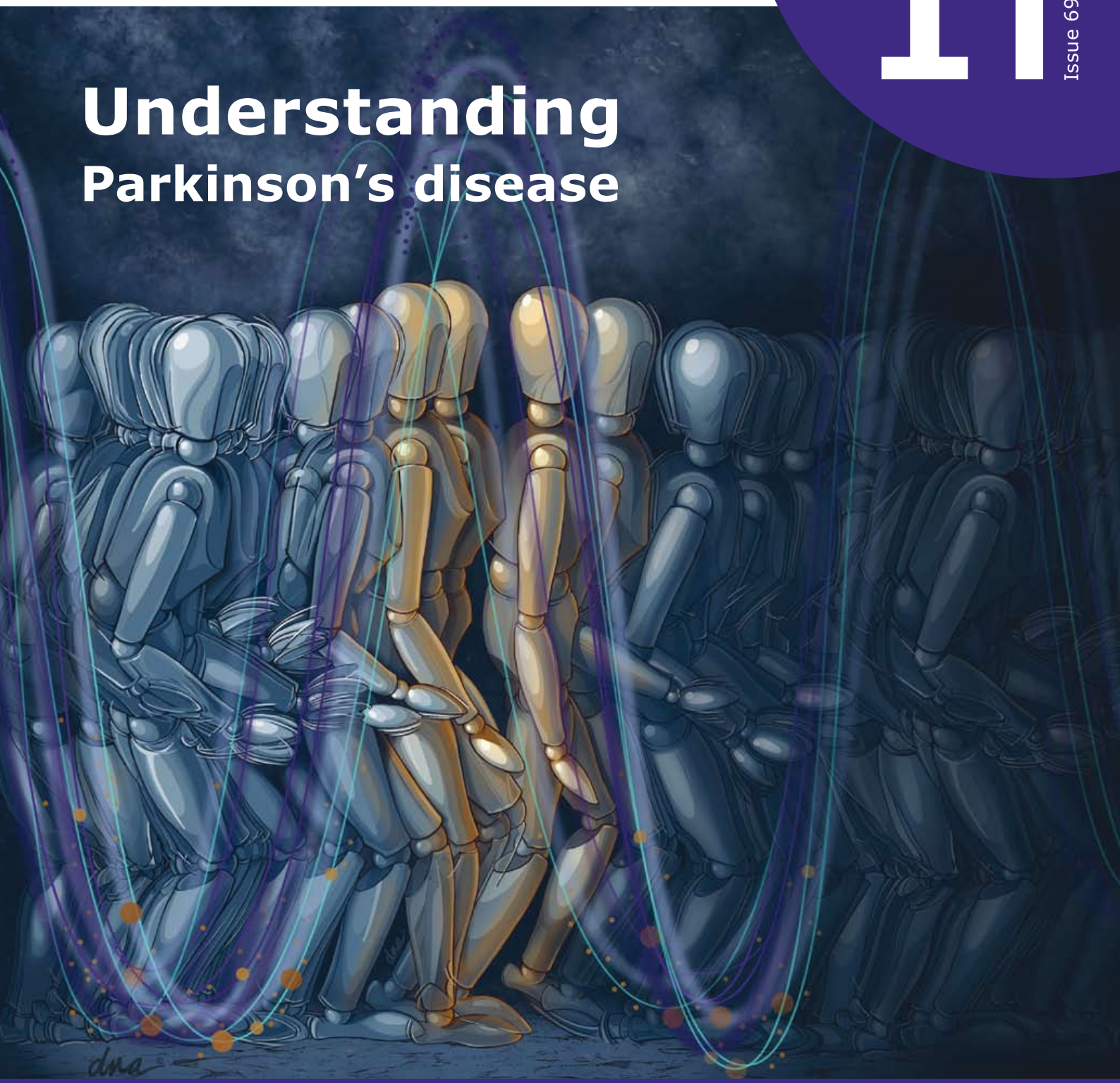
Phone numbers and email addresses for individual members of staff are unchanged

Email : enquiries@innovation.ox.ac.uk

Isis insights

Ii
Issue 69 Autumn 2012

Understanding
Parkinson's disease



Also inside: Consultancy, training, new Oxford technologies and more

The latest innovations, collaborations and technology transfer

ISIS INNOVATION

Issue 69
Autumn 2012

Understanding Parkinson's disease

Contents

Targeted approach
Potential cure for some Parkinson's disease patients

Carers' questionnaire
Evaluation for carers of people with Parkinson's disease

Ii is produced by Isis Innovation Ltd, the technology transfer company owned by the University of Oxford.

Cover image: Conceptual illustration of the impact of Parkinson's disease on mobility. (see pp 8,10)

Newsflash

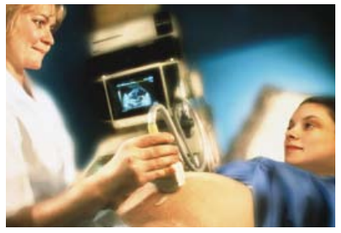
Isis is a research and technology commercialisation company owned by the University of Oxford.

Software start-up success

TheySay, one of the early successes from the Isis Software Incubator, is working with partners to provide a data (and sentiment) analysis solution for a new information system co-ordinated by QinetiQ. The system will enable the Care Quality Commission to analyse the opinions expressed by thousands of service users, plus Care Quality Commission assessors and inspectors, about the performance of health and social care providers. This is all made possible through the introduction of the new information system.

Improving the supply of organs for transplantation

An Isis spin-out from 2008, OrganOx, has raised additional investment of just under £1m to fund 'in-man' clinical investigations of its device that maintains organs in a fully functioning state during transport and storage. The technology increases the number of viable organs available for transplant. The company is preparing for market launch in 2013.



Saving taxpayer money

Interpreting images from ultrasound scanners is not easy, and requires highly-trained staff. A new company, Intelligent Ultrasound, spun-out from the University of Oxford by Isis, uses software to enhance the quality of ultrasound images, allowing more automation and less work for the experts. The NHS National Innovation Centre is a co-founder of the company, which offers improved patient care and has the potential to save the NHS in excess of £40m per year in cardiology diagnostics alone.

Spanish growth

Isis has been growing its activities and resources in Spain over the past year with the appointment of Manuel Fuertes as General Manager and the opening of an office in the prestigious Parque Científico de Madrid. Isis is working constructively with the Spanish government, who are focussed on stimulating innovative new businesses and expanding the knowledge based economy. We are holding the second meeting of the Oxford Innovation Society in Madrid on 21st November, with support from PWC, Fundación Barrié and FECYT. Following last year's successful event this is an excellent opportunity to support our growing network of university, investor, industry and government contacts in Spain. The event will promote our success in linking early stage technologies in Spain with Chinese business opportunities. (See p22 for more on this story.)

Enterprising Consultancy

News from **Isis Enterprise** and **Oxford University Consulting**

Technology Management courses

Isis Enterprise is offering new and bespoke courses in Technology Management based on its international experience in over 50 countries managing and advising on knowledge transfer and commercialisation of research.

The courses allow innovation professionals in the public and private sector, including employees of technology transfer offices, researchers, company R&D professionals and consultants from government bodies, to learn best practice expertise. IE is providing training in the facilitation of institutional, legal and financial environments surrounding innovation and technology transfer, as well as the day to day management of commercial technology ventures, throughout the autumn and into the winter.

Successful Consulting

Organisations seeking specialist help to solve a technical problem, or an authoritative consultant to advise on strategy and direction can access the University's world-class expertise via Oxford University Consulting (OUC).

OUC's consulting service, which operates across all divisions of the University, matches businesses with relevant academic consultants, negotiates contracts and manages administration so that the academics are free to focus on the intellectual challenge. Oxford consultants are also supported with advice and training, for example OUC recently hosted a workshop entitled 'Acting as an Expert Witness', exploring some of the unique challenges with this kind of work.

Backed by the University, OUC operates to ISO 9001:2008 standards of quality assurance and handles several hundred enquiries a year, with over 900 registered consultants on its books.

The University is also keen to ensure that its research equipment and facilities are fully utilised so, where appropriate, OUC can arrange for external organisations to access specialist equipment and technical services based in University departments.

Recently, OUC posted a significant increase in its annual key performance indicators, demonstrating solid growth in its activities across both the public and private sectors. In the year to 31 March 2012, OUC completed 243 consultancy contracts, up 31 percent on the previous year.

For more information, please contact:

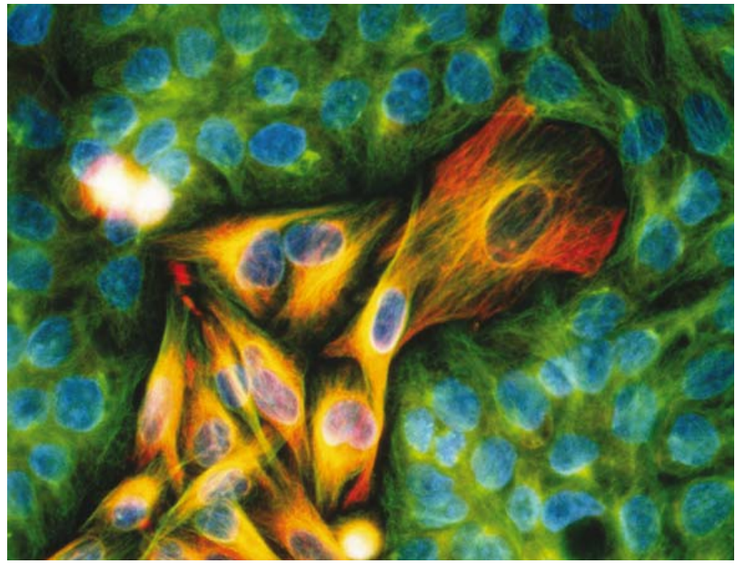
Andrew Goff,
Head of Oxford University Consulting
T +44 (0)1865 280866
E andrew.goff@isis.ox.ac.uk

The portfolio

The latest **spin-out** and **investment** news

iOx Therapeutics: Developing innovative immunotherapies for cancer and infectious disease

Researchers at the University of Oxford, in collaboration with the Ludwig Institute for Cancer Research (LICR), have developed a series of novel compounds which stimulate an essential component of the immune system, natural killer T cells (NKT). These NKT agonists are potent immune modulators and have the potential to act as adjuvants to vaccines for cancer and infectious disease, in combination therapies with existing cancer drugs or potentially as the basis of a monotherapy. A new company (iOx Therapeutics) is to be created to develop novel immunotherapies based upon this core technology. The creation of iOx Therapeutics represents the culmination of many years of collaboration between Professor Vincenzo Cerundolo, the director of the MRC Human Immunology Unit based in the Weatherall Institute of Molecular Medicine, and LICR. The relationship began with the original concept of designing improved analogues of the well characterised NKT cell agonist alpha galactosylceramide.



Immunofluorescent light micrograph of melanoma cancer cells

Immune regulators

NKT cells share some features of T lymphocytes – which are an important component of the adaptive immune system – helping to mount antigen-specific responses. T lymphocytes are characterised by their T cell receptors (TCRs) which are specific for peptide antigens in complex with cell surface molecules known as MHCs. In contrast, NKT cells recognise lipid and glycolipid antigens bound to a different antigen-presenting molecule called CD1d and their function appears to be as immune regulators, helping to promote cell-mediated immunity to tumors and infectious organisms. Paradoxically, they can also suppress the immune responses associated with autoimmune disease and rejection of transplanted tissues. Whilst the specifics of these contrasting functions is uncertain, it is known that activation of NKT cells results in the rapid release of effector molecules, called cytokines, that promote or suppress certain aspects of the immune response. Their regulatory function makes NKT cells a very attractive target for clinical intervention.

Pre-clinical experiments have demonstrated that the new compounds developed by Professor Cerundolo can significantly enhance both T cell and antibody responses and can induce regression of tumors in a mouse cancer model. Further pre-clinical work is underway to test safety, efficacy and further elucidate the mechanism of action of these innovative compounds.

Rationally designed adjuvants

iOx Therapeutics is to be based in Oxford, and through close collaboration with the University, NHS and LICR, will take the lead compound into a clinical trial to test its safety in a cohort of healthy volunteers. Following this there will be a series of efficacy trials in patients with melanoma, some of whom will also receive a new cancer vaccine developed by LICR. In parallel the company will develop NKT agonists for use as adjuvants to enhance the efficacy of vaccines for the prevention and treatment of infectious diseases such as hepatitis B, influenza and human papilloma virus. These compounds will represent the first rationally designed vaccine adjuvants ever to be developed.

For more information, please contact:

Andrea Alunni
Seed Investment Manager
Isis Innovation
T +44 (0)1865 280843
E andrea.alunni@isis.ox.ac.uk

Shionogi & Co.

Headquartered in Osaka with regional offices in Europe and the US, **Shionogi** has a strong heritage in the discovery and development of globally important therapies. Yayoi Matsumoto explains their open innovation strategies and introduces the Shionogi Science Programme.

Shionogi is a well established pharmaceutical company, with over 130 years' experience of research, development, manufacturing and marketing activities. We strive constantly to supply the best possible medicine to protect the health and wellbeing of patients, their families, and healthcare providers. Headquartered in Osaka with regional offices in Europe and the US, the company has a strong heritage in the discovery and development of globally important therapies.

The global pharmaceutical industry is facing many critical challenges such as escalating healthcare costs, falling R&D productivity, and patent expiry of blockbuster therapies. As a successful company operating in this fast-evolving field, Shionogi are managing such challenges via our ethos of **S**peedy decision-making, an **O**pen mind that fosters out-of-the-box thinking, **N**ever failing passion, and a **G**lobal presence. Our approach is nicely summarised as Shionogi's **SONG** for Real Growth in this critical phase of industry-evolution.

Open innovation at Shionogi

From an R&D perspective, Shionogi's vision is to constantly engage the frontiers of science and strive to be an innovative pharmaceuticals company. As a result, the company has embraced the concept of global open innovation that fosters collaborative relationships and shared incentives by multiple parties across the world. Creating such opportunities is the responsibility of the Global Development body, which is charged with consolidating control over important decisions concerning "when," "where," "who," and "what studies at what cost." The team is responsible for speeding up drug development through timely and flexible decision-making. Unified management enables us to prioritise – that is, to selectively allocate resources to projects that are believed to have higher added value and will confer a competitive advantage.

Industry-academic collaboration

In order to generate new medicines that can be adopted worldwide, Shionogi works with academic researchers to exploit the seeds of drug development openly, fostering them from the "idea stage". It takes a long time to see results from such early-stage industry-academia collaborations, but speed is vital for decision-making at Shionogi. Via fast decision making and a flexible approach to collaboration, the two imperatives are compatible and hold a lot of promise for the future. These efforts complement Shionogi's conventional licensing effort as a new platform for industry-academia collaboration.

Isis Innovation has advised Shionogi and its staff on the UK environment, in order to effectively promote the Shionogi Science Programme.

Key members of the Global Development Team (left to right): Tsuneaki Sakata, Head, Innovation Design Office; Yayoi Matsumoto, Innovation Design Office; Takuko Yamada Sawada, Senior Executive Officer and Executive General Manager

Shionogi Science Programme 2012

Scientists and strategists in the Japanese headquarters have identified key therapeutic areas and specific patient populations as their targets for the Shionogi Science Program. Researchers from across selected countries are invited to submit innovative and world-class ideas with the hope that together the team can create superior pharmaceuticals for those who suffer from diseases all over the world. Via the SSP, Global Development at Shionogi are looking for promising seeds in the following categories:

- Novel target molecules for drug discovery to treat pancreatic islet dysfunction related to type 2 diabetes, chronic kidney diseases, HIV or emerging and re-emerging infectious diseases.
- Novel target molecules, analytical methods and promising models for drug discovery for cancer immunotherapy, psoriasis, atopic dermatitis and/or allergy immunotherapy
- Novel target molecules, analytical methods and animal models for drug discovery to treat AD/HD and sleep disorder, or for neuroprotective and neuroregenerative drugs
- Ideas for novel next generation biologics (for example, next generation antibody drugs, next generation nucleic acid drugs, etc.)
- Ideas for novel technology of drug formulation

Winning candidates will be selected based on criteria such as: synergy with the needs of the company; originality of research; rationality; future potential; the possibility of commercialisation. The research period is determined at the time of adoption, with a maximum of five years, although contracts will be renewed each year and the research period may be shortened upon consultation. Collaborative budgets are determined at the time of adoption and may range from ¥5 - 15 million per year per project.

Web link

www.shionogi.co.jp/ssp/contents.html

For more information, please contact:

Yayoi Matsumoto
Innovation Design Office
Global Development
T +81 6 6455 2395
E yayoi.matsumoto@shionogi.co.jp
www.shionogi.com

The Oxford Innovation Society (OIS) is a network which exists to encourage Open Innovation between academia, industry and business.

Many of the world's leading companies are, or have been, members. Introductions and networking opportunities are provided for members to meet leading academics and other business leaders, and Isis provides early access to new technology available to license.

Members can promote their products and services to each other and to the Oxford 'ecosystem' through various channels, including articles such as this one.

Targeted approach

Andy Self explains how allele specific silencing has the potential to prevent or cure Pakinson's disease in patients with the G2019S mutation.

Parkinson's disease (PD) is a degenerative disorder of the central nervous system which results in a debilitating loss of motor functions, with symptoms including shaking, rigidity, slowness of movement and difficulty in walking. It is estimated that PD affects 5-10 million people worldwide and there is no known cure. While existing Parkinson's medicines help with symptoms, they don't slow the progression of the disease. There is therefore an urgent need for new treatments.

For many years PD was not thought of as a hereditary disease. Then, in 2004, an association between a protein called LRRK2 (leucine-rich repeat kinase 2) and PD was discovered. It is now estimated that around 1-2 percent of all PD patients contain a mutation in LRRK2 gene (the 'G2019S mutation') which results in the chances of developing PD increasing to 20-80 percent in a person's lifetime, compared to 0.3 percent in the general population.

At least 15 other genes have since been implicated in PD, which are jointly predicted to account for around 5-10 percent of PD patients. Although the disease remains poorly understood, LRRK2 has emerged as an attractive target for the development of new drugs for PD, due to its known association with hereditary PD and relatively high prevalence in PD patients.

There are a number of small molecule drugs in development for LRRK2 PD patients, which act by inhibiting the activity of the LRRK2 protein. However, due to the way hereditary forms of PD occur this approach is likely to face challenges. The LRRK2 protein naturally exists to perform important cellular functions in the body and in LRRK2 G2019S Parkinson's patients both normal and mutant, disease causing versions of the LRRK2 protein are produced. Small molecule inhibitors are unable to discriminate between the normal and mutant forms of the LRRK2 protein, resulting in the inhibition of both forms of the protein, which could result in unwanted side effects. An approach to specifically target just the mutant form of the LRRK2 protein could offer much improved results.

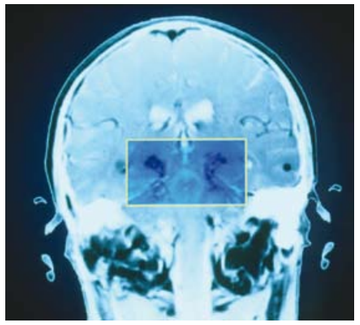
University of Oxford scientists have achieved this targeted approach through a technique known as allele specific silencing. Site-specific mismatched siRNA has been developed to specifically block the production of the defective version of the LRRK2 protein, at the RNA level, whilst allowing the normal LRRK2 protein to be produced and continue its essential functions.

Research engine

The G2019S mutation was brought into the spotlight in 2008, when Google co-founder Sergey Brin discovered that both he and his mother, who suffers from PD, carry the mutation. Since then Brin has accelerated his funding of PD, donating more than £85 million to Parkinson's research including research on LRRK2.

"I know early in my life something I am substantially predisposed to," Brin has said. "I now have the opportunity to adjust my life to reduce those odds (e.g. there is evidence that exercise may be protective against Parkinson's). I also have the opportunity to perform and support research into this disease long before it may affect me. And, regardless of my own health it can help my family members as well as others."
An international LRRK2 consortium has also been set up, with research into the gene gathering increasing momentum.

Whilst established for other dominantly inherited diseases, such as Huntingdon's disease, this is the first time allele-specific silencing has been successfully demonstrated in Parkinson's disease against this important mutation.



MRI scan of a brain with Parkinson's disease

Whilst established for other dominantly inherited diseases, such as Huntingdon's disease, this is the first time allele-specific silencing has been successfully demonstrated in Parkinson's disease against this important mutation. Should these results be confirmed in further studies, allele-specific silencing of LRRK2 has the potential to prevent or cure Parkinson's disease in patients with the G2019S mutation, by specifically blocking the production of the defective LRRK2 protein responsible for the onset of the disease in these patients. Isis is looking for partners to progress development.

Web links

Wired magazine article, July 2010:
http://www.wired.com/magazine/2010/06/ff_sergeys_search/all/

Bloomberg article, May 2012:
http://www.bloomberg.com/news/2012-05-11/google-s-brin-makes-strides-in-hunt-for-parkinson-s-cure-health.html

For more information, please contact:

Andy Self
Senior Technology Transfer Manager, Isis Innovation
T +44 (0)1865 280831
E andy.self@isis.ox.ac.uk
Ref 7925

Carers' questionnaire

Dr David Churchman presents the Parkinson's Disease Questionnaire-Carer, which measures quality of life among carers for people with Parkinson's disease.

Carers can be an important source of help and support to people with long-term conditions, such as Parkinson's disease (PD). Carers for people with PD can face numerous responsibilities arising from the need to provide support and assistance to the person they care for. This is particularly relevant to those caring for a person with a progressively disabling disease and can have direct implications upon their quality of life. The PDQ-Carer is a new questionnaire to address the impact of caring on the quality of life of informal carers of people with PD.

To ensure consistency with best practice, the views of carers for people with PD have been incorporated throughout the development of the PDQ-Carer questionnaire. There are 29 items in the PDQ-Carer, representing four discrete scales:

- Social and personal activities (12 items)
- Anxiety and depression (six items)
- Self-care (five items)
- Stress (six items)

Validation

The PDQ-Carer was developed at the University of Oxford by the researchers responsible for the development of the Parkinson's Disease Questionnaire-39 (PDQ-39), the most widely used and validated disease-specific Patient Reported Outcome (PRO) measure in PD.

The procedure used to develop the PDQ-Carer replicated the methods used to develop the PDQ-39 (also available from Isis Outcomes) and follows recommendations for best practice. It has been shown to be:

- valid and reliable – the PDQ-Carer demonstrates good content validity,
- construct validity and nternal consistency
- easy to administer – the PDQ-Carer is a short (29 items), self-adminis-tered questionnaire
- simple to score and interpret
- acceptable to carers – interviews with carers and high completion rates suggest that the PDQ-Carer is acceptable within the test population
- complementary – can be used in conjunction with the developers' patient questionnaire (the PDQ-39) to allow test administers to correlate quality of life scores of a person with PD and their respective carer's score

PROs in profile

Isis Innovation has a portfolio of patient self-completion, quality of life assessment tools (example on facing page) to measure efficacy of treatments. **Dr David Churchman** explains how these PROs are used in conjunction with clinical trial data to show the benefit of treatments given to condition-specific patient groups.

The Oxford PROs

The PROs from Oxford are all condition-specific questionnaires and include questionnaires for Parkinson's disease and Amyotrophic Lateral Sclerosis (ALS) / Motor Neurone Disease assessment.

Parkinson's disease

The PDQ-39 questionnaire is the most widely used Parkinson's disease specific measure of health status and has been used extensively throughout the pharmaceutical sector. The PDQ was developed at the University of Oxford's Department of Public Health and contains thirty-nine questions, covering eight aspects of quality of life. It is used to monitor changes that may occur during clinical trials of therapeutics for Parkinson's disease.

It has been repeatedly demonstrated that the PDQ-39 is feasible and acceptable for use by patients, but there may be occasions where a simpler/shorter form of the questionnaire may be required. For these situations the short–form, PDQ-8, was developed which delivers results almost identical to those of the long- form PDQ-39 questionnaire. A 114-page user manual supports both the PDQ-39 and PDQ-8. In addition, the lead author is available for advice on the scoring system and how to interpret the data should you require it. The PDQ has been widely validated and translated into over fifty languages.

Amyotrophic Lateral Sclerosis (ALS)/Motor Neurone Disease

The ALSAQ-40 is a patient self-report health status questionnaire, used to measure subjective well-being for patients with motor neurone disease / amyotrophic lateral sclerosis (MND/ALS). The ALSAQ–40 contains questions covering five dimensions of subjective health status: physical mobility, activities of daily living and independence, eating and drinking, communication, and emotional reactions.

Using the questionnaires

The above Oxford PROs and others are available for licence. Further information and requests for a licence can be found at: http://www.isis-innovation.com/licensing/healthoutcomes/

For more information, please contact:

Dr David Churchman
Senior Technology Transfer Manager, Isis Innovation
T +44 (0)1865 280857
E david.churchman@isis.ox.ac.uk

ISIS OUTCOMES

Isis Outcomes is an activity within Technology Transfer at Isis Innovation Ltd, dedicated to the provision and support of the highest quality PROs for healthcare providers and the pharmaceutical industry. It manages a large library of over 200 translated versions of the Oxford PROs, commissions user support materials, such as manuals, and arranges consultancy advice to customers from PRO experts in Oxford.

Skin cell cancer therapies

Dr Richard Reschen examines how dendritic cells derived from a patient's own skin cells promise to be the ideal starting point for the development of effective new cancer therapies.

A team of researchers led by Dr Paul Fairchild, Co-Director of the Oxford Stem Cell Institute, have developed a method of turning skin cells taken from a patient into large numbers of dendritic cells. This breakthrough may lead to the development of new cancer therapies.

Skin cells to stem cells

In the past, scientists have extracted dendritic cells from cancer patients, exposed the dendritic cells to cancer cells in the lab, and then re-injected them into the patient. These activated dendritic cells then activated cytotoxic T-cells and showed some success in fighting the tumour. Unfortunately, extracting sufficient cells has proven time-consuming and costly, so it is impractical to target tumours in this way.

Recently, scientists have uncovered the existence of a subset of dendritic cells in humans that are particularly good at cross-presentation. Oxford researchers have now worked out how to make large numbers of cross-presenting dendritic cells quickly and relatively cheaply – a world first. They first harvested skin cells from a patient, then instructed these cells to become "induced pluripotent stem cells" (iPS cells). Stem cells are master cells capable of differentiating into a range of cell types such as skin, heart, etc. The researchers showed that by adding a particular cocktail of chemicals, the iPS cells will differentiate into dendritic cells with enhanced abilities to cross-present. This method should be suitable for the production of dendritic cells in the large quantities required for therapeutic use.

Fighting cancer

In order to demonstrate their potential for use as a cancer vaccine, the researchers exposed the dendritic cells to a component from melanoma cells and showed that they activate T-cells and B-cells. This is an important proof-of principle as it shows that these cells could potentially fight cancer if reintroduced into the body. In theory any cancer could be treated this way; samples of a patient's cancer could be presented to dendritic cells grown from the patient's own skin cells, then injected back into the patient in large numbers.

Licensing opportunity

Isis Innovation is now looking for commercial partners who would like to license this technology and develop it further for the benefit of patients.

IPC cells differentiate into dendritic cells with enhanced abilities to cross-present.

Immune watchdogs

The immune system is divided into two arms – the innate immune system and the adaptive immune system. The innate immune system provides a first line of defence against infection, whereas the adaptive immune system reacts more slowly but provides a stronger targeted response together with long-lasting protection against previously encountered pathogens. The adaptive immune system is based mainly around B-cells and T-cells. T-cells safely kill cells that are part of tumours or have become infected, while B-cells produce antibodies that remove pathogens found outside of cells.

Dendritic cells play a key role in activating the adaptive immune system by a process known as antigen presentation. Antigen presentation involves engulfing pathogens, dead virally infected cells or cancer cells, chopping them up into small pieces and presenting them on the cell-surface. Cross-presentation, a particular type of antigen presentation, is important for cytotoxic T-cells to target tumours. Unfortunately, only small numbers of dendritic cells are capable of cross-presentation and cancer cells are often missed by the immune system.

For more information, please contact:

Dr Brijesh Roy
Technology Transfer Manager,
Isis Innovation
T +44 (0)1865 280842
E brijesh.roy@isis.ox.ac.uk
Ref 7381

Surgery not required

Dr Nikolaos Chalkias presents a drug candidate for Dupuytren's disease which prevents the development of this common, debilitating hand condition and hence the need for surgery or collagenase treatment.

Dupuytren's disease is a common disorder affecting approximately 5% of the white Caucasian population. There is no cure for Dupuytren's disease and current treatments address only late stage disease. Surgery represents the mainstay of treatment; however, recovery times are long. Collagenase injections can also be used to relieve the contracture but are only suitable for some patients and are associated with high recurrence rates.

The early manifestation of Dupuytren's disease involves small lumps of tissue (called nodules) developing on the palm of the hand. The nodules progress into a fibrous cord that contracts, making it difficult to straighten the fingers. As Dupuytren's contracture progresses, fingers are eventually pulled into a permanently flexed (bent) position. The disease can make day to day tasks, such as holding a glass, using a keyboard or shaking someone's hand difficult and embarrassing.

Addressing contractility

Oxford researchers recently identified new drug candidates that address early stage contractility. There is no animal model for Dupuytren's disease and by using cells from tissues excised from patients with Dupuytren's disease they have identified novel mechanisms that control the development and activity of the contractile cells. These results pave the way for the first early-stage drug for Dupuytren's disease and may also help prevent recurrence following surgery, needle fasciotomy or collagenase treatment.

A therapeutic for early stage disease that can be injected on an out-patient basis would provide significant time and cost benefits both for the patient and health service providers. The cost for the surgery ranges from £3,500 to £5,000 and the recovery time for the patient is up to three months. A course of three collagenase injections costs £3,000 and is associated with a recurrence rate of more than 30 percent within three years. In contrast to these approaches, it is envisaged that the new early-stage drug candidate would be administered during the early development of nodules. The drug would prevent the development of cords and hence the need for surgery or collagenase injection.

The invention may also prove effective in treating a number of other diseases with similar pathophysiology, including frozen shoulder, Ledderhose and Peyronie's disease.

The invention may also prove effective in treating a number of other diseases with similar pathophysiology, including frozen shoulder, Ledderhose and Peyronie's disease.

Market opportunity and IP protection

The invention represents a significant commercial opportunity. It has the potential to generate a new market for an indication that is not addressed at an early stage. Furthermore, it targets the main Dupuytren's patient population (white Caucasians), including those that do not qualify for surgery or collagenase injection.

Robust IP protection is in place and two international patent applications have been filed. The invention is at preclinical stage and the next phase is to trial the best drug candidate in humans. The drug candidates are known molecules with well described safety profiles. In addition, the researchers have access to an existing pool of patients and in collaboration with Isis Innovation are making preparations for a proof of concept clinical trial.

The envisaged final product would be based on the local and targeted delivery of the drug into a fibroproliferative nodule. Targeted delivery would be achieved via a protected method as described in the patent filings. This ensures localisation of the drug at the injection site, thereby improving efficacy.

Isis is actively looking for collaborators and licensees to bring this opportunity to the market.

Images: below left, a sketch of a hand affected by Dupuytren's disease. The contracted fibrous cord is seen in two fingers and the disease is at a progressed stage. Border, collagen fibres

For more information, please contact:

Dr Nikolaos Chalkias
Technology Transfer Manager
Isis Innovation
T: +44 (0)1865 614429
E: nikolaos.chalkias@isis.ox.ac.uk
Ref 8638/8851

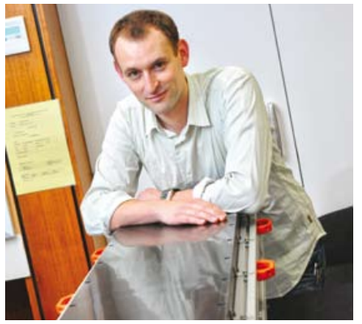
Applications

- Early stage treatment of Dupuytren's disease, Peyronie's disease, Ledderhose disease, and frozen shoulder.
- Prevention of recurrence for Dupuytren's disease following surgery, needle fasciotomy, or collagenase treatment.

‘Scintillating’ security solution

Oxford researchers, in collaboration with Imperial College London, have developed an efficient way to detect neutrons. One commercial application for these detectors is within Radiation Portal Monitors to help ensure national security. **Dr Jon Carr** discusses this and details the latest developments from a prototype study.

The Oxford detector is based on a lithium-6 fluoride neutron capture design combined with an inorganic composite scintillator material.



Images: Oxford’s Dr Antonin Vacheret and the neutron detector technology

Since the events of September 11th 2001, there has been an increasing focus on protecting countries from terrorist attacks. This protection is no longer limited to conventional weapons as a radiological and/or nuclear attack has also become a serious threat. Technologies that can detect radiation are at the forefront of this effort. Instruments used to detect nuclear and radioactive material are generally placed into the following categories: personal radiation detectors (PRDs), radioactive isotope identification devices (RIIDs) and radiation portal monitors (RPMs).

Radiation Portal Monitors

RPMs are portals through which vehicles can pass. The first portals designed were criticised for their inability to distinguish gamma radiation originating from benign cargo types that naturally emit radioactivity (including cat litter, porcelain and bananas) and that gamma photons could be easily suppressed by high-density shields (and therefore not detected by the monitors). This was solved by the portals also containing a specific neutron detector. However, first generation neutron detectors relied on a rare isotope of helium called helium-3, in order to function and due to increasing global demand by the security and medical sectors, supply can no longer meet demand1. This has led to increased pressure for new types of detectors to be developed.

Commercial opportunity

Over 11 million shipping containers pass through the 361 ports in the USA each year and the American government is faced with the difficult task of making sure none containing illicit radioactive or nuclear material get through. In 2009, President Obama requested a budget of $14.2 billion over five years to reduce the global nuclear threat by detecting, securing, safeguarding, disposing and controlling nuclear and radiological material. Part of this is the Second Line of Defense (SLD) programme, which will attempt to work not only in the US, but around the world to strengthen the capability of foreign governments to deter, detect, and intercept illicit trafficking in nuclear and other radioactive materials across international borders and through the global maritime shipping system.

Oxford invention

The Oxford detector is based on a lithium-6 fluoride neutron capture design combined with an inorganic composite scintillator material. A scintillator is a material which exhibits scintillation, the process of luminescence, whereby light is emitted following the absorption of radiation. Importantly, the neutron capture releases charged particles rather than gamma rays, which are converted into light by the scintillator material, allowing the Oxford system good discrimination of gamma ray-only sources. The light produced is collected quickly and then a specific light guide efficiently transfers the light to a semi-conductor photon detector over large distances (metres).

Readiness for market

The group were awarded a University Challenge Seed Fund to make a full size prototype neutron detector. This has been completed and testing carried out at the National Physics Laboratory with a calibrated neutron source showed good efficiency (over 2.5 neutron counts/second per 1ng Californium source at a distance of two metres) and good gamma discrimination (GARRn of 1.0). The system has relatively low bulk material costs compared to many competitor systems and the scalable design could lead to additional applications such as large neutron detector arrays for the nuclear reactor industry, detecting neutrons’ directionality, and an efficient antineutrino detector.

References: 1 CRS Report for Congress, “The Helium-3 shortage: Supply, Demand and Options for Congress”. Report 41419 (2010)

Advantages over alternative neutron detectors:

- Lower bulk material costs
- Excellent discrimination from gamma rays
- High neutron absorption cross-sectional area
- Lower power consumption
- Does not contain hazardous materials

For more information, please contact:

Dr Jon Carr, Technology Transfer Manager, Isis Innovation
T +44 (0)1865 280907
E jon.carr@isis.ox.ac.uk
Ref: 8187

Smart nano-structures

Dr Mark Gostock introduces a rapid, inexpensive and straightforward method for reversibly solubilising and stabilising any type of nano-structure for use in smart drug delivery, nano-electronics and pollution treatment.

Preparation

Preparation of the solubilised nano-structures is;

- simple
- inexpensive
- rapid
- reversible
- independent of type or size of nano-structure
- independent of DNA size or sequence

Storage

Solubilised nano-structures may be stored:

- frozen at -120°C and up to 45°C
- lyophilised for reformulation
- in aqueous at pH 5-12
- in physiological media
- in organic solvents

Stability has been shown for at least six months or more, without significant aggregation of the nanostructures.

Nano-structures formed from a plethora of materials such as silver colloids, dendrimers, nano-pores, quantum dots and semi-conductors have unusual properties. As such, these nano-structures are useful in a variety of applications in the field of nano-technology including drug delivery, tissue engineering, electronics, micro electrical mechanical systems (MEMSs) and optics.

However, manipulation of nanostructures like carbonaceous nano-tubes is made difficult due to their instability in solution and tendency to rapidly aggregate forming macro-defunctionalised complexes. This presents significant difficulties for manufacture of such nano-structures on a commercial scale and complicates the provision of nano-structures in soluble form, for applications where this is necessary.

Solubilising nano-structures

Research by Dr. Sonia Trigueros has culminated in the development of technology for solubilisation, manipulation, storage and sorting of nano-structures. The Oxford invention uses induced DNA wrapping of nano-structures as a means to improve and exploit the functionality of these materials. As the DNA does not directly bind to the surface of the nano-material (either covalently, electrostatically or through conjugation), but is instead wrapped around the structure, the coating is therefore not dependent on the particular nano-material, size or shape.

Stable formulations

Coating of the structures is simple and convenient, requiring only commercially available materials with processing under ambient conditions and in a range of aqueous solutions, pH or organic solvents. Additionally, the coating is simply and readily reversible, allowing the nano-structures to be released after delivery, storage or sorting.

Examples of nano-particles and structures to which the technology may be applied include:

- carbon nano-tubes
- fullerenes
- polymer and metal nano-composites
- nano-bones
- nano-pores
- magnetic nano-particle
- semi conductors
- silver colloids
- liposomes
- dendrimers
- quantum dots

Drug delivery, photovoltaics and many other applications

The coated nano-structures are particularly suitable for medical applications since they are soluble and stable in physiological media such as bacteria growth medium, yeast growth medium and serum. This is of particular use where the solubilised nano-structures are to be used for delivering therapeutic agents in the treatment of humans and animals or during surgery.

Within the healthcare sector this solubilisation technology also lends itself to the application of diagnostic tools such as chemical or biological sensors, chips or other nano-diagnostic devices. The therapeutic or diagnostic agent may be covalently or non-covalently attached to the nano-structure or to the DNA wrap itself.

DNA-wrapped nano-structures may also be used for cell therapy, tissue engineering or in nano-devices for medicine or surgery, where the DNA coating makes the structures amenable to sorting, i.e. based on the size of the nano-structures. Such techniques include DNA electrophoresis, size-exclusion chromatography and silica adsorption.

Nanostructures are useful in a variety of applications.

Physical sciences will benefit from this technology in energy applications such as solar cells, photovoltaics, batteries and ultra-capacitors. Research in micro and nano-electromechanical systems, nano-electronics, ceramic engineering and environmental pollution control will all benefit from this Oxford technology.

DNA wrapping and solubilisation of nano-particles can be applied to:

Life Science
- drug delivery
- surgery
- diagnostic tools
- cell therapy
- tissue engineering
- nano-devices
- chemical/biological sensors

Physical Science
- MEMS and NEMS systems
- Nano-electronics
- food packaging
- textiles and nano-fabrics
- ceramic engineering
- structural composite materials
- environmental nano-technology
- treatment of air or water pollution

Commercial opportunity

The underlying technology is the subject of a UK patent application and Isis welcomes contact from parties interested in licensing this opportunity.

For more information, please contact:

Dr Mark Gostock
Technology Transfer Manager,
Isis Innovation
E mark.gostock@isis.ox.ac.uk
T +44 (0)1865 280856
Ref: 8172

Accessing mental health therapies

Through an agreement negotiated by Oxford University Consulting, **David Clark**, Professor of Experimental Psychology at Oxford, assists the Department of Health in his role as National Clinical Advisor for the Government's Improving Access to Psychological Therapies (IAPT) programme. **Andrew Goff** outlines the programme's development and its impact.

According to the Department of Health, one in four adults experience mental illness at some point during their lifetime and one in six experience symptoms at any one time, making mental illness one of the most significant health concerns in our society today.

Started in 2008, the six year IAPT programme aims to vastly increase the availability in the NHS of evidence-based psychological therapies to treat depression and various anxiety disorders by training up to 6,000 new psychological therapists and deploying them in specialised psychological therapy services. At just over half way through the programme IAPT services are established in 95 percent of primary care trusts and around 500,000 people per year are using the services. Once the programme has been fully rolled out it is expected that 900,000 will be using the services each year.

Traditionally, mental health services have not been good at collecting systematic outcome data. However, IAPT uses a simple session-by-session measurement system based on one that David Clark initially piloted in Northern Ireland when setting up a service to treat psychological problems suffered by victims of the Omagh car bomb. This monitoring system allows IAPT services to obtain pre and post treatment data on over 90 percent of people who receive treatment. The results show that the programme is achieving good outcomes with 44 percent of people recovering and around two thirds showing reliable improvement.

In an unprecedented move that brings much needed transparency to mental health services, the outcomes of each IAPT service are published on the NHS Information Centre website (www.ic.nhs.uk) every quarter.

IAPT is unique in its approach, offering adults of all ages first-line psychological therapy combined, where appropriate, with medication.

Many people contributed to the development of the IAPT programme. With Richard Layard from the London School of Economics, David produced a cost-benefit analysis that helped secure initial Treasury support for the programme. He also co-authored the Depression Report which was distributed by the Observer in 2007 and helped raise public awareness of depression/anxiety and the value of psychological therapies in their treatment. In his role as National Clinical Advisor, David has helped develop national curricula and quality standards for therapist training, service models, and commissioner guidance. The cognitive therapies for panic disorder, social phobia and posttraumatic stress disorder that his team have developed are included among the range of evidence-based treatments that are available in the services. With colleagues, he has conducted analyses of the initial IAPT data that identified features of services that are associated with particularly good outcomes. These findings are now being used to improve overall recovery rates and reduce variability between services.

IAPT is unique in its approach, offering adults of all ages first-line psychological therapy combined, where appropriate, with medication, which in the past was often the only treatment available. It supports a cross-Government mental health strategy, 'No health without mental health'. A related, but separate, IAPT programme for children and young people is also being developed and David assists several of the committees associated with this programme.

Weblink

http://www.iapt.nhs.uk/services

For more information, please contact:

Andrew Goff,
Head of Oxford University Consulting
T +44 (0)1865 280866
E andrew.goff@isis.ox.ac.uk

Professor David Clark

David studied Experimental Psychology at Oxford (MA, DPhil) before training in Clinical Psychology at the Institute of Psychiatry (MPhil), where he became Professor of Psychology and Director of the Centre for Anxiety Disorders and Trauma at the Maudsley Hospital. The American Psychological Association presented David with their Award for Distinguished Scientific Application of Psychology in 2010, citing his work as "pure genius with a real world application". The London School of Economics also recently awarded him an Honorary DSc in recognition of his working on mental health and economics. In 2011 David returned to Oxford to take up the Chair of Experimental Psychology and established the Oxford Centre for Anxiety Disorders and Trauma.

Supporting Spanish innovation

Manuel Fuertes, Isis' General Manager for Spain, discusses the projects and relationships Isis has established within the Spanish innovation ecosystem.

For decades Spain has been producing high quality science from its excellent research institutions, fuelled by public funding. Despite the quality of the scientific research, only a small fraction is commercialised. The current economic situation has reinforced the need for better technology transfer, with one of the biggest challenges being the gap between the research base and the private investment industry.

Isis Innovation established an office in the Madrid Science Park in April 2012 to help bridge this gap, and bring the level of academic engagement with industry in line with the quality of its research output. This strategic move was endorsed by Spanish Secretary of State for Innovation, Carmen Vela, and Her Majesty's Ambassador to Spain, Mr Giles Paxman, who attended the opening.

Spanish Success Stories

FECYT (Spanish Foundation for Science and Technology) Training Course

FECYT is the public entity belonging to the Ministry of Economy dedicated to promoting Science and Technology within Spain. FECYT has a yearly course that trains technology transfer specialists to improve their practices and skills. This year, Isis experts were given the task of training selected specialists to be able to commercialise Spanish technology in the global market. One of the course initiatives, led by Dr Viraj Perera, was the simulation of investment pitches for different types of investors around the world.

Fundación Barrié Technology Fund Support

Fundación Barrié is one of Spain´s leading foundations, serving to support the transfer of Galician technologies to society. Isis has supported the Foundation with the due diligence and commercialisation activities of its €5.5mn tech fund over the past three years.

Isis has also collaborated with Fundación Barrié to promote a training programme to technology transfer staff of Spanish universities and other research institutions. The programme improves the participants' skills in areas such as identification, evaluation, protection and commercialisation of research output.

University of Santiago de Compostela's Proof of Concept Technology Fund

"One of Spain's biggest challenges, as it is for many other countries in the world, is to prepare their scientific results for private investment," says Isis' Dr Steve Cleverley. With this in mind, Isis is delighted to support the creation of the Universidad Santiago de Compostela's (USC) Proof of Concept Technology Fund and advance the route-to-market of technologies from this prestigious University. The fund has now been launched and USC have started working with researchers to develop their first round of projects.

SETEP (Sino-European Technology Commercialization Programme)

The platform transfers European technologies to China by means of a strong, reputable and solid partner, RITS (Tsinghua's Institute of Research in Shenzhen), and with the collaboration of Isis's Hong Kong office.

One of Spain's biggest challenges, as it is for many other countries in the world, is to prepare their scientific results for private investment.

IE at the University of Santiago (above) and the OIS event in Madrid last year (left and right)

Madrid Science Park

Madrid Science Park is one of Spain´s most active and innovative players in terms of international technology transfer, especially in relation to Latin America. Through our cooperation agreement the Park has strongly supported Isis' entry to Spain as well as to other Latin American countries. Isis, in return, coaches the park management and companies in transferring technology to other parts of the world.

Oxford Innovation Society Dinner and Forum

The 2011 Oxford Innovation Society dinner in Madrid brought together 150 of Spain's top decision makers, investors and corporations to discuss the trends and strategies for international technology transfer. Sponsors included FECYT, PWC and the Fundación Barrié. This year the dinner will again be presided by Carmen Vela and will be complemented by all kind of workshops around the topic of transferring and commercialising Spanish technology. Other new initiatives being considered at the time of going to press included the incorporation of a Latin American cooperation table and the attendance of investors from China (SETEP Programme) and other parts of the world. The event is scheduled to take place on November 21st, again in Madrid.

For more information, please contact:

Manuel Fuertes,
General Manager for Spain, Isis Enterprise
T +44 (0)1865 614413
E isis@manuelfuertes.com

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Blake Lapthorn

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Andrew Davies
Corporate Director
Barclays Bank
T: 07775 548803
E: andrew.j.davies@barclayscorporate.com

Nicola McConville
Partner - Technology Team
Blake Lapthorn
T: 01865 253284
E: nicola.mcconville@bllaw.co.uk

Sue Staunton
Partner - Technology Group
James Cowper
T: 01865 200500
E: sstaunton@jamescowper.co.uk

Oxford Innovation Society

Forthcoming meetings of the Oxford Innovation Society will be held on the following dates:

- Thursday 20 September 2012
- Thursday 6 December 2012
- Thursday 21st March 2013

Meetings are held in Oxford for OIS members and invited guests, and are followed by a formal reception and dinner in an Oxford college hall.

Isis Innovation Limited, Ewert House, Ewert Place, Summertown, Oxford OX2 7SG
T +44 (0)1865 280830 **F** +44 (0)1865 280831
E innovation@isis.ox.ac.uk **W** isis-innovation.com

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