



Ii

Issue 60 Summer 10

Isis insights

The latest innovations, collaborations and technology transfer

Naturally innovative

Responding to a changing world.....



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ISIS
INNOVATION

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Welcome to Isis insights

Isis is excited to announce the launch of our first summer newsletter.

Issue 60 brings you all of the latest news on Isis Innovation, emerging technologies from Oxford University and licence agreements, as well as some new features including investment news and sector focus articles. This issue presents a feature on telemedicine technologies on pages 10-11, kicking off a selection of healthcare inventions on pages 12-24.

Isis insights also marks a new design direction for the publication with a fresh new look which we hope you enjoy.

Oxford start-up Plink Search purchased by Google

Oxford start-up Plink Search has become the first UK company to be purchased by Google Inc.

The firm was founded in 2009 by Mark Cummins and James Philbin, two graduate students from Oxford University's Department of Engineering Science, to commercialise technology stemming from their doctoral research.

They decided to form a company to develop an application that could recognise art work from photos taken by mobile phones, using the FabMap code licensed from Isis as a starting point. Mark said: "It was a good baseline to start building Plink. The technology that a robot uses to recognise places versus how we do painting recognition on a mobile phone is really very similar." "Mark and I were both involved in developing visual search during our DPhils," said James. "Mark's research focused on visual place recognition for robot navigation, which culminated in the FabMap software. My own research looked at how visual search could be scaled robustly and efficiently to handle millions of consumer images crawled from sites such as Flickr."

Oxford Innovation Society to celebrate 20 years in September

The Oxford Innovation Society, the open innovation forum run by Isis, is celebrating 20 years of bringing together some of the world's most innovative multinationals with researchers and inventors from Oxford as well as spin-outs, technology transfer professionals, local companies and venture capital groups.

Established by Isis in 1990, Society members meet three times a year to network, hear from one of the University's leading researchers about new technology and sit down to a College dinner. They also receive priority access to new intellectual property being marketed by Isis.

The September 2010 meeting will be extended to a full afternoon of presentations and networking, followed by a dinner at Christ Church.



The latest news
from **Oxford**
University
Consulting and
Isis Enterprise

The

Loop

Greater knowledge of the brain's function, structure and pathologies

There are many exciting, yet practical applications that result from brain imaging research, including insights into human cognitive processes (e.g. facial recognition, memory and pain endurance), as well as new approaches to personalising drug therapy, early diagnosis of brain disorders and rehabilitation strategies.

Oxford's Centre for Functional MRI of the Brain (FMRIB) is a multi-disciplinary research centre involved in neuroscience research and related technologies. They are at the forefront of such research with a leading edge software toolset (FSL), available to license through Isis Innovation. The tool uses Magnetic Resonance Imaging (MRI) to track brain activation, produce high-resolution images of brain structure and maps the brain connectivity patterns. A recent licensee of the software also made good use of the expertise available in FMRIB with consultancy contracts to advise, train and support the application and use of the software.

"We hope our advances in image analysis technology will lead to earlier diagnosis and improved treatment of many conditions," said Professor Smith of FMRIB. "The various FSL tools should allow us

to learn more about the nature of different brain diseases, and the healing effects that drugs can have. A more long-term goal is that we can also make a big difference for healthcare in the individual, providing more tailored medicine through improved diagnosis."

The installation of new 7T and 3T MRI scanners at FMRIB this summer will enable even higher resolution imaging.

For further information about the software see the FMRIB website at www.fmrib.ox.ac.uk/fsl.

For further information on licensing the FSL software please get in touch with Brendan Spillane, Isis Innovation.

For consultancy and expertise enquires please contact Susan Clark, Oxford University Consulting.

Hands-on support from Isis Enterprise

Learning from training courses and workshop exercises can only take you so far. To really learn about the methods for commercialising early stage technology the best tactic is to be mentored by someone with experience. In addition to bespoke training programmes and postings to our offices in Oxford, Isis Enterprise offers secondments of our staff to clients from both the public and private sectors.

Isis staff have recently been based for extended periods of time with clients in Croatia, Malaysia and even deepest, darkest North Oxfordshire. Assignments have varied from an in-depth review of a client's portfolio of 120 patent applications to provision of an extra pair of hands during maternity leave.

Speaking on his work in Malaysia, Terry Pollard says: "Helping other people through practical training and workshops is very rewarding. However, there is nothing more illuminating than working with a client in their own environment which enables you to truly understand the challenges they face. I particularly enjoy adapting the lessons I have learnt in Oxford to a client's particular circumstances – be they a shortage of follow-on funds, lack of familiarity in dealing with academic researchers or incomplete institutional policies.

"On my current assignment in Malaysia I am hoping that I will be able to make a real difference by introducing technologies to technology companies, partners or investors from our global networks; facilitating the transfer of new ideas into products and services in much the same way we do in Oxford."

For more information on seconding staff from Isis contact David Baghurst.

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The Portfolio



Oxford YASA Motors

Oxford YASA Motors (OYM) was the 65th spin-out from the University of Oxford and was formed in September 2009 to commercialise a novel electric motor developed by the Energy and Power Group. OYM has made significant progress since formation, achieving initial product sales turnover in its second month of operation and more than £100k by the 6 month point, validating predicted motor performance and strengthening company IP. The company currently has a qualified sales pipeline worth more than £13m with a number of major deals being discussed that could dramatically accelerate business growth and market position.

OxEmS

OxEmS uses RFID technologies to deliver the most cost effective solution to the problem of locating, identifying, and maintaining buried utility assets such as pipes.

These technologies have resulted from work within the Department of Engineering Science as part of the UK's "Mapping the Underworld" programme.

UK utilities are upgrading their networks, installing polyethylene pipes that cannot be located using traditional technology, to replace ageing iron pipes. The Oxford solution consists of a combination of inexpensive 'omega' tags, low frequency (LF) point tags, a unique 'bar-code' type system and a locator solution. The omega tags are deployed along the length of a pipe and significantly enhance accuracy of detection and identification, at a very competitive price.

The LF tags are used in situations where additional specific points need to be identified such as joints in water pipes as they are able to operate in wet ground such as when there is a water leak.

OxTEX

OxTEX is a medical device project which provides novel soft tissue expansion solutions. The tissue expander addresses unmet needs in reconstructive surgery and dentistry. More details can be found on page 14.

The self-inflating tissue expander has a delayed onset and rate of expansion and can be directionally controlled and shaped by the surgeon at the point of intervention.

To support product roll out the business will provide training in the use of the tissue expanders. The project is based on key intellectual property, with a US priority patent application filed in October 2009.

The primary market for this technology is the dental market, as a complementary product for use with implants and in treatment of periodontal disease. Other applications include surgical reconstruction, particularly following trauma and oncological resection, and for the treatment of disorders such as cleft palate, syndactyly (fused digits) and other birth defects.

Oxford Biotrans

Oxford Biotrans is a University of Oxford project supported by 10 years of research led by Dr Luet Lok Wong in the Department of Chemistry. The team is committed to commercialising new enzymatic routes to speciality chemicals, flavours and fragrances. The technology also has applications in agrochemicals and pharmaceuticals.

The production of ethanol from ethane and methanol from methane are the first applications and ethanol has been proved at the laboratory scale.

Biotrans' P450 enzymes have been designed to catalyse specific bio-transformations, where in each case the feedstock is a low cost material and the product is a high value product. These include:

1. Limonene to Menthol
2. Valencene to Nootkatone
3. Pinene to Verbenone

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Technology Steps Forward

Isis signs vaccine licence agreement with Imaxio

Isis Innovation has entered into a reciprocal licence agreement with biopharmaceutical company Imaxio to develop a new series of vaccines jointly researched at one of the world's premier vaccinology institutions, Oxford's Jenner Institute.

This agreement will allow Imaxio to use its proprietary aXent adjuvant technology with viral vectors such as Modified Vaccinia Ankara (MVA) and adenoviruses. The University of Oxford is internationally recognised for its expertise in the creation and development of virally vectored vaccines.

"The technology Isis has licensed to us further validates the ability of Imaxio's aXent™ technology to enhance immune responses to current and future vaccines, and particularly those using viral vectors," said Francois Miceli, Chief Executive Officer of IMAXIO. "Oxford and the Jenner Institute have been excellent sources of innovation in the vaccine field."

Oxford also benefits, as it secures the right to use the Imaxio adjuvant in developing its own vaccine candidates, which would then be made available for partnering and further development through Isis. The current agreement is the result of a collaboration which started in 2004 and has already led to joint patent filings. This collaboration is financed in part by the Grand Challenges in Global Health consortium, a programme supported by the Gates Foundation to promote innovation in global health.

Both Imaxio and Oxford expect to see some of their projects enter into clinical trials this year, addressing globally important medical needs particularly in infectious disease.

About Imaxio

Imaxio is based in France and has programmes in the areas of oncology and infectious diseases. It aims to create new recombinant vaccines and new medicines (derived from its oncology screening platform) as well as new diagnostic and prognostic tools for common cancers. Imaxio was formed by the merger in 2006 of Diagnogene and Avidis, which was created in 2000 as a spin-off from the UK Medical Research Council and the University of Cambridge. Imaxio has several awarded and pending patents for the technologies aXent™, OverExpress™, Diagnogene™ and PepAptamer™.

www.avidis.fr

About the Jenner Institute

The Jenner Institute was founded in November 2005 to develop innovative vaccines against major global diseases. It is a unique partnership between the University of Oxford and the Institute for Animal Health, focusing uniquely on diseases of both humans and livestock.

A major theme is translational research involving the rapid early-stage development and assessment of new vaccines in clinical trials. The Jenner Institute investigators, through the support of many funders, are now developing promising new vaccine candidates against major global infectious diseases.

New vaccines against malaria, tuberculosis and HIV are in field trials in the developing world. The clinical activities of the Institute are at the Centre for Clinical Vaccinology and Tropical Medicine, with strong links to units in developing countries.

The Institute comprises the research activities of over 20 Jenner investigators who head leading research groups spanning human and veterinary vaccine research and development. Together the Institute investigators comprise one of the largest non-profit sector research and development activities in vaccinology.

www.jenner.ac.uk



Isis works with vaccine stabilisation technology

A simple and cheap way of making vaccines stable – even at tropical temperatures – has been developed by scientists at the University of Oxford and Nova Bio-Pharma Technologies.

Isis Innovation is working with the Oxford inventors and the company to put a commercial strategy in place for the development of the technology.

The British technology has the potential to revolutionise vaccination efforts, particularly in the developing world where infectious diseases kill millions of people every year, by removing the need for fridges, freezers and associated health infrastructure. The work, funded by the Grand Challenges in Global Health partnership with other funds from the Wellcome Trust, is published in the journal, *Science Translational Medicine*.

Preparing vaccines that do not need refrigeration has been identified as one of the major unsolved problems in global health.

“Currently vaccines need to be stored in a fridge or freezer,” explains lead author, Dr Matt Cottingham of the Jenner Institute at the University of Oxford. “That means you need a clinic with a nurse, a fridge and an electricity supply, and refrigeration lorries for distribution.

“If you could ship vaccines at normal temperatures, you would greatly reduce cost and hugely improve access to vaccines,” he says. “You could even picture someone with a backpack taking vaccine doses on a bike into remote villages.”

In the proof-of-concept study, the team showed it was possible to store two different virus-based vaccines on sugar-stabilised membranes for 4–6 months at 45°C without any degradation. The vaccines could be kept for a year or more at 37°C, with only tiny losses in the amount of viral vaccine re-obtained from the membrane.

“We’ve developed a very simple way of heat-stabilising vaccines and shown it works for two viruses that are being used as the basis for novel vaccines in development,” says principal investigator, Professor Adrian Hill of the University of Oxford. “This is so exciting scientifically because these viruses are fragile. If we are able to stabilise these, other vaccines are likely to be easier.”

The team’s method involves mixing the vaccine with the sugars trehalose and sucrose. The mixture is then left to slowly dry out on a simple filter or membrane. As it dries and the water evaporates the vaccine mixture turns into a syrup and then fully solidifies on the membrane. The thin sugary film that forms on the membrane preserves the active part of the vaccine in a kind of suspended animation, protected from degradation even at high temperature. Flushing the membrane with water rehydrates the vaccine from the membrane in an instant.

“The beauty of this approach is that a simple plastic cartridge, containing the membrane with vaccine dried on, can be placed on

the end of a syringe,” explains Dr Cottingham. “Pushing a liquid solution from the syringe over the membrane would then release the vaccine and inject it into the patient.”

The process is general and could be used for many types of vaccines and sensitive biological agents.

Professor Hill adds: “The World Health Organisation’s immunisation programme vaccinates nearly 80% of the children born today against six killer diseases: polio, diphtheria, tuberculosis, whooping cough, measles and tetanus.

One of the biggest costs is maintaining what’s called the cold chain – making sure vaccines are refrigerated all the way from the manufacturer to the child, whether they are in the Western world or the remotest village in Africa. If most or all of the vaccines could be stabilised at high temperatures, it would not only remove cost, more children would be vaccinated.”

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Miko Neri explains how Oxford Innovation Society members, Emergent BioSolutions plays an important role in protecting lives and transforming global healthcare.

Emergent BioSolutions is a biopharmaceutical company that is focused on the development, manufacture and commercialisation of vaccines and antibody therapies that assist the body's immune system to prevent or treat disease. Emergent's global operations span three continents.

Making progress together

Emergent knows that developing vaccines and therapeutic antibodies requires significant investment and collaboration. Because of that, the company actively works to bring together the best scientific, business, and public policy minds in order to partner with

Protecting Life across the Globe



“Fighting disease is a complicated job. However, while a lot about the company’s business may seem complex, the company’s mission remains stunningly simple: to protect life”.

government and non-government entities in pursuit of common product development goals.

Emergent formed a joint venture with the University of Oxford, known as the Oxford-Emergent Tuberculosis Consortium, to further develop MVA85A, the world’s most clinically advanced tuberculosis vaccine candidate. The JV has secured development funding from the Wellcome Trust and Aeras Global TB Vaccine Foundation. A Phase IIB clinical trial in infants in South Africa commenced in 2009 and a second Phase IIB trial in a second targeted population cohort is anticipated to begin in various sites in Africa in 2010.

The company also recently completed a Phase IIa clinical trial in Vietnam and a Phase IIB clinical trial in the U.S. for Typhella™, Emergent’s single dose, oral typhoid vaccine candidate.

“Across the globe and on a daily basis, the Emergent team lives out the company mission of protecting life - a commitment to make meaningful contributions to address unmet medical needs especially in underserved markets,” said Fuad

El-Hibri, chairman and chief executive officer of Emergent BioSolutions. “Our product pipeline targets infectious diseases and includes programmes focused on anthrax, tuberculosis, typhoid, flu and chlamydia.”

Investing in core competencies

Operating as a matrix organisation, with empowered management teams and committees, the Emergent culture encourages an entrepreneurial spirit and teamwork. It starts from the top. Emergent’s chairman and CEO, Fuad El-Hibri, was named an Ernst & Young 2009 Entrepreneur of the Year for the Greater Washington Region. The company recently ranked 23rd on the Forbes list of 200 best small companies in the U.S. For 2009, the company grew revenue from both product sales and development contracts and grants. While maintaining profitability, Emergent continued to invest in its product pipeline as well as expand its manufacturing infrastructure, which the company considers a core competence and competitive advantage.

“I am proud of Emergent BioSolutions’ track record of growth and financial strength. These

successes are clearly a direct result of the entrepreneurial spirit and commitment of our employees,” said Mr. El-Hibri. “Looking ahead, we anticipate continued growth in our operations and financial performance. We will also continue to actively pursue initiatives that have the potential to broaden our product pipeline as well as expand our sources of revenue.”

Emergent employs approximately 650 people, and the company has been recognised for its contributions to economic expansion and job growth in the United States.

The corporate headquarters are in Rockville, Maryland and the primary manufacturing site, a 12.5-acre campus, is located in Lansing, Michigan, where the company has invested over \$80 million in a new, large-scale state-of-the-art vaccine manufacturing facility. Emergent’s marketed product, BioThrax® (Anthrax Vaccine Adsorbed), is the only vaccine approved by the U.S. Food and Drug Administration for the prevention of anthrax disease. Since 1998, the U.S. government has procured over 42 million doses of BioThrax and more than 9.4 million doses have been administered to nearly 2.4 million military personnel.

For over a decade, Emergent has been a proud partner to the U.S. government, as well as other non-U.S. governments, in developing, manufacturing and supplying critical biodefense medical countermeasures to address overall preparedness goals and objectives.

Fighting disease is a complicated job. However, while a lot about the company’s business may seem complex, the company’s mission remains stunningly simple: to protect life.

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The Oxford Innovation Society is the leading forum for open innovation, fostering links between business and the academic community. For more information please email us at innovation@isis.ox.ac.uk

Telemedicine Technologies



Isis Innovation looks at predicting patient care and treatment at the touch of a button.

Will your mobile phone become a key part of your healthcare in the near future?

For some patients with depression, cardiac disorders and some chronic conditions such as diabetes, it already is.

Oxford has become a focus for this kind of innovation: where medicine and communication technologies are combined to deliver better patient care.

Isis is already working with a number of technologies which can be broadly described as "telemedicine".

Monitoring mood

One of these - which has already received awards and accolades - is a simple, reliable method of obtaining patient-reported ratings of mood from people with bipolar

disorder, for which self-monitoring of mood is a key component of care. The system, which combines medicine, software engineering and communication technology, is based on keeping in touch with patients regularly via automatic text messages to which patients respond with an indication of their mood - from depression to euphoria. A bespoke system captures data for each patient and emails it each week to their psychiatrist in numerical and graphical form, including a visual rating of the severity of individual symptoms. This is copied to the GP and the patient.

The system is currently being developed by the University of Oxford's Department of Psychiatry and Computing Laboratory, funded by Oxfordshire and Buckinghamshire Mental Health Trust. It has been such a success that it is now being expanded from a 150 patient pilot to

being evaluated as part of a comprehensive National Institute of Health Research funded project.

Professor John Geddes, of Oxford's Department of Psychiatry said: "We wanted to create a system that was pretty low-tech and was very easy for patients and not too burdensome."

"This system also allows healthcare professionals to hit the ground running: when we meet patients we know how they have been feeling and can focus on trying to help them and their treatment."

Professor Geddes said the system could probably be adapted to monitor people with other mental health disorders, such as less severe schizophrenia.

Isis is working with Professor Geddes and the team to provide guidance to make the system commercial and available to a much wider patient population. They have introduced a group of software specialists to create a commercial system, capable of operating at scale. Isis is also negotiating with organisations who will provide the route to market. This process has been successfully managed by Isis staff with experience in software commercialisation in both start-up and large corporate environments.

Health "apps"

A number of other mobile phone-based technologies are being developed at Oxford for the remote monitoring or diagnosis of key health indicators such as heartbeat, respiratory patterns and blood pressure.

Isis is working with the researchers to manage the software and intellectual property underpinning these new applications, and ensure that they are brought to market efficiently with appropriate commercial partners.

The inventors of these applications are based at the Centre of Excellence for Personalised Healthcare at Oxford's Institute of Biomedical Engineering.

For the developing world - with limited access to healthcare, but better access to telecommunications - "telemedicine" technologies are particularly important. The Oxford teams have identified conditions that affect significant numbers of people in these countries, where early remote diagnosis can lead to great improvements in treatment.

The Centre is also studying how electrode implants can be used to alleviate pain and motion disorders.

"Other mobile phone-based technologies are being developed at Oxford for the remote monitoring or diagnosis of key health indicators."



Measuring the benefits of therapy from the patients perspective

Over the past ten years, there has been a huge growth in the use of Patient-Reported Outcome (PRO) measures to assess the benefits to patients of different therapies. Traditionally used in a paper-based form, these PROs are now starting to be deployed in more efficient ways through the use of mobile phones (e.g. Interactive Voice Response, IVR, for both mobile and landlines), web-based delivery (Interactive Web Response, IWR) or PDA/Tablet formats. PROs or "quality of life questionnaires" have already found widespread use throughout public and private healthcare as well as the clinical phases of drug development to assess the efficacy of surgery or new drugs. The new e-PROs promise to assist physicians to put patient experience and outcomes first.

Oxford has a wealth of condition-specific PRO's including the well-known and widely used Parkinson's Disease Questionnaire (PDQ), Oxford Hip and Knee Scores (for assessing total hip and knee replacement surgery outcomes) and the Endometriosis Health Profile (EHP).

The benefits of e-PROs are:

- Better completion rates by patients.
- Increased data integrity and quality.
- Better data capture.
- Providing better visibility of data (in real-time).
- Reduced data entry and data cleaning costs.

Isis Outcomes, the Health Outcomes business at Isis Innovation is currently looking to deploy its portfolio of condition-specific PRO's to customers through electronic delivery formats.

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Bringing Bench to Bedside

Dr John Wilson briefs us on a small portable diagnostic technology which has been developed for the point-of-care and home diagnostics sector. The technology has the advantage of being able to detect multiple markers in a single test, increasing speed and accuracy whilst reducing cost.

The multi-marker test

Today, many home and point-of-care diagnostic kits diagnose a condition by detecting a single biological marker. Researchers at the University of Oxford have developed a technology that will allow multiple markers to be tested in a single kit. For example glucose and lactate, both energy metabolites, could be measured simultaneously, both of which are monitored closely in diseases such as diabetes, obesity and cancer. Other indications and areas where multiple markers are required include:

- Cardiac risk.
- Neonatal screening.
- Renal and liver care.

The technical advantages

A micro-electrode array device has been designed to allow the detection of multiple analytes and to optimise the performance of each enzyme-based detection system. The



surface of the electrode array can be functionalised with various biopolymers, especially enzymes that will only give an electrochemical response to a specific compound or analyte. Typical enzymes include glucose dehydrogenase and lactate dehydrogenase. This invention represents the first example of a biopolymer based micro-array biosensor.

Specifically the design has the following advantages over the current single electrode technology:

- Low energy use, utilising a small charging capacitance.
- High sensitivity, utilising radial diffusion kinetics.
- Rapid response time, less than 2 minutes.
- High S/N ratio.

The point-of-care diagnostics market is expanding rapidly. It is dominated by the US, which accounts for 50 per cent of the overall market and 55 per cent of the professional use market. In the US, point-of-care testing products are in widespread use in the hospital, physician's office and consumer settings. Growth is driven by self-testing products due to the high prevalence of conditions such as diabetes and cardiovascular diseases.

Rapid diagnostics

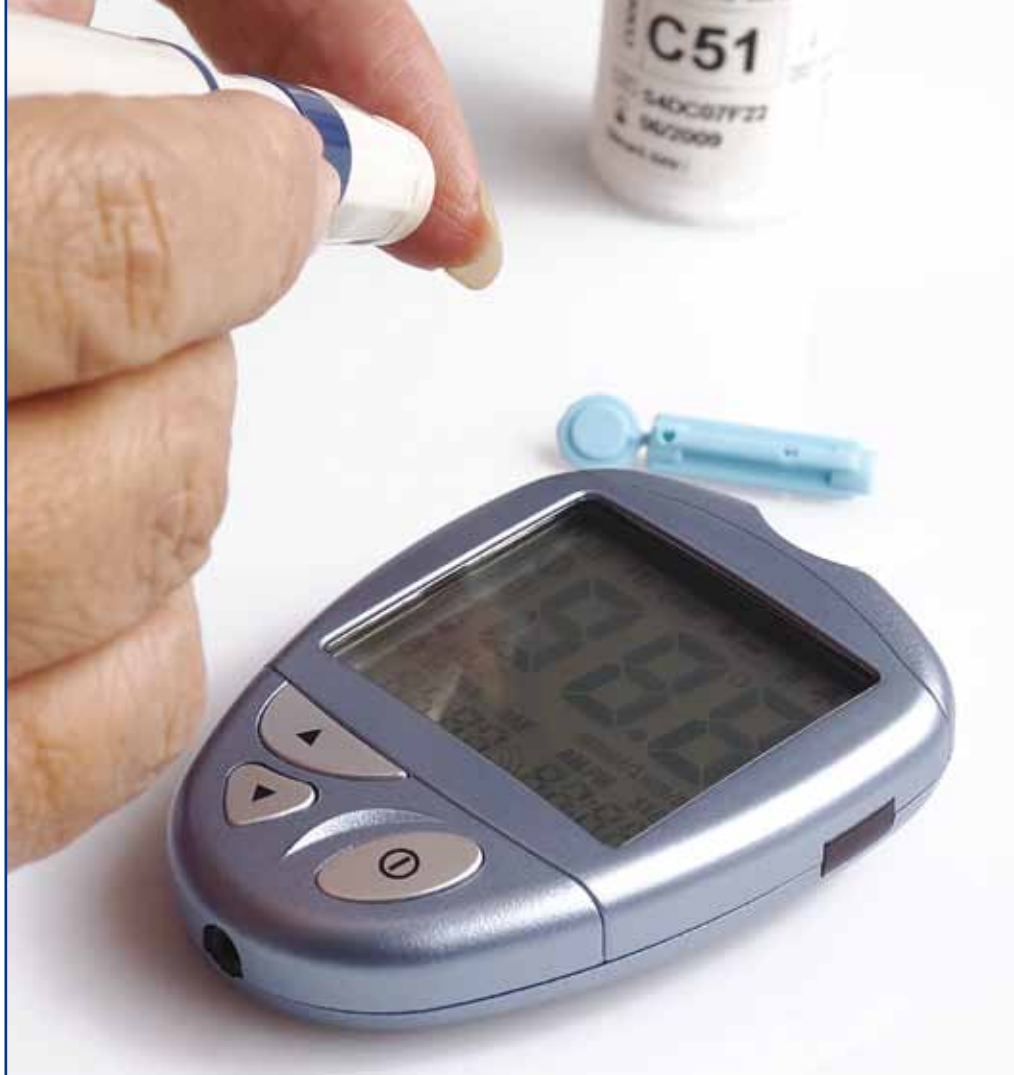
Improved accuracy and tests for a wider number of conditions will continue to see the self-test market develop rapidly. But the major challenge - and opportunity - for the manufacturers of point-of-care products is to improve their penetration in primary and secondary care settings. The Oxford technology will also reduce the cost of point-of-care tests by allowing multiple markers to be tested in a single kit, with no reduction in sensitivity. The multi-marker device is the same size as current single marker kits.

Market readiness

The Oxford invention has a granted patent in the USA. Isis would like to talk to companies interested in developing the commercial opportunity.

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“The Oxford technology will also reduce the cost of point of care tests by allowing multiple markers to be tested in a single kit, with no reduction in sensitivity.”





Talking Technology

Dr Angela Oldacres discusses the benefits of using a hydrogel material for improving dental implants, and treating cleft palates - a birth defect that affects 1 in 700 babies in the UK.

The hydrogel, currently being commercialised by Isis can also be used in many other cases of congenital disorders and surgical reconstruction, and improve routine dental applications.

The research and development is being led by Jan Czernuszka and a team of researchers including Jinhyun Hannah Lee and Zamri Radzi from the University of Oxford's Department of Materials. Surgeons from the John Radcliffe Hospital, including Mr Marc Swan, of the Department of Plastic and Reconstructive Surgery, and researchers from Georgia Institute of Technology in the United States also played an important role.

The team used the Science and Technology Facilities Council's ISIS neutron source to look at the hydrogel polymer's molecular structure in order to see how the

material might be used as part of a simplified surgical treatment.

For example, with cleft palate the treatment will involve inserting an anisotropic hydrogel material - similar to that used in contact lenses - under the mucosa of the roof of the mouth. Once inserted, the hydrogel gradually expands as fluid is absorbed, encouraging skin growth over and around the plate.

After sufficient skin has been generated to repair the palatal cleft, the plate is removed and the cleft is repaired using this additional tissue. The success of the preliminary studies of the self-inflating anisotropic hydrogel tissue expander has led to the first clinical trials being expected to take place early in 2011.

The technology is also useful for a wide range of other surgical applications. One key field is dental

treatments, including restorative dentistry, implant surgery and treatment of periodontal disease.

The hydrogel provides a reliable method for expansion of soft tissue, in procedures such as implant surgery where bone augmentation is required. Its use will improve patient outcomes and the predictability of outcomes. In the UK alone 80,000 dental implants are fitted every year, with an estimated 50 per cent of cases requiring bone augmentation. Other applications of the material include soft tissue expansion following removal of carcinomas, treatment of congenital birth defects, scar tissue and wound repair.

The work was awarded £72,500 by the Oxford University Challenge Seed Fund in July 2009 to accelerate the commercialisation of the technology, and fund a post-doctoral researcher to further develop the method of limiting the rate of hydrogel expansion, increasing the number of potential applications and markets for the device.

Isis welcomes contact from industry partners to take the technology to market.

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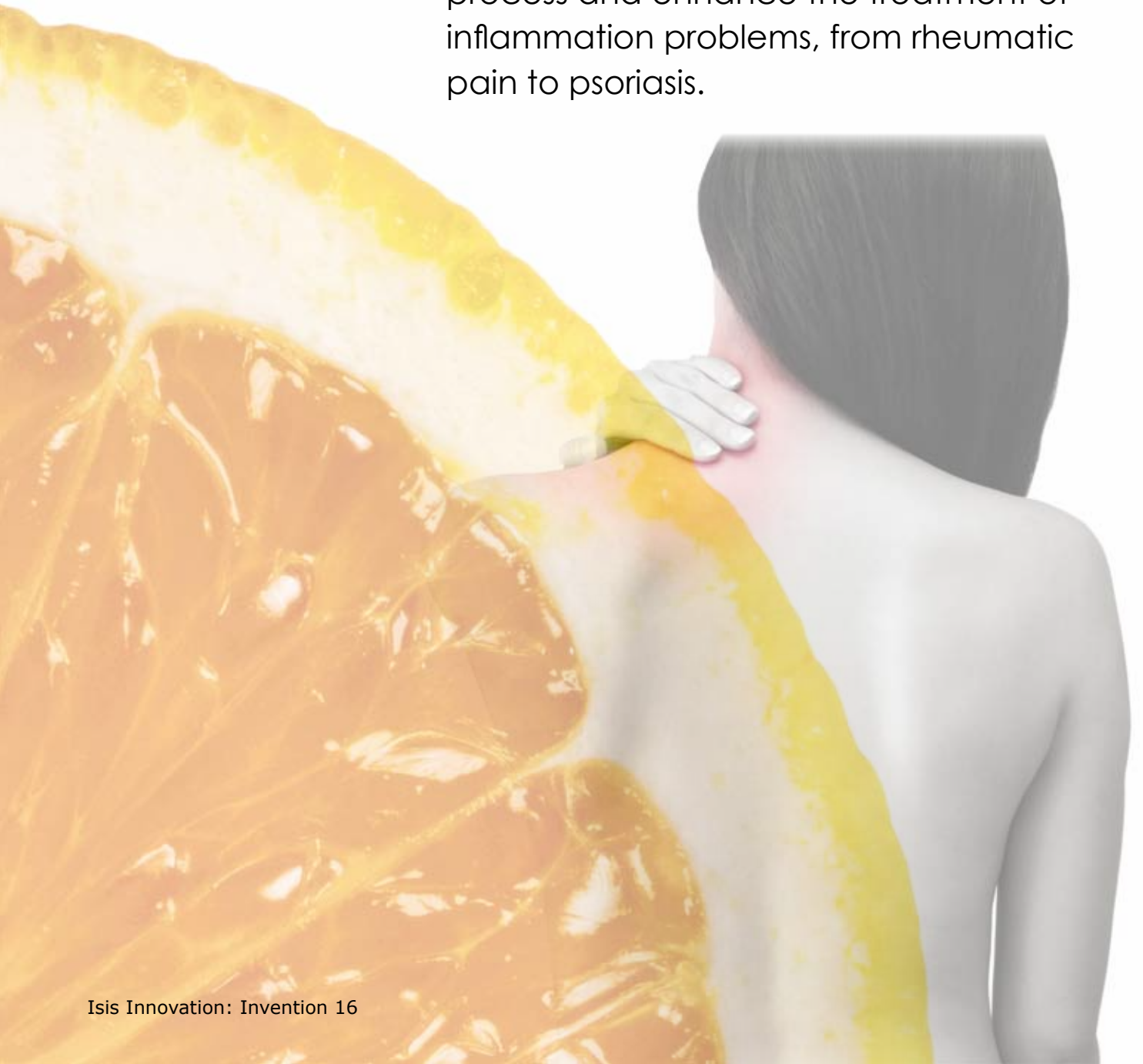
“In the UK alone 80,000 dental implants are fitted every year, with an estimated 50 per cent of cases requiring bone augmentation.”



Supplementing Steroids



Andy Self discusses an invention that could lead to an improved form of steroid, incorporating vitamin C to help the healing process and enhance the treatment of inflammation problems, from rheumatic pain to psoriasis.



“This new invention could lead to an improved combination therapy.”

Preventing tissue damage

The use of steroids represents a common and effective treatment for a wide variety of conditions in which inflammation causes pain, swelling and other issues. Glucocorticoids, such as prednisone and dexamethasone, are commonly used in injections for the treatment of inflammation and pain, and have a dramatic anti-inflammatory effect on tissues, particularly joints and tendons. Other forms of glucocorticoid, such as hydrocortisone, are an effective treatment for a variety of skin conditions, such as eczema and psoriasis.

It is known that glucocorticoids can cause substantial damage to skin, bone and other musculoskeletal tissues, and therefore excessive steroid use is a major clinical concern. For example, clinician's typically see an increased incidence of tendon re-rupture in patients who undergo glucocorticoid treatment, whereby the steroid is hindering the healing process by a previously unknown mechanism. Long term use of steroid creams can also cause side effects such as damage to and thinning of the skin. Consequently there is a need to identify the cause of the side effects caused by glucocorticoids and to develop methods to alleviate this damage.

Researchers within the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences at the University of Oxford have for the first time identified the cellular mechanism responsible for glucocorticoid induced tissue damage. The research focused on tenocytes (the cells that form tendons) and led to the discovery that the activation of the glucocorticoid induced signalling pathway results in two potentially damaging effects - 1) a reduction in cell proliferation and 2) the generation of Reactive Oxygen Species (ROS). ROS are highly

active, oxidative molecules that can lead to DNA damage and cell death.

Researchers within the department treated tenocytes with glucocorticoids in combination with vitamin C, known for its powerful anti-oxidant properties. They found that the combination therapy prevented glucocorticoid induced damage. Furthermore, researchers have identified the mechanism by which this occurs.

Long term patient care

In the UK alone, >500,000 glucocorticoid injections are administered annually. This new invention could lead to an improved combination therapy, offering significant improvements to standard steroid therapy. By substantially reducing the damage caused by glucocorticoids patients will benefit from a safer, longer term treatment.

The invention is likely to be of interest to companies in the pharmaceutical, cosmetic and veterinary industries. Examples of the potential benefits of this new approach include improved steroid injections for tendon rupture, dermatological creams for skin disorders such as eczema and psoriasis, and eye drops for conditions such as glaucoma.

Status

This invention is the subject of an international patent application and Isis would like to talk to companies interested in developing the commercial opportunity.

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X Radiotherapy

Dr Jamie Ferguson explains how radiotherapy enhanced by nanoparticles could be instrumental in treating deep-tissue tumours more effectively.

Researchers at the University of Oxford have developed a new system to treat cancer cells using reactive oxygen species (ROS) with little or no damage to neighbouring healthy cells, using existing radiotherapy facilities in a minimally invasive procedure. With the new method, ROS are generated by nanoparticles excited by x-rays.

The Oxford solution is based on the administration of doped titanium dioxide nanoparticles, which are highly tuned to absorb X-rays and efficiently converted into ROS to destroy malignant cells.

Nanoparticles are known to passively accumulate within tumour tissue due to the fenestration of the tumour vasculature and the Enhanced Permeability and Retention (EPR) effect. X-ray excitation of localised nanoparticles would be minimally invasive and utilise existing clinical facilities. The accumulation of nanoparticles in cancer cells will either be used to enhance the irradiation of cancer cells using radiotherapy, or to enable lower doses of radiation to be used without loss of efficacy. In addition, short life-times and diffusion distances of ROS permits cancer cell destruction.

Deep tissue treatment

Titanium dioxide is known to have high photocatalytic activity and to generate ROS under ultraviolet (UV) excitation. ROS can react with biological macromolecules, modify the structure and function of proteins and cause oxidative damage to DNA. ROS damage cellular DNA through destruction of bases and by producing single strand breaks. In addition, oxidants are known to act directly on mitochondria to trigger the initiation of apoptosis.

Consequently, specific generation and control of ROS at a tumour site





“It is believed that the Oxford nanoparticles, used in conjunction with conventional X-ray radiotherapy, will enhance cancer treatment.”

can be used as a tool for specific killing of malignant cells. Indeed, a technique known as photodynamic therapy which uses UV light to stimulate nanoparticles is already used for skin cancers. However, since UV light is not very penetrative, treatment of deep tissue tumours via UV excitation would be practically very difficult.

Existing treatment, new technology

In a cancer cell treatment model, cells were incubated with nanoparticles and irradiated with a clinically relevant X-ray dose (3 Gy), left to recover for 24 hours and then irradiated once more. Multiple cell lines have been tested and the results demonstrate that cells devoid of nanoparticles were damaged by the X-rays, but continued to proliferate and return to approximately 80% of their pre-treatment level after 48 hours. In contrast, cell lines incubated with nanoparticles showed 70% cell death with little evidence of cell growth resuming.

Helping to save lives

Cancer is a class of diseases in which a group of cells display uncontrolled growth, intrusion and destruction of adjacent cells and metastasis. It is the highest cause of death worldwide and, according to the World Health Organisation, accounted for 13% of all human deaths in 2007. Early cancer diagnosis, in combination with precise cancer therapies could eventually save millions of lives. It is believed that the Oxford nanoparticles, used in conjunction with conventional X-ray radiotherapy, will enhance cancer treatment.

Status

The Oxford invention is the subject of a UK patent application. Isis would like to talk to companies interested in developing the opportunity.

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Ready, Steady... GO₂

Dr Brijesh Roy talks us through a new **breath-by-breath respiratory gas analyser developed by researchers at the University of Oxford** which could help enhance athletic performance, and transform critical care and anaesthesia.

Mass consumption

Measuring the oxygen consumption of humans is valuable in a wide range of clinical and non-clinical settings. At one extreme, measurement of oxygen consumption is generally considered the best indicator of aerobic fitness and cardiorespiratory endurance for sportsmen, and is widely used to develop optimum training and nutritional strategies. At the other extreme, it is routine to monitor the blood oxygen content of patients that have been admitted to hospital intensive care units.

There are a wide range of products on the market for the measurement of oxygen consumption, including patient monitoring devices used widely in hospitals. However, the respiratory gas analysis capabilities

of these are limited due to the use of 'sidestream' analysers. In these devices, as the patient breathes out, a sample of the gas is diverted away from breathing tubes down a long catheter for remote analysis. The resulting response times are slow and variable, making calculation of gas exchange occurring at the lungs very difficult. This is particularly true in the clinical settings of anaesthesia and critical care where the gas flow rates and the inspiratory gas compositions may vary, for instance, by the addition of extra oxygen and anaesthetics.

In-line analysis and measurement

The Oxford invention is an apparatus for 'in-line' analysis that uses laser spectroscopy to measure directly the concentration of oxygen, carbon dioxide and water vapour in the breathing tube.

Advantages of the Oxford invention:

- Removes the limitations associated with sidestream analysis.
- Allows the calculation of gas exchange occurring at the lungs under conditions where both inspiratory gas compositions and flow rates are varying.



- A fast response time (an order of magnitude faster than most current instruments).
- Simple and reliable device with no moving parts.
- Greatly reduced size and cost relative to mass spectrometry devices with similar capabilities.

Prototype

The Oxford invention is being developed by Professor Gus Hancock, Head of Physical and Theoretical Chemistry in collaboration with Professor Peter Robbins of the Department for Physiology, Anatomy and Genetics. Their approach combines Hancock’s expertise in the chemistry of optical absorption and Robbin’s expertise in human respiratory physiology. A working laboratory prototype has been developed and the inventors have received an MRC translational award to fund ongoing development of the device appropriate for use in a clinical setting.

Patient monitoring

Following successful development, it is expected that the technology would be incorporated as a standard component of clinical patient and intensive care settings. In 2008, the patient monitoring market was estimated to be worth \$2bn in Europe alone.¹ The use of respiratory analysis in the sports, exercise and defence markets has



“A further clinical driver for the development of this technology has been the desire to establish whether measurement of oxygen consumption could form the basis for target-based resuscitation of patients in hospitals.”

yet to be fully exploited, but is likely to present a significant opportunity for early revenues.

A further clinical driver for the development of this technology has been the desire to establish whether measurement of oxygen consumption could form the basis for target-based resuscitation of patients in hospitals. Until now, the lack of suitable technology has prevented proper exploration of this idea. It is expected that once the device is ready for the clinic, it would be used as a key technology underpinning a programme of clinical trials with potential to unlock an additional stream of longer-term revenues.

¹ Frost and Sullivan – Patient Monitoring, Dec 2009

Patent Status

The Oxford invention is the subject of an international patent application. Isis would like to talk to companies interested in developing the commercial opportunity.

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Force of Nature

Dr Angela Oldacres talks Traptavidin, a new protein that is set to replace Streptavidin in a broad range of biotechnology applications where improved binding properties are advantageous.

Ultra-stable streptavidin

The University of Oxford has engineered a streptavidin mutant that binds biotin-conjugates more stably than wild-type streptavidin.

The new "Traptavidin" mutant has the potential to replace streptavidin in many applications, including arrays, surface-plasmon-resonance, point-of-care diagnostics, immunoassays, purification and imaging.

The streptavidin-biotin system is already widely used in many fields and Traptavidin increases the effectiveness of streptavidin by making the interaction more stable, and effective in a wider variety of conditions.

Traptavidin has the potential to replace streptavidin in many of its applications due to its;

- 10-fold decreased off-rate
- Increased thermostability
- Increased mechanical stability
- Similar ease of expression

Widely-used

Streptavidin is a 52,800 dalton tetrameric protein purified from the bacterium *Streptomyces avidinii*. It is one of the most widely used tools in molecular biological research, due to its extraordinarily strong affinity for biotin (also known as vitamin H). The dissociation constant (KD) of the biotin-streptavidin complex is on the order of 10^{-14} M, which is one of the highest affinity interactions known in nature.

The strong streptavidin-biotin bond can be used to attach various biomolecules to one another or onto a solid support. The streptavidin-biotin binding is widely used in nano-assembly, immunoassays, purification and imaging. Despite the strength of the streptavidin-biotin interaction, the stability of this interaction is limiting for many applications because it has been shown to fail in certain conditions including low pH, when attaching to nanoparticles and in the presence of mild shear force, as well as in the path of molecular motors and at high temperatures. Although streptavidin has been the

focus of numerous engineering efforts for many years a streptavidin mutant has never before been successfully produced with binding stronger than wild-type.

Demonstrated and validated

This mutant, known as Traptavidin was made by site-directed mutagenesis. Its increased utility has been demonstrated by investigation into the translocation of FtsK, the fastest known linear molecular motor which is also important for bacterial chromosomal segregation.

Status

The Oxford invention is the subject of a patent application. Isis would like to talk to companies interested in developing the commercial opportunity.

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"Traptavidin has the potential to replace streptavidin in many of its applications."





Science Naturally

Dr Emma Sceats and **Dr Brijesh Roy** explain how scientists at the University of Oxford have been looking to nature to develop new protein-based drugs.

Small molecule drugs have been the cornerstone of the pharmaceutical industry for well over a century, but so-called large molecule drugs, such as proteins and peptides, are becoming increasingly important. Oxford researchers have developed a broad toolkit of protein modification strategies that alter protein function and assist in the development of protein-based drugs.

The pharmaceutical industry has a long history of using large molecules for medicinal purposes, including insulin for diabetes, and the cowpox vaccine, developed in 1796 as an immunisation against smallpox. Clearly, large molecule drugs are not a modern phenomenon, so why have they not been developed or used as widely as their small molecule counterparts?

This can be explained by the properties of larger molecules which make drug development particularly challenging. For example, developing protein drugs that can be administered by mouth is difficult because the acids and enzymes in the human gut are very effective at destroying protein drugs. Large molecules are often quite insoluble so getting them into a liquid form where they can be introduced via injection is also difficult.

In spite of these challenges, the market for therapeutic proteins is large (\$37 billion in 2003) and growing (>15% growth p.a.), with

over 150 FDA-approved protein-based drugs used in the treatment of various conditions including cystic fibrosis, cancer, diabetes, anaemia, arthritis, heart attack and stroke.

Next generation protein drugs

With large molecule drugs becoming increasingly well established, pharmaceutical companies must find more ingenious ways to overcome the challenges posed by working with these complex molecules. Companies are particularly keen to apply principles that have been successful in small molecule drug development to larger drugs.

Professor Ben Davis, fascinated by the structural and functional diversity achieved in nature through the process of protein alteration (post-translational modification), has looked to take advantage of the control of chemistry to develop new, more specific protein modification strategies.

Reducing side effects and saving money

Professor Davis' team at Oxford's Chemistry Research Laboratory has developed a toolkit of chemical methods that enable scientists to pursue more logical and

“These strategies are expected to yield therapeutic proteins offering a number of benefits.”

efficient development strategies for protein drugs. For example, it will be possible to decorate proteins in a very specific manner with biological molecules such as sugars and peptides to yield well-defined, homogenous, modified proteins (e.g. glycoproteins, PEGylated proteins). The toolkit offers choices in the conjugation strategy, provides methods that are compatible with a broad variety of peptides, proteins and conjugates, and allows scientists to tailor the links between the protein and its conjugate. Other advantages over existing modification strategies include excellent reproducibility, reliability and high yields of protein-based products.

These strategies are expected to yield therapeutic proteins offering a number of benefits:

- **Improved protein drugs:** modifications that enhance drug activity or ensure that a drug remains in its pharmaceutically-active state for longer can benefit patients by minimising drug doses and reducing side effects. Modifications that improve drug-receptor interactions, prolong plasma half-life, or reduce immunogenicity may be useful in this regard.
- **New protein drugs:** chemical methods enable the

development of modified proteins that mimic natural products and offer routes to proteins with novel (synthetic) modification patterns.

- **Salvaging failed drugs:** the failure of drugs in clinical trials is expensive for developers and disappointing for patients who might otherwise have benefited from the drug. Failures linked to the sub-optimal absorption, distribution, metabolism or toxicity of the drug might be turned around, for example, through protein modifications which can enhance drug targeting of diseased tissues.
- **Active ingredients:** the efficacy of existing protein-based therapeutics, for example, erythropoietin a glycosylated hormone used in the treatment of anaemia, may be improved by developing drugs that contain only the most active glycoforms. Chemical modification methods provide unique access to these specific glycoforms.

Moving forward

Professor Davis is working with several international collaborators to explore the use of these methods in the development of drugs and vaccines for the treatment of diseases affecting the central nervous system and the immune system including HIV/AIDS.

This toolkit of technologies is available for licensing from Isis Innovation and is protected by granted patents and a number of international patent applications.

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Sowing

the

seeds

of future

success



In 2009 Oxford University Consulting identified an expert with the right mix of scientific credentials and management experience to join a team for an independent review of one of the UK's most respected public institutions, the Royal Botanic Gardens, Kew.

Oxford University Consulting provides access to Oxford experts by setting up consulting arrangements with businesses and governments worldwide. In the last financial year, OUC managed over 150 consulting agreements.

Emeritus Professor Hugh Dickinson, former Sherardian Professor in the University of Oxford's Department of Plant Sciences, was science and education consultant to the "Independent Review of the Royal Botanic Gardens, Kew" commissioned by the Department for Environment, Food and Rural Affairs. Its report was released in February 2010.

Dickinson, a former Trustee of the Royal Botanic Gardens, Kew and Keeper of the Oxford Botanic Garden, brought to the project considerable experience gained from a distinguished career managing large research departments. A member of the Governing Council of the renowned John Innes Centre, Dickinson has also sat on the boards of several Research Council committees, including the BBSRC's Integrated Epigenetics Initiative.

Over a period of four months, Dickinson met with a wide range of stakeholders and staff at the Royal Botanic Gardens, Kew. Benchmarking other botanic gardens was particularly valuable in that it put the challenges faced by Kew into an international context.

"An institute as large as the Royal Botanic Gardens, Kew is highly complex, and under very different pressures from a wide range of stakeholders," said Dickinson. "Our overall view was that Kew should focus on its core business - developing its excellent collections, carrying out high quality research, and providing a first-class 'public face'."



"Identifying these priorities should help Kew to focus and thrive. Kew's collections are truly world-class; in addition to the better known collections of living plants, seeds and herbarium specimens, they include paintings, books and manuscripts and ethnological artifacts. For this reason they need to be curated and researched by specialists who are in turn well managed and resourced."

The report outlines fifty recommendations, including a proposal that the Natural History Museum, the Royal Botanic Gardens, Kew and the Royal Botanic Garden in Edinburgh share resources to develop and maintain their plant collections in an integrated fashion. Other recommendations cover research strategy, visitor experience, horticulture,

management and Kew's Millennium Seed Bank.

The team was led by Sir Neil Chalmers, Warden of Wadham College, Oxford and former Director of London's Natural History Museum. Dickinson said Oxford University Consulting provided a smooth service in setting up the contracts, administration and financial arrangements for his consultancy, allowing him to focus on the review itself.

"It's the breadth and depth of experience of people such as Professor Dickinson here at Oxford which allows OUC to provide the right person to enhance a business or government project such as this," said Steve Lee, Head of Oxford University Consulting.



"Identifying these priorities should help Kew to focus and thrive. Kew's collections are truly world-class."



Playing with the **Fate** of the World

**Oxford University
Consulting** gives us
a preview of a new
climate change game
which includes real
prediction models
from Oxford.

University of Oxford climate change expert, Dr Myles Allen, has provided state-of-the-art climate science for Oxfordshire games company Red Redemption's "Fate of the World" game - currently scheduled for release in the third quarter of 2010. Dr Allen's consultancy to the company was arranged by Oxford University Consulting.

"Fate of the World" is a nail biting set of global warming scenarios covering 200 years of Earth's existence. The game lets players explore the next two centuries, trying out geoengineering, fusion power, wildlife adaptation, and many other brain teasing and sometimes alarming, options. The player must manage a balancing act of protecting the Earth's resources and climate versus the needs of an ever-growing world population, who are demanding more food, power, and living space.

At the heart of the game are 10 'Masterplans' where the player calls the shots for all mankind including 'Apocalypse' where the goal is to raise the planet's temperature to a lethal degree; 'Lifeboat' where the goal is to save only the player while abandoning everyone else to

whatever catastrophes await them; and 'Utopia' where a player can try to build a perfect society while battling population growth.

It is a sequel to the successful "Climate Challenge" game developed by Red Redemption and sponsored by the BBC, which has been played by nearly 1 million people since its launch in 2007.

Dr Allen is project leader on ClimatePrediction.net, a program that lets interested people from around the world take part in climate modelling. "Fate of the World" uses a model reviewed in Nature (April 2009) - the international weekly journal of science.

Dr Allen said: "Providing science for games is a new field for me, but public engagement with the issues surrounding climate change is vital and games are a great way of reaching millions of people."

Ian Roberts, designer of "Fate of the World" said: "Accurate real-world data is used in many videogames. Take a motor racing game, you need to know how a car responds when a player brakes or turns too sharply. A climate based game is similar but

you can't test drive the climate. So we needed the expertise of a real scientist. That's why Dr Allen's input is so important."

Oxford University Consulting was approached by Dr Allen after he and a former colleague who works for Red Redemption discussed how to provide realistic climate change calculations for the game's outcomes.

"The aim of Oxford University Consulting is to help business access the right experts, and to help academics engage with industry. The work of the environmental and climate change experts at Oxford is very relevant to a whole range of groups, and Dr Allen's consultancy is just one example of business accessing this expertise through a consultancy arrangement," said Steve Lee, head of Oxford University Consulting.

Based in Oxford, England, indie games company Red Redemption makes games that provoke and challenge. "Fate of the World" is a PC & Mac title being released in Q3 2010.

<http://www.red-redemption.com>

"A climate based game is similar but you can't test drive the climate. So we needed the expertise of a real scientist. That's why Dr Allen's input is so important."

“If your current networks cannot help you – meet some new people!”

Research funding organisations throughout the world are turning their attention to the impact their funding has on society through the exploitation of research results. Studies have been commissioned, reports written and observations made. Due to the time lag between research funding and exploitation, and the difficulties in linking any individual research project to specific outcomes, the overriding conclusion is that it is very hard to measure impact with any degree of certainty.

Given our background in technology transfer, Isis Enterprise has been commissioned by a number of organisations across the world to evaluate research impact. When we speak to researchers who have been involved in developing new products or services a consistent message is that publishing research papers is not, on its own, sufficient for ensuring research adoption and long term impact.

In the age of information overload the chances of an individual research publication getting into the hands of someone in a position to exploit the results is diminishing. Here we offer ten practical steps which can be undertaken by researchers, or technology transfer staff, in order to maximise the chances of achieving (with apologies to Harry Callaghan, better known as “Dirty Harry” in the Clint Eastwood films) a ‘Sudden Impact’.

1. Look backwards

What history can tell us is that exploitation of research results is hard and the key to success is finding someone with the drive to make it happen. To learn from history we recommend you find someone who has acted as an exploitation champion – the impact vigilante – and listen to their advice!

2. Look forwards

The journey taken by individual research outputs through to new products and services can be complicated. Some innovations are subject to regulatory hurdles, whilst others rely on the implementation of legislative changes. Understanding these factors early on can reduce the time it takes to get innovations into practice.

3. ‘Phone a friend’

Being a champion of an early stage technology project is lonely. Setbacks are common and the journey to successful technology transfer is littered with dead ends. It is important to share your challenges with colleagues and get their ideas.

4. Meet new people

Any commercialisation project can be viewed as a series of questions: “who can improve my prototype?”, “where can I find more funding?”

Sudden IMP

10 practical steps to
streamline research
exploitation

Theorists have developed the concept of social capital – a measure of the power of contact networks in problem solving. If your current networks cannot help you – meet some new people!

5. Publish in trade magazines

Generally academics read academic papers. Industrial researchers and clinicians read patents, trade

magazines, clinical guidelines and some academic papers. Publish outside academic literature to increase awareness.

6. Collaborate

Having found other parties interested in your project it is important that you commit to transferring your know-how. Mechanisms include research collaboration, contract research and consultancy.

7. Do more research

When research activity results in publication the temptation is to stop. However, a few selected further experiments can make an enormous difference to the prospects of getting third parties interested.

8. Patent before publication

If taking your promising research results through to a product or service will be costly and will involve a commercial company you need to file a patent. Without the market protection associated with patent rights, no company will be prepared to invest.

9. Open sourcing

Giving technology away to get it used is a valid technology transfer mechanism in some circumstances.

10. Report back

Research funding organisations get their money from other organisations. They increasingly need to demonstrate the impact of their funding. It is important to let them know of your successes.

Isis Enterprise offers advice on all aspects of research impact.

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“When research activity results in publication the temptation is to stop.”

ACT

Dr David Baghurst, Isis Enterprise explores the challenges involved in achieving research adoption and long term impact, and provides immediate practical advice.



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Oxford Innovation Society

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

- Wednesday 22 September 2010
- Thursday 9 December 2010
- Thursday 24 March 2011

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.



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