

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 <u>www.isis-innovation.com/</u>... are automatically redirected to our new domain, <u>www.innovation.ox.ac.uk/</u>...

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

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Isis insights

APPLIED BIOLOGY

Software solutions from Oxford's medical scientists, p12-15



The latest innovations, collaborations and technology transfer



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Applied biology

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NEWS

Commercial success for established spin-outs

One of the largest ever transactions involving an Oxford spin-out was finalised in December when US social games company Zynga acquired NaturalMotion Ltd, a spin-out from 2001, for more than \$527m. Isis worked with Torsten Reil, an Oxford Zoology DPhil student, to patent the underlying technology and attract initial investment from business angels. Reil successfully grew the company to 260 people with international offices, applying its technology to highlyrated games such as CSR Racing and Clumsy Ninja (pictured).

To find out more about Isis's economic impact, including the \$64m Nasdaq success of Oxford Immunotec Global PLC, turn to the accompanying booklet or www.isis-innovation.com.

New spin-outs from Isis and Oxford

"This is a time of bustling activity for Isis Innovation..." wrote Technology Transfer Tactics in February, noting the number of recent spin-outs formed.

• £12m investment in treatment for blindness

A gene therapy for choroideremia, an inherited form of progressive blindness, has been developed by Professor Robert MacLaren at Oxford's Nuffield Laboratory of Opthamology and is to be further developed and commercialised by Nightstar. Syncona, a subsidiary of the Wellcome Trust, will invest £12m in the new company. Professor MacLaren's discovery was featured in The Lancet last year.

• Secure mobile communications

Patented security protocols are the core technology of a new spin-out from Oxford, Oxcept. Developed at the University's Department of Computer Science under Professor Bill Roscoe, the methodology will allow peer-to-peer payments and secure ad-hoc data sharing in disaster recovery scenarios and other insecure environments.

• Ultrasonic drug delivery

Oxsonics, a new spin-out from Oxford's Institute of Biomedical Engineering has been formed with £2.7m funding. Using ultrasound to trigger the collapse of nanoscale bubbles allows drugs to be safely targeted into tumours and organs. Oxsonics initially aims to address metastatic liver cancer, but the technology has potential in many diagnostic and therapeutic applications.

New international members for the Oxford Innovation Society

The Oxford Innovation Society, an open innovation network managed by Isis, provides members from around the world with opportunities to learn more about new technologies from Oxford, and to explore areas of common interest with each other. Recent new members from the USA, Holland and Mexico include Sensient Technologies, Philips, SCG Chemicals and Centro Kappa de Conocimiento, S.C.

Investing in Oxford spin-outs

A new fund, managed by Parkwalk Advisors, has been launched to facilitate investment into spin-outs from Oxford. The University of Oxford Isis Fund allows private investors to support the commercialisation of new technologies from Oxford whilst qualifying for income tax relief under EIS/SEIS rules.Details of the fund are available from Parkwalk Advisors at http://parkwalkadvisors.com/pw_uoif/.



Information

Enterprising Consultancy

News from Oxford University Consulting and Isis Enterprise



Robots in the desert

Oxford University Consulting (OUC) recently arranged for mobile robotics expert Professor Paul Newman to spend a week in the Omani desert. He was there to experience, first-hand, some of the practical challenges faced by the teams who work for one of the world's leading geoscience companies, CGG.

CGG is a fully integrated geoscience company providing leading geological, geophysical and reservoir capabilities to its customers, primarily from the oil and gas industry. It is renowned not only for its creation of value by optimising the discovery and the development of natural resources, but also for operating safely and with integrity, across its operations worldwide. "CGG's strong commitment to research and development drives our innovative approach and this led us to Oxford," says CGG's Advanced Projects Manager, Jonathan Grimsdale.

CGG have been discussing with Professor Newman how best to use mobile robotics to support their highly experienced land crews operate safely, with the very latest geophysical technology to record the most insightful data in any location around the globe. As Professor Newman says, "the collection of such data, sometimes under very challenging conditions, is all about coordinated and precise movement of assets – the very definition of mobile robotics".

Kyoto collaboration

Isis Enterprise, a division of Isis Innovation, is working with Kyoto University to promote a portable device for elementary analysis of rare-earth elements at mining sites and steelmaking slags.

Associate Professor Susumu Imashuku, at Kyoto University, has developed a novel, high-sensitivity detector featuring cathodoluminescence that uses visible light in combination with simultaneously generated X-ray.

This electron-ray device uses pyrelectric crystal and a battery under low vacuum. The device can detect several rare-earth elements that could not be detected with X-ray.

Only one pre-treatment, a crushing process, is required and high-selectivity enables detection of elements that are undetectable with conventional portable detectors.

A prototype of the device has already been produced and the basic analysing performance has been confirmed. Kyoto University seeks business partners to license the patent for practical application of the invention on an industrial scale.



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The portfolio

The latest **spin-out** and **investment** news **Material value: Designer Carbon Materials**

Isis is seeking to raise £250,000 to form a spin-out company, Designer Carbon Materials, which is focused on meeting increasing demand for an advanced form of nanocarbon: endohedral fullerenes.

Cage-like structure

Although attracting less publicity than graphene, fullerenes are another allotrope of carbon that have been shown to possess highly attractive chemical, physical, magnetic and electronic properties. One of the most interesting features of fullerenes is that due to their cage-like structure, they can trap atoms inside their empty "shell" producing structures known as endohedral fullerenes.

Endohedral fullerenes offer opportunities for exciting advances in the development of a number of fields, including energy harvesting in organic photovoltaics, magnetic resonance contrast agents and radiotracers for biomedical applications.

Current status

Research at the University of Oxford's Department of Materials by Dr Kyriakos Porfyrakis has led to the development of a patented process for the production of endohedral fullerenes and higher fullerenes (C₇₆, C₇₈, C₈₄ etc) at quantities sufficient for research and development purposes. Using prototype equipment, small quantities of these highly valuable materials have already been sold to research groups. Further enquiries for gram quantities of endohedral fullerenes and tens of grams of higher fullerenes are being received from around the world but these cannot be fulfilled on existing prototype equipment.

These are extremely high value materials; endohedral nitrogen fullerenes have been sold at a price of \$100/mg and they cost approximately \$5/mg to make. "There are believed to be no other companies or research groups with alternative processes that can reliably produce such high purity endohedral fullerenes and higher fullerenes"

There are believed to be no other companies or research groups with alternative processes that can reliably produce such high purity endohedral fullerenes and higher fullerenes. An exciting opportunity has been identified to develop a business that could meet this need, by scaling up the production and purification processes of the Oxford technology by several orders of magnitude, and investment is being sought for this purpose. We aim to spin-out Designer Carbon Materials to meet this unfulfilled market demand.

Matched funding grant applications for up to £100,000 will be made to the Technology Strategy Board, potentially allowing for a £150,000 investment.

Strategy

As the end-markets for endohedral fullerenes develop, sales volumes will increase, but the company also has the opportunity to generate additional intellectual property and value. These opportunities exist around the materials, the production processes and the end-applications. An exit by trade sale to a major advanced materials or chemical producer may be sought within five years.



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LAYTONS

Paddy Kelly, Partner at Laytons Law Firm, outlines some of the investment routes and sources available for energy projects

Availability of funding for energy projects depends on the maturity of the technology and the scale of deployment. Funding for early stage technology development is the hardest to obtain, and in order for investors to spread their risk there is usually a need for pooling of their investments. Laytons offers legal support in areas related to securing or providing funding.

Laytons law firm has acted as lawyers to a range of fund managers in setting up investment funds operating in this field including The Finance Yorkshire Fund (a £90 million fund), the Rising Stars Growth Funds and The North West Fund (a £155 million fund). Laytons also advises fund managers focusing specifically on University spin-outs such as the £32m UMIP Premier Fund, a fund investing in Manchester University spin-outs. Such work involves combining and applying a knowledge of financial services fund law with a knowledge of institutional and EU funding sources; both the North West Fund and The Finance Yorkshire Fund have been financed by the European Regional Development Fund and the European Investment Bank.

A paper presented by Kate Bingham, of the SV Life Sciences Advisers LLP Law Firm, at the OSEM 2012 Conference called for creative strategies for life science spin out project using of EU funding, and there have been developments in such funding for both large scale energy infrastructure projects and smaller scale projects through investment funds. The greatest advantage to be had from such funding will arise if Oxford University and the wider regional funding community can use EU resources to sponsor such investment funds.

Investment funds for energy and life science spin outs

The North West Fund has two sub funds focusing on energy and life sciences: The North West Fund for energy and environmental places specific emphasis on businesses in the Energy and Environmental sector while The North West Fund for Biomedical invests in companies in pharmaceuticals, biotechnology and clinical research. These funds were financed by the European Regional Development Fund and the European Investment Bank under the European Commission's Joint European Resources for Micro to Medium Enterprises Initiative and are focussed specifically on the North West region of England. There is no reason in principle why these fund types cannot be replicated in other areas within the UK although alternative sources of funding would need to be established.

"Laytons is available to assist with the legal aspects of the funding of both energy related spin-outs and larger projects"

UK infrastructure guarantees

The UK government has a programme to support nationally significant infrastructure projects, including those in the energy sectors, by issuing government guarantees to support debt financing of such projects that are ready to start construction within 12 months of the guarantee being given; that are financially credible; dependant on the guarantee to proceed or not otherwise financeable in a reasonable time; and give good value to the tax payer on a risk reward assessment.

Energy projects whose funding has been secured by such guarantees include the Neart Na Gaoithe 450MW wind farm in the Forth Estuary, Scotland and projects to convert Drax and Eggborough power stations from coal to biomass fuel.

Laytons is available to assist with the legal aspects of the funding of both energy related spin outs and larger projects, such as those covered in this article, using EU and other government related funds.

EU project bonds initiative

The European Commission has set up a financing scheme to stimulate investment in EU transport energy and broadband infrastructure and to support debt capital markets funding such projects. The credit rating of the projects, promoter is increased once the scheme has backed it with a loan or guarantee from the European Investment Bank. The increased credit rating allows the promoter of the project to issue more financially robust bonds that will be acceptable to a wider investor pool such as pension funds as well as corporate investors.

A £316million project bond funding structure has just been used to fund the purchase of the transmission assets – substations, cabling, electrical equipment – of the 504-megawatt, 140-turbine Greater Gabbard North Sea wind farm.

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Meeting energy demand

Speaking at the Oxford Innovation Society Meeting in December, **Professor Sir Chris Llewellyn Smith**, Oxford University's Director of Energy Research, addressed the question of whether the world's future energy needs can be met with or without fossil fuels, and gave examples of the contributions of over 180 senior Oxford researchers who work on energy

Energy use is more or less constant in developed countries, but is rising rapidly in the developing world, where a large increase is needed to allow billions of people to emerge from poverty. The magnitude of the increase will depend on future lifestyles. It does not seem possible for the per capita energy use in the USA to become universal, which today would require a fourfold increase in total energy consumption. Less energy intensive lifestyles will be necessary and/or demand must, if possible, be lowered by means that do not compromise lifestyles. Energy must also be used very much more efficiently.

While large efficiency gains of 40 percent or more look possible technically, they are not being realised for reasons that are analysed by researchers in Oxford and elsewhere. With the right measures in place, perhaps 10 percent savings could be achieved beyond those expected anyway as technology improves. Seeking such savings is vital but they won't be enough to do more than curb the expected increase in energy use. Energy needs are therefore expected to continue to increase in the coming decades. Whether the needs can be met will depend on the future price and availability of fossil fuels and of the alternatives. The world is awash with fossil fuels. Much is in forms and places that until recently made extraction look economically or technically out of reach. It is sometimes argued that as the world becomes increasingly reliant on these new sources, costs will rise steeply. Perhaps, but history suggests that technological advances could undermine this view, and I believe that with fossil fuels it will be possible to meet demand for at least 50 years, beyond which time prognosis becomes increasingly difficult.

The world should of course be weaned from fossil fuels, to reduce pollution, to improve energy security in countries that rely heavily on imported fossil fuels, to reduce the scale of climate change, and because in the long run fossil fuels will become increasingly scarce and expensive. Doing without fossil fuels, which provide some 80 percent of the world's primary energy, will however be incredibly difficult even in principle, and impossible – with current technology – at

"According to the World Health Organisation, outside urban air pollution causes 1.35 million premature deaths a year, including 11,000 in the UK"

"Oxford's development of perovskite based solar cells could lead to large reductions in the cost of solar energy"

a price society would be willing to pay. The alternatives currently contribute small amounts, and many are much more expensive than fossil fuels, ignoring externalities, and/or have limited potential.

The stark conclusion is that without a secure fossil fuel supply, the poor of the world will remain poor for the foreseeable future. Moreover, without vigorous development and expansion of non-fossil sources, the goal of decarbonisation will not be achieved. Given that the world will be heavily reliant on fossil fuels for decades to come, high priority should be given to using them as efficiently as possible, while coal should be replaced by gas wherever possible, both to mitigate climate change and to reduce pollution.

Oxford's response

I will illustrate Oxford's response to the energy challenge with just three examples. First, Oxford physicist Dr Henry Snaith, one of Nature's top ten 'scientists who matter' in 2013; Dr Snaith has pioneered the development of perovskite based solar cells, creating great excitement world-wide as they could lead to large reductions in the cost of solar energy. Second, Oxford has a powerful programme in nuclear materials, focused on lifetime extension of existing reactors, and - in collaboration with EDF and Rolls-Royce – on materials for future fission reactors, as well as fusion reactors. Third, Oxford scientists think they may be able to understand why cows are 20 times more effective than existing man-made bio-digesters at turning plants into methane. This could have a huge impact. Numerous other examples of Oxford's wide-ranging contributions to energy technology, economics and policy can be found at the recently launched website www.energy.ox.ac.uk.

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Creating energy connectedness

Catherine Bottrill, the CEO of Oxford energy-saving start-up Pilio, presented at the December OIS Event on the company's eclectic range of services and clients

In debates about meeting the energy challenge, building energy efficiency is repeatedly cited as the 'low hanging fruit' because it offers some of the cheapest and effective solutions. However, World Energy Outlook identified in their 2012 Report that despite the policies and technologies available, 80 percent of the potential in buildings would go unrealised.

This missed opportunity for energy savings is in part due to energy managers having to wrestle with collecting and organising their energy data from a complexity of hardware and software. Many are reliant on excel spreadsheets for performing energy analytics, which quickly become unwieldy with multiple buildings and insights cannot be easily shared with colleagues.

Pilio spun-out from building energy research at Oxford's Environmental Change Institute to provide energy managers with the energy analytics necessary to accurately assess and target energy performance. Pilio has created a number of software products – sMeasure for business, iMeasure for homes and wMeasure for weather data – to contextualise and connect people to their energy use and provide the evidence for appropriate energy saving actions to be taken. Pilio has been working with the Church of England for the past two years to help them understand their energy use across a complex estate of 16,000 churches and 4,000 schools to improve energy management. Pilio is also working with Whitbread Plc, to assist them with weather-energy analytics across their portfolio of Premier Hotels, so they know the true energy performance of their buildings (not skewed by mild or severe winter weather).

Finally, Pilio has been working with hundreds of arts organisations in partnership with Julie's Bicycle to embed good energy management practices in buildings. This work has involved calculating revised energy performance benchmarks for performing arts buildings.

All these clients are exciting to work with as they each provide touch points to make visible and engage a wide audience in the importance of energy saving. Going forward, Pilio is committed to creating intelligent and accessible software applications to make energy saving action compelling so the low hanging fruit is picked.

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Understanding consumption

Navetas' Chief Scientific Officer **Jim Donaldson** described to the OIS how its core technology informs itemised energy readings to enable savings for customers

In today's climate, consumers need to manage and control the energy that they use. However, whilst we can all follow simple rules such as turning off lights and not leaving the TV on standby, the reality is that most people do not have a clear understanding of how they use their energy. When shopping at the supermarket, each item is individually priced and clearly itemised at the checkout. Similarly, when receiving a phone bill, the cost of each call is accurately and clearly illustrated. In contrast, as well as being inaccurate and intermittent, energy bills lack any information which can help people understand how they use gas and electricity, and what they can do to reduce their expenditure.

Navetas solution

Dubbed 'disaggregation', Navetas's core technology solution consists of advanced software algorithms which are able to analyse the electricity supply at a single point in the house and accurately break down the energy consumption into each of the major loads. Typically the technology is located either inside the meter cabinet, or inside the meter itself.

Navetas has recently signed a license agreement with a large US based metering provider to develop disaggregation technlogy for the North American market with a launch scheduled for the latter half of 2014. In addition, Navetas continues to seek partners in Europe and Asia to develop its technology to address the global market.

Navetas, the back story

Founded by Jim Donaldson and Malcolm McCulloch, Intelligent Sustainable Energy (ISE) spun out of the Department of Engineering in 2008 with initial funding from Navetas Energy Management, a start-up in the field of energy management.

Following a merger of the two companies in 2009, Navetas (www.navetas.com) continues to develop a range of innovative and advanced technologies to help consumers better understand and reduce their energy consumption.



Navetas Energy Monitor

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Invention

Clinical trial management

Dr James Groves presents an online clinical trial randomisation system that delivers the skill of a highly experienced statistician packaged into a complete and customisable user-friendly platform

The majority of new methods to diagnose, treat or prevent disease may show only modest improvements over existing approaches. Such subtle effects therefore require validation in clinical trials involving a large and often varied population of participants, where great care is needed to ensure that individuals are appropriately balanced across treatment/intervention groups.

Randomisation is an effective method of controlling for factors such as age, sex, medical conditions and treatments, as well as smoking, alcohol consumption and exercise, which if not accounted for could falsely enhance or mask the genuine effect of an intervention.

While randomisation of participants in a clinical trial is fundamental to its overall validity, the procedure is complex and requires a deep understanding and application of a wide range of statistical methods (e.g. simple block, stratified, and covariate adaptive methods). This has forced researchers across the world to either build their own randomisation systems or seek assistance from outside organisations. However, these options are far from ideal, generating software that suffers from either a poor level of usability and customisation, unwanted bias or high costs. Frustrated by such limitations and aware of a clear and widespread need for improvement, clinicians and statisticians

from the Nuffield Department of Primary Care Health Science at the University of Oxford came together to build a solution.

A complete solution

Sortition is an online randomisation system builder designed to incorporate a wide range of powerful statistical and minimisation algorithms delivered through an intuitive and user-friendly interface. It is a complete participant allocation system that allows full auditing, email notifications and treatment resource management. It is also fully customisable and ensures that control remains firmly in the hands of the user, regardless of their experience or location in the world.

Supported by a secure server network managed by the University of Oxford, Sortition can handle clinical trials of all sizes, regardless of the number of users, participants, trial sites, intervention groups, stratification factors or levels. The system uses a double-blind approach where concealing knowledge of the treatment groups from both the experimenter and participant is necessary to protect the study from unintentional bias. However, if concerns arise for the health of a participant enrolled in a trial, the web-based interface of Sortition is able to provide any medical practitioner with quick and easy access to the patient's history.

RGEN

"Sortition is well validated and has been adopted by clinical trial units both throughout the University of Oxford and across the world"

Mobile and global statistical expertise

Sortition is well validated and has been adopted by clinical trial units both throughout the University of Oxford and across the world. The intuitive and mobile nature of Sortition has generated positive feedback from both researchers tasked with setting up a clinical trial as well as the nurses, GPs, and field workers who input patient data. For example, field workers in a Cape Town community centre, investigating the use of mobile technology to improve the self-management of high blood-pressure, have used Sortition with minimal training to randomise over 1300 patients.

Widespread application

While Sortition was designed primarily with clinical trials in mind, its ability to package complex algorithm processing into an intuitive and user-friendly system has potential to benefit researchers across a wide range of disciplines.

Sortition is offered on a subscription basis. Please contact Isis Innovation for more details.



Key advantages

- Clean and uncluttered interface
- Accessible over the internet
- Wide range of powerful randomisation and minimisation methods
- Works for both open and blind studies
- Fully customisable and scalable
- Full audit trail
- Secure management
- Email notifications
- Built-in treatment resource management reporting and monitoring tools

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Advantages of the Oxford invention

- Random feedback matrices improve generalisation to data not seen during training
- Feedback Alignment is often quicker than existing methods. Novel network dynamics allow learning steps which approximate second order techniques, with no more computation than that required for a first order technique
- The technique is more robust to network initialisations, and is successful even when other algorithms struggle to learn at all
- Decoupling the feedback function avoids the central difficulty with training deep neural networks, the 'vanishing gradient' problem

Accelerating machine learning

Showcasing an algorithm for quickly and efficiently training artificial neural networks

The Feedback Alignment Algorithm allows systems such as those used for speech and image recognition to learn from data more quickly and enables such systems to be exploited in ever smaller devices.

Oxford's approach

In machine learning, deep neural network architectures – inspired by the multiple layers of neurons in the brain – have recently been used to set records on speech and image recognition datasets. Conventionally, these artificial neural networks are trained using a training set of inputs and corresponding external outputs. An error signal (generated from the difference between the expected and actual outputs) is then fed back to adjust the connection weightings of each layer and improve the accuracy of the system.

However, it would be impossible for the brain to implement the highly complex algorithms currently used to train these deep neural networks on a computer. This understanding has led to the Feedback Alignment Algorithm, based on much simpler circuitry requirements and has provided a number of unexpected benefits.

Oxford's Feedback Alignment Algorithm uses random feedback matrices to process errors and deliver updates to network parameters. Networks are trained quicker using this method than via alternative techniques such as 'back propagation of errors'.

Easy to implement, with rapid benefits

The technique is general purpose and can be applied very broadly. It is quick to implement and can be used to train both feed-forward and recurrent network architectures on regression and classification problems. Existing neural network tools can easily be modified to take advantage of the technique.

In silico neural networks

The Feedback Alignment Algorithm can also simplify the design of hardware-based neural networks. Such networks compute faster than software versions and can be installed in small devices like cameras or mobile phones. Previously, training these 'on-chip' networks has proven complex, due to the difficulty in writing circuits with the required error-feedback precision. The Oxford algorithm removes the need for this type of precision, making it ideal for training hardware based neural networks.

Patent status

A US patent has been applied for: US Application No. 61858928.

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Tackling malaria

Presenting an online tool for estimating malaria parasite clearance

Anti-malarial testing

The Parasite Clearance Estimator (PCE) represents a key component of the toolkit developed by the World Wide Anti-malarial Resistance Network. WWARN comprises a global network of experts supported by the Bill and Melinda Gates foundation and managed by the University of Oxford. The PCE online tool provides a consistent, reliable and accurate method for measuring malaria parasite clearance based on the linear portion of the slope of the log-parasitaemia versus time relationship.

This standardised approach facilitates routine monitoring of artemisinin combination therapy (ACT) efficacy and allows comparisons over time and space. Such information is critical to enable the detection of early changes in Plasmodium falciparum sensitivity to artemisinins and supports timely responses in treatment guidelines when needed. It is also being used to support an FDA application for a novel anti-malarial drug.

Parasite Clearance Rate – an early indicator of anti-malarial resistance

The emergence and spread of resistance to antimalarial drugs threatens the efficacy of existing drug treatments. Parasite clearance rate is an important measure of drug efficacy. The rate can be used to assess in vivo responses to treatment withartemisinin derivatives, evaluate new antimalarial drugs and assess therapeutic response in severe malaria and hyperparasitaemia. Emergent artemisinin resistance in Western Cambodia wasfirst signalled by a significant reduction in parasite clearance rates following artesunate treatment of falciparum malaria. Resistance subsequently manifested in increased failure rates following ACT.

A uniform method to describe the delayed clearance phenotype is an essential research tool when assessing antimalarial efficacy data for signs of change. Only by comparison with baseline parasite clearance rates can prolonged clearance, an important early warning sign of resistance, be identified. To address this need, WWARN teams developed the PCE online tool.

Reference

Flegg JA, Guerin PJ, White NJ, Stepniewska K. Standardizing the measurement of parasite clearance in falciparum malaria: the parasite clearance estimator. Malaria Journal 2011; 10:339. doi:10.1186/1475-2875-10-339

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Cardio care

Dr Matt Carpenter introduces a potential treatment for various cardiac diseases based on a repurposed heart-rate-lowering agent that selectively inhibits the cardiac pacemaker current, overcoming safety limitations associated with existing alternatives

Global killer

Cardiovascular diseases (CVDs) are the principle cause of non-communicable disease related deaths worldwide. In 2008 the World Health Organisation estimated that CVDs led to approximately 17 million deaths worldwide. Whilst mortality rates from CVDs in high-income countries like the United Kingdom continue to fall, it is still the most common cause of death and accounts for more than 900,000 patients per year coupled with approximately one million NHS inpatient bed days. CVDs are also the main cause of death in the EU, killing over two million people annually and costing the economy nearly €192 billion. With ageing populations and unhealthy lifestyles it is projected that the levels of CVD-related morbidity and associated health-economic costs will continue to rise significantly over the next 25 years.

Bradycardic agents

Commonly used treatments for CVDs and related symptoms include β -blockers and calcium-channel blockers but these agents have significant limitations. β -blockers, for example can cause hypotension, cardiac failure, bronchospasm, worsening of asthma symptoms, and rebound flare of angina. It is well established that a high resting heart rate increases the risk of a cardiac event such as arrhythmias and

sudden cardiac death. Consequently, agents that induce a reduction in heart rate (bradycardia) without affecting ventricular contractility are of major interest as potential treatments for ischaemic heart disease and heart failure. Ivabradine (Procoralan, Servier Laboratories) is currently the only marketed drug which is a bradycardic agent that selectively and specifically inhibits the cardiac pacemaker If current, which controls the spontaneous diastolic depolarisation in the sinus node and determines heart rate. However, Ivabradine is not without its drawbacks and is known to cause a number of side-effects, most notably a temporary brightness in the field of vision ('luminous phenomenon'). Furthermore, the clinical utility of Ivabradine is limited in certain patient groups, including children, pregnant women and the visually impaired. Developing new selective heart rate-reducing agents to treat a specific subset of cardiovascular disease patients represents a significant opportunity for further innovation in the field.

Re-purposed drug

Scientists from the Departments of Physiology, Anatomy & Genetics and Pharmacology at the University of Oxford have discovered that a well-known, generic drug ('drug X'), the safety of which is well documented, acts as a low-dose, heart rate lowering agent by targeting the if current. The initial discovery was made by Dr Rebecca Burton who made a chance observation that drug X induced a reduction in heart rate. Using traditional electrophysiology techniques on isolated sinoatrial node cells the research team of Dr Burton, Professor David Paterson, Professor Derek Terrar, Dr Gil Bubb, Dr Neil Herring and Dr Rebecca Capel have been able to show that drug X acts at very low doses to specifically block the if current, leading to a reduction in heart rate. Further pre-clinical studies funded by an award from the University Challenge Seed Fund which is managed by Isis Innovation using whole atrial preparations and in vivo have confirmed these findings and demonstrated that whilst drug X is a highly effective bradycardic agent it has no apparent effect on blood pressure.

These findings suggest that drug X could potentially be of interest in modulation of the If current at appropriate clinical doses for the treatment of a variety of CVDs including systolic heart failure, diastolic heart failure, sinus tachycardia and cardiac syndrome. The well-established safety profile and widespread use of drug X for other indications will greatly facilitate the regulatory route and the scientists are in the process of planning a phase II proof of concept study in patients with mild systolic heart failure as the next step.

Intellectual property

Isis has filed a priority patent application (GB1312386.4 'Pharmaceutical Compounds', 10th July 2013) and the scientific team have compiled a comprehensive pre-clinical data package which will form the basis of translational funding applications and ethical approval for the phase II clinical trial. We would welcome contact from companies who are interested in licensing this technology and developing the next generation of safe, low-dose specific bradycardic agents.



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Providing purity

Dr Andrew Bowen presents a process with the potential to desalinate water and purify carbon dioxide in a single closed-loop system

Climate change, energy supply and water security are three of the major challenges that face society today. With a growing global population it is increasingly difficult to supply adequate fresh water for human consumption and agriculture. Reverse osmosis desalination (forcing water through a semi-permeable membrane to remove salt) is increasingly being used throughout the world to provide a source of water in countries without adequate freshwater resources. But reverse osmosis plants tend to be expensive, energy intensive and inefficient, and significantly increase the cost of water supply.

There are also pressures to reduce carbon emissions, particularly from major emitters such as electricity generators and cement producers. Carbon capture and storage (CCS) is one of the leading methods with the potential to effectively reduce carbon emissions by depositing purified carbon dioxide (CO_2) where it will not enter the atmosphere. However, there are major technological challenges in implementing CCS schemes, one of which is the availability of a pure source of CO_2 . Most industries do not produce waste streams containing high-purity CO_2 so an effective method of purifying the gas is essential.

The Oxford approach

Researchers from Oxford's Department of Engineering and The Oxford Martin School have combined their expertise in desalination and carbon capture to develop a novel system that links both processes.

The proposed system couples the removal and purification of CO₂ from a waste stream containing the gas, such as the flue gas of a power station, to the desalination of water by forward osmosis. Forward osmosis also passes water through a semi-permeable membrane to remove salt and other contaminants. However, unlike reverse osmosis, which uses high pressure to force water through against the osmotic gradient, forward osmosis uses a concentrated solution to draw water through a membrane. This means that the process is extremely energy efficient.

Desalination method	Advantages	Disadvantages
Reverse osmosis	 Proven at industrial scales Good performance High purity water produced 	 Very inefficient High energy cost High capital costs Problems with membrane fouling
Forward osmosis	 Extremely efficient Low energy costs Low(er) capital costs Extremely efficient 	 Unproven at industrial scales Currently performance cannot match reverse osmosis Recycling of draw solution is technically challenging

Table: Summary of reverse osmosis vs forward osmosis.

"The process is specifically designed for power stations, however the process would be equally applicable to other industries that produce large volumes of CO2 such as cement manufacturers and chemical producers"

The two cycles rely on a novel draw solution (calcium bicarbonate solution) that is formed by the reaction of CO_2 with water and calcium carbonate. This draw solution pulls water from a saline source through a semi-permeable membrane. Low-grade heat such as waste heat from a power plant can then be used to separate the water and CO_2 , and regenerate the calcium carbonate solution. The calcium carbonate solution is then reused in the first step of the process, meaning that the whole cycle is self-contained.

Depending on the application, some extra processing might be necessary to ensure that the desalinated water is potable. The process is specifically designed for power stations, particularly gas-fired power stations, with easy access to a body of saline water. However, the process would be equally applicable to other industries that produce large volumes of CO₂ such as cement manufacturers and chemical producers. The inventors have already received some proof-of-concept funding from the Engineering and Physical Sciences Research Council (EPSRC) and are now looking for further support to produce prototypes and continue to develop the technology.

Patent protection

This technology is now the subject of a PCT patent application and Isis welcomes enquiries from parties interested in developing this opportunity.



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Diagnosing Crohn's disease

Dr Richard Reschen discusses the difficulties in diagnosing an unpleasant bowel disease, and reveals how a discovery at Oxford may make future diagnosis easier

Oxford scientists have discovered that a particular molecular pathway is defective in some Crohn's disease patients, representing an exciting new diagnostic possibility and – in the longer-term – a potential new treatment strategy.

The causes of Crohn's disease are not completely understood and there is currently no cure for the condition. Instead, treatments seek to reduce symptoms such as intestinal inflammation. In addition to being difficult to treat, Crohn's disease is hard to diagnose, as the symptoms are similar to those of many other conditions. There is therefore an urgent need to develop new ways to both accurately diagnose and treat Crohn's disease.

Shedding light on the causes of Crohn's disease

Crohn's has a strong genetic component with 40 percent of patients with the disease expressing variants in a gene called NOD2. NOD2 helps to control immune responses against gut bacteria by activating or deactivating inflammatory immune pathways. NOD2 normally turns off these processes when they are no longer needed by increasing the production of a molecule called micro RNA-29 (miR-29). By doing this, NOD2 may help prevent the body from overreacting to the normally helpful bacteria found in our intestines. Oxford researchers have now discovered that the variants of NOD2 found in some Crohn's disease patients do not work properly, leading to decreased production of miR-29. In experimental animals, the absence of this molecule leads to the worsening of intestinal inflammation. This suggests that the same process may occur in human Crohn's patients.

Crohn's disease biomarker

Reduced miR-29 levels in patients presenting with chronic intestinal problems may represent a useful diagnostic marker (biomarker) for Crohn's disease. These patients may develop a more aggressive disease requiring a lower threshold for treatment with biological therapies earlier in the course of the disease. miR-29 levels may be indicative of disease sub-phenotypes that would be amenable to different therapeutic approaches. miR-29 levels can be measured in dendritic cells, which can be isolated from blood, hence it may be possible to develop a simple blood test for this biomarker, and thus for certain forms of Crohn's disease.

"Patients with reduced miR-29 levels may develop a more aggressive disease, requiring a lower threshold for treatment earlier in the course of the disease"

Future treatment direction

While some patients with Crohn's disease respond to conventional immunotherapies a significant proportion fail to do so, requiring treatment with antibody-based therapies or repeated surgery. Oxford researchers have found that miR-29 acts to reduce a panel of inflammatory and fibrosis mediators in human cells, including IL-12p40/IL-23. Replacing miR-29 restores normal functioning in cells taken from Crohn's disease patients, and could resolve inflammatory lesions by suppressing drivers of inflammation. It also suppresses fibrosis factors such as collagen and elastin which are likely to play a role in advancing stricturing disease (a severe form of Crohn's disease). Therapeutic administration of miR29 in an appropriate delivery vehicle might therefore represent a new treatment option for Crohn's.

Technology status

The technology is at the pre-clinical research stage and is the subject of a patent application. Isis would like to speak to companies involved in therapeutics or biomarker development who are interested in developing and commercialising this technology.

Crohn's disease – The Consequences

Crohn's is a chronic, debilitating form of inflammatory bowel disease, which may result from a breakdown in the immune system's ability to recognize the normal bugs or microflora in the intestine as 'self'. This is thought to result in the immune system attacking the lining of the intestine, resulting in inflammation. In turn, this can cause unpleasant symptoms such as diarrhoea, abdominal pain and fatigue. Fortunately, Crohn's disease is relatively uncommon, but it still affects around 150,000 people in the UK alone.

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Lightweight composite

Dr Jon Carr presents a high strength aluminium composite offering superior strength at elevated temperatures.

There is great demand for the development of new bulk alloys that can enable a step-change in performance in respect of strength and toughness at elevated temperatures. Various technology roadmaps for aerospace, defence and automotive industries are calling for such development, along with the worldwide aluminium supply chain. Furthermore, legislative and environmental requirements have applied pressure to the transport industries, which now need to introduce vehicles with lower weight, greater efficiency and reduced emissions.

The team

A team of researchers from Oxford's Department of Materials have collaborated with the University of Buenos Aires over the past decade to work specifically on developing nanostructured and metal matrix alloy composites. The research has resulted in alloys with world class high temperature performance. The team is investigating how these alloys will be manufactured on a large scale and how these alloys could be used in specific applications.

Advantages

Global production of aluminium in 2012 totalled 45 million tonnes and the material is often seen as a cheaper alternative to other materials. More expensive materials such as titanium have, until now, offered a superior performance, particularly at elevated temperatures. This latest technology uses nanostructure and metal matrix alloys to ensure good strength and toughness characteristics at elevated temperatures, while still having the specific properties to allow cheap powder production. These alloys use aluminium as a bulk component of the alloy to keep bulk material costs down. A comparison of conventional commercial alloys and Oxford's novel range (red lines) can be seen in the graph (below right) showing strength vs temperature.

"Researchers from Oxford's Department of Materials have collaborated with the University of Buenos Aires over the past decade to work specifically on developing nanostructured and metal matrix alloy composites"

Supporting data

Please refer to: "Nanoquasicrystalline Al-Fe-Cr based alloys with high strength at elevated temperatures" Galano, M., Audebert, F., Escorial, A.G., Stone, I.C. and Cantor, B., Journal of Alloys and Compounds, 495(2), 2010, 372-376 and "Nanoquasicrystalline Al-Fe-Cr-Nb alloys produced by powder metallurgy" Audebert, F. Galano M., Triveño Riosc, C., Kasama, H., Peres, M., Kiminami, C., Botta, W.J. and Bolfarini, C., Journal of Alloys and Compounds, 577, 2013, 650-657

Patent protection

The technology is now the subject of an international patent application, and Isis would like to discuss with interested companies the licensing of the technology.



Comparison of conventional commercial aluminium alloys (dotted lines) and the researchers' novel range (red lines), showing strength (MPa) versus temperature(°C) data

Benefits to industry

Aerospace and automotive sectors

The aerospace and automotive industries will benefit from a new family of Al alloys offering a significant jump in strength at both room temperature and elevated temperature. Example applications include dynamic car engine parts, such as pistons; fans and compressors for gas turbines; specialised areas of aeroplane wings.

Aluminium alloy supply chain

New Al alloys will compete with steel and Ti alloys.

Aluminium alloy powder producers

Aluminium alloy powder producers will benefit from increased demand for alloys produced via the gas atomised powder metallurgy route.

Technology providers

New demand for atomising and other specialist metallurgical processing equipment.

IT companies

The new composites could provide better smart phone casing performance.

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Inspiration

Bench to bedside

Andrew Goff, Head of Oxford University Consulting, discusses the growing take up of diagnostics in primary care and how OUC consultancies in the sector will benefit patients

Diagnostic tests have an increasingly important role to play in 21st century health care – ruling in or ruling out particular conditions, monitoring people with established diseases, or screening asymptomatic people for disease. Nearly three quarters of all the clinical decisions made are done so on the basis of the results from standardised diagnostic tests (e.g. blood results or imaging results). The UK is the fifth largest market for in-vitro diagnostics in Europe and the UK medical technology industry consists of over 3,000 companies with a combined turnover of £15bn.

It is perhaps surprising therefore that, in contrast to pharmaceutical products, there is currently no single European institution that evaluates diagnostic tests. This has hampered a standardised approach to generating evidence and its subsequent evaluation not only for regulatory approval but also for impact analysis. While in the USA FDA approval is required before the introduction of a new test, for introduction in Europe the majority of diagnostic tests need only CE marking (EU conformity compliance), requiring no formal evidence to demonstrate clinical utility, impact on health outcomes or cost effectiveness. This 'void' between industry, clinicians and researchers risks stifling innovations that could both improve health care and strengthen the UK's life sciences

industry, particularly in the rapidly growing international market for point of care testing.

So it is exciting that a team of Oxford academics - OUC consultants - has now been nationally recognised as the UK's leading experts in the assessment of in-vitro diagnostics (IVDs), particularly in primary care. By 'assessment' we mean the generation of robust evidence for clinical validity, clinical utility and cost effectiveness, as well as care pathway benefits. Directed by Dr Matthew J Thompson and Professor Carl Heneghan, the team, many of whom are also active GPs working for the Oxford Health NHS Foundation Trust, has recently been designated a Diagnostic Evidence Co-operative (DEC) by the National Institute for Health Research (NIHR).

"The focus of the DEC is to improve the bench-to-bedside processes needed to implement new IVDs in primary care," says Dr Thompson. "The ultimate aim is to improve the quality and effectiveness of diagnostic tools available within the NHS. We will develop collaborations between frontline clinicians, diagnostic test researchers, the diagnostics industry, NICE diagnostics programme, and other relevant NHS groups to bring into primary care the newest medical technology across a range of common diseases."

"The consultancies will lead to improvements in healthcare services"

The team works across five multidisciplinary research themes which aim to:

- Develop methods to identify and prioritise new and emerging diagnostic technologies, through meeting with the diagnostics industry and scanning both journal and industry resources.
- Evaluate which IVDs are needed in primary care settings in the UK and other western countries, to help prioritise R&D efforts.
- Find better ways of integrating point of care tests with laboratory services and clinical information systems.
- Understand the impact of diagnostic tests on patients and front line clinicians in order to facilitate wider implementation of IVDs by utilising the team's considerable experience of point of care testing in hospital settings, primary care settings and in patient homes/nursing homes.
- Improve the efficiency of research designs for diagnostics, including better ways of translating research findings from one type of clinical setting to another.

Through these activities, the team is developing a "diagnostic evidence toolkit" which will propose a common approach to understanding the evidence needs at each step from test development to adoption, including what evidence is needed, what study designs are appropriate, which research designs are most efficient, and which translate between countries and different settings. In parallel, the team is undertaking consultancy through OUC to advise IVD companies on the evidence base required to support the adoption of their new IVDs while simultaneously promoting better informed clinical decision-making and improved NHS commissioning. This will lead to improvements in healthcare services as patients will access the most appropriate treatments more quickly and help the NHS make the best uses of its resources.

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Abu Dhabi Innovation

Dr Chris Moody highlights some of the interesting technologies developed in the Emirate that Isis Enterprise's internationally-facing consultants are helping to commercialise

Isis Enterprise is continuing its work in Abu Dhabi, an increasingly important regional hub for innovation in research from industry and universities. The Emirate, through the Technology Development Committee (TDC), is working closely with universities and research institutes to accelerate the commercialisation of innovations emerging from their research. Isis is partnering with the TDC to advise and assist these institutions with their projects.

The Abu Dhabi Government has given priority to a number of Science and Technology areas and has already committed and will further commit significant investments to specific priority industry sectors, including oil and gas services, semiconductors, aerospace, clean tech and information and communication technologies. Isis Enterprise is currently working with the United Arab Emirates University (UAEU), Khalifa University of Science, Technology and Research, the Mazdar Institute and the Petroleum Institute of Abu Dhabi on projects that range from medical science to water resources and clean energy.

There are a variety of world-class research programmes in Abu Dhabi and the TDC is seeking to more rapidly move their creative innovations out into the world. Isis has been meeting with researchers in the institutions to discuss and make recommendations on ways to successfully commercialise their ideas. After the initial reviews, we are conducting "deep dive" commercialisation work on selected projects. This second phase work includes evaluating the market, establishing potential licensing partners, and guiding the process through to completion with the interested companies.



Dr. Mohamed Rezeq, Assistant Professor of Physics, Department of Applied Mathematics and Sciences, Khalifa University, has been granted a US patent for the creation of the world's smallest semiconductor transistor.

"Isis Enterprise is currently working with the United Arab Emirates University, Khalifa University of Science, Technology and Research, the Masdar Institute and the Petroleum Institute of Abu Dhabi on projects that range from medical science to water resources and clean energy"

Our work with Khalifa University includes advanced semiconductor device concepts, composite materials and IT network technologies from the Etisalat BT Innovation Center (EBTIC).

Isis' work at the UAEU has included projects in new chemical sensor technologies and biomedical innovations. We are working with the Mazdar Institute on a number of projects including improved technologies for desalinisation of water and power management.

The Petroleum Institute of Abu Dhabi is the largest specialised research institute in the Emirate. Isis is currently working with them on strategies for commercialising advanced polymer formulations. This spring, Isis will conduct a new round of IP portfolio reviews and thorough commercialisation work with the TDC and the research institutions in Abu Dhabi. In addition to the work with commercialising specific technologies, Isis is assisting the institutions in Abu Dhabi with refining and optimising their intellectual property policies and strategies for IP protection. This will involve workshops with the senior decision-makers in the institutions.

We are also providing training to technology transfer managers and staff to expand their capability to engage in international licensing, create successful spin-out companies and optimise the management of the tech transfer organisations and their processes.

The Abu Dhabi government is demonstrating a strong commitment to building a broad technology based economy for the future and Isis is delighted to be a part of these important initiatives.



Dr Alexandra Bush and Dr Chris Moody at the Mazdar Institute of Science and Technology.

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Oxford Innovation Society

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

Thursday 20th March 2014 Thursday 18 September 2014 Thursday 4 December 2014

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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