



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

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

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

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

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Cognitive developments

Also: Pre-eclampsia diagnostic, migration study, Tomsk technologies and more

The latest innovations, collaborations
and technology transfer



ISIS
INNOVATION



Cognitive developments

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Isis Innovation Ltd is a growing and profitable business owned by the University of Oxford.

Isis and the Oxfordshire economy

The extent of Isis' involvement in the local economy was highlighted recently by Iain Gray, head of the UK's Technology Strategy Board. The TSB has supported 50 technology businesses in the region and Isis is closely involved with many of these. Of these 50 technology companies, 14 are companies spun-out of Oxford University by Isis, 14 are consultancy clients for Isis and four are members of the Oxford Innovation Society. Isis contributes to the vitality of the local economy, generating revenue and jobs by creating new businesses and facilitating the supply of services from the University of Oxford.

Isis welcomes Chinese Vice-Premier for Economic Policy to Oxford

In September the Chinese Vice-Premier for economic policy, Mr Wang Qishan, visited Oxford and heard from Isis about Oxford's successful Technology Transfer model. Isis has a particular focus on the Chinese market, having opened its first overseas office in Hong Kong in 2009. By managing seed capital, raising investment, and identifying experienced management, Isis boasts an impressive success rate when bringing new technologies to market, and is keen to expand by applying its experience and knowledge in China through high technology company formation, technology licensing, and consultancy engagements.

Oxford Innovation Society in Spain

Isis held a meeting and dinner of the Oxford Innovation Society in Madrid in early November. The event brought together 150 prominent figures from the fields of technology, academia and finance to discuss Spanish technology transfer and research commercialisation, and of course involving the Members of the OIS. The event was supported by Fundación Barrié, PriceWaterhouseCoopers and Spanish innovation agency FECYT. This is the second overseas meeting of the Society, the first being in Hong Kong in July this year. Over sixty meetings of the Society have been held in Oxford since its formation by Isis in 1990.

Imaging spin-out launched by Isis

Oxford Imaging Detectors is developing high performance scientific imaging detectors capable of studying structures and processes at the atomic level. Initially focused for use in electron microscopy, the detectors were developed at the University's Department of Materials. They provide significant advantages over existing technology, exceeding the current state of the art in speed, contrast, efficiency and resolution. **Four recent Isis spin-outs are profiled on pages 5-9.**



Enterprising Consultancy

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

Innovating for the environment



Isis Enterprise (IE) is assisting Nampak, the UK market leader in plastic milk bottles, with the international exploitation of their recent innovation – the Infiniti® bottle. Nampak has developed this new design in order to reduce the weight and plastic consumption of its bottles by an average of 15%. This results in cost savings through materials reduction and reduces the bottle's environmental impact.

Nampak went back to first principles and moved the moulding seam (and with it the handle) to the diagonal. This allows rounder corners and thinner walls whilst maintaining the strength and improving user ergonomics. Nampak spent £1 million on developing this new bottle design and will invest a further £9 million over the next few years to implement the new range across its production facilities. The first bottles have already appeared on the market in some UK supermarkets.

While not as complex as the majority of innovations that Isis has traditionally worked with, this innovation is extremely important due

to the volume of production. The UK uses around 4 billion bottles per year, and Nampak alone will save 10,000 tonnes of plastic.

Licensees are being sought around the globe for the granted and pending patents, but this is not limited to the milk industry. It is anticipated that the principles of the innovation can have uses beyond just food packaging such as chemical or automotive fluids.

IE can assist all manner of companies when it comes to getting the most from their intellectual property, be it finding new technologies to licence in, reviewing existing portfolios and building expertise, or licensing out innovations for non-core markets.

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Learning across life

Oxford University Consulting (OUC) is delighted to support the University's Department of Education in their programme of active engagement with external organisations, helping to make a positive societal impact through department-based consultancy projects. Rated first equal in the UK in the 2008 Research Assessment Exercise, the Department's research profile is outstanding and demonstrates its focus on learning across the life-course. Their research themes provide insights into areas ranging from the role of families in early learning and literacy, through to the links between the acquisition and use of skills and knowledge, production and product strategies and economic performance – be it of individuals, organisations or countries.

Through consultancy, the department is actively applying its research to support many key challenges facing education today, including engagement with nursery organisations, school improvement programmes, apprenticeships, financial education in schools, and vocational education and training across Europe. Through OUC, the Department is able to provide consultancy to a wide range of clients such as NGOs, charity organisations, international bodies, governments and educational consultancy firms. To find out more about the Department's expertise please view their website: www.education.ox.ac.uk.

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The portfolio

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

Butterfly effect



Pilio, the first company to graduate from the Isis Software Incubator, causes a flutter

A recent spin-out from the University of Oxford, Pilio Limited, provides a cost-effective online tool enabling small and medium sized businesses to monitor and manage their energy usage, potentially saving up to 40 percent of their energy budget. The company is named after a butterfly in reference to the butterfly effect whereby small changes can have a big impact. This symbolises the positive effect that informed energy usage could have on the environment.

Pilio's online energy monitoring tool, sMeasure, was developed and piloted at the University's Environmental Change Institute. It has been available online for three years and in the last year has been used by over 400 businesses to monitor their energy use. sMeasure works by combining two sets of data: gas and electricity meter readings provided by the customer and weather data to accurately assess a building's energy efficiency. It requires no additional meters or devices.

Pilio CEO Catherine Bottrill said, "Energy costs are going up significantly this winter. Many businesses will be looking for a way to save money. sMeasure allows companies to implement their environmental and energy policy. We have kept the cost for our customers low at a subscription of £120 a year per building. Using the tool requires



The Isis software incubator offers support to emerging software ventures.

only five minutes a week to input meter readings. sMeasure helps companies to use their own common sense to stop energy being wasted in their buildings. They can look at their patterns of energy use over time so they can spot peaks, troughs and abnormalities, which will alert them to problems with their building control settings or prompt them to carry out maintenance work."

The Chief Executive of the Royal Albert Hall, Chris Cotton, is sold. "We have used sMeasure for the last three years. It is an inexpensive, simple to access, and extremely effective tool to allow those running businesses to get a snapshot of their energy consumption over a day, week or year and then take appropriate action to improve efficient use of energy." Pilio's UK clients also include the Greater Authority of London, Julie's Bicycle, Ebico and Severn Wye Energy Agency.

sMeasure is expanding into the US market as part of the Innovator Pilot Project with Sierra Business Council. This project is supported by Pacific Gas and Electric, the largest utility in the US. Over the next year, the company aims to increase the number of UK and US SMEs it works with four-fold. Pilio has spent one year in the Isis Innovation Software Incubator and has been supported by a £15,000 investment of working capital from the Oxford University Challenge Seed Fund, also managed by Isis. Companies can visit the Pilio website and get a free 30 day trial of sMeasure. No downloads or kit are necessary.

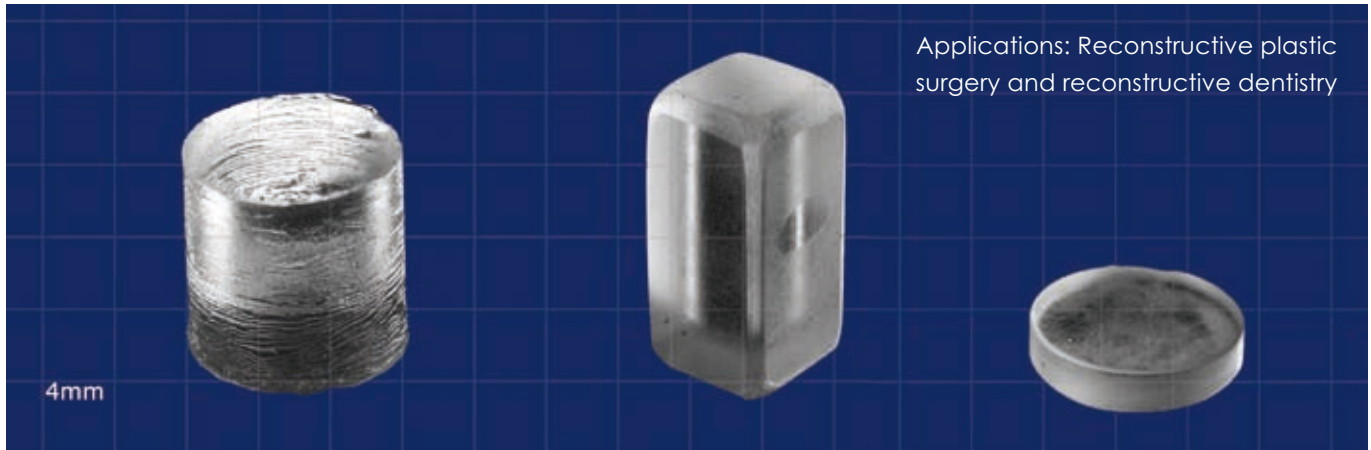
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Technology steps forward

The latest licences, agreements and developments from Isis

Tissue expansion spin-out Oxtex aids surgeons and dentists



Oxford researchers have developed an intelligent hydrogel material for use as a surgical tool in soft tissue expansion. The tissue expander devices will allow surgeons and dentists to accurately and predictably control the direction, timing, and rate of soft tissue expansion in the body. This reduces the risk of soft tissue damage and associated complications, meaning that clinicians can treat more cases, at a lower cost, and with better results.

The built in level of control makes these devices ideal for use in delicate anatomical locations, particularly in the treatment of children.

To ensure that this technology is developed into a commercially available medical device, Oxtex Limited was successfully spun out from the University in the summer. A strong team was put together with a CEO, David Jackson, who has experience in building start up companies, and seed funding from investors who have a strong track record of funding and supporting successful medical based start ups.

Oxtex is currently focusing on establishing manufacturing facilities and aims to undertake first clinical trials

with the hydrogel device in 2012. The company and the University are working collaboratively with the Harvard School of Dental Medicine and the University of Malaya. These activities and the establishment of research collaborations will lead to the provision of soft tissue expansion solutions that address a wide range of clinical applications across reconstructive plastic surgery and restorative dentistry.

Potential

The potential of Oxtex as a newly-founded medical device company was recognised at the OBN Annual Bioscience Awards, where it recently won the Best Emerging Medtech category. Oxtex is also well on the way to completing establishment of its new clean room facility, located in the University's Department of Materials, to be certified as compliant with medical device standards. Oxtex is close to completion of its bespoke Quality Management System (QMS). Certification of the clean room and QMS are essential components for the production of a medical device. These will both aid in the scale up and production of a range of different tissue expanders to be used in clinical

trials in 2012, once ethics approval has been given.

The novel concept of anisotropic self-inflating tissue expansion evolved as a result of a collaboration between two material scientists (Jan Czernuszka, Lecturer in Materials at the University of Oxford, and David Bucknall, currently Professor of Materials Science at the Georgia Institute of Technology, USA) and two plastic and reconstructive surgeons (Marc C. Swan and Tim Goodacre from the John Radcliffe Hospital in Oxford). Their research and commitment to achieving the successful development of their technology led to ongoing research and the filing of two patent applications. These formed the foundations for building Oxtex into a successful medical device company.

Weblink

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The name Oxtex comes from the surgical shorthand abbreviation for tissue expansion (tex).

Oxford Imaging Detectors spin-out to improve scientific imaging

Scientific imaging will be given a boost by a new company spun out from the University of Oxford. Oxford Imaging Detectors, which is developing high performance scientific imaging detectors capable of studying structures and processes at the atomic level, has been set up by the University's technology transfer company Isis Innovation.

Initially focused for use in electron microscopy, the detectors were developed by the research group led by Professor Angus Kirkland at the University's Department of Materials. They provide significant advantages over current technology, exceeding the current state of the art in speed, contrast, efficiency and resolution.

Professor Kirkland explained, "These detectors, coupled to state of the art imaging instruments, are one of the most powerful tools in a scientist's toolkit. Materials scientists, chemists, biologists and physicists increasingly need to examine objects at the atomic level. The Oxford Imaging Detectors' products will support critical research in diverse areas spanning automotive catalysis, molecular medicine and new engineering nanomaterials."

Dr Grigore Moldovan – who joins Oxford Imaging Detectors as Research Director from Professor Kirkland's group – said, "These detectors combine the latest developments in particle sensing with novel semiconductor design and technology to provide the best imaging performance. Key features include single-electron detection, simultaneous imaging of multiple independent regions of interest, and radiation hardness."

Oxford Imaging Detectors' instruments also have potential applications in a number of other



areas, including X-ray, other microscopy techniques, and machine vision.

Oxford Imaging Detectors will be initially be funded by an equity investment from a corporate investor alongside a sponsored research and development contract.

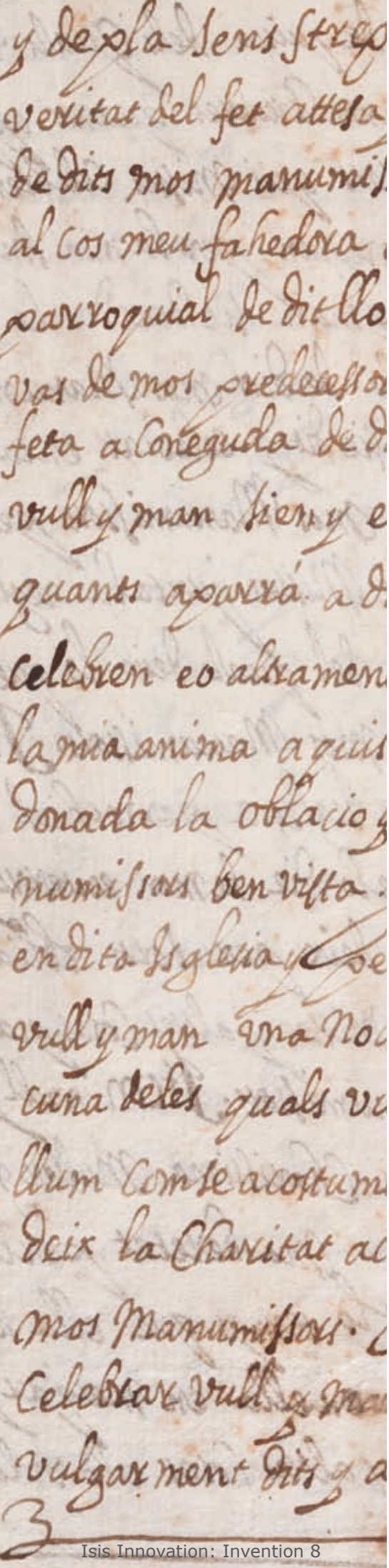
Oxford Imaging Detectors CEO Geoff Foote said, "The market for new high

performance detectors is growing as research into nano-scale technologies and materials becomes increasingly important. Oxford Imaging Detectors will provide state of the art sensors to enhance the capabilities of existing instruments, and extend the possibilities for future developments. We believe that this will have a profound impact on the emergence of new research areas, benefiting both existing and emerging industries."

These detectors combine the latest developments in particle sensing with novel semiconductor design.

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Documenting the detail

Renate Krelle looks at an Oxford scanner which reveals the secrets of ancient and modern documents.

A scanner which combines the convenience of a desktop design with the functionality of a powerful laboratory imaging device has been developed at the University of Oxford's Classics Department, and is now being commercialised by a new company – Oxford Multi Spectral Limited – spun out by Isis Innovation.

The scanner was developed for imaging ancient papyri and the technology has been used to successfully scan, restore and archive over a quarter of a million historically significant manuscripts.

Oxford Multi Spectral Limited (OMS) will focus on the applications in restoring manuscripts and art, as well as the huge potential market for detecting forged security and border control documents, bank notes and forensic evidence.

The Oxford scanner could be used to

analyse a huge variety of samples, including crime scene samples such as counterfeit and altered documents as well as documents bearing erased or faded entries and signatures. The portable nature of the scanner means that it will be a great resource when document examiners are required to undertake examinations out of the laboratory environment, such as at Court Registries or the offices of opposing lawyers.

"We anticipate that using the Oxford scanner will be like moving from using a dark room to using a modern digital camera," says Paul Westwood, managing director of Forensic Document Services, the biggest forensic document company in the Asia Pacific. "We can use it to detect what is currently invisible and make it visible. The compact design and powerful imaging and analysis will be of great benefit to document examiners worldwide."



Papyrology patenting

The research project – which began in 1998 under the direction of Dr Dirk Obbink, University Lecturer in Papyrology and Greek literature – was initiated to capture digitised images of Greek and Latin papyri housed at Oxford and Naples. A sizeable number of these ancient manuscripts, which date back to the 3rd century BC, had sustained heavy damage and the text on many was regarded as irretrievably lost. The research was thus aimed at developing a technique to image texts from these seemingly unreadable but priceless documents.

Over the past decade multispectral imaging techniques have been successfully applied to such

degraded manuscripts at Oxford, in an attempt to recover and transcribe texts that were previously undetectable by other scientific techniques. The impressive results of Dr Obbink's team were achieved through the use of very expensive, technically challenging and process intensive MSI systems.

In spring 2009 Dr Alexander Kovalchuk, a physicist working within Dr Obbink's group, was inspired to combine two well established technologies: a simple, convenient flat bed scanner and the powerful imaging capabilities of multispectral imaging.

Isis recognised the commercial

potential of this invention and facilitated application for a patent two years ago. In February 2010 Isis awarded a UCSF grant to the project which allowed Dr Kovalchuk to develop the optical, electronic and mechanical systems and overall design of the new multispectral flatbed scanner. The UCSF grant also provided funds both for purchasing equipment and materials necessary for building alpha and beta prototypes of this device. January 2011 saw the first live demonstration of the prototype to a Chinese investor, which subsequently led to the investment necessary to form Oxford Multi Spectral and bring the technology to market.

"OMS delivers multispectral imaging capabilities superior to large laboratory systems in a very cost-effective apparatus," according to OMS CEO, Mike Broderick. "Current multispectral imaging kits use cameras, but they are large, expensive and need specialist operators. Our scanner uses well-proven flat-bed scanner technology and powerful image processing to scan visible and 'invisible' features which absorb and reflect light at different wavelengths such as inks, pigments, polymers or papers."

An ordinary colour image has three layers: red, green and blue. A multispectral image has many more layers, some of which are invisible to the human eye, but all of these layers contain potentially useful information. The Oxford scanner is capable of registering an unlimited number of layers.

Dr Dirk Obbink, University Lecturer in Papyrology and head of the research group which developed the scanner explains, "The technical leaps we made mean many ancient documents which were previously unreadable can now be scanned and read. We can take digital images at different wavelengths of the light band and layer them on top of each other, using

software to analyse them. We can set the equipment to interrogate a feature we are interested in: the surface structure, fibres, stains, watermarks, fingerprints, or alterations. We can detect an artist or writer's signature under multiple layers of paint or the pencil sketch under a watercolour."

OMS has secured an investment of £250,000 from a Chinese investor, Changsha Yaodong Investment Consulting Co, and its UK based partner RTC Innovations to commercialise, manufacture and market the scanners globally. It received £47,600 from the University Challenge Seed Fund last year for prototyping work.

OMS will be the first spin-out from the University of Oxford's Classics department and indeed from the University's Humanities Division.

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Lombard Medical

Oxford Innovation Society member **Lombard Medical** is a fast growing and innovative medical technology company with expertise in the design, manufacture and commercialisation of cutting edge endovascular products.

The flagship product, the Aorfix™ endovascular stent graft, addresses previously unmet clinical need for a conformable and flexible graft in the rapidly developing global abdominal aortic aneurysm (AAA) market.

Aorfix™ combines pioneering design and technology that results in outstanding clinical performance in EVAR patients with complex anatomy. The only endovascular stent graft approved in the EU to treat complex aneurysms up to 90°, Aorfix™ broadens clinicians' treatment options and opens opportunities for treating more patients less invasively with Endovascular Aortic Repair (EVAR).

Over 2,000 patients worldwide have been treated with Aorfix™ and the growing body of clinical evidence confirms that Aorfix™ reduces EVAR complications such as proximal

endoleaks, graft migration and iliac occlusion in patients with both standard and complex AAA anatomies.

Lombard Medical has achieved the number three market position in the UK and is continuing to grow its presence in key EU markets. The company has recently submitted an application to the US Food and Drug Administration (FDA) with a view to entering the United States, the largest global market for endovascular repair.

To support these activities Lombard Medical grew its workforce rapidly during 2011. As an innovator and manufacturer of complex medical devices, engineering is one of the key skills within the company. Engineers can join the development team in working on new products, the quality team in ensuring processes are in place to comply with medical device





Aorfix™ endovascular stent graft.

regulations, or the manufacturing team in safeguarding that devices are produced in the most efficient and stable manner.

Lombard Medical offers a dynamic, friendly working environment and a focus on innovation and responsiveness is a key driver for all teams. Throughout the business staff evaluate current practices and ensure that tools for business efficiency are used to best effect. When determining how to expand manufacturing capacity, improvement teams have been formed from a range of disciplines including shop floor production staff. All employees recognise that their input is valuable and they all impact on the success of the company.

Website

If you would like to learn more about Lombard Medical, please visit:
www.lombardmedical.com.

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Back to basics

Professor Yiannis Ventikos, of the Department of Engineering Science, discussed the Role of Basic Research in Innovation and Entrepreneurship in his presentation to the Oxford Innovation Society in September.

When I was first asked to present to the OIS, I felt that this might represent both the easiest and most difficult of tasks. Easy, because I was absolutely certain regarding the topic I wanted to cover in my talk; difficult, because the diversity and excellence of the audience that usually congregates at the Society's events meant that the point I wanted to make had to be, at the same time, succinct and accessible. Non-technical, yet properly documented.

When the subject is slightly controversial, and rather unpopular nowadays, the challenge doubles.

The theme I chose to present was, I believe, particularly topical: the importance and relevance of basic research in the development of a successful and wealth-creating national research agenda. There are clear signs in the international research funding community in general and in the UK in particular of a perception that emphasis should be placed on applied research, research with *immediate* tangible outcomes.

I chose to defend an almost diametrically different position: that research cannot be seen as whole and that starving one component of resources (or motivation) will inevitably have repercussions across the entire spectrum, ultimately with

grave consequences in innovation outcomes, job creation and wealth.

I felt at ease making the scientific argument. I drew from my own personal experience in fluid mechanics basic research and from how work connected with identifying fundamental hydrodynamic processes and mechanisms – entirely curiosity-driven in the first place – led to the development of ideas that warranted patenting and commercial exploitation.

Even at the microscale of a single research group (albeit in Engineering), the interdependence of basic, applied and translational research is evident and we have experienced the benefits of pursuing and interrelating all tracks many times.

We have also suffered when the links have been broken and when the leaps ahead that successful fundamental research provides were not there to supply novelty and competitive edge to the more translational components of our work.

However, making the wider societal argument, and, more importantly, showing with some certainty that there is indeed a quantifiable link between investment at the basic research level and returns in tangible economic growth and job creation, is more complicated.

Even at the microscale of a single research group (albeit in Engineering), the interdependence of basic, applied and translational research is evident.



Needless to say, this is rarely a point an engineer needs to make or defend in a scientific conference! In other words, *knowing* something as an abstract concept, based on personal experience, observation or gut feeling, and *convincing* an audience of businessmen, scientists and policy makers are two very different things.

So, the way I proceeded was compatible with the most basic advice I would give to a graduate student encountering a technical problem: "When you do not know, look it up!"

My literature survey (scientific and popular) yielded numerous gems that unfortunately I cannot share with you in their entirety here. A few items, however, are definitely in need of mentioning.

In an excellent article looking at this very question, C.H. Llewellyn Smith, former Director-General of CERN, argued, among other things, that pursuing investment *only* in applied and translational research (since

this type of research only allegedly translates directly to entrepreneurship and wealth creation) is equivalent to saying that one must only buy shares that will go up. This is, of course, self-evident and completely intuitive, but it assumes that you know which shares will actually increase in value. I am sure very few people would disagree that this is not easy to infer.

Actually, even the most knowledgeable – even those credited with the very fundamental science breakthroughs that have transformed our society – often cannot predict the consequences of their discoveries. Dismissing the prospects of harnessing atomic energy, Ernest Rutherford, the father of nuclear physics, famously said, "Anyone who looked for a source of power in the transformation of the atoms was talking moonshine."

In an effort to quantify the return-on-investment question, E. Mansfield published an excellent paper in *Research Policy* (vol. 20, 1991) where a survey of leading companies' CEOs



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steady stream of innovation and technology translation, or, even more importantly, to ensure that the transformative technological breakthroughs that revolutionise the way we do things and generate the step-changes in growth, revenue and quality of life, actually take place, we must nurture the climate that makes this possible. It is in everybody's interest and it requires everybody's efforts and commitment.

and R&D executives, asked about new products that would not be launched without basic academic research that paved the way for the innovation, yielded an astounding result.

Public investment in basic science generates a return of 28%. It is understood that this figure is approximate and contingent upon the assumptions made, but it is still a very striking conclusion, that substantiates the argument. Others have produced even higher estimates, based however on more anecdotal evidence.

It is by no means implied that a linear model of basic research feeding applied research holds. Nothing could be further from the truth. If I may paraphrase slightly G. Porter (Nobel Laureate in Chemistry, 1967), fundamental thermodynamics, for example, owes more to the steam engine than the steam engine owes to thermodynamics.

The message that emerges is, I believe, that scientific research is an indivisible whole and no component should be starved. To establish a

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In his talk to the OIS in September, the Universities and Science Minister David Willetts was unequivocal about the importance of universities to enterprise and growth. He highlighted five areas where the links between enterprise and higher education were important.

- Enterprise helps pay for education. Many of today's universities were founded by philanthropists who had made their money from business. Royal Holloway was an example cited.
- Higher Education produces smart customers. Concentrations of university educated customers are necessary for the success of hi tech and innovative businesses.
- Universities provide research that drives business. It is important not to make universities go through banal attempts to predict impact.
- Teaching of entrepreneurial and business skills. Being an entrepreneur is not a rare genetic gift, but can be learnt. 1 in 7 students in the UK are pursuing a form of business studies.
- Universities can link up businesses and entrepreneurs to provide services aimed at the creation of Technology Innovation Centres (TICs), which will improve things in this space. The minister also professed to be a fan of innovation vouchers, and noted that Sir Tim Wilson's report would inform policy in this area.

Diagnosing pre-eclampsia

Dr Angela Calvert looks at a promising new method for assessing the risk of developing pre-eclampsia during pregnancy.

Pre-eclampsia (or PE) is a disease affecting up to 3% of pregnancies that can be life threatening to both mother and baby. It is a leading cause of maternal mortality in the developing world and even in the developed world it remains a cause of maternal death. Now, researchers from the Nuffield Department of Obstetrics & Gynaecology at the University of Oxford have identified a novel biomarker, sST2, that is significantly raised in the circulating blood of pregnant women suffering from PE and, most importantly, it is detectable before the onset of clinical symptoms.

Pre-eclampsia: the impact

Approximately 50,000 women die each year from complications arising from pre-eclampsia, which is characterised by the onset of hypertension (high blood pressure) and proteinuria (protein in the urine) in the second half of pregnancy. Maternal complications of pre-eclampsia include liver and renal failure, clotting disorders and stroke. Eclampsia (maternal seizures) is the end stage of the disease.

Pre-eclampsia cannot be prevented and the only effective 'treatment' is the delivery of the baby and placenta. Drug therapies (such as anti-hypertensives) can be used once pre-eclampsia has been detected, which only address the symptoms of the condition, although they may reduce the likelihood of complications caused by high blood pressure, such as stroke.

The fetal complications of pre-eclampsia that arise most commonly are as a result of pre-term delivery. In addition a poorly functioning placenta may mean that the baby suffers nutritional insufficiency and consequently restricted growth.

Prediction difficulties

Although there are known risk factors for pre-eclampsia it remains difficult to reliably predict which women will develop the disease. To date, several molecules produced by the placenta have been suggested as potential biomarkers that may indicate those women who are at high risk of developing the disease, but these are still only used in the context of research. Currently there are no biomarkers for pre-eclampsia which are used routinely in clinical practice.

Ideally a biomarker that will be used to identify patients with a high risk of developing pre-eclampsia should be detectable as early as possible, so patient care can be adjusted accordingly and lead to improved pregnancy outcomes.

The Oxford Invention

- Studies compared blood samples from women with and without PE (n=50 in each group). The Oxford biomarker, sST2, was significantly higher in the PE group than in the normal pregnant group ($p < 0.001$). The largest differences observed were in early onset PE (21-28 weeks).

Ideally a biomarker that will be used to identify patients with a high risk of developing pre-eclampsia should be detectable as early as possible.

- sST2 was measured in blood samples from both groups throughout each trimester of pregnancy, with an additional sample taken at the time of diagnosis (n=15). There was a significant increase in sST2 in the third trimester of both groups compared to the first and second trimesters ($p < 0.01$). sST2 levels were significantly higher in the third trimester of pre-eclamptic pregnancies compared to third trimester samples from 'normal' pregnancies ($p < 0.001$) even before the onset of clinical symptoms.

Although larger studies are still required to identify precisely how far in advance of disease onset sST2 is elevated, it is possible that alone, or in conjunction with other proteins, it may effectively stratify pregnant women into high or low risk for pre-eclampsia, allowing antenatal care to be tailored accordingly.

The work undertaken by the Oxford researchers on detection of sST2 has demonstrated a high level of robustness and reproducibility, which they believe is essential for the development of a future clinical diagnostic tool. Many of the other existing markers are related to angiogenesis (the growth of new blood vessels), whereas sST2 may actually be related to inflammatory changes as a result of pregnancy, therefore providing complementary information about pregnancy. This gives the exciting possibility for the detection of sST2 to be carried out alongside other biomarkers, thereby enhancing overall clinical effectiveness in assessing the risk of pre-eclampsia.

Ongoing research

Further work is ongoing at the University to investigate sST2, including a systematic screen to determine exactly how early in pregnancy sST2 changes that are predictive for pre-eclampsia can be seen.

Reference

Granne et al. (2011) ST2 and IL-33 in Pregnancy and Pre-Eclampsia. PLoS ONE 6(9): e24463. doi:10.1371/journal.pone.0024463

The sST2 biomarker

- Can be identified from testing blood samples.
- Immunoassay based marker.
- Detection possible via an antibody that binds to sST2

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A vertical image on the left side of the page shows several spherical, spiky cells in shades of blue, purple, and orange. In the background, a semi-transparent DNA double helix is visible. The overall aesthetic is scientific and futuristic.

Stem cell ‘revolution’

Dr Bharti Ranavaya looks at the health benefits made possible through cryopreserving pluripotent stem cells.

Human embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) derived from adult cells have the potential to revolutionise healthcare. Some of the most serious medical conditions and currently untreatable diseases such as Alzheimers, heart disease, diabetes and cancers could be treated – or cured directly or indirectly – using pluripotent stem cells. This potential is represented by stem cell therapy and regenerative medicine. ESCs and iPSCs can also be utilised for new drug and therapeutic development.

With large-scale stem cell therapies and industrial applications of pluripotent stem cells (ESC and iPSC) on the horizon, a significant challenge is the establishment of controllable, reproducible and scalable culture methods that preserve growth rates, genetic stability and pluripotency. Furthermore, whether it is to support large-scale *in vitro* screening systems or the manufacture of cell

products for preclinical and clinical studies, banking and preservation of ESCs and iPSCs is important. ‘Off-the-shelf’ availability of hESCs and iPSCs is a must, to ensure that their potential is harnessed.

Current banking methods have a number of obstacles to overcome, for instance they are only able to preserve a small number of cells. Common banking practices often fail to preserve the functionality of these cells, due to slow freezing methods. Additionally, expensive apoptosis inhibitors, such as inhibitors of the Rho-associated protein kinases (ROCKs) are used. The common practice is also characterised by low recovery, slow growth rate and a high incidence of short-term spontaneous differentiation which results in the original stem cell phenotype being lost. For example, the expression of stem cell markers has been shown to be as low as 10 percent of the recovered cell population, indicating that the stem cell phenotype is

Pluripotent stem cells: the challenges

Working with pluripotent stem cells is notoriously complicated because the cells are particularly sensitive to their environment and require complex culture conditions. The storage of pluripotent stem cells by standard cryopreservation techniques is characterised by low recovery, slow growth rate and a high incidence of short-term spontaneous differentiation which results in the original stem cell phenotype being lost.

Low post-cryopreservation recovery rates are closely correlated to slow-cooling and the use of cryoprotective agents. The expression of stem cell markers has been shown to be as low as 10% of the recovered cell population, indicating that the stem cell phenotype is poorly maintained. These problems are particularly prevalent for human pluripotent stem cells such as human embryonic stem cells (hESCs) or human induced pluripotent stem cells (hiPSCs).

The methods include a novel treatment of the cells before they undergo cryopreservation and a recovery process that is independent of apoptosis inhibitors.

poorly maintained. These problems are particularly prevalent for hESCs and hiPSCs.

Researchers from the University of Oxford have devised novel methodologies for cryopreserving pluripotent stem cells which do not suffer from the problems associated with existing methods. The methods include a novel treatment of the cells before they undergo cryopreservation and a recovery process that is independent of apoptosis inhibitors.

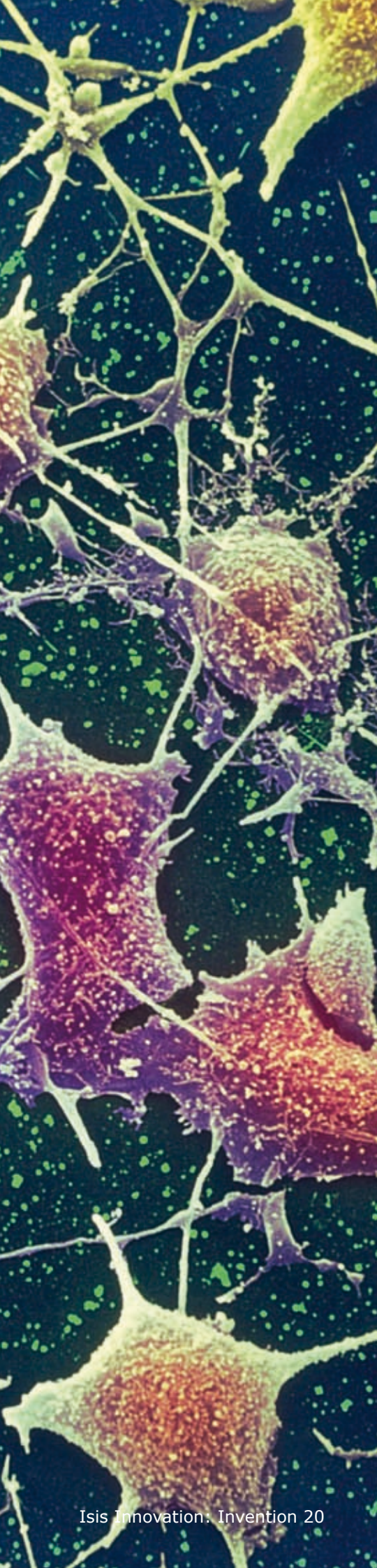
The underlying innovation has been protected by a UK patent application. Isis would like to talk to companies interested in commercialising and developing this opportunity.

Benefits offered by the Oxford invention over existing cryopreservation methods include:

- increased post-thaw survival rates
- decreased apoptosis rates
- inhibition of spontaneous differentiation
- no requirement for apoptosis inhibitors
- a decrease in DNA damage

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Cognitive empowerment

Dr Ruth Barrett presents a B vitamin formulation for treating Mild Cognitive Impairment, often a precursor of dementia.

Mild Cognitive Impairment (MCI) is a recently recognised condition defined as “cognitive decline greater than that expected for an individual’s age and education level but that does not interfere notably with activities of daily life.” MCI affects around 16 percent of those over 70-years-old (translating into 14 million sufferers in Europe, and another five million in the US), and there is no proven therapy currently available. As about 50 percent of these people will go on to develop dementia such as Alzheimer’s disease within 5 years of diagnosis, MCI is often thought of as prodromal for Alzheimer’s, and underlines the need to intervene early in the disease process.

Treatment hypothesis

Even in cognitively healthy adults the brain shrinks with age. Individuals with MCI show intermediate atrophy rates and those with the highest rates go on to develop Alzheimer’s. Therefore, slowing the rate of atrophy might reduce the likelihood of an individual developing MCI or conversion of MCI to Alzheimer’s. High homocysteine levels are already known to be associated with increased rates of atrophy and cognitive decline. As certain B vitamins are involved in the metabolism of homocysteine, it was hypothesised that high doses of B vitamins might lower the homocysteine concentration in the body, and therefore also slow the rate

of atrophy and associated decline in cognitive function.

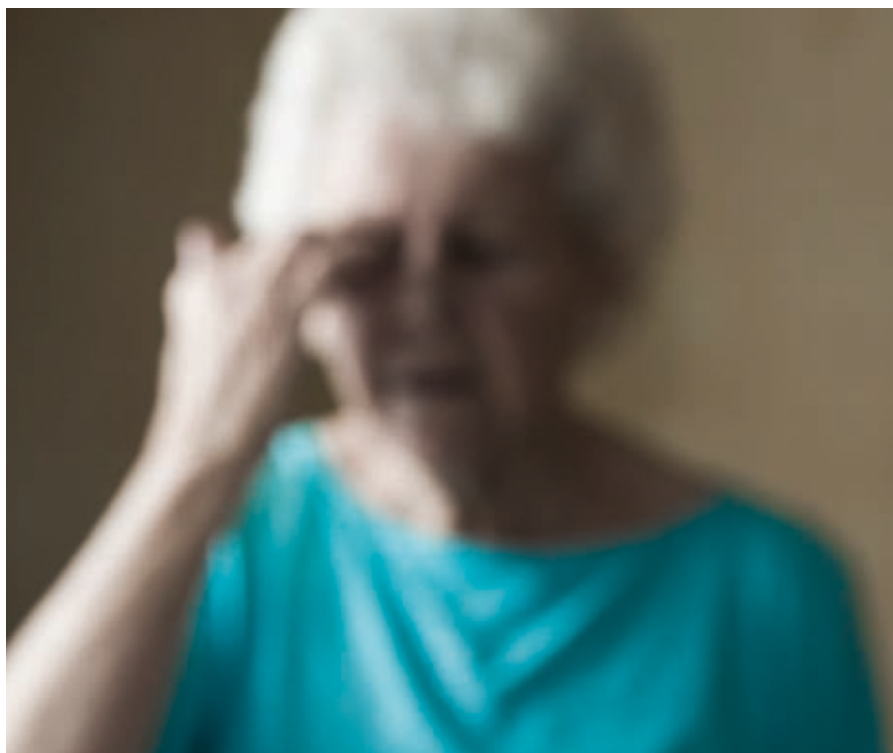
Proven efficacy

A B vitamin formulation protected by a patent application filed by Isis has been shown to have efficacy in slowing cognitive and clinical decline, and to reduce brain atrophy in MCI. Led by Professors David Smith, Helga Refsum and Robin Jacoby, a single centre, randomised, double-blind, placebo-controlled two year trial (VITACOG) was conducted at Oxford, involving 271 people diagnosed with MCI. Half of the participants were treated once daily with a high dose combination tablet containing 0.8mg folic acid, 20mg vitamin B₆ and 0.5mg vitamin B₁₂.

Volumetric MRI scans and cognitive tests (mini mental state exam, episodic and semantic memory tests, and executive function tests) were done at the beginning and end of the trial. Analysis of this data showed that both brain atrophy and cognitive decline were significantly reduced, with the greatest efficacy seen in those individuals with the highest homocysteine levels at the start of the trial. Brain shrinkage was reduced by up to 53%. Homocysteine levels in the plasma dropped on average by 22.5%.

The parallel effect of the treatment on cognition and on brain atrophy

Analysis of trial data showed that both brain atrophy and cognitive decline were significantly reduced.



suggests that the B vitamins are able to modify the disease process.

Safe and simple

There was no treatment-specific occurrence of serious adverse events, indicating that this formulation may be well tolerated and safe. Furthermore, compliance and adherence were good, with 78% of participants taking 75% of their medication.

Product opportunity

The Isis filing covers a range of B vitamin combinations that may be used to treat MCI, and is now available for licensing. This application presents an opportunity for companies interested in developing a B vitamin combination for use in MCI. Due to the high vitamin doses used, a prescription product or medical food may be developed, or alternatively over-the-counter may be considered in some territories, if desired.

Patent status

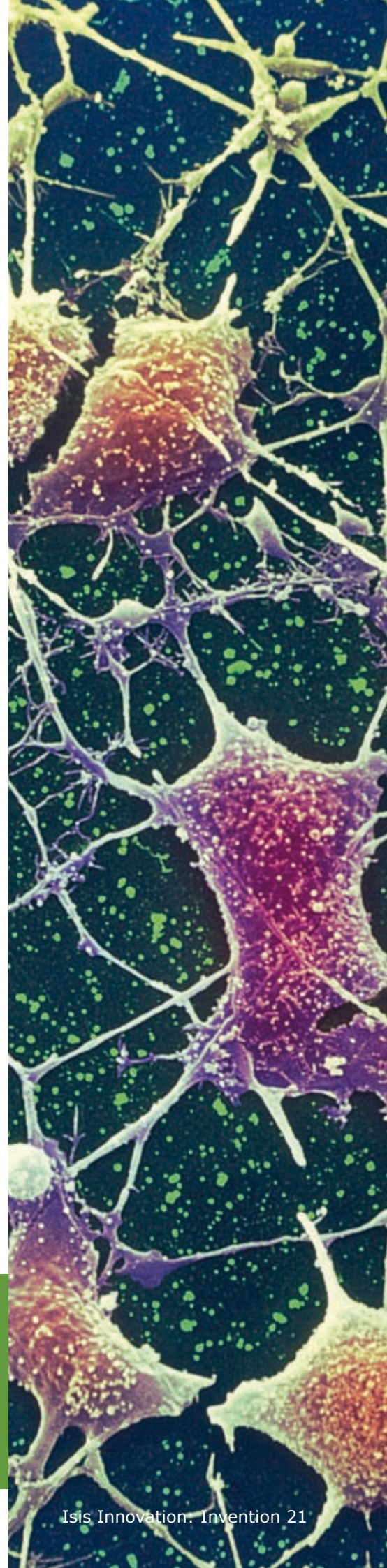
The Isis filing is now at PCT and is unpublished as yet.

References and examples of press attention:

PLoS One. 2010 Sep 8;5(9):e12244. Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment. A randomized controlled trial, Smith AD et al.
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Mind control

Dr Mark Gostock reveals how an automated device engineered at Oxford for studying fruit fly behaviour can be used as a platform to identify mechanisms and compounds for treatment of human memory disorders.

Writing memories

It is widely accepted among neuroscientists that if the activity of all neurons could be recorded, the mysteries of brain function would be unlocked and the inner workings of the human mind understood. However, with trillions of neurons in the human brain firing off signals, attempting to understand the code used by the brain through deciphering all the recorded activity patterns would be just as difficult as understanding the brain that produces them.

In order to make progress, the code needs to be broken. If the activity of neurons can be controlled, considerably more could be learnt about the complexities and intricacies of the brain.

The Oxford technology spins conventional thinking and concepts on their head, and rather than trying to understand how the brain works in order to control its function, it seeks to control the brain in order to understand how it works.

Cognitive therapy development

Researchers at Oxford have developed an experimental apparatus, which can be used to train and evaluate learning experience of fruit flies by using exposure to external stimuli. A fly's reaction to chemical signals and odours is neither innate nor invariant but influenced by experience. The Oxford technology can exploit these similarities in the learning behaviour of fruit flies and humans, to screen

compounds for therapies targeted at improving learning and memory.

The fly study technology replaces crude and invasive electrical implants typical of conventional approaches to probing the nervous system, with passive, non-invasive stimuli that are capable of reengineering some of the brain's neuronal elements. Studies have demonstrated that the reactionary circuits of a fly's brain can be reinforced through diffusively broadcast signals such as odours, light and electrical stimuli.

Multiplexed training

The olfactory training system allows simultaneous monitoring and behavioural analysis of up to 20 flies in separate chambers. Individual control of the stimuli applied to each fly is facilitated by customisable experiment control software, which allows for action-contingent (operant) conditioning protocols, and for both trained and control groups to be included in a single experiment. Automated stimulus control standardises protocols and allows fewer operators to collect more data than from existing olfactory training systems.

Quantitative data is obtained from the fully automated experimental system, in which all variables and stimuli are readily accessed and controlled from the scripted software interface, including:

- airflow
- odour concentration

“Rather than trying to understand how the brain works in order to control its function, the Oxford technology seeks to control the brain in order to understand how it works.”

- stimulation voltage
- training pulses
- evaluation periods
- rest periods
- time of training

Market readiness

This highly engineered *Drosophila* training device, multiplex instrument control software and data analysis platform are mature and market ready. The technology will be of interest to biotechnology and pharmaceutical companies involved in discovery of drug treatments for memory dysfunction and improvement of cognitive function as an alternative to traditional screening platforms. Additional application of the technology includes analysis of decision making, walking speed, activity bouts, motor responses to painful shock and other behavioural metrics, which can either be assayed in separate experiments or simultaneously during learning experiments.

References

A. Claridge-Chang, R.D. Roorda, E. Vrontou, L. Sjulson, H. Li, J. Hirsh & G. Miesenböck, 'Writing Memories with Light-Addressable Reinforcement Circuitry', *Cell*, 139: 405-415, (2009).

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Silence, please

Andy Self describes an exciting new approach to correcting abnormal gene expression, prevalent in a range of diseases from cancer to neurodegenerative disorders.

RNA interference, (RNAi), the ability to switch off the expression of a gene by the use of a specific sequence of RNA, holds promise as a powerful new approach to correcting abnormal gene expression. Oxford scientists have developed a new long-lasting approach to gene silencing which has several advantages over traditionally used techniques.

The RNAi therapeutics market, whilst still in its infancy, is expected to become a prominent force over the next 20 years, with the first products expected by 2015. Despite this, each of the classes of RNAi therapeutics in clinical development have disadvantages, and improved technologies are required to broaden the therapeutic use of RNAi drugs. The Oxford mirtron technology discussed here represents an exciting alternative approach to gene silencing.

Gene regulation

RNAi is a naturally-occurring gene regulatory mechanism in cells, where it controls which genes are active and how active they are. The potential simplicity and specificity of mimicking this natural mechanism has seen intense scientific research in the RNAi pathway over the past decade. This has led to the development of a number of synthetic approaches to RNAi.

The three most advanced methodologies in development are microRNAs (miRNAs), short hairpin RNAs (shRNAs) and short interfering RNAs (siRNAs), each of which has an effect at a different point in the RNAi pathway. Therapeutics based on these methods are currently in clinical development. However, all of these approaches have disadvantages (such as rapid degradation in the body,

Marvelous mirtrons

- Longer-term silencing compared to siRNAs
- Reduced toxic effects due to independence of Drosha processing
- Can be integrated into viruses for gene therapy use
- Well suited for gene knockdown and replacement approaches
- Ability to silence multiple targets in a biological pathway within one construct
- Multiple mirtrons can be delivered within one reporter gene
- Ability to achieve temporal and spatial expression by virtue of using host transcript promoters

toxicity and off-target effects) that may limit their therapeutic usage and new approaches continue to be sought to expand the range of diseases treatable by gene silencing.

Mirtrons

Oxford researchers have developed a novel synthetic RNAi system based on mirtrons. Mirtrons are a naturally-occurring type of miRNA, which were first discovered in fruit flies (*Drosophila*) but until recently little had been known about their role in humans.

Oxford researchers have shown that the mirtron system does exist in humans and have exploited this system to develop a novel synthetic gene-silencing approach.

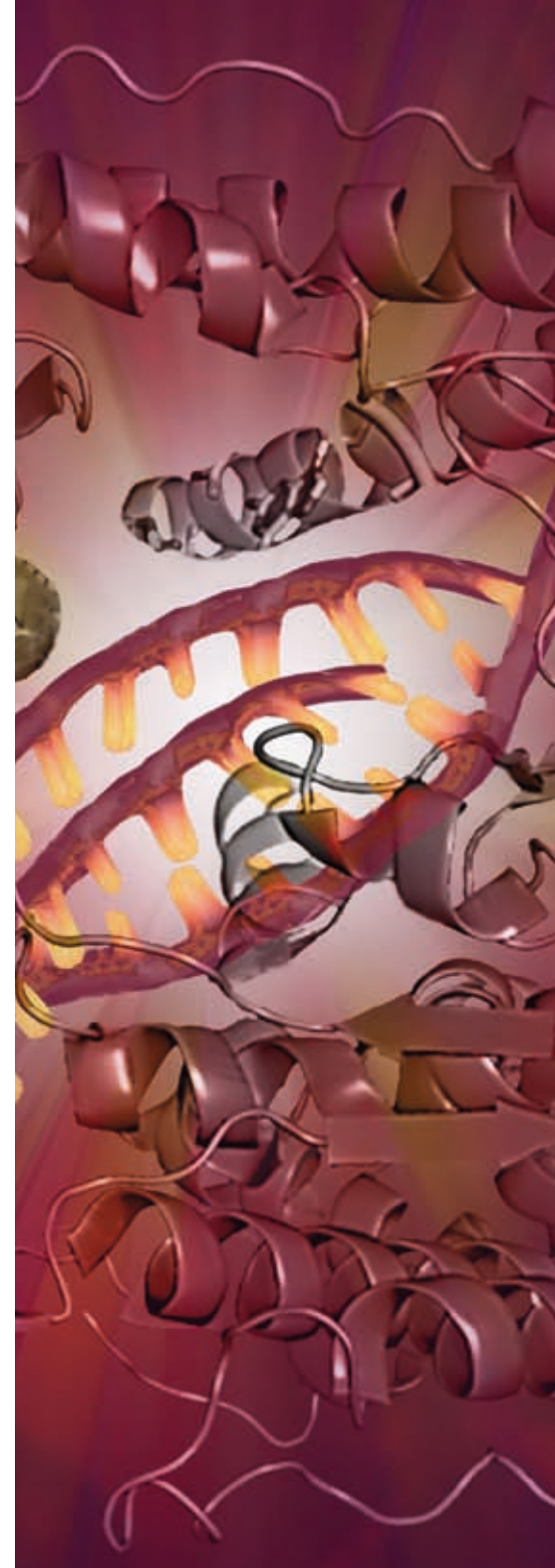
Mirtrons have a number of advantages over traditional techniques. Importantly the researchers have shown that mirtrons bypass the Drosha processing step of the RNAi pathway. Drosha processing can be a rate-limiting step in the RNAi pathway and saturation with synthetic therapeutics, such as miRNAs, can lead to toxic effects. RNAi therapeutics with reduced dependence on Drosha are therefore highly desirable due to the enhanced safety that they would offer. Mirtrons instead rely on a different mechanism, intronic splicing, to achieve their silencing effect.

The Oxford researchers have successfully designed synthetic mirtrons against several target sequences and shown excellent levels of silencing activity over a prolonged duration without any toxic effects.

Oxford Scientists have developed a new long-lasting approach to gene silencing which has several advantages over traditionally used techniques.

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Mercury rising

Dr Jon Carr explains how a new range of crystals developed at the University of Oxford will facilitate remote temperature sensing.

Many sensors have limited temperature range and suffer from electromagnetic interference. One example is that of temperature measurement sensors which use pyroelectric material, typically a crystal, placed in the target environment.

Changes in temperature result in a voltage change. Such sensors require the crystal to be intimately combined with the rest of the sensor as wires must be connected to the crystal to detect the voltage changes in it. Resilience of these ancillary components, other than the crystal, therefore limit where the sensor can be used.

The remote temperature sensing market is growing. In these systems, interrogation is operated remotely and only the crystal itself needs to be located in the environment. All other components such as the light source, measurement and processing electronics can be situated remotely.

This allows greater freedom of design both of the electronics and the housing, leading to these sensors having improved temperature range and resistance to electromagnetic interference.

Birefringent crystals

Birefringence is the decomposition of a ray of light into two rays when it passes through certain materials. Birefringent crystals can be used to measure temperature by monitoring an interrogating light beam to detect changes in the birefringence as the temperature changes.

Performance of current birefringent crystals used to measure temperature is critically dependent on both crystal thickness and orientation. These can be difficult to control from device to device and each has to be independently calibrated. Furthermore, the use of white light can wash out the birefringence colours, and therefore for accurate measurement the use of monochromatic light such as that from a laser becomes necessary. These issues contribute significantly to manufacturing costs.

Specially designed crystal

Researchers from the University of Oxford have developed a new range of materials and it is now possible to obtain crystals with optimum birefringence whereby the change becomes independent of thickness, and either a white light source or monochromatic light can be used, with

Prime applications include temperature measurement near electromagnetic, radio frequency and high voltage environments, where other types of sensor are normally subject to large errors due to interference.

no drop in quality. The new crystals have birefringence that is close to zero in magnitude in all directions i.e. the material is close to being optically isotropic, just like glass.

Collaboration with the University of Warwick has shown that the slightest temperature change induces a rapid increase in birefringence in these materials, forming the basis of a very sensitive method for detecting temperature changes within the Millikelvin range.

Applications

A recent Frost and Sullivan survey ("World temperature sensor and transmitters") stated a current \$4 billion per annum total temperature sensor market, with a compound annual growth rate of over 6%. Prime applications include temperature measurement near electromagnetic, radio frequency and high voltage environments, where other types of sensor are typically subject to large errors due to interference. Examples include temperature measurement within the vicinity of MRI scanners in hospitals, industrial microwave dryers and high voltage transformers. It is also envisaged that these crystals could be used in the future within a thermal imaging design set-up.

Patent protection

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

The light source, measurement and processing electronics can be situated remotely.

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Steering Siberia

Dr Steve Cleverley showcases the technologies being commercialised with the support of Isis Enterprise in Siberia.

Isis has begun engagement in a multiyear programme devised to support the international commercialisation of technologies from within the Tomsk region of Siberia, in partnership with The Eurasia Consortium. Each year, invitations are extended to technology providers from Tomsk to apply to be part of the entrepreneurship training and support scheme. Successful applicants attend a week long course of intensive training, run by the Eurasia Consortium in Oxford, at the Saïd Business School. Themes of the training programme include The Oxford Model of Technology Transfer, Entrepreneurial Activity and University Research, and Managing High Tech Start Ups.

As a follow-up service, Isis Enterprise offers practical advice and support to the participants with the aim of identifying and brokering deals with prospective partner organisations outside of Russia. This involves ongoing contact from Oxford,

supplemented by assistance from patent attorneys, product designers and finance or business strategy experts, and quarterly visits to Tomsk by Isis Enterprise consultants.

This year, programme participants brought a broad range of technology ideas – from software to fertilisers – at varying stages of commercial readiness.

Tomsk Technologies

Some of the technologies we are helping to partner in Europe include:

Triaxes – Glasses-free 3D technology

Current consumer 3D TVs rely on glasses to select which image is seen by which eye. Glasses-free systems display many different images simultaneously, projected in different directions so that each eye sees two different, adjacent views. However, stereo 3D (requiring glasses) is

Destination Tomsk

Tomsk, the administrative centre of Tomsk Oblast and located on the river Tom, is one of the oldest cities in Siberia. Since its foundation in 1604, Tomsk has become one of the main educational, scientific, cultural and industrial centres of Siberia. With a population of just over 500,000, it is home to seven local universities and several branches of Russian and foreign institutes and universities.



s_singarov

The innovation potential of the city is underpinned by its 47 scientific institutions – among them nine research, engineering and design institutes of the Russian Academy of Sciences, five institutes of the Russian Medical Academy, 20 organisations focused on industrial sciences, and 11 research institutes linked closely to the universities of Tomsk.



prevalent, both in terms of production equipment and media back-catalogue. Triaxes have developed software solutions to extract the depth information from a normal stereo 3D movie and use it to then generate all the different viewpoints required for a 'glasses-free' display. Implementations are available for real-time broadcasting, off-line production and set-top-boxes. Isis Enterprise is assisting Triaxes with developing commercial partnerships abroad.

Sibspark – Micro-plasma sterilisation technology

Equipment to be cleaned and sterilised is placed into an electrolytic solution and a micro-plasma discharge is generated at the interface between the equipment and the fluid. This plasma causes pressures of up to 2,000 atmospheres to be generated at the phase interface between the equipment surface and the contaminants attached to it, thus removing the contaminant quickly and with minimal heating. Simultaneous cleaning and sterilisation can occur within minutes at low temperature and without the need for hazardous and toxic sterilisation chemicals. The process does not harm the equipment increasing the lifespan over traditional methods. The combination of the fluid and micro-plasma discharge can penetrate very small and intricate crevices and complex shapes. Isis Enterprise is working with SibSpark to find further commercial partners/ licensees for the micro-plasma sterilisation technology.

iPhar – Innovative anti-ulcer therapeutic

Peptic ulcers are among the most common diseases of internal organs, affecting 2-3% of adults. A common consequent illness called gastroesophageal reflux disease occurs in more than 20% of the adult population. Acid-related diseases constitute the third largest sector in the pharmaceutical market, with global revenues exceeding \$30 billion. Proton-pump inhibitors (PPIs) are the current standard of care and the most potent inhibitors of acid secretion available today. iPhaR (Innovative Pharmacology Research) has identified a drug candidate that addresses the clinical gaps left by existing standards of care such as traditional PPIs. Consultants at Isis are working with iPhar to understand these unmet needs and identifying potential development partners for this innovative anti-ulcer therapeutic.

Isis Enterprise continues to support both technology providers and technology seekers through our international service offerings.

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Migrating the debate

An ongoing study involving Oxford University Consultancy is demonstrating the positive impact of migration on rural development, food security and poverty reduction, as **Susan Clark** explains.

The Commonwealth – as recorded by the Interim Report for the Ramphal Commission on Migration and Development – is one of the major migration arenas, accounting for 45 million international migrants, or one fifth of the global total. The Commonwealth also contains some of the most food-insecure countries in the world.

While migration is all too often seen by nations as a problem to be solved rather than as an instrument to be used for positive benefits, evidence of the development potential that migration can bring is now being highlighted.

The Ramphal Centre, with the assistance of the Commonwealth Foundation, is working with the UN Food and Agriculture Organisation on a significant and dynamic study on the role of diasporas in the food

security and development of countries of origin.

Through analysis of eight Commonwealth countries the study reflects the increasing recognition of diasporas in the contribution they can make to development potential for food security. The central question the study addresses is: *in what ways and to what extent can migration be an instrument to combat rural underdevelopment, poverty and food insecurity in rural areas?* The recently published report, based on this study, proposes a series of recommendations for the creation of an enabling environment for investing remittances in the agro-rural sector within the Commonwealth.

Recommendations

At the Commonwealth level, the creation of a Commonwealth Office

The organisations behind the study

The Ramphal Centre is an organisation set up by the Commonwealth's 53 Member States to operate as an independent intellectual hub, advising on policy issues to support member states in their efforts to meet the environmental, developmental and governance challenges of the 21st Century. The core activity of the Centre is to carry out policy studies of the highest quality.

Dr. Thomas Lacroix, of the International Migration Institute – which forms part of the Oxford Department of International Development – was commissioned by the Ramphal Centre through a consultancy agreement arranged by Oxford University Consulting to synthesise the findings of the study in a report.

The World Bank has reported that remittances sent home to developing countries from migrants totalled \$325 billion in 2010, representing a lifeline for the poor and supporting development of general wellbeing, food security and entrepreneurship.

for Migration and Development would provide a platform where issues of migration and development could be discussed. The board of the COMD would include policy makers of sending and receiving countries and representatives of migrant and pro-migrant associations.

At the national level, states should enlarge their capacity at two distinct levels. The creation of dedicated institutions should tackle migration-related issues such as migrant rights and migration management, while migration and development issues should be part of the agendas of institutions in charge of development strategies. The research has extrapolated four proposals likely to improve the migration and rural development relationship:

- Maximising internal remittances through innovative channels such as mobile phone transfers to reduce transport costs.
- Linking agriculture and immigrant entrepreneurship to build up international market chains.
- Developing integration policies in Northern states to encourage openness to increased capacities of immigrants.
- National bonds and other incentives to channel investment into rural areas.

At the local level, joint co-funding programmes fostering synergies between migrant organisations, local authorities and civil society should target the infrastructure deficit in rural areas. A particular emphasis

should be given to female poverty. Measures should be taken to enlarge the possibility for women to use remittances, to grant them better access to economic assets and to help them participate in development strategies at the local level.

The Commonwealth will benefit from this work through a greater understanding of the effects of diasporas and migration on agricultural development to reduce poverty and food crises.

The findings of the report were used to inform the debates on migration and development during both the FAO conference on food security in Manila and the Commonwealth Heads of Government Conference at Perth, both events being held in November 2011.

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Oxford Innovation Society

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

- Thursday 8 December 2011
- Thursday 22 March 2012
- Thursday 12 Sept 2012

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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