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

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

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

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

Email : enquiries@innovation.ox.ac.uk

Isis insights

Issue 72 Summer 13

The latest innovations, collaborations and technology transfer

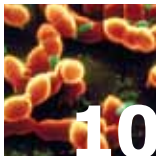
UNIVERSITY OF OXFORD

ISIS INNOVATION

Ii

Issue 72
Summer 2013

Contents



'Shotgun' proteomics
Disease diagnostics: malaria and pneumonia

Upscaling with nanomaterials
Production analysis and manufacture

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

Newsflash

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


OXFORD UNIVERSITY

Press Release NOT FOR PUBLICATION BEFORE

A quarter century not out

25 years ago the University of Oxford formed Isis to file patents and commercialise IP – we recall and celebrate some of the highlights in our centre pages this issue. Both the breadth of our activities and the geographic reach of Isis have grown enormously during that time, and our 2012-13 financial year was another record-breaking performance. Details will be published in our Annual Report later this year.

Spin-outs and start-ups, old and new

Companies from Oxford, formed by Isis, continue to make the news.
Oxitec's recent Brazilian trial showed a 96 percent reduction of the wild mosquito population in the target area after only six months.
Perspectum, the 70th company spun-out by Isis since 2000, is commercialising a new technique that can spot early liver disease. The new scan uses standard MRI technology and costs half as much as a biopsy.
OrganOx's metra™ device (pictured here) maintained donar organs for several hours ahead of two successful human liver transplants, a major milestone for the spin-out. This technique could potentially double the number of livers available for transplant.
Colwiz, an early entrant to the Isis Software Incubator, announced a development partnership and strategic investment from the American Chemical Society, the world's largest scientific society. Colwiz is a research management, collaboration and productivity software company.

Engaging globally

A second Isis joint venture company in China was created in June. In addition to providing technology transfer services between the rest of the world and China, the Guangxi Liuzhou Jinhui International Science and Technology Company will manage a newly established 10,000 metre squared innovation centre and create an industrial product development consultancy. The new joint venture is a collaboration between Isis, a government agency and local/international investors. Guangxi's main industries include automotive, heavy industrial equipment, mining and agriculture.

Malaria diagnosis

Following nearly five years working in sub-Saharan Africa, and 12 months of intensive work in Oxford, Dr Climent Casals-Pascual and his team from the Wellcome Trust Centre for Human Genetics at the Nuffield Department of Medicine have identified a parasite protein that is an accurate indicator of both the presence and severity of malaria. This marks a critical step towards developing a quick and accurate diagnostic kit. Since most deaths occur within the first 24 hours, it is critical to diagnose and treat malaria patients promptly. *See page 10 for more.*

Enterprising Consultancy

News from Isis Enterprise and Oxford University Consulting

Stopping the spread

M-Trap is a new approach and technology for controlling cancer metastasis. Although a range of treatment options are available, cure rates fall drastically once cancer reaches the metastatic stage, the most devastating event in oncology.

If the pattern of tumour dissemination can be controlled, then it is possible to transform a systemic disease back to a localised one, where surgery, radio- and chemotherapy have proven efficacy.

M-Trap interferes with this pattern of metastatic dissemination through the generation of a preferential site of implantation. Its insertion in the peritoneum captures the tumour cells that circulate from the primary lesion towards the M-Trap device, allowing them to be isolated and removed. Therefore M-Trap can effectively prevent metastasis, transforming life threating metastatic cancer into a manageable chronic disease.

This technology originated from research at the Translational Medical Oncology Group of the Health Research Institute of Santiago-IDIS and the University Hospital of Santiago-SERGAS (Spain), in collaboration with the Cell Cycle and Oncology Group and the NANOBIOFAR Group. The Technology Fund of Fundación Barrié is supporting the project, with Isis Enterprise offering project management support and commercialisation services.

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Fluent consulting

Medical translators PharmaQuest Ltd have highlighted the contribution that Oxford academics, working with Oxford University Consulting (OUC), have made to the international success of the Patient Reported Outcomes (PRO) measures provided by Isis Outcomes (IO).

OUC supports IO activity by incorporating academic expertise into the IO business model. IO, managed by Dr David Churchman, provides its clients with fully supported access to high quality PRO measures developed at the University of Oxford and elsewhere. Users of PRO measures may need to deploy the questionnaires into many territories for their study, requiring careful translation. IO and OUC have formed a relationship with Pharmaquest, an Oxfordshire-based medical translation company, which specialises in the translation and linguistic validation of PRO measures. OUC works closely with both IO and PharmaQuest to organise Developer Reviews by the creators of each PRO, for every translation.

Rebecca Two, Translation Director at PharmaQuest, said, "Working with academic consultants from OUC has added real value to the quality of our PRO translations. Their input throughout the translation process aids our understanding of the concepts behind the questionnaires, which, as a result, improves the harmonisation and quality of the final translations. We have always found OUC to be highly responsive and a pleasure to do business with."

In addition to supporting translation activities, OUC also facilitates access to other specialist expertise, offering advice on the best use and interpretation of data from PROs.

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See also p22

The portfolio

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

OneTriax: An update on the exciting 'GPS-alternative' company in the pipeline

Prospective Oxford spin-out, OneTriax is targeting the location, navigation and tracking market, with a unique technology that addresses the deficiencies of global positioning satellites (GPS). Smartphones and other mobile consumer devices generally retrieve localisation data from GPS satellites. However, GPS positioning can be unreliable in some environments such as when used indoors or underground, leading to situations where a user has little or no location information available to them.

Unique solution

OneTriax aims to bring to market a new and unique 3D positioning solution with sub-metre accuracy. The technology is based on the generation and detection of Very Low Frequency (VLF) fields, which have the capability to penetrate walls, soil, rock and fresh water. The technology is thus ideally placed to provide accurate position input for location and navigation applications where GPS does not typically work. It also overcomes the deficiencies of other indoor location technologies, such as those based on WiFi.

The development of the technology started in 2008 with a project from the University of Oxford focusing on technology to track badgers underground. In 2011 Isis Innovation saw the potential of the research and started the commercialisation process, successfully pitching for £70,000 of seed funding from the University Challenge Seed Fund (UCSF). This has been invested in designing and producing a working demonstrator on an Android platform.

Target markets

The proposed spin-out is focusing on two distinct markets: Enterprise and Consumer. The Enterprise market includes industries seeking specific solutions to problems in location, tracking, safety, emergency response and security. Encouragingly, companies in the healthcare, nuclear, marine and mining sectors have already identified specific needs and are engaged with the OneTriax team. For example, in the mining industry – where improving efficiency and miner safety is a strong market driver – the ability to locate people and equipment through rock is a tremendous opportunity afforded by the technology.

Location-based advertising

In OneTriax's business plan, initial adopters of the technology in the Enterprise market will provide early revenue streams for the business and establish a proving ground for future applications in the Consumer market. These are largely based around Location Based Services (LBS) including Location Based Advertising (LBA), with apps on phones providing information on, for instance, where nearby shops, restaurants, or services are located. Usually the app will then show a route on a map or provide directions, as well as potentially providing shop owners with vital information about customer behaviour. However, these location apps do not function where there is no GPS signal, which precludes their use in buildings such as supermarkets, shopping malls or museums, or wherever there is poor GPS reception such as in city streets with high buildings.

With global sales of smartphones forecast to reach 1.1Bn units in 2015, and given that around 80 percent of 'consumer time' is spent indoors, the potential for this technology is clear. It is anticipated that OneTriax will be spun out from the University to begin deploying the technology in these markets.

Mining is one of the sectors identified by the OneTriax team

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jamescowper
Accountants & Business Advisers

Sue Staunton, a Partner at the firm, discusses how the OIS member company manages "minutiae and strategy" for start-ups and spin-outs.

Companies spinning-out from the University of Oxford have quite distinct characteristics from more conventional business start-ups in the UK. Although they are probably not intending to generate revenue in the short to medium term, they will very often have international aspirations and ambitions. While they may initially be operated on a shoestring, they will have a focus on satisfying the requirements of existing and future third-party investors. And although they will start with a very small complement of staff – often outsourcing early activity – they will tend to put in place employee incentive schemes from the outset.

Because of these apparent dichotomies in choosing advisers to work with them, the spin-out companies need specialists with significant experience spanning both the minutiae of issues any early stage will need to address – how to run a payroll, when to register for VAT etc – and the bigger, more strategic issues such as how best to set up overseas in order to gain benefits from local state-aid.

As accountants and business advisers, James Cowper's specialist technology team are accustomed to covering the gulf of advisory requirements for our clients. We are local – with an office in Oxford – and international. We play a lead role in the Kreston International network of accountants and business advisers, which has over 21,000 professional and support staff globally along with 700 offices in 105 countries.

We have been working with Isis for a number of years, supporting companies such as OrganOx, Particle Therapeutics and Oxford Cancer Biomarkers with their bookkeeping, payroll and annual compliance requirements. We also provide advice as required on international issues, obtaining R&D tax credits, structuring for investor tax opportunities and implementing tax-efficient share option schemes.

We are also increasingly working with businesses from the Isis Software Incubator, which have a range of very different characteristics from the "normal" spin-out businesses that come out of the Isis melting pot. However, our work with Isis goes beyond advising spin-outs.

As accountants and business advisers, James Cowper's specialist technology team are accustomed to covering the gulf of advisory requirements for our clients

We have advised Isis itself on a number of matters, including international issues. We help to run training courses on financial matters in technology businesses for non-financial people and on issues for non-execs to consider when invited onto the board of a technology-based business.

We are passionate about our work with Isis, its spin-outs and its start-ups, because we enjoy helping the founders achieve their financial objectives and we love working with diverse businesses. For example, we have recently worked with one providing automated background and reference checking services for employers [Onfido] and another working on the commercialisation of a medical device enabling the repairs and preservation of livers prior to transplantation [Perspectum Diagnostics]. We believe that one of the considerable strengths of Isis and its teams is the ability to foster the successful and sustained commercialisation of ideas across a broad spectrum of technologies and platforms, and we feel very proud to play our part with them in this.

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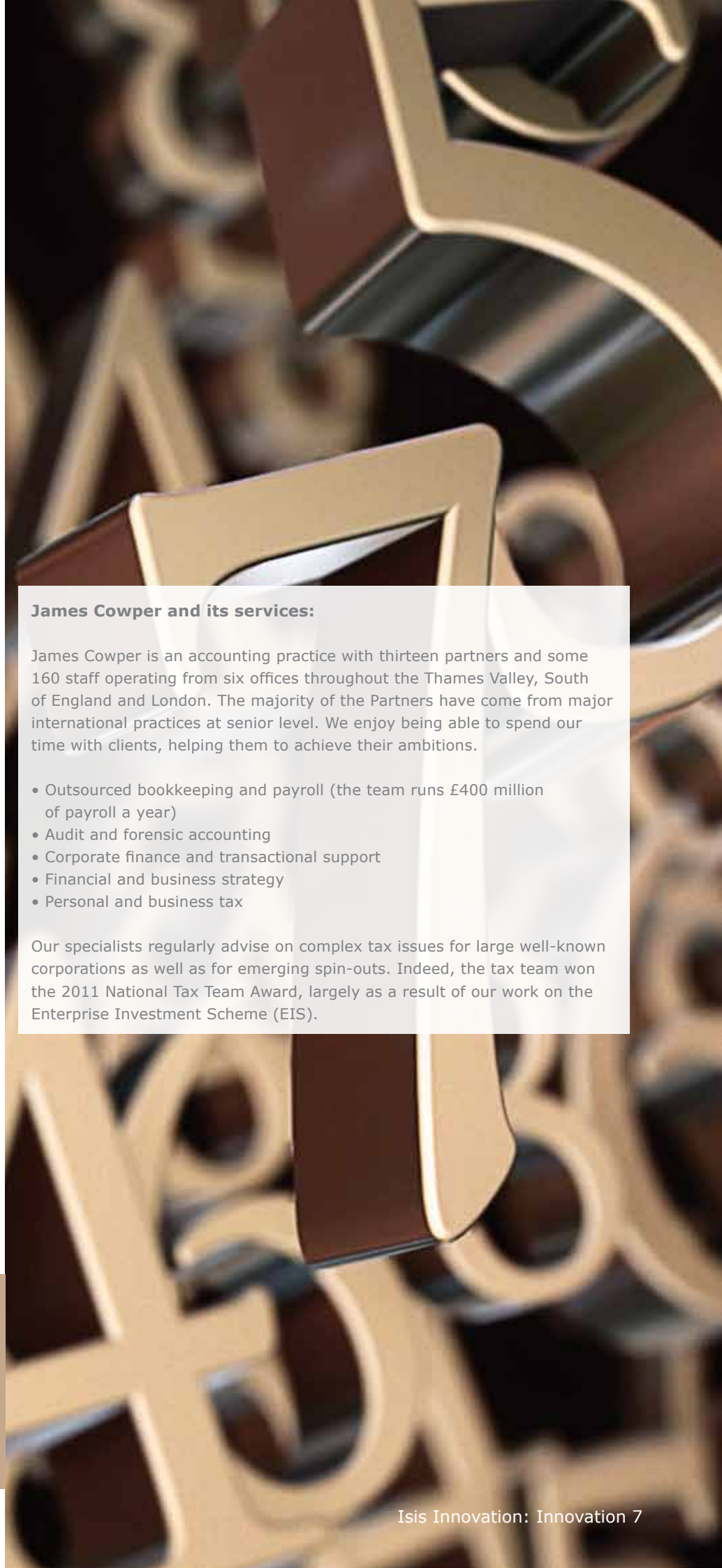

James Cowper and its services:

James Cowper is an accounting practice with thirteen partners and some 160 staff operating from six offices throughout the Thames Valley, South of England and London. The majority of the Partners have come from major international practices at senior level. We enjoy being able to spend our time with clients, helping them to achieve their ambitions.

- Outsourced bookkeeping and payroll (the team runs £400 million of payroll a year)
- Audit and forensic accounting
- Corporate finance and transactional support
- Financial and business strategy
- Personal and business tax

Our specialists regularly advise on complex tax issues for large well-known corporations as well as for emerging spin-outs. Indeed, the tax team won the 2011 National Tax Team Award, largely as a result of our work on the Enterprise Investment Scheme (EIS).

Innovation through collaboration

EPSRC, sponsors of the March OIS dinner, asked BP's **Dr Bob Sorrell** to discuss innovation ecosystems. Here's what he had to say, on an illuminating evening at Oriel College, Oxford.

The energy industry faces a major challenge: how to meet increasing energy demand in a way that is affordable, secure, reliable and that does not harm the environment. As a global energy company committed to tackling these challenges, BP recognises that innovation has a central role to play. Consequently we employ a research philosophy that is based on fostering an innovation ecosystem, believing that through collaborative partnerships key technology challenges can be progressed. This ecosystem includes our own dedicated technology centres, commercial research partnerships, venturing and academic institutions.

BP's Energy Outlook projects that demand for energy will grow by around 40 percent over the next two decades, equivalent to another China and another USA being added to the world's energy demand by 2030. This increase in demand - driven in a large part by growing populations and rising standards of living in developing societies – means that over the coming decades we will need to produce more energy than we do now.

However, while on the one hand the world is demanding ever greater amounts of energy, the world also wants it to be secure, affordable and sustainable. Achieving these goals will require significant investment, new infrastructure and better technology. It also means that the world needs to innovate both in respect of its existing technologies – for example finding new ways to get more oil out of the ground – as well as for new ideas, such as developing highly efficient biofuels that do not use food crops or valuable farmland.

An 'innovation ecosystem' model

In BP we take a focused approach to technology, selecting and developing those which enable us to be successful within our industry and make us distinctive at the point of competition. For example, seismic imaging, real-time corrosion management and product differentiation through formulated products. We do this using significant internal capability of our own, but we also recognise that by identifying and forming the right partnerships we can access a larger innovation ecosystem and, through collaboration rather than competition, enjoy opportunities for wider insights and technology developments.

To enjoy the full benefits of such an ecosystem, we include many different types of collaboration. We

Fostering relationships is central to our ability to pull science and technology through into our businesses in a meaningful way

have strategic partnerships with large multinational organisations. An example of one of these is with GE, with whom we have a shared interest in developing the oil and gas market. We partner with SMEs through our venturing team, allowing them to access the skills and insights that a large company is able to offer and enabling us to immerse ourselves in new technologies through their market development. We involve ourselves in public private partnerships such as the UK's Energy Technologies Institute (ETI), which among other benefits has provided us with strategic insights at a national level. We also maintain a great number of university relationships, frequently investing in major collaborative research projects with them.

Making collaborative partnerships work

In BP's experience, the most successful alliances are long-term, mission-orientated, stable commitments. In establishing new partnerships we therefore place great emphasis on this, as exemplified in one of our most recent initiatives, the BP International Centre for Advanced Materials (ICAM). This is a ten-year, $100m investment programme which will support 25 new academic posts, along with 100 postgraduate researchers and 80 post-doctoral fellows. It operates as a hub-and-spoke model, with the hub at the University of Manchester and the spokes at Imperial, Cambridge and the University of Illinois at Urbana-Champaign. Its structure will allow all sides to bring their ideas to bear and to input to the research agenda, another aspect which our experience shows is essential for successful collaboration.

Fostering relationships such as these in our innovation ecosystem is central to our ability to pull science and technology through into our businesses in a meaningful way. This is essential for us as we seek to play our role in addressing the energy challenges that the world faces in the coming decades. We are confident that by adopting an innovative approach – not only to our technology but also to our partnerships and business models – we can be successful in translating great science into great outcomes.

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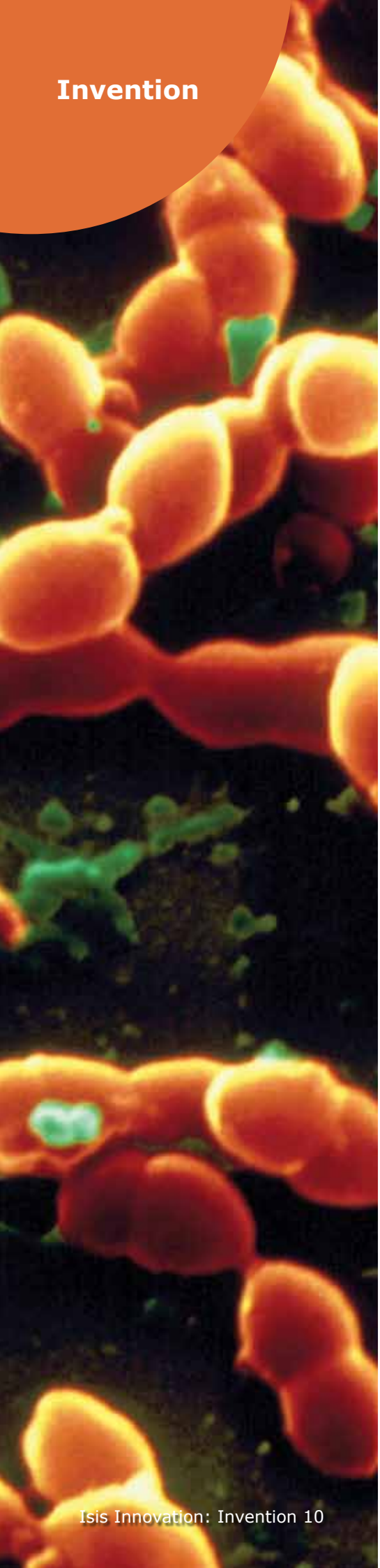
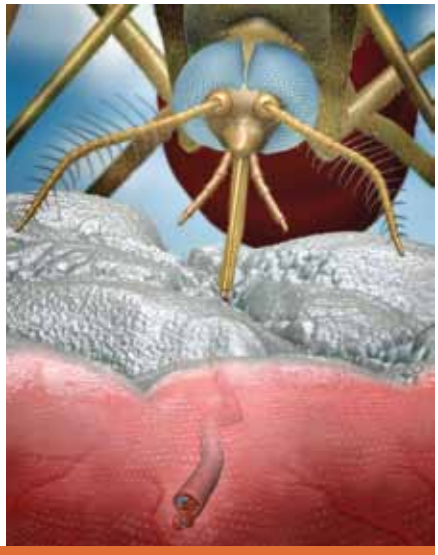


‘Shotgun’ proteomics

Dr Christine Whyte describes how a team headed by Dr Climent Casals-Pascual from the Wellcome Trust Centre for Human Genetics, Nuffield Department of Medicine are using proteomic techniques to identify novel molecular markers of life-threatening diseases including malaria and pneumonia.

In work funded by the Medical Research Council, Dr Casals-Pascual’s team has painstakingly analysed patients’ plasma samples to identify proteins associated with malaria and pneumonia. Their proteomics work has identified proteins which could help in the rapid and more accurate diagnosis of these conditions.

The team searched for proteins from the malaria parasite Plasmodium falciparum in plasma from infected individuals. This proved to be a major technical challenge, akin to searching for a needle in a haystack. The team started with an approach called “Shotgun” Proteomics using mass spectrometry to identify, with remarkable accuracy, tiny protein fragments in the samples. Over 12 months of intensive work 8,905 unique protein fragments were identified in plasma from patients with mild or severe malaria, but only a small fraction – 65 proteins – corresponded to malaria proteins. The team then accurately measured the amount of these proteins in individual samples. This is something usually done with specific antibodies but these were not available so the team used a specialised technique – targeted proteomics – to identify the proteins. A significantly higher concentration of a protein called pfHPRT was found in the plasma of patients with severe malaria compared to mild cases; they also observed that levels of this protein decline rapidly after treatment. The data is now published in the Journal of Proteome Research (2013) 12: 1211-1222.



Malaria

Approximately half of the world’s population is at risk of malaria, caused by Plasmodium parasites transmitted by mosquitoes. The first symptoms – fever, headache, chills and vomiting – may be mild and difficult to recognise, but if patients are not treated within 24 hours, Plasmodium falciparum malaria can progress to severe illness, even death. In 2010, malaria caused approximately 660,000 deaths, mostly among African children. Early diagnosis and treatment reduces disease, prevents deaths and helps reduce spread of the disease.

In collaboration with Dr Stephen Howie at the MRC Laboratories in The Gambia, the team used 'shotgun' (bottom-up) proteomics to look for human proteins associated with tissue damage caused by another devastating disease, pneumonia. They analysed samples from children with severe and mild pneumonia, finding that the concentration of certain proteins correlated with disease severity. These biomarkers could potentially predict severe pneumonia and identify those patients who should receive antibiotics. Invasive pneumococcal disease in children causes life-threatening septicaemia, meningitis and pneumonia. Detecting these new biomarkers could be faster and more sensitive than traditional blood cultures to predict bloodstream infections. Bacterial culture-methods can take at least 24 hours, however rapid detection of these biomarkers could give a diagnosis within hours.

In sub-Saharan Africa, respiratory distress in children may be due to malaria or bacterial bloodstream infections. The team found that by comparing the levels of two different biomarkers it was possible to accurately distinguish pneumonia from malaria in these patients.

Isis has filed UK patent applications describing the newly identified malaria and pneumonia biomarkers and welcomes contact from companies interested in developing them as diagnostic tests.

Pneumonia

Respiratory infections are among the top four causes of morbidity and mortality worldwide, with pneumonia accounting for 2 million deaths every year in children younger than five. Prompt diagnosis is crucial not only in children, but in adult patients with immune-suppression, HIV or solid tumours and also in the frail and elderly.

Delayed diagnosis is an important risk factor for death in children with pneumonia and is hampered by the lack of specificity of respiratory symptoms, which are shared with other conditions causing respiratory distress (eg: viral infections, malaria).

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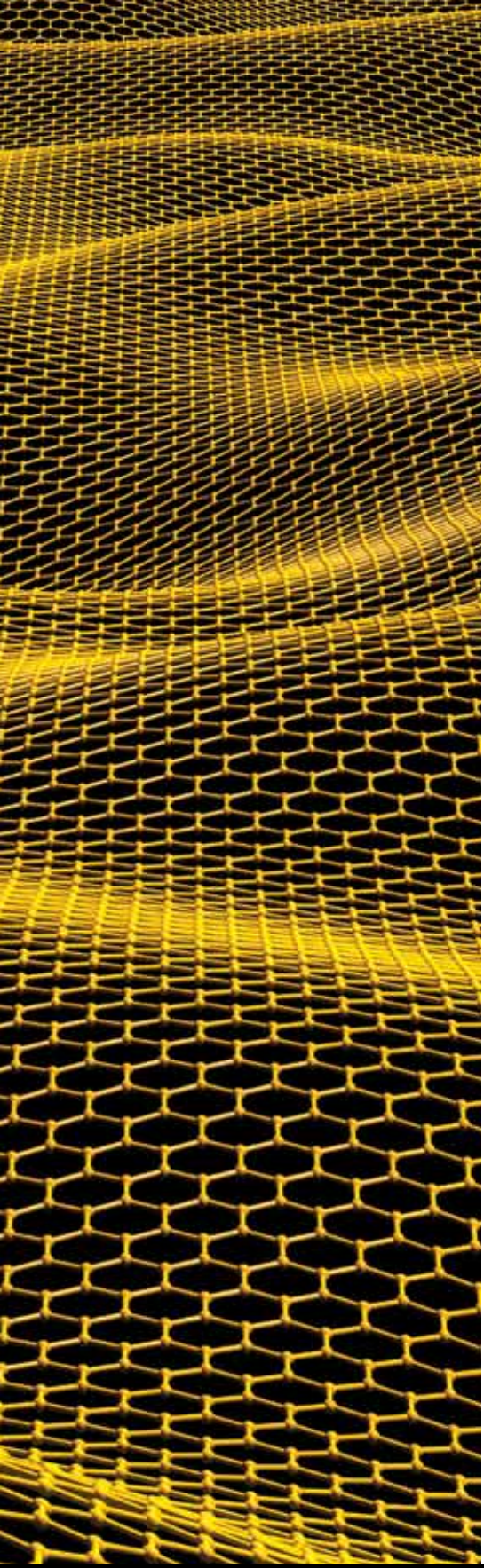

Up-scaling with nanomaterials

Chim Chu explains how two nanomaterial technologies from Oxford will exploit the potential of advanced materials like graphene.

Project 8336: Nanomaterial production analysis

A new system from Oxford will optimise and calibrate industrial scale production of nanomaterials and other analytes in chemical reactors. The invention permits monitoring of the chemical reaction in-situ, can reveal how the reaction is progressing in real time, and helps identify intermediates.

Quality control of commercial scale nanomaterial production is vital to successfully exploit the materials in future applications, for example as components in electronic devices, super-strong and lightweight composite materials, energy generation and biomedicine.

An analytical device developed at Oxford will enable quality-assured nanomaterials to be made faster, more cheaply and in commercial quantities, when used to control a manufacturing process within a range of reactors, such as those for chemical and physical vapour deposition (CVD & PVD). Mainstream industrial monitoring of production of analytes (gas, liquid, solid phases or mixtures) from drying, baking, and roasting ovens and refrigerators – from -100C to 1500C – is also possible when used with appropriate, commercially available instrument analysers.

Capabilities and features

Two working prototypes have enabled detailed analysis of a wide range of reaction chambers used for nanomaterials synthesis, and have been successfully tested with a quadrupole mass spectrometer (a highly-sensitive gas analyser). The device:

- Can collect any analyte from specific positions inside the reactors with minimal interference from the atmosphere and from reactions in the reactor.
- Enables control of the thermodynamic parameters of analytes (avoiding any alteration or modification such as breaking, binding and/or condensation) of collected molecules, ions or atoms as they transfer to the instrument.
- Can be made in a variety of shapes and sizes to fit particular applications.
- Has high mechanical, thermal and chemical stability in a wide range of extreme atmospheres.
- Is the subject of an international patent application with 35 claims.
- Is at Technology Readiness Level 3-4.

Isis insights

25

The latest innovations, collaborations and technology transfer

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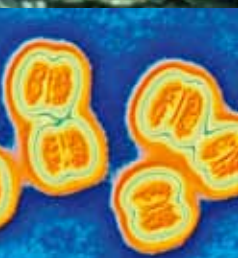
Isis INNOVATION











Twenty five
years of innovation

Isis Innovation was established by the University "to ensure that the results of research, having been adequately protected by way of patents, bring reward to the University and the inventors". Since then Isis has filed 1500 new patent applications on Oxford inventions, concluded 750 technology licence agreements with industry around the world and helped establish 80 new Oxford technology companies, which have raised in excess of £500m investment finance. Isis has also developed to provide many new activities to support the University, transferring technology and expertise to industry and society.

Tom Hockaday, Managing Director, Isis Innovation

"Isis was formed at a time when there were no established models of how to successfully commercialise university IP. We are incredibly proud to have been a trailblazer in this area, bringing the benefits of new technologies to society, contributing to the economy in raising investment and creating jobs, and playing a key role in establishing relationships between the University, industry, and investors."

Professor Andrew Hamilton, Vice-Chancellor, University of Oxford

"The University of Oxford, like all universities, thrives when it engages with society. Academic freedom to generate and develop new thinking drives progress, and tangible benefits from research are made accessible through commercialisation. Isis has been at the heart of this activity for Oxford for 25 years and its contribution to the University is highly valued and appreciated. Congratulations!"

Jonathan Flint, CEO, Oxford Instruments

"Isis has led the way in developing models of interaction between academia and industry, a major area of interest to innovative technology companies. The technologies that Isis has commercialised through licensing and spin-outs epitomise the sources of economic growth that are so important for the future, and its success has inspired other organisations both in the UK and abroad."

Professor Màrius Rubiralta Alcaniz, University of Barcelona

"In Spain we are proud of our world-class research and manufacturing capability. There is still huge potential for further growth through commercialisation of research and we have been delighted with the support that Isis has provided in developing new ventures."

Selected Activities

Some examples demonstrating the breadth of Isis activities and successes over the years

Oxford Innovation Society

The OIS allows companies to have a window on Oxford science and fosters links between academics, industry, professional services firms and government. Two hundred organisations have benefited from membership down the years, with the 70th meeting and dinner to be held at Keble College this September

Pre-natal testing

Safe, reliable, non-invasive prenatal tests have long been a holy grail in medicine. A new test developed at Oxford will require only a small blood sample to be provided by a pregnant woman. The test harnesses a discovery by Professors Dennis Lo and James Wainscott, who said, "We found a significant percentage of foetal DNA in the mother's blood plasma, up to 20 percent, and this can be used for a non-invasive test". Isis licensed the technology to US-based genetic analysis specialist Sequenom, which is making the test available via testing laboratories and health services in many countries worldwide.

Creative Spin-outs

NaturalMotion is a leading games and technology company based in Oxford, London, Brighton and San Francisco. The technology side of the business provides leading animation software engines: endorphin and euphoria. NM Games has recorded over 30 million game downloads to date. Isis helped develop the business plan and raise the finance to launch the company in 2001.

Auditing the Auditors

Oxford University Consulting, part of Isis since 2002, supports the UK Government's National Audit Office by providing expert reviewer services for the NAO Value for Money reports. OUC has managed the independent and objective review of over 200 NAO VfM reports over eight years, identifying Oxford academics to comment on the NAO reports.

Clean Energy

Isis helped set up Oxford Catalysts Group in 2005, having supported the commercial development of the technology for many years. The company is now regarded as the leading technology innovator for clean synthetic fuel production, designing, developing and commercialising technology for producing synthetic oil from waste gas, stranded gas, renewable sources such as waste biomass, as well as coal via Fischer-Tropsch (FT) synthesis – a potential market of 25 million barrels of fuel a day.

Beyond Oxford

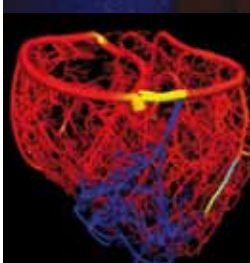
Isis now has staff in Hong Kong, China, Spain, Japan, Mexico and Australia promoting technology transfer from Oxford, investment into Oxford technologies, as well as providing platforms to connect global technologies, industry and investors.











ISIS MILESTONES

1988	Isis Innovation Ltd is formed
1990	Isis establishes Oxford Innovation Society
1990	Oxford University research funding at £47m (2012: £546m)
1991	Isis spin-out Oxford Molecular hosts visit from UK Prime Minister John Major
1994	Oxford wins The Queen's Anniversary Prize for higher and further education, for exploitation of intellectual property for wealth creation, citing Isis Innovation and the Oxford Innovation Society
1997	Isis files 100th patent application
1999	£4m Oxford University Challenge Seed Fund established
2000	Oxford and Isis sign £20m Chemistry IP deal with Beeson Gregory (now IP Group)
2002	Oxford University Consulting becomes part of Isis
2003	Oxford University Challenge Seed Fund awarded "UCSF of the Year'
2004	Isis Enterprise established to provide technology transfer expertise globally
2006	50th Meeting and Dinner of the Oxford Innovation Society
2008	Isis MD wins inaugural Science: Business Academic Enterprise Award
2009	Isis Innovation (Hong Kong) Ltd formed
2010	Oxford Invention Fund established
2011	Isis Software Incubator formed
2012	Spanish, Chinese and Japanese Offices established by Isis
2012	Oxford/Isis spin-outs (since 2000) raise over £500m total investment
2013	Isis sales income £11.5m in 25th anniversary year

GLOBAL MILESTONES

1988	Copyright, Designs and Patents Act
1990	Hubble space telescope launched
1991	First website created at CERN, Internet begins
1992	European Union formed by The Maastricht Treaty
1994	Channel Tunnel open to traffic linking UK to France
1995	First item sold on Amazon.com
1996	Scientists in Scotland clone a sheep (named Dolly the Sheep)
1998	Google search engine launched
1999	First circumnavigation of the earth in a hot-air balloon (Bertrand Piccard and Brian Jones)
2000	Millennium celebrations postponed due to widespread computer failures (only joking)
2001	First draft of the complete human genome published in Nature
2002	Euro currency launched, adopted by 12 major countries in Europe (not UK)
2003	Last commercial flight of Concorde
2004	Ireland becomes first country in the world to ban smoking in public places
2005	Kyoto Protocol on climate change came into force
2008	Global Financial Crisis, Lehman Brothers declares bankrupcy
2010	Iceland volcano Eyjafjallajökull erupts closing European airspace for 6 days
2010	Burmese pro-democracy campaigner Aung San Suu Kyi released from arrest; collects her Oxford honorary degree in 2012
2012	London hosts the Olympic Games and the Paralympic Games

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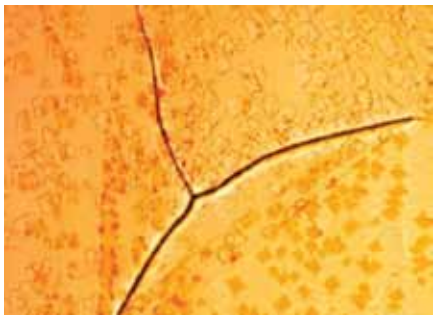
UNIVERSITY OF OXFORD

ISIS INNOVATION

Glass image:Dr Stephen Hicks Catalysts image:Oxford Catalysts Racing car image: Jakob Ebrey Photography

While substantial investments are being made into researching graphene properties, it must be commercially available in affordable, quality-assured quantities for full exploitation of its properties in emerging applications

Project 8727: Graphene manufacture technique



Optical micrograph showing graphene domains formed across grain boundaries

A commercial process for producing graphene and other 2D nanomaterials by chemical vapour deposition (CVD) using cheap copper foil has been devised at Oxford. The invention enables the growth of large sheets of defect-free CVD graphene on relatively cheap copper foils, making CVD an ideal off-the-shelf technique for industrial-scale production.

Graphene – a one atom thick carbon layer – has promising potential for many applications in the energy and health care sectors. "While substantial investments are being made into researching graphene properties, it has to be made commercially available in affordable, quality-assured quantities, in order to fully exploit its properties in emerging applications" says Professor Nicole Grobert, leading the team behind the research in the Department of Materials.

Existing processes for producing large-area CVD graphene films suffer from the many small flakes (domains) that are randomly oriented on the copper surface, giving grain boundaries in the graphene sheet which reduce its mechanical strength and degrade its electrical properties. Oxford's technique overcomes this limitation by controlling the crystallographic orientation of the copper substrates and aligning the flakes. By varying the pressure during growth it is possible to selectively grow single-layer graphene domains or bilayer domains of graphene (a double layer of carbon atoms which display unique properties for electrical applications). This technique also represents an important tool in manufacturing process innovation for general nanomaterial application development.

Readiness for market

Initially the subject of a UK patent application with 29 claims, the Technology Readiness Level is rated at TRL 2. Development of the process is supported by a multinational materials measurement equipment maker using reference source materials produced from the invention.

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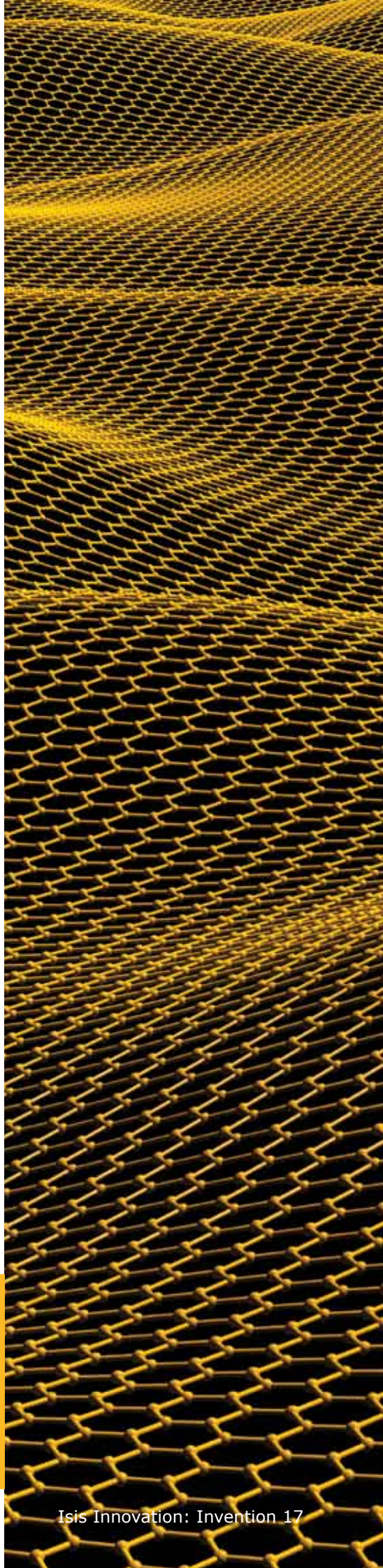


Careful probing

A novel probe sheath conceived by surgical clinicians at the Oxford University Hospitals NHS Trust makes viable the routine use of intra-cardiac echo (ICE) probes in interventional heart surgery procedures. **Dr Louis Pymar** explores the impact the invention will have on patients and the NHS.

Oxford's ultrasound probe sheath will allow for Intra-cardiac echo (ICE) probes to be both safely positioned and re-used. Currently, ICE probes are discarded after a single use. In using a sheathing device the sterility of the probe is maintained, making it possible to re-use the expensive hardware whilst discarding only the inexpensive sheath.

The cost of a single 2D ICE probe, of the sort in clinical use across the NHS, is approximately £1,500. By using the Oxford invention, a hospital performing ICE procedures on 5-10 patients per week would save over £400,000 a year in ICE probe costs alone.

A growing medical need

Ultrasound probes are increasingly used in cardiac intervention procedures, including procedures for the treatment of coronary artery disease and heart defects, and preventative measures guarding against stroke and heart attack.

A widely used alternative to intra-cardiac echocardiography (ICE) is trans-oesophageal echocardiography (TOE), which involves the placement of an ultrasound probe into the patient's oesophagus for imaging of the heart. This procedure requires a team of medical personnel including three anaesthetists and causes discomfort and procedural stress to patients. ICE avoids these disadvantages whilst also providing clearer images and shorter procedural times. However, the principle disadvantage of ICE is the cost of ICE probes, which limits widespread adoption of ICE as a routine procedure by healthcare providers.

Intelligent by design

The sheath concept has been progressed in partnership with an independent clinical design team. The resulting prototype includes a number of unique enabling features, refined over the course of an iterative design process, and is now the subject of a patent application. Whilst conceptually simple, the sheath will improve patient experiences and health outcomes by making the positioning of the ICE probe safer, as well as increasing the availability of ICE procedures to more patients.

Next generation 3D ICE probes promise to deliver enhanced imaging quality and so are expected to cost significantly more. It is anticipated that use of the novel probe sheath will facilitate the routine use of such

Whilst conceptually simple, the sheath will improve patient experiences and health outcomes

probes, by removing the cost burden to healthcare budget holders.

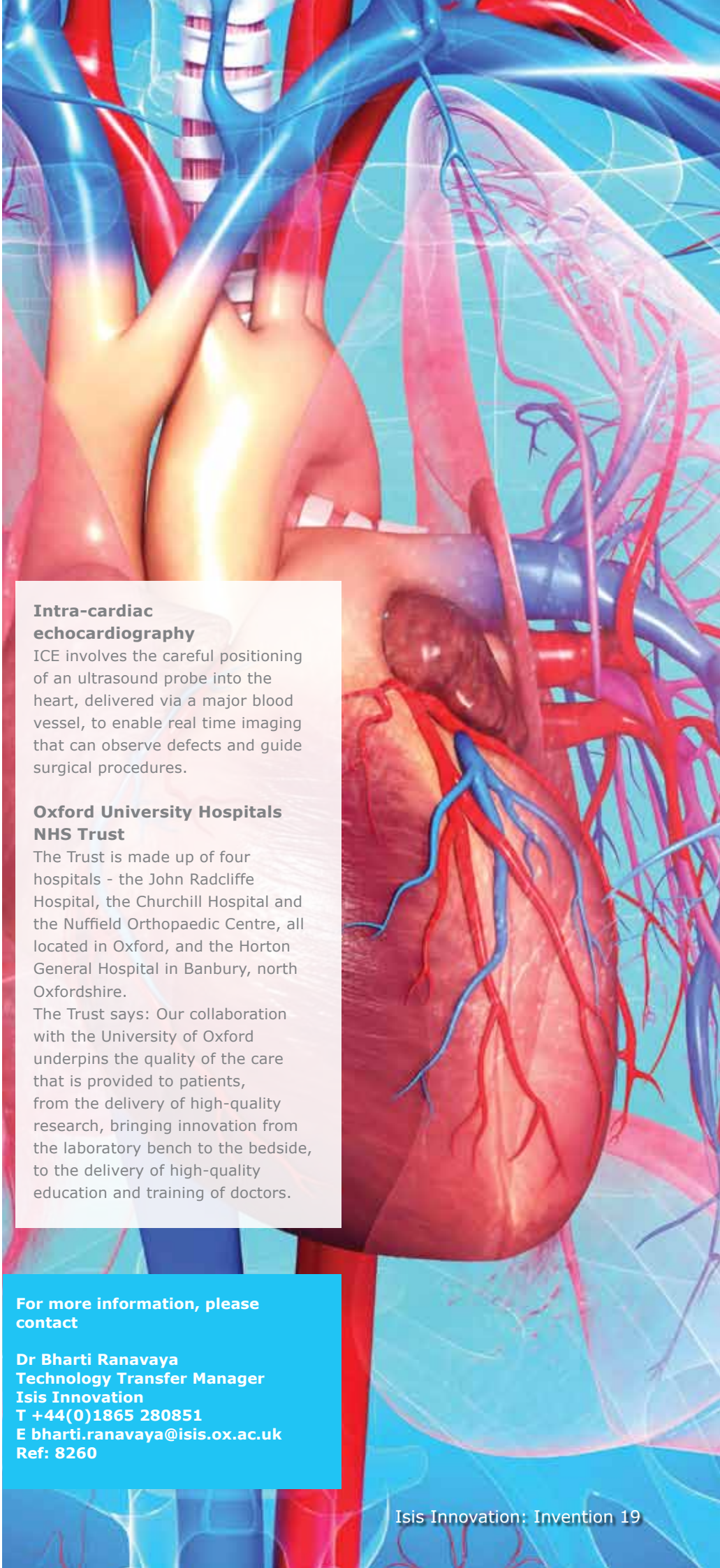
Innovation in practice

The idea of using a sheath for an ICE procedure was borne out of the necessity of treating a patient with a medical complication that made a traditional TOE procedure impossible. In this case it was necessary to deliver the ICE probe into the heart via delicate valve structures to image the left atrium, and to allow the surgical team to implant a device to reduce the patient's risk of suffering from stroke.

By first positioning an improvised flexible sheath into the heart, it was shown that the relatively inflexible ICE probe could be easily and safely delivered to the heart via the sheath, with no risk of causing damage, and with no detrimental effect on the quality of image acquired.

A new healthcare innovation pathway

This invention, conceived entirely by NHS clinicians, is being managed by Isis Innovation following a 2011 agreement which paved the way for all inventions from the Oxford University Hospitals NHS Trust to be commercialised by Isis. Isis is now inviting interest from medical technology companies to support full clinical and commercial development of the sheath.



Intra-cardiac echocardiography

ICE involves the careful positioning of an ultrasound probe into the heart, delivered via a major blood vessel, to enable real time imaging that can observe defects and guide surgical procedures.

Oxford University Hospitals NHS Trust

The Trust is made up of four hospitals - the John Radcliffe Hospital, the Churchill Hospital and the Nuffield Orthopaedic Centre, all located in Oxford, and the Horton General Hospital in Banbury, north Oxfordshire.

The Trust says: Our collaboration with the University of Oxford underpins the quality of the care that is provided to patients, from the delivery of high-quality research, bringing innovation from the laboratory bench to the bedside, to the delivery of high-quality education and training of doctors.

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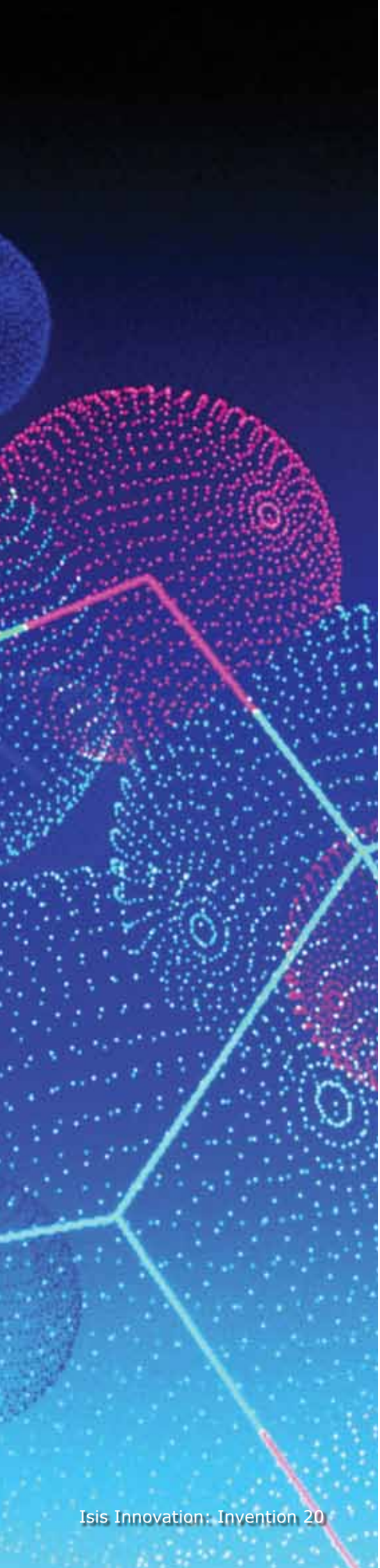


Diabetes – the patient's perspective

Dr David Churchman introduces a diabetes questionnaire – a Patient Reported Outcome measure – for recording the efficacy of care.

Patient Reported Outcome (PRO) measures are rapidly gaining recognition as essential tools for measuring the effectiveness of diverse health care interventions. Condition-specific PROs for diabetes provide meaningful insight from the patient's perspective on their Health Related Quality of Life (HRQoL) relating to their diabetes. They offer a depth of understanding to study investigators of the practical efficacy of treatments, over and above that offered by a simple physiological blood glucose test. One such measurement tool is the Diabetes Health Profile (DHP), now available from Isis Outcomes.

The Diabetes Health Profile (DHP)

The DHP is a scientifically robust diabetes-specific PRO developed to evaluate the psychological and eating behaviour of people living with Type-1 and Type-2 diabetes. Developed using a multi-method process, including significant patient input consistent with industry best practice, the DHP is available as either a specific 32-item measure for use with insulin-dependent and insulin-requiring patients (DHP-1) or as an 18-item measure (DHP-18) for use across all treatment groups including insulin-dependent, insulin-requiring, oral and diet. The DHP has demonstrated highly satisfactory performance and psychometric qualities including reliability, and content and construct validity across a range of settings.

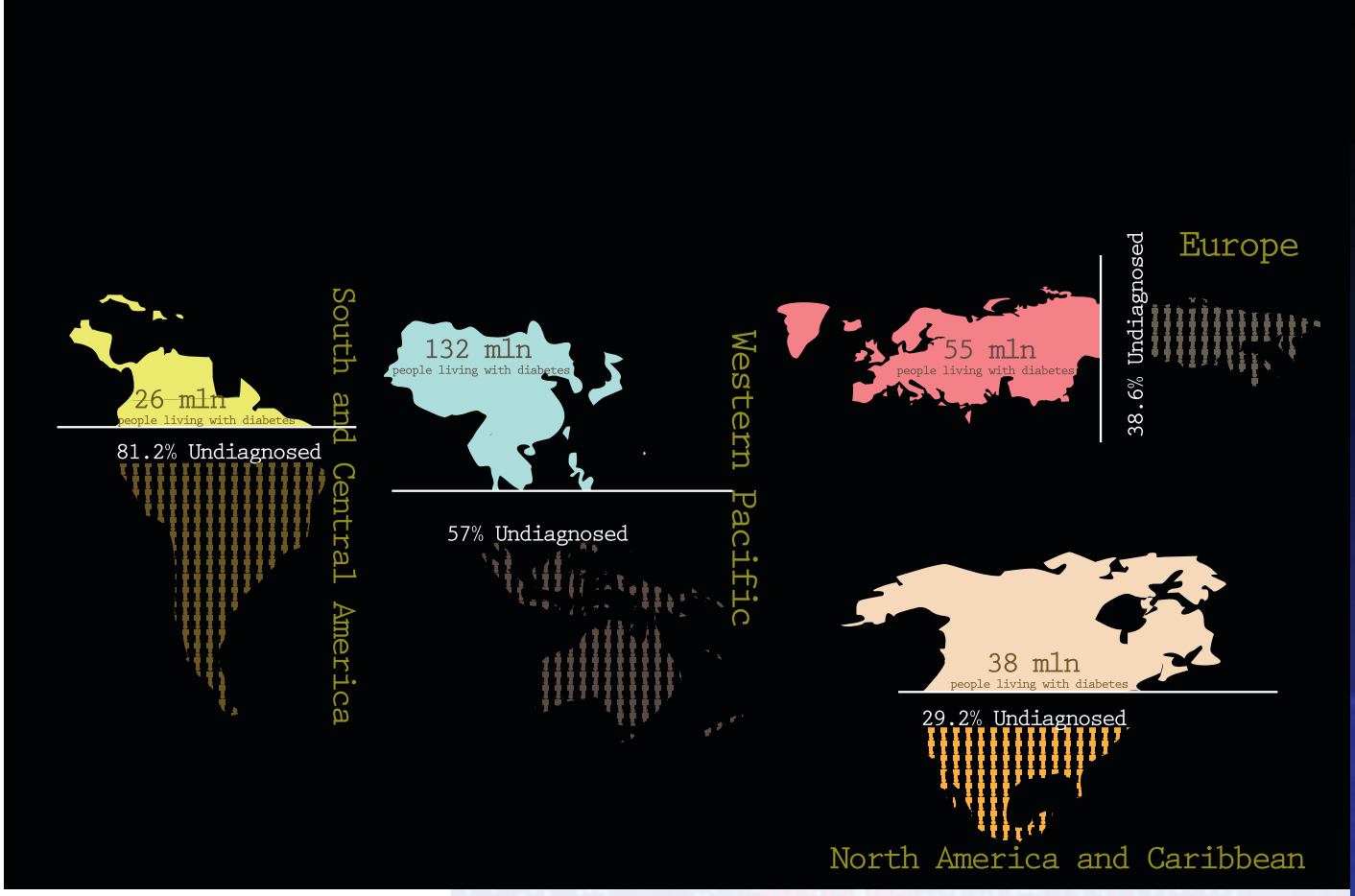
The DHP was developed to be applicable for use across a range of study settings, including drug development and the evaluation of clinical interventions, and measures those aspects of living with diabetes considered most important to patients. Based on a conceptual model, the DHP measures three HRQoL domains: psychological distress, barriers to activities, and disinhibited eating.

Benefits of the DHP

- Comprises three dimensions: psychological distress; barriers to activity; disinhibited eating – which, despite its importance in the management of diabetes, is not included in other diabetes-specific PROs
- Easy to use – is short and simple in format so that it can be widely used and results in high response and completion rates
- Relevant content, highly acceptable to patients
- Applicable in a range of clinical and population settings including screening for unmet need, assessing treatment effectiveness and for intervention programmes
- Available in 29 different language versions
- Expert advice available from the developer of the DHP on all aspects of using the DHP

The DHP has been widely deployed, to over 10,000 diabetic patients, including in many international studies. The DHP has also been recently adopted by the Department

The DHP measures those aspects of living with diabetes considered most important to patients



of Health in the UK for the second generation NHS PROMs programme, and will be used to assess health outcomes of diabetes sufferers treated throughout the NHS.

Possible uses

- Evaluating health improvement and psychological and behavioural outcomes
- Diabetic population monitoring
- Evaluating health programmes
- Evaluating treatment effectiveness
- Enhancing doctor-patient communication

Available for licence

The DHP is now available for licence from Isis Outcomes, a business activity within the technology transfer group at Isis Innovation. Isis Outcomes has exclusive rights to market and licence the DHP. Extensive support in the use of the DHP is available from Isis Outcomes.

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Diabetes demographics

According to the World Health Organisation (WHO), diabetes is predicted to become the seventh leading cause of death in the world by the year 2030. It has rapidly become a global epidemic, affecting more than 347 million people, forecasted to increase to 438 million within the next two decades. In North America and the Caribbean, one in nine adults suffers from diabetes, whilst in the Western Pacific one in three adults are affected by the disease. In the UK alone 2.9 million people were diagnosed with diabetes in 2011.

Long-term health complications linked to diabetes often include heart disease, kidney failure, neuropathy (damage to the nervous system) and retinopathy (blindness caused by damage to the small blood vessels of the retina). Alongside these physical health problems, diabetes can also have an adverse effect on the patient's psychological and emotional well-being, impacting social activity and behaviours.

Rheumatoid Arthritis Diagnostic

Dr Richard Reschen explains how a new biomarker discovered at the world-renowned Kennedy Institute of Rheumatology may help to identify patients who suffer from a particularly severe form of Rheumatoid Arthritis (RA), enabling these patients to receive earlier treatment with appropriate medicines.

A range of drugs is now available to treat RA, with the most commonly used ones being methotrexate or one of the numerous TNF-α inhibitors. Unfortunately around 40 percent of RA patients do not benefit from these therapies and require different treatments (e.g. anti-IL-1 antibodies or B-cell depletion). Existing biomarkers for RA – such as Rheumatoid factor and CCP –do not allow doctors to predict which patients will fail to respond to methotrexate/ anti-TNF-α drugs, meaning that these patients may go on to suffer joint damage. Many of these patients have a particularly severe form of RA known as Erosive RA, which leads to extensive joint destruction.

Tenascin C – a potential biomarker for Erosive RA

TNC is a protein that is not normally expressed in healthy adults, but which is induced upon tissue damage, where it drives the repair response. During normal tissue repair, levels of TNC are downregulated after repair is complete.

Oxford's researchers have found that circulating TNC levels are consistently higher in patients with inflammatory diseases such as RA, when compared to healthy controls. The researchers also found that higher levels of TNC were specifically associated with higher levels of joint erosion. This is the first time that a biomarker has been specifically linked to joint erosion. Further studies are now needed to confirm the exciting possibility that TNC levels in early disease may be predictive of the development of severe Erosive RA, when used in combination with other biomarkers that are specific for RA.

TNC would be an ideal component of a biomarker panel for RA diagnosis, as it can be easily monitored in serum samples using standard ELISA assays*, making it straightforward and cost-effective to test for. The test could be easily incorporated into existing systems used in hospital laboratories.

The Oxford researchers found that higher levels of TNC were specifically associated with higher levels of joint erosion

** ELISA assays: Enzyme-linked immunosorbent assays are tests that use antibodies and colour changes to identify substances.*

Tenascin C levels may predict drug response

Many patients do not respond well to anti-TNF drugs, a mainstay of RA treatment. Oxford's researchers have found that patients who have high levels of TNC before they start treatment with an anti-TNF inhibitor are more likely to have unresolved joint problems one year after treatment. This suggests that high levels of TNC may be predictive of a poor response to anti-TNF drugs. Again, further studies in larger patient cohorts will be needed to confirm this finding. If larger clinical studies support this, it could greatly improve RA treatment by allowing patients to be stratified according to the likely severity of their disease, informing clinical decision making as to which drug is appropriate for that patient.

Technology and patent status

This technology has been tested in cohorts of RA patients. Funding is currently being sought to undertake larger studies and to assess the predictive value of this marker in patients with early RA or even before disease onset. This discovery is subject to an international PCT patent application, and Isis would like to hear from companies who wish to license this technology for further development or engage in collaborative research.

Rheumatoid Arthritis

Rheumatoid Arthritis (RA) is a progressive autoimmune disease which affects around one percent of the world's population. It results when the body's immune system attacks the membrane (synovium) surrounding the joints, resulting in swelling as well as subsequent tissue and cartilage destruction. RA can cause intense pain and progressive disability as joints become fused or stiff. In some cases RA can also affect other areas of the body, such as the membranes around the heart and lungs. Early treatment is recommended as soon as symptoms appear, in order to prevent joint destruction.

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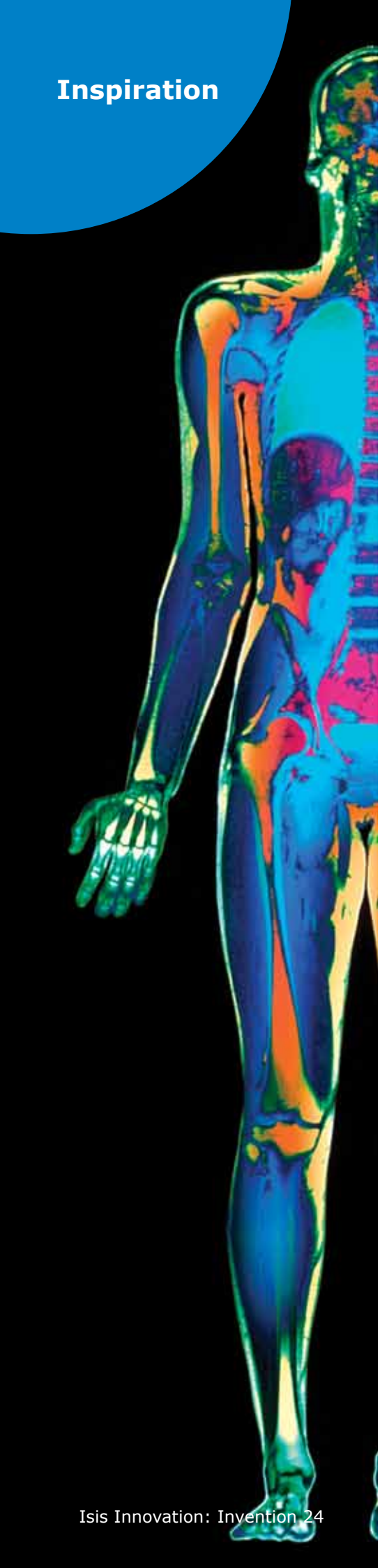

Imaging with GlaxoSmithKline

Working through Oxford University Consulting, leading academics from the University of Oxford have been supporting the Global Imaging Unit at GlaxoSmithKline (GSK), providing them with expertise across multiple imaging disciplines. **Dr Josef Walker** introduces the protagonists and highlights the outputs from a successful, on-going collaboration.

Clinical imaging has a key role to play in shaping the way in which new medicines are developed by providing non-invasive methods to understand disease and its response to therapy. As one of the world's leading research-based pharmaceutical companies, GSK is a strategic innovator in clinical imaging and seeks to apply such tools to areas such as cancer, inflammation and neuroscience. GSK has invested significantly in imaging sciences through key collaborations to access the diverse expertise required across methods and areas of application.

Regardless of the disease setting, optimising the MRI methodology used to generate clinical images forms the fundamental foundations for all subsequent analyses. Peter Jezzard is Professor of Neuroimaging at Oxford's Functional Magnetic Resonance Imaging of the Brain (FMRIB) Centre and a world-expert on MRI physics and the development of new imaging techniques for yielding information on the human brain. Through consultancy arrangements, GSK have benefitted from Professor Jezzard's expertise for improving imaging processes for neurological applications.

Once imaging has been performed, generating images and deriving meaningful data from them so that clinical assessments of the patient can be made presents a unique set of challenges. Stephen Smith, Professor of Biomedical Engineering and Associate Director of FMRIB, leads the FMRIB analysis group who research new methodologies for the analysis of functional and structural brain imaging data such as being able to segment brain images into different tissue types. GSK has worked with Professor Smith to improve study designs that involve a functional MRI component and develop strategy across multiple programmes.

Continuing the image analysis theme, GSK's imaging group is also working with Alison Noble, Professor of Biomedical Engineering at Oxford's Institute for Biomedical Engineering. As the Director of the Biomedical Image Analysis Laboratory, Professor Noble leads multi-disciplinary research across varied areas of human health and the development of new imaging techniques including the improvement of ultrasound as a clinical imaging modality. Image analysis tools are vital to ensure imaging methods are translated into quantitative, decision-making tools. The GSK imaging team is consulting with Professor Noble to

Working with the researchers in GSK's Global Imaging Unit is a very positive interaction, not least due to their strong belief in fundamental science, and a valuable opportunity to create additional impact in human health

ensure awareness of novel imaging analysis methods, informing their strategy and guiding best practice.

In addition to optimising scanning methods and image analysis techniques, there is great scope in the development and application of novel molecular imaging probes (particularly for PET). In this respect, the GSK imaging team has sought the expertise of Professor Ben Davis from the Department of Chemistry – a world-expert in chemical biology with active research in labelling strategies for smart imaging agents.

"The area of molecular probes for clinical imaging is an exciting field and understanding the fundamental chemistry and biology that underpins them is critical," Professor Davis said.

"Working with the researchers in GSK's Global Imaging Unit is a very positive interaction, not least due to their strong belief in fundamental science, and a valuable opportunity to create additional impact in human health."

At GSK, the potential for applying innovative clinical imaging across multiple disciplines is recognised amongst its priority areas for collaborative research.

"Clinical imaging forms a key part of our strategy to support R&D programmes," said Dr Philip Murphy, Senior Director and Head of GSK's Global Imaging Unit. "We are exploring how to better integrate these approaches to increase success in new drug development, ensuring the delivery of innovative medicine. Access to these expert consultants provides a valuable adjunct to our internal knowledge-base, allowing us to access the right expertise when we need it as well as helping us to build important networks with leading academics for future research projects."

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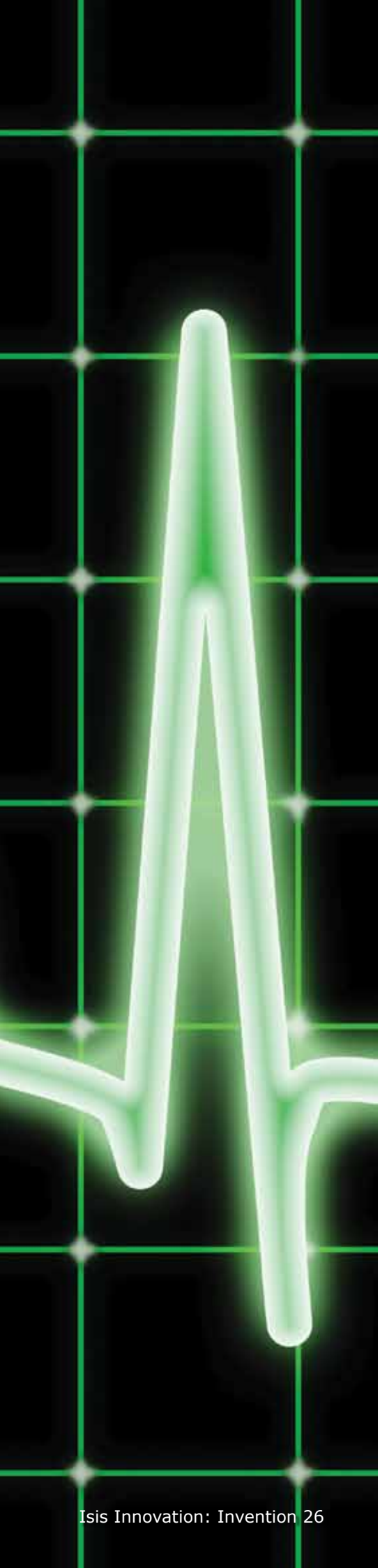

Cardio conclusion

Isis Enterprise's **Dr Wenming Ji** tells the story of the novel cardio disease screening technology that is set to underpin the formation of two new companies this summer.

Isis Enterprise, working with the Ukrainian academic founders, recently reached Heads of Terms with private Chinese financiers in a deal that will see two companies formed for the commercialisation of unique, non-invasive cardiac screening technology. With the investors injecting £2m in return for an equity position, one company will be registered in the UK to hold the IP and commercialise Cardiomox technology for the European market, and the other will be incorporated in China to commercialise and supply the Asian markets under licence.

How the technology works

Cardiomox represents a first level diagnostic tool for the initial evaluation of patients at risk of cardiac disease or defects. The technology allows detection of serious cardiac disease such as ischemia, arrhythmias and defects that may not be detected by electrocardiograms (ECG). Cardiomox offers visualisation of the electrophysiological state of the myocardium.

MCG is the imaging of the magnetic field generated by the heart, specifically from the electric impulses created by the sinoatrial node that triggers contraction of the heart. This happens through the use of extremely sensitive devices – a Superconducting Quantum Interference Device (SQUID) and an Inverse Problem Solution – and advanced mathematical algorithms. All of these, when combined, enable the software to map the current density vectors by region and time.

The Cardiomox technology enables MCG measurements to be recorded during the depolarisation and repolarisation processes, mapping the direction and density of the flow of ions relative to spatial-temporal distribution in order to identify abnormalities. MCG uses multichannel sensors to measure the magnetic field and creates a map of the magnetic field over the chest, drawing conclusions and taking from mathematical algorithms that account for the conductivity structure of the torso. This makes it possible to locate the source of the activity.

Accurate screening

Cardiomox MCG is not a replacement for ECG but rather a complementary technology to make first level cardiac screening more accurate and efficient. Because of its low cost, ease of use and rapid scan time, there is a need and strong economic justification for Cardiomox scanning capability

Cardiomox MCG is not a replacement for ECG but rather a complementary technology to make first level cardiac screening more accurate and efficient

to be present in every hospital and community health clinic. Cardiomox MCG scanning will reduce the number of invasive and expensive next level diagnostic procedures by providing more accurate initial cardiac screening. The Cardiomox system saves money and saves lives by preventing, through early diagnosis, a significant percentage of sudden cardiac events. The emergency and critical care provision for these events is a major expense incurred by healthcare systems.

Global solution

It is estimated that China will have 32 million heart disease patients in 2013, with the costs incurred totalling up to CNY 327.6 billion. The death rates from myocardial infarction (MI) during the same period could reach 719,000, while 1.8 million lives could be lost from all heart disease.

There is the potential for Cardiomox MCG to be adopted as a standard clinical screening procedure in the UK, Europe, China, North America and the rest of the world. This should rapidly develop into a market of hundreds of systems per year for the foreseeable future.

International business model

International technology transfer brings with it many challenges, but the lessons learned from this venture may well be harnessed when realising the formation of further international companies in the future. It took many years for this research to progress to Heads of Terms, but the final outputs and patient benefit more than justify the journey.

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Oxford Innovation Society

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

- Wednesday 18 September 2013
- Thursday 5 December 2013
- Thursday 20th March 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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