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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Isis insights

Issue 68 Summer 12

Sight for the blind

Also inside: Proteomics, Dengue developments, Intellectual Property workshops

The latest innovations, collaborations and technology transfer

ISIS INNOVATION

Issue 68

Sight for the blind

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Dengue discovery
Vaccine within reach

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

Cover image: CAD drawing of Oxford's bionic glasses, offering augmented sight through stereo cameras (see p12)

ISIS INNOVATION

Newsflash

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

Global reach

Isis is becoming well-established in China, having attracted funding for spin-out companies from Chinese investors and having won contracts for consultancy and management of a Bioincubator in Jiangsu Province. Following a visit to Oxford from a high-level delegation led by the Mayor of Changzhou City in March, the "2012 Changzhou Industry-University-Institute Cooperation Contribution Award" was recently presented to Isis in recognition of the successful collaborative work with Changzhou government and companies over several years.

Isis Angels Network

The recent IAN Event in April showcased four new companies from Oxford. With a keynote speech from Professor Geoff Hale of BioAnalab and sponsored by James Cowper, the event drew attendees from investor and professional services communities to meet the founders of companies including 'Smart Specs' (see cover story on p12 for more on the bionic glasses).

Oxford test for statins risk launched in US

The benefits of taking cholesterol-lowering statins are frequently discussed. However, there is an associated risk, for some users, of developing myopathy: muscle aches, spasms and pain. This condition can be extremely unpleasant and, for some, completely debilitating. Boston Heart Diagnostics recently licensed a diagnostic test from Isis, developed from work in Oxford's Clinical Trials Services Unit, and has now launched it in the US market. Isis has filed patents covering the test in several other territories and is seeking partners to develop the diagnostic method in the UK and other countries.

Wired

"Are the Dreaming Spires becoming Silicon Spires?" asked wired.co.uk in April. Featuring spin-out and start-up companies from Oxford, an article highlighted ten exciting and successful technologies that have come from Oxford. The downside? "Undergraduates and foreign language students will continue to have to fight entrepreneurs for their seats in Starbucks" according to Wired.
http://www.wired.co.uk/news/archive/2012-04/24/silicon-spires

Images, top to bottom: Changzhou signing ceremony, IAN speaker Professor Geoff Hale, the Multi Spectral Scanner as featured in Wired.

Enterprising Consultancy

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

Extracting value from hot air

Tomsk oil field

A commercially viable method for utilising associated petroleum gas (APG) found in small, remote oil wells has been established in Siberia. As part of Isis Enterprise's continued efforts to support the international commercialisation of technologies from the Tomsk and Novosibirsk regions, we are actively seeking co-development partners and licensees for this technology.

APG, a form of natural gas worth £24billion a year at today's prices, is a common by-product of oil production. Unfortunately the remote nature of many oil reservoirs means it is not feasible to bring in specialised equipment to tap and transport the APG as a secondary product, and so instead the gas is 'flared' or burnt off. Russia flares about £7.5billion of APG annually. The loss in potential revenues and contribution to global warming has prompted the Russian government to sponsor development of technologies offering a solution.

One such technology is a piston-cylinder reaction chamber with crystalline aluminium oxide coating. This coating, which is formed by Plasma Electrolytic Oxidation (PEO), is tough, durable, has a low coefficient of friction and protects the reaction chamber from the extreme conditions required by the reaction process i.e. 100bar and 3000°C.

It is these conditions that allow for a single-stage conversion of APG to longer chain hydrocarbons (as opposed to the traditional, complicated and more expensive two-stage catalytic approach). These can be transported and stored more easily than APG, allowing the by-product to be commoditised rather than flared.

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Childcare research

The National Day Nurseries Association (NDNA) has renewed its engagement with Professor Kathy Sylva (OBE) of the University of Oxford's Department of Education through Oxford University Consulting.

Professor Sylva, who is also a voluntary member of the National Policy Committee and Educational Advisor to the NDNA, will continue to develop the NDNA's research expertise.

The Educational Psychology Professor will be involved in supporting a project entitled 'Exploring barriers and opportunities for parental engagement in childcare settings', which aims to identify best practice in nurseries and highlight innovative methods to engage families.

Professor Sylva said, "This project provides an ideal opportunity to capture the expertise of those at the frontline of the sector, feeding into further research and informing future improvement guidance for nurseries."

NDNA
PROMOTING QUALITY IN EARLY YEARS

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The portfolio

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

Social media goes tribal

"We don't need to know who you are, just where you are and what your interest is in that location," explains Selwyn Lloyd, CEO of Oxgeos, an original social media start-up conceived at the University of Oxford. "Your interest might be the local cricket team or your college. We differ from other social platforms because each group, club etc gets its very own app."

The company's geo-social technology will be provided in Oxford initially, after a dedicated app was created for University colleges. College members will be able to interact in a dedicated social scene that matches them with other users based on a shared affiliation. Even when they are not in Oxford, college members will be able to view content and people related to their college, far and wide. In fact, the range is up to them.

While dominant social media giants are battling for the minds of friends, work colleagues and family, Oxgeos has set out to win the loyalty of users with strong affiliations to their real world activities in partnership with their real world clubs, passions and other social interests.

"It's this ability to partner location-based brands to forge more meaningful social networks that really counts for us," says Lloyd.

Oxgeos believe they have identified a game changing opportunity in geo-social technology. When you pin location-sensitive advertising to 21st century tribalistic social identities, consumers are not merely satisfied, they become enthusiastic ambassadors, it is claimed.

Oxgeos is one of a number of software ventures receiving support through the Isis Software Incubator

In return for their daily banter, sharing and participation in location based ads, the fans' or members' subjects of interest are paid advertising royalties. The users, meanwhile, receive timely offers, discounts and other perks via the Oxgeos app.

Football is one of four channels being prototyped in Oxford colleges and Oxgeos is building multidisciplinary teams to execute this.

The Oxgeos mission is to create social currency and to be the first choice platform for geo-social engagement applications and technology. We want to add value both to end user consumers and to supplier advertisers via fun, interactive products and services.

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Triteq

In just 20 years Oxford Innovation Society member **Triteq** has grown to become one of the UK's best known medical product design and development companies. Technical Director Ken Hall tells the Triteq story.

Creativity, innovation and technology are areas frequently cited as key drivers for economic growth in the private sector. These same ingredients also represent the core elements that underpin what Triteq stands for. A glance at Triteq's portfolio underlines its ability to work across an extensive range of projects, whilst maximising on collaboration and knowledge exchange. This occurs both internally and externally, through interaction with global partners and clients.
Jackie Berry and Steve Lane founded Triteq in 1992 with a shared understanding that skills, experience and commercial reality bring success. They have subsequently achieved uninterrupted, sustainable and responsible growth, with ongoing investment in building a talented team.

The duo began working in the medical product market early on in the company's development and since then Triteq has established an enviable track record for taking concept development through each stage of the product life cycle and all the way through to various competitive and demanding markets.

Emerging trends and technologies

Strategic product designer Joseph O'Connor joined the company and was tasked with building an in-house design team to support clients through all stages of product development. Understanding behavioural changes ensures that a client's product provides not just what its target audience needs today, but what it will be looking for tomorrow.

The team excels at listening to client ideas and developing strategies to bring products to life. Intelligent design brings multiple benefits to millions of people and Triteq attributes its success to applying a clearly defined focus to each client's vision, aware of the potential to help create tomorrow's life changing product. Our extensive experience in identifying opportunities and risks early adds value and commercial reality to early stage projects and increases intellectual property value. Triteq has streamlined the product development roadmap from initial concept definition to gaining approvals, reducing development timescales and costs whilst retaining quality and innovation. When the practise of incorporating data into healthcare products began to accelerate, Triteq was already involved in a number of projects in this field. Now, telemedicine and mobile health has become a clearly defined strategy adopted by healthcare companies, the telecoms industry and health connected organisations, all eager to increase market share by giving

Understanding behavioural changes ensures that a client's product provides not just what its target audience needs today, but what it will be looking for tomorrow.

consumers the option to manage their lives more effectively. Triteq is rapidly becoming expert in this area and is currently engaged in projects in monitoring, measuring and tracking devices and communications using near field, 3G, Bluetooth, GPS, GSM, RFID and Zigbee.

Choosing a partner

Triteq brings skills, knowledge and experience to every project and has the proven ability to fulfil varying requirements for clients from start-ups looking to bring exciting new projects to market to large corporations looking for intelligent partnerships to work with them on demanding and technically challenging propositions.

All of Triteq's teams engage in external learning opportunities to ensure trends and emerging technologies are incorporated into its working methods. The AP@home project is a good example of Triteq's cooperative working processes. It forms a key part of the consortium which is bringing together world-leading experts in the fields of diabetic medical device development, clinical researchers and modelling and control algorithm experts, including seven academic partners. Pushing the boundaries of current technologies using an automated closed loop software algorithm, continuous glucose monitor (CGM) and a continuous subcutaneous insulin infusion (CSII) could help many thousands of diabetes patients around the world lead improved lives by providing an artificial pancreas. www.ap@home.eu

Quality assurance

Wishing to give external reassurance to clients as to Triteq's rigorous working methods resulted in the devising of a process and system of working which received ISO13485 and ISO9001 approval. Medical approval and regulatory standards are stringent and achievement of these standards is a clear demonstration of the exacting standards that Triteq works to. Awareness of new standards is vital to quality management. IEC62034 is a recently introduced regulation for developing medical device software; Triteq prepared for the introduction in advance and were invited by EMDT magazine to explain the new classification and help other organisations assess the impact on their work.

"The IEC62034 safety classification has a tremendous impact on the code development process. It is therefore in the interests of medical device manufacturers to get this right the first time to avoid expensive, time-consuming rework late in a project." Ken Hall, Triteq Technical Director in EMDT magazine 2010

Image: Technicians weaving medical product

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

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

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

Manufacturing with droplets

Speaking at the Oxford Innovation Society meeting in March, **Professor Patrick Grant** explained how new materials with previously unattainable properties can be made from spray-formed droplets.

Professor Grant is Cookson Professor of Materials in the Department of Materials at Oxford University. A materials scientist, his work focuses on manipulating the structure of materials in order to control their properties. The real-world problems his group addresses have led to industrial collaborations with leading companies worldwide.

Industrial uses for droplets and sprays cover an enormous range – from ink-jet printing to spraying concrete on tunnel walls. The process is common to all, albeit with eight orders of magnitude difference in the flow rate. Each starts with atomisation of a fluid, produces droplets that are accelerated and heated (or cooled), and concludes with the collection or deposition of material to form the final product.

The droplets formed can be directed accurately and with a controlled flow rate. Because they can be directed only where they are needed, complex shapes can be formed and scarce materials conserved. Droplets, with their inherently high surface area to volume ratio, cool, heat or react very efficiently. The engineering challenge is to control and manipulate their transition from liquid to solid form so that, for example, useful elements that would not naturally combine can be alloyed into structures under controlled conditions. New materials can also be created by applying and mixing different droplets layer by layer. The process suits applications that must meet critical performance standards - coatings to create insulating ceramic components in jet engines, for example, or synthetic bone for hip replacements. The manufacturing cost is inevitably higher than that of conventionally produced materials, and so practical applications for droplet technologies are those where some or all of the special features provide a clear economic advantage.

In his talk, Professor Grant illustrated three application areas – manufacture of a solid mass of material, 3D structures, and energy storage.

Using video taken in his laboratory at the Begbroke Science Park, Professor Grant showed how large scale production of complex metallurgical alloys is achieved using spray forming. Alloys can be produced in a controlled environment, with material built up under real-time control. By extracting and reusing overspray, the yield of this production-scale spray forming can be as high as 95%. Real world applications have been developed where material quality and consistency is paramount, such as sputter targets for LCD panels and DVD coatings.

Aerospace and automotive applications also benefit from spray forming technology. Alloys can be created with stiffness, strength, and corrosion resistance tuned to meet specific applications.

Working with industrial partners, Professor Grant's team has created

an advanced spraycast Al-MgLi-Zr alloy for a lightweight all-terrain vehicle with structural efficiency and crashworthiness.

Professor Grant then explained how spray forming can be used to make 3D structures. The demand and economic rationale are clear – leadtimes associated with conventional tool-making form the critical path for new vehicles, meaning that design iterations become prohibitively expensive. Spray formed tools can offer greater flexibility, reducing leadtimes by up to 50 percent.

Having realised the key was to control tool accuracy during manufacture and studying deflections under various process conditions, the group developed a feedback control mechanism that virtually eliminated the tool deformation that otherwise occured. A spray formed tool for the door inner panel of the Ford GT40 has been used for more than 100,000 pressings.

Professor Grant concluded by discussing how droplet technology can be used to improve energy storage in supercapacitors. Characteristics of these devices include a fast charge/discharge rate, higher power density (W/kg) than conventional batteries, and higher energy density (Wh/kg) than conventional capacitors. Applications are therefore found wherever instantaneous high power is needed e.g. in hybrid power vehicles, and for deploying emergency chutes on planes.

Spray deposition of thin electrode films allows high performance pseudo-capacitive electrodes to be made in safe materials. By using sprays various nanoparticle, and nanowire, electrodes have been made, including the construction of graphene supercapacitors with extremely high power density and low resistance.

This exciting work signals the way to smaller, flexible, safer supercapacitors, without binders or additives, and with non-flammable electrolytes. The group is currently exploring the feasibility of scaling-up the technology to manufacture thin-film Li-ion battery electrodes. Whilst established technology will continue to meet the needs of the mass market, spray deposition opens up the possibility of many material combinations, and may address the particular demands of niche markets.

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Isis Innovation: Invention 10

Value through partnerships

The Engineering and Physical Sciences Research Council (EPSRC) Chief Executive, **Professor David Delpy**, explains the role EPSRC plays in supporting research and PhD training.

EPSRC is the main UK sponsor for research and PhD training in engineering and physical sciences. In 2012-13, we will invest around £950 million in world-class research, training and knowledge exchange via partnerships with universities, business users, the third sector and government.

Our focus is on research that precedes development and demonstration and enabling both the breadth and depth in university/business partnerships across engineering and physical sciences. Forty percent of all the research grants we award are collaborative with users, including business, while 80 percent of our Centres for Doctoral Training (CDTs) receive business support, either in cash or 'in kind', adding to our initial investment of £300 million. Over 2,000 different user organisations including businesses, charities and government organisations collaborate on EPSRC research and training grants.

What makes EPSRC unique in the research and innovation landscape is the quality of partnerships it has nurtured over the years with both business users – EPSRC current boasts 27 active Strategic Partnerships, 17 of which are with business – and with the universities it supports. The University of Oxford is among the 20 higher education institutions that receive 80 percent of EPSRC funding. In fact, Oxford is currently the fourth largest recipient of EPSRC funding with 278 active grants totalling £285 million. Many of EPSRC's industrial collaborators also partner with Oxford,

investing another £6.8 million in cash in EPSRC-funded projects at the University, and much more in other 'in kind' contributions.

The last year was very challenging for everyone, business and universities alike. An increasing number of voices are calling for a focus on sustainable growth, rather than growth for its own sake. Levels of business investment in R&D continue to go down and, increasingly, strategic investment decisions are being made in headquarters overseas. EPSRC has been working hard with its strategic business partners to make the case for continued co-investment in the UK research base as it has maintained its level of excellence in spite of strong international competition.

One of EPSRC's key priorities for 2012-13 is to continue to develop leaders through tailored support for the best individuals at all stages of their careers. One example that typifies this

commitment is that of Professor Paul Newman, one of EPSRC's Leadership Fellows, who runs the Autonomous Vehicles Research Group at Oxford (featured in Isis Insights 67). EPSRC recognised Paul's potential early on and, through proactive sponsorship, enabled him to develop his research career and his research group. Paul's expertise has since been recognised by a number of industrial partners with which he actively collaborates including BAE Systems.

One of the many ways we have demonstrated leadership as a sponsor over the years is through the provision of high-quality PhD training, much of which is in collaboration with business users. EPSRC's model for Centres for Doctoral Training, first developed in the 1990s and refined over the past 10 years, is now being adopted by other agencies around the world and has long been recognised by business as an excellent way to prepare bright students to the reality of the workplace – particularly through industrially-focused CDTs. EPSRC will announce a new call for CDTs in 2013.

Another prime focus for EPSRC in 2012-13 is on delivering further impact from its research investments. In order to do this, all researchers must play their part in explaining clearly how their research can contribute to economic and societal challenges faced by the UK today.

The impact of UK research is truly outstanding and we must continue to work closely together with universities and users to demonstrate the impact engineering and physical sciences research is making on the economy and particularly on growth. EPSRC is working on ways to enable business users to gain greater access to its research and training portfolio. In partnership with key universities we are currently collecting data in order to capture information about the outputs and outcomes of our funded research (the 'Research Outcomes System'). The continuous need for knowledge sharing between universities and business was highlighted in Tim Wilson's recent review. We, in EPSRC, have worked on making this happen for many years, and 2012-13 will be no different. We will, for example, work to provide greater flexibility to

The impact of UK research is truly outstanding.

universities to exchange students and personnel with business, as knowledge sharing is always best realised through people. We are also engaging with our university and business partners in deciding on the future priorities for investment in Centres for Doctoral Training.

Finally, the engineering and physical sciences community cannot afford to be complacent as future growth is anything but guaranteed. Under-investing in long-term research and innovation now, in an environment of competing priorities, carries a risk that cannot be overestimated and could have damaging consequences on the economy in the years to come. The triangular EPSRC-Universities-Business relationship that we have worked to develop over the past 10 years is starting to show real impact on growth and the importance of this triangle must be articulated as widely as possible. EPSRC is doing its bit and I sincerely hope others will help to push this agenda.

Weblinks

Our 2011-2015 Delivery Plan (www.epsrc.ac.uk/plans/approach/deliveryplan/Pages/default.aspx) sets out our priorities and investments over the next three years.

To find out more about the EPSRC portfolio of research and PhD training investments please consult http://www.epsrc.ac.uk/ourportfolio/Pages/default.aspx.

To get to know more about opportunities for commercial partners to engage with EPSRC, and the research and researchers it supports, see http://www.epsrc.ac.uk/funding/grants/business/Pages/default.aspx

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Vision realised

Dr Mark Gostock introduces a high-tech yet inexpensive and inconspicuous portable device. Smart Specs provide improved spatial awareness and object recognition for the legally blind.

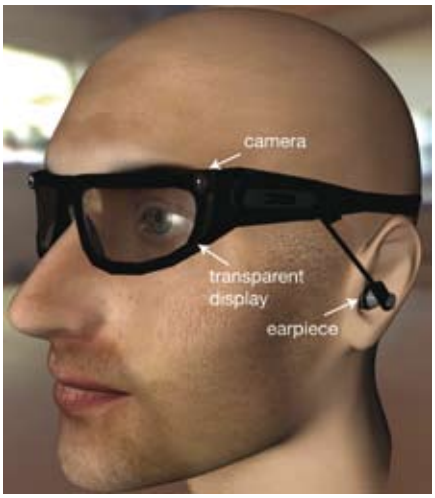
The impact on an individual's ability to navigate and negotiate their environment following sight loss is both obvious and great. Many individuals suffer reduced mobility as a result of their visual impairment and the personal difficulties faced by someone who is blind cannot be overstated. Many aspects of everyday life become increasingly difficult, such as the ability to travel independently and use public transport, to walk safely around the environment and to make complex journeys. Many individuals are prevented from performing any work for which eyesight is essential, and depression is common amongst the visually impaired population.

Over 360,000 people are registered as blind in the UK, with the majority suffering retinal disease such as age-related macular degeneration, diabetic retinopathy or glaucoma. However, up to 90 percent have some form of residual vision function, sufficient to differentiate between light-dark contrast and motion.

Illuminated vision

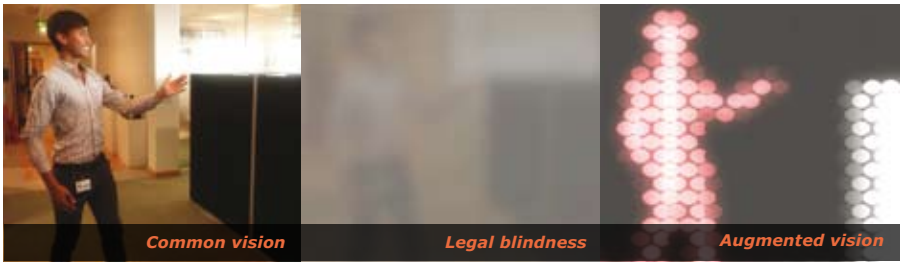
Typically, the only mobility aids available to visually impaired individuals, not withstanding guide dogs, are manual probes (white sticks) or auditory devices similar to echolocation. Never before has light been used to enhance visual input to the eye, even though visual stimulus is the most natural way to interact with objects. Technology designed by Dr Stephen Hicks and researchers in the Nuffield Department of Clinical

- Transparent visual display: inconspicuous design, allows eye contact between wearer and others.
- Navigation assistant: GPS and compass sensors locate the wearer on a digital map and set visible waypoints on the displays to guide individuals safely to their destination.
- Public transport assistant: Downloads real-time information about public transport to improve accessibility and alerts wearer to an approaching vehicle.
- Depth imaging: Rapidly draws connections between display and objects in the real world, enabling avoidance of obstructions.



Tiny stereo cameras – embedded in the frame of lightweight spectacles – capture simplified images of a scene and send them to a series of small LEDs, set within the surface of transparent lenses

Up to 90% of legally blind individuals have some residual vision, enough to see motion and light-dark contrast.



Neurosciences at the University of Oxford has been developed to increase the independence of blind people, by improving their ability to recognise objects and obstacles in their immediate environment.

Tiny stereo cameras – embedded in the frame of lightweight spectacles – capture simplified images of a scene and send them to a series of small LEDs, set within the surface of transparent lenses. A unique and fast image processing solution developed to be intuitive to the wearer, converts depth images from the cameras into a brightness scale. When items are identified an appropriate subset of LEDs illuminates, thus mimicking the local field of vision such that nearer objects appear bright, and distant objects fade into black. People and obstacles can be seen by the device. Common items like coffee mugs and telephones are potentially visible too.

Independence

Audio is another function of the bionic glasses. Words on street signs, bus stops, supermarket price tags and newspaper headlines can be synthesised into speech and read-out aloud to the wearer via headphones, with different modes of the software controlled through voice activation. Further advantages can be found in the inconspicuous looking design of the glasses, the portability of the unit as a whole and the low cost of the components. Additionally, the application can be extended to dementia sufferers, who could be helped by the prosthetic to improve their ability to recognise faces and locations.

Prototype study

Results from a pilot study of sight impaired individuals showed that all were able to describe the location of people and other objects in the local environment within five minutes. Subsequently, the research has received widespread media coverage in print, TV, radio and online, winning many awards and accolades, including selection for the prestigious Royal Society Summer Exhibition.

Commercial opportunity

Parties with an interest in investing in this remarkable, IP protected (PCT patent application) technology are invited to contact Isis Innovation.

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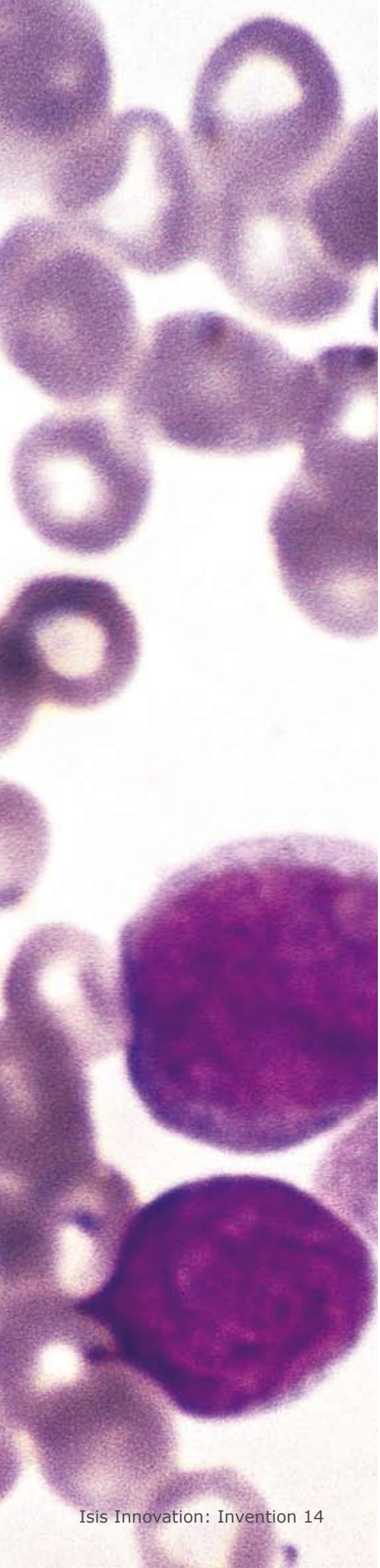


Leukaemia lifeline

Oxford researchers, in collaboration with the University of Birmingham, have discovered a combination of cell-surface biomarkers for Acute Myeloid Leukaemia (AML) that provide improved sensitivity in diagnosis and prognosis. **Dr Natasha Tian** details the developments.

AML is an aggressive cancer of the myeloid line of white blood cells and is the most common adult acute leukaemia, affecting over 15,300 people a year in the US and UK combined. Since AML is more common in adults aged over 65, with an overall survival rate of just five percent in this patient group, its prevalence is expected to increase as the population ages.

Leukaemic stem cells and resistance to therapy

AML is currently treated by chemotherapy, with the aim of reducing the amount of bone marrow leukaemic cells to less than five percent. However, most patients relapse without further chemotherapy or a stem cell transplant to eliminate leukaemic cells that resist therapy. AML is organised as a loose cellular hierarchy, which is maintained by self-renewing leukaemic stem cells (LSC) that are thought to be responsible for sustaining disease by resisting current chemotherapeutic regimens. Therefore, the identification and eradication of all LSCs is required for a complete cure.

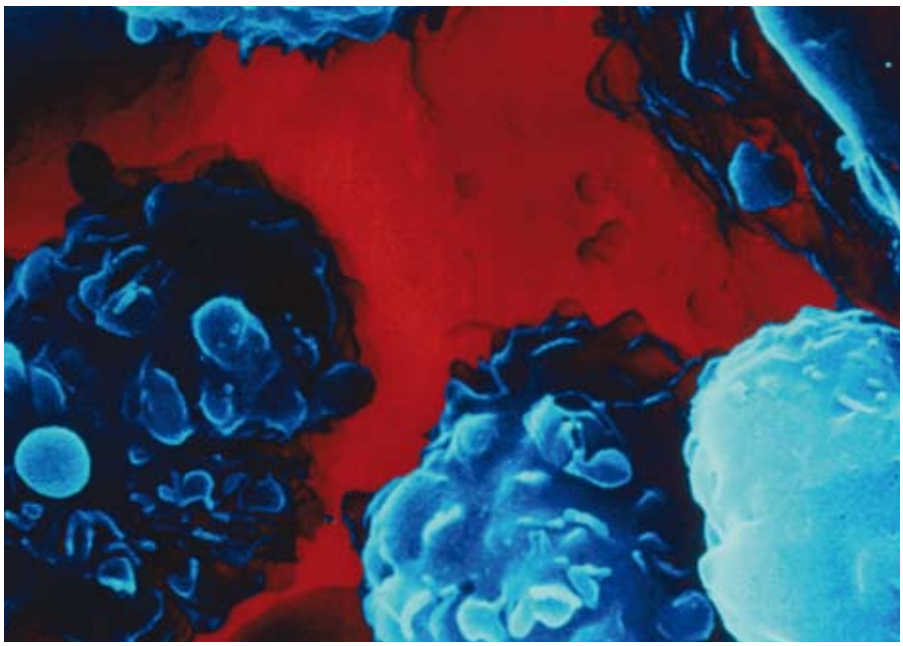
Recent studies have identified several antigens – proteins on the surface of these stem cells –that are expressed on AML stem cells and not on normal stem cells. A better understanding of LSC-specific antigens will help clinicians monitor the disease in AML patients and aid the development of effective therapies, such as antibody therapies targeting LSCs.

Oxford biomarkers

Dr Paresh Vyas and Dr Nicolas Goardon at the University of Oxford's Weatherall Institute of Molecular Medicine, in collaboration with researchers at the University of Birmingham, have discovered a novel combination of LSC-specific cell-surface biomarkers (CD molecules) that can more accurately follow AML disease progression.

The advantage of the newly discovered biomarkers is that they follow LSC populations directly and

The new biomarkers offer improved sensitivity by detecting leukaemic stem cells at lower levels than previously possible.



SEM of blood with myeloid leukaemia.

hence provide a better strategy for following disease progression. The new biomarkers offer improved sensitivity by detecting LSC at lower levels than previously possible.

Commercial opportunity

The researchers are currently working towards developing an antibody-based kit for the diagnosis and prognosis of AML in the majority of patients. They are continuing to collect clinical and in vivo proof-of-concept data showing that the biomarker combination unequivocally identifies LSCs and that the specific antibody combination is capable of detecting LSCs.

Patent position

A PCT patent application has been made with a filing date of 21st December 2011. The claims include use and method claims for biomarkers for AML.

References

Goardon N et al., Cancer Cell 2011; 19 'Coexistence of LMPP-like and GMP-like Leukemia Stem Cells in Acute Myeloid Leukemia.'

Sarah J. Horton and Brian J.P. Huntly Haematologica April 17, 2012 Recent advances in acute myeloid leukemia stem cell biology.

Advantages of the biomarkers

- Improved sensitivity in AML diagnosis and prognosis
- Patient care stratification, saving time and money by avoiding inappropriate treatments and improving patient wellbeing
- Assessment of treatment efficacy

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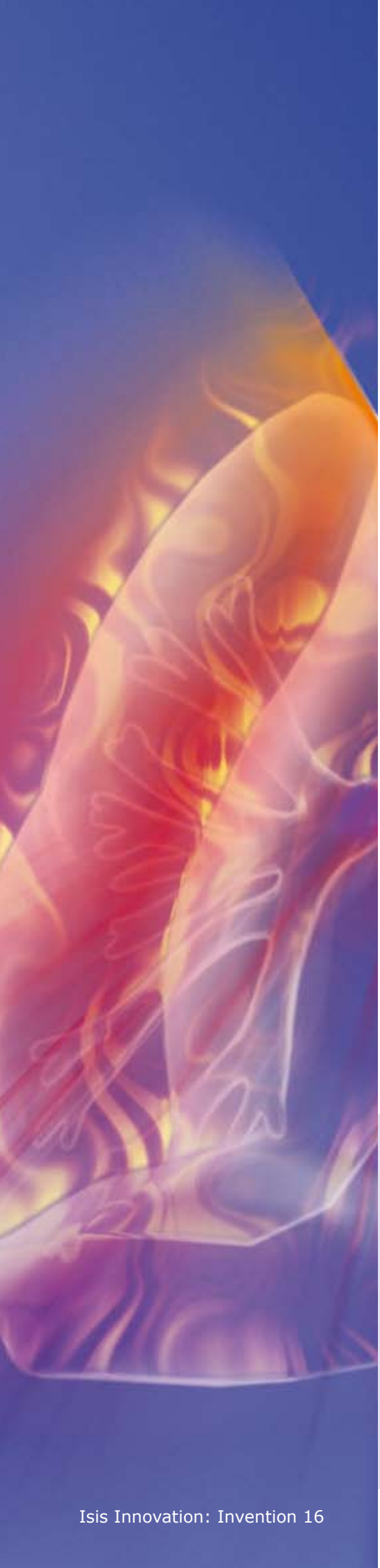

Breath of life

Dr Bharti Ranavaya discusses the 'asthma whistle' that makes possible the remote monitoring of patients with respiratory diseases.

Within both developing and developed countries there is a growing requirement for effective remote monitoring of patients.

Within the UK, for instance, the NHS faces major financial challenges and reform which will see healthcare delivery shifting into the local community to reduce hospital administration and the use of beds. In developing countries such as South Africa and India a large percentage of the population live within rural areas, where constant monitoring and hospital access is difficult and expensive. Remote healthcare workers have been employed by government and healthcare providers in such areas to aid in alleviating some of these problems.

Low cost, easy to use medical devices which allow for early diagnosis, on-going monitoring and analysis by a doctor hundreds of miles away are in global demand.

Now, a low-cost spirometer and phone application, developed by researchers at the University of Oxford, enables remote assessment of lung function to be immediately relayed to a doctor. This allows for remote diagnosis and monitoring of asthma, chronic pulmonary disease (COPD) and other respiratory conditions.

Early diagnosis

In February 2009 the World Health Organisation reported that COPD accounts for 3300 deaths in South Africa and 1200 in the UK each year. Asthma itself causes the death of 4600 people in South Africa and 300 in the UK annually.

Technical and commercial advantages

Researchers from the University of Oxford have developed a portable spirometer that leverages mobile phone technology. Key features include the ability to:

- Characterise a flow-volume curve, from which peak expired flow (PEF), forced expired flow over one second (FEV1), and forced vital capacity (FVC) can be determined
- Allow healthcare workers to capture high quality flow-volume data with minimal training
- Transfer flow-volume data wirelessly to a central database for analysis and diagnosis by a trained expert
- Provide immediate feedback to the user on their results

Low cost, easy to use medical devices which allow for early diagnosis, on-going monitoring and analysis by a doctor hundreds of miles away are in global demand.

Early and ongoing monitoring of both conditions would reduce the number of fatalities and improve the patients' quality of life. This easy to use spirometer allows initial screening and regular monitoring to be done remotely, using a low-cost and robust device.

Product development

The spirometer prototype has been tested on volunteers at the Institute of Biomedical Engineering at the University of Oxford. Work is currently underway to develop the device using a pulmonary simulator in the Department of Anaesthetics in the John Radcliffe Hospital, Oxford.

A patent filing is currently being undertaken and Isis would like to speak to companies interested in licensing and/or developing this technology.

Cardiology application

As showcased in Isis Insights 67, this same portable technology also has uses within the field of remote cardiology monitoring. An Oxford-developed digital stethoscope and phone application enables basically trained healthcare workers to capture and transmit high quality phonocardiograms for expert analysis.

The device was initially developed to target tuberculosis pericarditis, which affects around 10% of all TB patients and has a high mortality rate (40%) because sufferers in developing countries struggle to reach a clinic before it is too late. The ability to pick up the early warning signs of this and many other conditions is made possible through the Oxford invention. In the future it could also be utilised for pulmonary auscultations and foetal heart sound examinations.

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Dengue discovery

Dr Nikolaos Chalkias explains how peptides identified by Oxford researchers will aid the development of a diagnostic test to analyse and predict immune responses to different serotypes of Dengue virus.

While Dengue infection may be asymptomatic at first, individuals who have previously been infected with Dengue are 100 times more likely to contract Dengue haemorrhagic fever (DHF). The pathogenesis of DHF is debated but there is epidemiological evidence that it is more common when subsequent infections occur with different serotypes. This phenomenon is called disease-enhanced immune response. There is currently no fast and reliable test to determine which serotype a person has previously been infected with. The World Health Organisation (WHO) and the Paediatric Dengue Vaccine Initiative (PDVI) listed "the differentiation of Dengue serotypes" as one of the primary needs for a Dengue diagnostic test. The absence of such a test has been a significant limitation for eradicating Dengue.

Oxford scientists have now identified specific, immunogenic epitopes for all four Dengue virus serotypes. Knowledge of these epitopes will enable the development of a diagnostic test and possibly a multivalent Dengue vaccine. Peptides generated from the identified sequences have unique advantages in that they are serotype-specific, non cross-reactive and originate from highly conserved regions of the Dengue viral genome.

Dengue diagnostics

The peptides can be used for the development of a diagnostic test to differentiate between immune responses to different serotypes. The test could determine which Dengue subtypes a person has previously been infected with and the subsequent responses to vaccination. This would be valuable for the characterisation of serotype-specific responses to vaccination. The use of the test would determine whether immune responses are modulated favourably through vaccination, both for vaccine serotype-specific responses and also for any pre-existing non-vaccine serotype-specific responses. These serotype-specific responses can be readily compared to serotype cross-reactive immune responses in order to develop a complete understanding of T cell responses to Dengue viruses before and after vaccination.

Dengue vaccine development

Unlike current approaches, vaccine development would be based on immunogenic peptides rather than an inactivated or attenuated virus. The identified peptides can be used in the development of a multivalent vaccine for Dengue. A vaccine based on this invention would avoid current

Dengue has received global focus with financial supporters like the World Health Organisation and NGOs such as the Bill and Melinda Gates Foundation.

potential safety limitations, namely using a vaccine that may induce disease enhancing immune responses to heterologous serotypes, should they be subsequently encountered by the vaccinated individuals.

Market considerations

The invention is the subject of a global PCT patent application and Isis would like to speak to companies that develop and commercialise in vitro diagnostic assays and kits as well as Dengue vaccine developers.
One of the immediate applications would be in Dengue vaccine clinical trials. For instance, a serotype specific test could:

- Validate whether previous Dengue serotype infections can influence the success of the developing vaccine
- Provide vaccines targeted to sub-groups

Proof of principle evidence

Preliminary clinical data has been generated as a proof of principle for a Dengue serotype test. Twenty healthy Dengue immune individuals were screened for IFNγ T cell responses to the serotype-specific conserved peptides from the individual Dengue serotypes. All showed evidence of previous Dengue infection (see data in border, right).

Dengue: a deadly disease

Dengue has four viral serotypes and is transmitted by the bite of an Aedes Aegypti mosquito infected with any one of the four Dengue viruses.

There are as many as 50 million Dengue cases each year and the disease is endemic in over 100 countries. The disease occurs in tropical and sub-tropical areas and it represents a substantial burden to local populations. An estimated 500,000 people with severe Dengue require hospitalisation each year, a large proportion of which are children.

About 2.5% of those affected die. There is no treatment for this severe form and the only prevention available is to avoid being bitten. Two promising vaccine trials are underway but no vaccines are available as yet.

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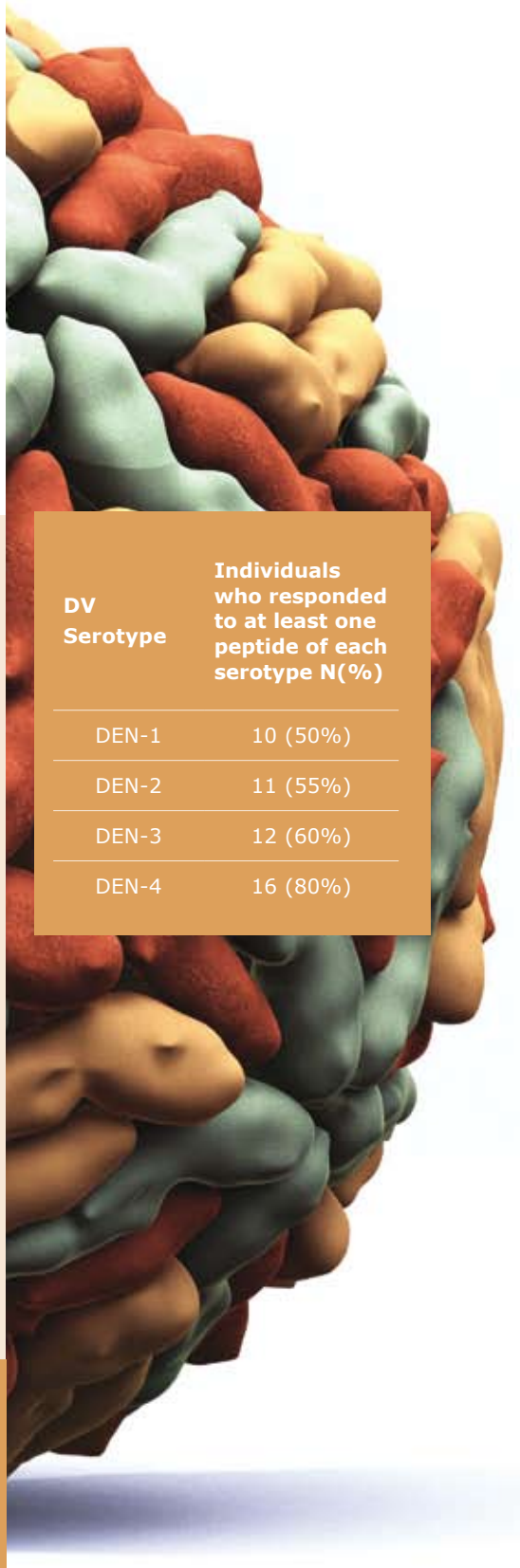


DV Serotype	Individuals who responded to at least one peptide of each serotype N(%)
DEN-1	10 (50%)
DEN-2	11 (55%)
DEN-3	12 (60%)
DEN-4	16 (80%)

Stronger, tougher alumina

Dr Andy Robertson presents a new class of engineering ceramics combining the cost-effectiveness of alumina with the performance characteristics of expensive alternatives such as silicon carbide.

Ceramic materials are increasingly being adopted for mechanical and industrial applications due to their electrical characteristics and their resistance to wear, corrosion and thermal shock. Aluminium oxide, known as alumina, is one of the most widely used engineering ceramics due to its properties (mechanical and electrical) and low cost. Unfortunately, if high strength or high wear resistance is required then other more expensive materials must be specified. Finding alumina-based materials with enhanced performance characteristics is highly desirable.

Performance superiority for an affordable price

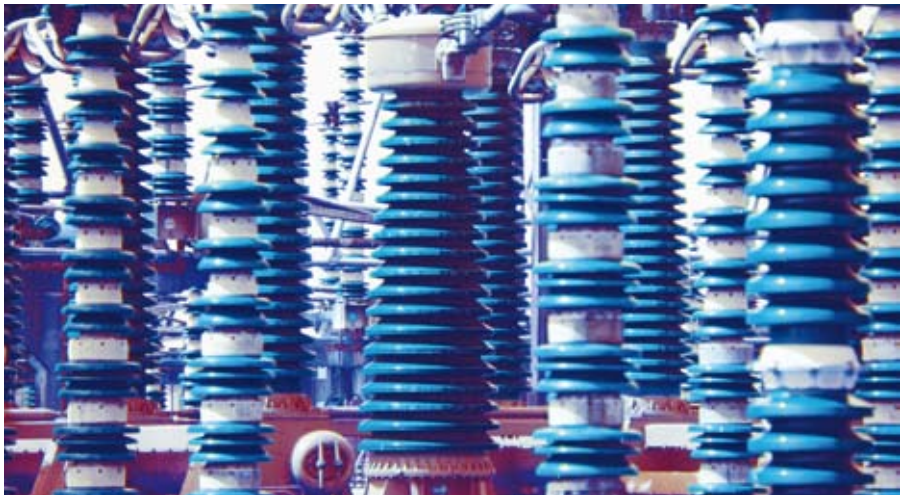
One approach to improving alumina's properties is to add a dispersion of a second ceramic material e.g. adding silicon carbide to form alumina-silicon carbide. Although this method can produce better performance characteristics, the production techniques required are expensive or complex. Employing non-standard sintering processes (such as spark plasma sintering, working at higher temperatures or using raw materials in nanopowder form) are other approaches that have been explored previously.

Oxford researchers have invented technology for processing a solid solution of alumina with a second material, e.g. iron oxide, and a dopant such as yttrium oxide to produce an alumina-based nanocomposite in situ. This delivers the desired improvements using standard production processes and without the need for expensive raw materials. The resulting nanocomposites therefore offer cost-effective performance improvements. Users of existing alumina applications can gain from the enhanced mechanical properties of these materials, but at the same time, users of other engineering ceramics – silicon carbide is an example - can also benefit by investigating the potential of this lower cost alternative for their products.

Improved characteristics now quantified

Alumina is used in a multitude of products from mechanical parts such as seal rings, through electrical insulators and wear components to ballistic armour. Tests on the new Oxford materials have demonstrated

Alumina is used in seal rings, electrical insulators and wear components to ballistic armour.



Images: above, ceramic insulators. Borders, ceramic car parts.

improved flexural strength (520MPa) and fracture toughness (4.7MPa√m) against standard "monolithic" alumina (around 300MPa and 3MPa√m respectively). It is expected that these improved material properties will further extend the range of applications for alumina.

Tests of the Oxford materials have demonstrated enhanced abrasion resistance: over 2.5 times the performance of a standard alumina part. For wear components such as threadguides or nozzles for abrasive slurries this means longer lasting components and less maintenance downtime.

Impact resistance

Alumina has been widely used for impact resistant applications such as ballistic armour for personnel or vehicles. For example, alumina can be used in a laminated composite, containing a ceramic (alumina) front layer and a metal (steel) backing layer. In this arrangement the ceramic's hardness and compressive strength are intended to fracture the projectile and reduce the local pressure on the backing layer, which then serves as an absorber for remaining energy from the projectile. Weight – typically represented as mass per unit area or areal density – is also a critical factor in armour applications. Experimental testing of the Oxford invention indicates enhanced impact resistance properties without significantly increased weight.

Readiness for market

The underlying technology is the subject of an international patent application published as WO 2011/061534. The current Technology Readiness Level is rated at 3 as laboratory studies to produce the new materials and verify their performance have been completed successfully. Further work to refine the specification of the process and develop manufacturing know-how is continuing. Companies interested in learning more about this project should contact the Isis Technology Transfer Manager.

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Carpeting the market

Chim Chu profiles a technique to modify the structural features of nanotubes, making them suitable for heat sinks, brake pads and more.

It's not often the word carpet is used to describe carbon nanotube glass composites. But that's exactly what has been forged from the collaboration of Professors Nicole Grobert (nanomaterials) and Richard Todd (ceramics) in the innovation labs of the Materials Department: usefully sized aligned carbon nanotube/ glass composite carpets made from a near-to-market industrial scale production technique

The two Oxford Professors (aided by DPhil student Geoffrey Otieno) have developed a technique to modify the structural features of nanotubes, making them suitable for thermal interface materials for heat sinks, thermal/gas/electrical sensors, high performance brake pads and molecular filters.

A number of organisations in defence and mainstream advanced materials manufacture are in discussion with the inventors to assess the potential for up-scaling this technique to enable advanced applications.

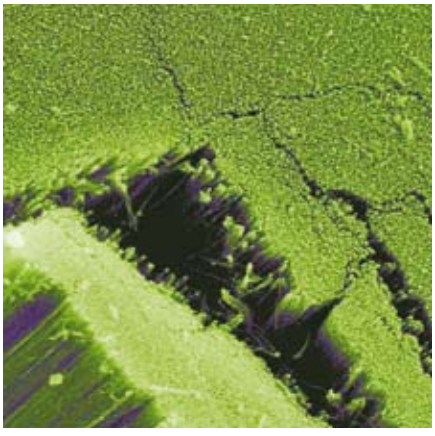
"Building block" materials

Industry experts calculate that products and applications based on carbon nanotubes represent a potential global market of up to hundreds of billion euros, and could create around 100,000 new jobs. It has been reported that virtually all areas of industry will benefit. (Inno.CNT, 2009). The nanotube materials currently available are limited as their properties have to be engineered and produced in useable commercial quantities at affordable prices. Hence, it is envisaged that the potential market for dedicated carbon nanomaterials exhibiting properties tailored to application requirements may be of a similar order, if not larger.

Only if nanomaterials are synthesised/processed systematically and with a strong focus on eventual application can the extraordinary properties of these materials be fully exploited as the building blocks for new electronic devices, super-strong and lightweight composite materials, energy generation/storage or biomedical devices.

There have been several attempts recently to make ceramic nanocomposites in which the reinforcing phase consists of carbon nanotubes," says Professor Todd. "None has resulted in a viable composite, either because the nanotubes have been destroyed by the high firing temperatures used, or because the nanotubes have not been properly dispersed in the ceramic matrix."

Geoffrey Otieno agrees. "These previous attempts to produce



Industry experts calculate that products and applications based on carbon nanotubes represent a potential global market of hundreds of billions of euros.

carbon nanotube (CNT) ceramic composites have usually resulted in poorly dispersed, unaligned and/or non-continuous CNTs in the composites. Consequently, property improvements have been limited. To avoid this, we produce dense composites by infiltration of aligned multiwalled carbon nanotube (MWCNT) preforms using aluminoborosilicate (ABS) glass sol."

Future technology application

The Oxford invention uses well established and highly versatile low cost techniques with minimum modifications. It permits in situ chemical functionalisation to tailor speciality nanocomposite materials for future technological applications. The resultant ceramic composite material is a strong uniform carpet able to transfer heat efficiently and rapidly via the aligned carbon nanotube (CNT) embedded in its structure.

Proven method

The production of aligned, multi-walled CNT/ceramic composite carpets using Sol Gel processing involves:

- An array of aligned CNT, produced by chemical vapour deposition
- Filling the interstitial spaces of the CNT with a ceramic matrix material using sol-gel processing and induced wetting of the CNTs
- Sintering the CNT ceramic matrix material to form the composite material

Technical performance

- The alignment of CNTs is confirmed by TEM and SEM
- Raman spectrum of the sintered composites shows little change in the D/G ratio
- All the fibre toughening mechanisms for conventional fibre reinforced ceramics are observed
- The thermal diffusivity is measured by a laser flash technique. This method is fast, accurate, uses small specimens, and can also be used at different temperatures.
- The 15 W/m K thermal conductivity of the composite is three times higher than the phase change thermal interface materials currently used

Readiness for market

The underlying Oxford invention is the subject of patent applications in USA and Europe. Of particular interest to industry is the claim that The Technology Readiness Level is rated at TRL 3 with tested, useably-sized sheet carpet thicknesses available.

Images: border, car braking system manufacture. Inset, customised carbon nanotubes.

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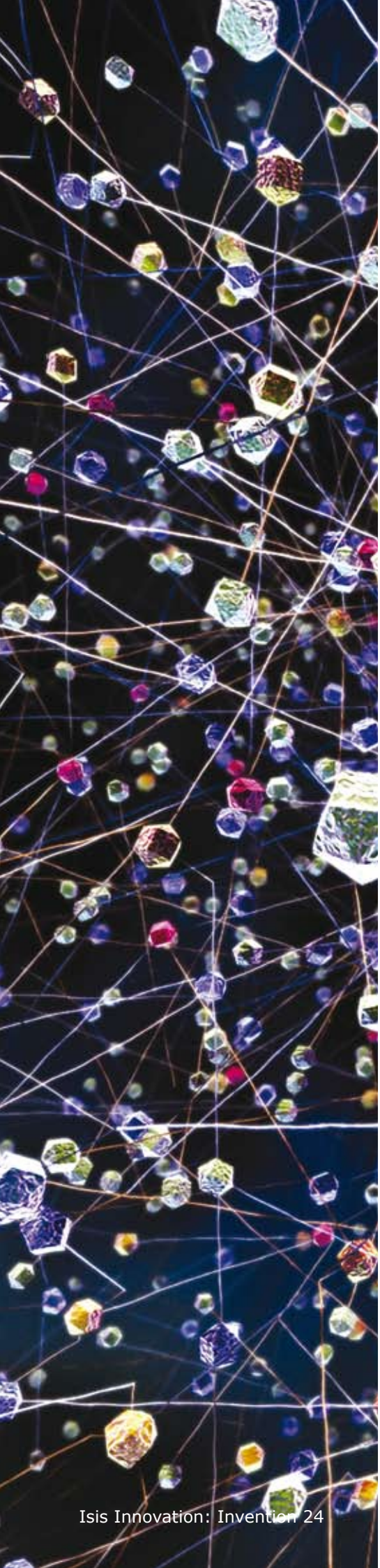
Nano-glossary

Sol-gel
The sol is a liquid that infiltrates the CNT carpets, set to a gel (like a jelly), so that it stays there and will then convert to glass when heated

bTEM
Transmission electron microscope/microscopy

Raman spectrum
Luminescent light emitted at particular wavelengths by solids when stimulated with a laser

D/G ratio
The ratio of the areas of two particular wavelength peaks in the Raman spectrum of CNTs. It is an indicator of the degree of perfection of the CNTs



Exploring the proteome

Oxford's protein-identification experts are working closely with Oxford University Consulting to help international cancer research groups and other sectors benefit from the academics' expertise.

With the advent of the genomic era and the subsequent explosion of data generated through transcriptomics, the desire to further complete the biological jigsaw fuelled the drive to develop the field of proteomics. The large-scale analysis of proteins in hundreds, if not thousands, of different biological systems has provided invaluable insights into diverse areas of science, including microbiology, plant sciences and medicine.

Proteomics has now progressed to the stage of being routinely deployed as one of the many tools at the disposal of the modern day biologist but the technical challenges needed to conduct such analysis require specialist skills, capital investment and a dedicated team to provide the services.

The Central Proteomics Facility (CPF) based in the Sir William Dunn School of Pathology at the University of Oxford is one such facility. It provides proteomic services to research groups across the University, working collaboratively with investigators to determine the best approaches and methodologies at the start of each individual project and supporting the group downstream with bioinformatics training and data interpretation.

Interactive approach

With many groups keen to capitalise on the advances in this field to extract maximum information from their experimental system, choosing the right method is critical. The CPF's approach is very interactive according to Dr Ben Thomas, the CPF's Permanent Technical Director. "We work closely with our colleagues and collaborators to make sure that they understand which particular method might best address the question that

Proteomics has now progressed to the stage of being routinely deployed as one of the many tools at the disposal of the modern day biologist.

The techniques available to do this are relatively complex and the Central Proteomics Facility is able to offer guidance on the most suitable approach.

they are seeking to answer, whether it's some simple single spot protein identification or complex quantitative multi-component analysis," he says. "We're always happy to discuss new projects and ideas and to provide advice on experimental design and optimising techniques. "

In order to enable external organisations to benefit from its expertise and resources, the CPF works closely with Oxford University Consulting. Typical projects have included protein identification for a research group in South America which is studying protein production in members of the brassica family (including broccoli), and the analysis of complex protein mixtures in human cell lines infected with different strains of human cancer viruses for an independent research organisation in southern Europe.

A number of groups have shown interest in working with the CPF for quantitative proteomic studies which involve not only the identification of the proteins in a given sample but also the reliable measurement of the amounts of each protein. This approach parallels the methods developed for transcriptomic analysis, allowing researchers to build more complete maps of the pathways from gene to transcript to protein to biological effect. The techniques available to do this are relatively complex and the CPF is able to offer guidance on the most suitable approach. "The key factors for choosing the right method depends upon the system which you are studying and whether you are looking for absolute or relative quantitation," says Dr Thomas. "Each method has its advantages and disadvantages and varies in the technical challenges required to implement them. We are careful to discuss these options for each project."

The organisations that have worked with the CPF have found the flexible and consultative approach very user-friendly, allowing access to the right expertise and the ability to generate proteomics data without the need for capital expenditure. Building links with a world-class university represents another great benefit.

Weblink

http://www.proteomics.ox.ac.uk/index.htm

Image: Protein crystals

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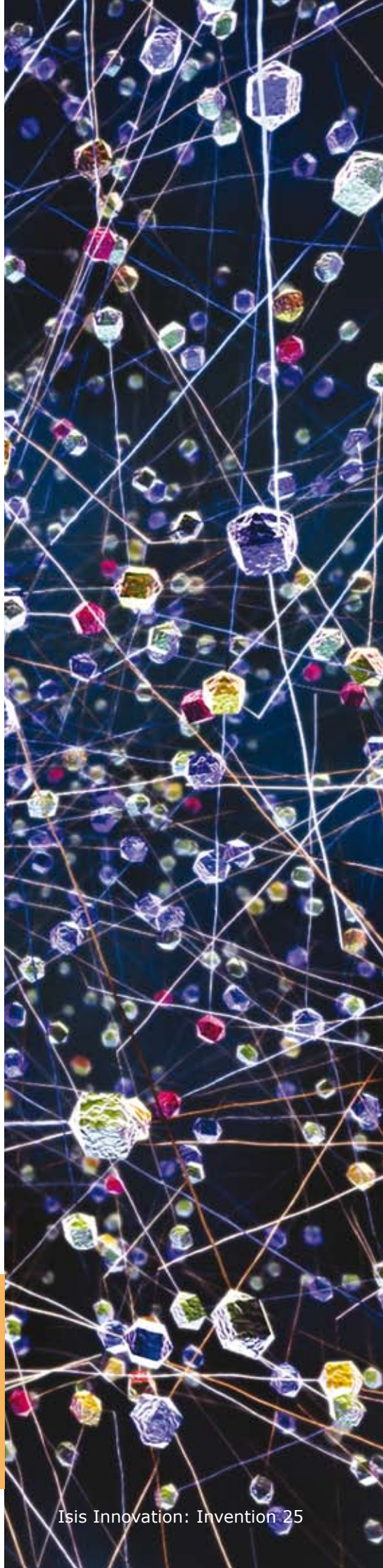

Strong foundations

Dr Chris Moody and **Rob Swerdlow** explain why having an intellectual property policy is at the heart of good IP management.

University and institutional leaders usually recognise the great potential value in the ideas and inventions created by their faculty, staff and students. However, a surprising number do not have well constructed and comprehensive intellectual property policies.

The absence of a good IP policy can lead to frequent case-by-case negotiations and sometimes sharp disagreements regarding the ownership of IP and the sharing of the financial benefits from IP. Because there are often different views regarding IP developed in the course of research, developing a comprehensive IP policy can be a challenging and lengthy undertaking. As a result, IP policy work is often put on the back burner by institutions.

However, creating or improving an IP policy can be a real opportunity to strengthen an institution and does not have to be a daunting or overwhelming project. Through our work with institutions around the world, Isis has accumulated a wealth of knowledge regarding different IP policies and considerations. Our expertise in the best practices for IP policy has led to the development of a methodology to help institutions create and improve their IP policies with less organisational stress and in a shorter period of time.

The fundamental purpose of an IP policy is to set out how intellectual property is managed within an institution or group of institutions.

To establish a successful IP policy it is crucial that the policy is fully understood and supported by its stakeholders. From Isis' experience, developing such policies in isolation, without the input of those it affects, such as the researchers and academics, is rarely successful. IP policy development is usually a process of negotiation between all of the stakeholders within the institution.

Through our own experience in this area and encounters with different universities and research institutions worldwide, it became apparent that often what was missing in the implementation was a suitable forum for all the relevant parties to discuss

With Isis acting as an independent advisor, the potential conflicts between stakeholders can be minimised.

The role of an IP policy

- Promotes innovation and creativity in the institution
- Establishes a mechanism for IP development
- Promotes the transfer of knowledge and technology generated in the institution through licensing and commercialisation
- Determines the rights and obligations of the institution, inventors, creators, sponsors of research, and licensees and other stakeholders
- Ensures that the legal framework is in compliance with national laws
- Avoids case-by-case negotiations around the split of equity for each project

all aspects of the policy, as well as the requisite knowledge to have informed discussions. To address these issues, Isis has developed our IP policy workshop methodology.

Typically lasting two days, the IP policy workshop invites senior decision makers within the university, technology transfer management, researchers and academics to meet, discuss and develop a mutually agreed and accepted policy.

The workshops are facilitated by an Isis expert, who leads the discussion, and manages the proceedings. During the workshops, the Isis representative takes the participants through key issues such as:

- Defining the roles of the stakeholders
- What types of IP are covered by the policy and owned by whom
- Specifying the split of equity and licensing revenues between the parties
- Addressing the IP constraints imposed by research funders
- Providing guidelines for dispute resolution

With Isis acting as an independent advisor, the potential conflicts between stakeholders can be minimised. The discussion can be moved along at a productive pace, drawing from the insights and alternatives put forward. We can add valuable advice on the

To establish a successful IP policy it is crucial that the policy is fully understood and supported by its stakeholders.

advantages and disadvantages, as well as the unintended consequences that may flow from various policy choices.

The workshop produces a draft IP policy that has basic agreement and buy-in from the key stakeholders. This method of developing IP policies has proven to be highly effective and can progress your institution from a low base to full policy adoption in a fraction of the time it might otherwise require.

Images: IP Policy workshop involving the Head of the Serbian IP office, the Rector of the University of Belgrade, the Vice Rector of the University of Belgrade, representation from the European patent Office and IE Managing Consultant Chris Moody.

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Oxford Innovation Society

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

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

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

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