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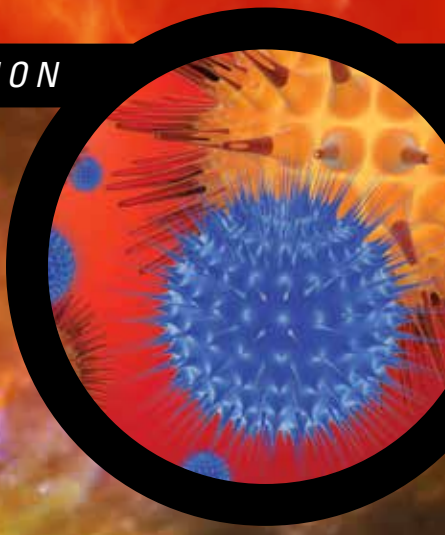
THE JOURNAL FOR SCIENCE, ENGINEERING AND TECHNOLOGY

advances WALES

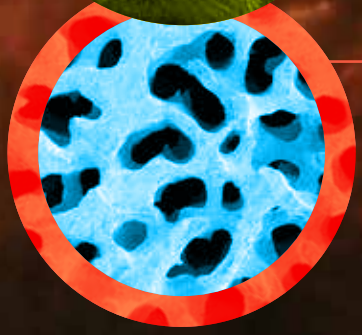
SPECIAL BIOSCIENCE EDITION



New frontiers New discoveries

How a Welsh instrument discovered a noble gas in space

SYNTHETIC BIOLOGY



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THE JOURNAL FOR SCIENCE, ENGINEERING AND TECHNOLOGY
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Synthetic biology:
Welsh universities explore potential of this emerging technology

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Guest Foreword

Professor Julie Williams CBE, Chief Scientific Adviser for Wales

As Chief Scientific Adviser for Wales, I am delighted to introduce you to this Bioscience special edition of Advances - launched in time for BioWales.

As one of the most vibrant life sciences events in the UK, BioWales will attract over 500 individuals to Wales' capital to hear a line up of high-profile speakers from across the world.

The Cardiff event provides an opportunity for businesses and investors to network and develop commercial opportunities, to partner with like-minded organisations in one-to-one meetings, and to investigate access to investment and new business.

Also, this issue's Special Feature investigates synthetic biology - an emerging science that some of our Welsh universities, namely Cardiff, Swansea and Bangor, are actively involved in. This field is poised to have an impact on almost every industry on earth. In the coming years we will be able to reliably build all manner of biological machines not found in nature for purposes such as the production of fuel and drugs from waste, sunlight and CO2, biosensors monitoring and responding to the progress of disease in the body and photographic bacteria, as highlighted on page 10.

Once again, Advances provides a showcase for many of Wales' companies and universities alike. Great research has led to many new and innovative technologies and ideas such as the Metabo- Lung from Cardiff University's Lung & Particles Research Group (page 26), MicroPharm's answer to C.diff (page 19) and a method of pest control from Swansea University (page 21), as well as new discoveries using Cardiff's SPIRE instrument (page 14).

Lucinda Dargavel, *Editor*

COVER IMAGE
W3, a giant cloud of gas and dust 6200 light-years away from Earth, undergoing intense star-formation, as pictured by Herschel's SPIRE and PACS cameras. (see page 14).
ESA/PACS & SPIRE consortia

PHOTOGRAPHY Sourced from organisations featured, their representatives and Shutterstock.

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Advances Wales is a high-quality, quarterly 'transfer of technology' journal produced by the Welsh Government to showcase new developments in science, engineering and technology from Wales. Devoted to concise reports and commentary, it provides a broad overview of the current technology research and development scene in Wales. Advances raises the profile of the technologies and expertise available from Wales in order to facilitate collaborative relationships between organisations and individuals interested in new technologies and innovation.

Commissioning Editor Alyson Pasch.
For information on how to contribute features contact the editor, Lucinda Dargavel (tel +44 (0)29 20473456, email advances@teamworksdesign.com).
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Scientists maximise renewable energy's potential

Siemens-owned Marine Current Turbines (MCT) is working with Bangor University's SEACAMS hydrodynamic modelling team in North Wales to understand the best sites for future development of marine energy farms.

The company is currently developing large scale tidal current energy generation technology and is set to deliver the first tidal energy converters in the UK.

With the industry moving towards large-scale commercialisation, the experts at the University's Centre for Applied Marine Sciences are vital. Bangor scientists are providing their state of the art facilities and expertise to companies through the SEACAMS programme, an initiative part-funded by Welsh Government. Their computer models accurately predict tidal currents, wave heights and other important measurements throughout the water column, helping to identify the best sea states, tidal flows and accessibility for wave and tidal devices, and to test the behaviour of prototypes and commercial scale turbines.

"It is fundamental that we have the best possible understanding of the environment our devices will be operating in. SEACAMS is providing the step change in the modelling capability required to accelerate the development of our industry."

Dr Scott Couch,
MCT Principal Resource Analyst

This sector is moving from being a developing technology to commercial viability and is forecast to deliver significant clean energy for the UK. "It's important that these technologies are supported through development and early commercial testing to build market confidence and investment" concluded Dr Stephanie Merry, Head of Marine at Renewable Energy Association.

www.seacams.ac.uk

IQE plays key role in US clean energy initiative

Hi-tech South Wales-based company IQE plc will play a key part in a consortium of high tech businesses and academia in a major Clean Energy Initiative announced by U.S. President Barack Obama.

President Obama announced the formation of a Clean Energy Manufacturing Innovation Institute which will be led by North Carolina State University and industry partners including IQE alongside ABB, APEI, Avogy, Cree, Delphi, Delta Products, DfR Solutions, Gridbridge, Hesse Mechantronics, II-VI, John Deere, Monolith Semiconductor, RF Micro Devices, Toshiba International, Transphorm, USCi, and Vacon.

The Institute is part of the U.S. Government's National Network for Manufacturing Innovation Initiatives (NNMI) announced by The White House in February 2013 to bolster the competitiveness of U.S. manufacturing.

IQE, based in Cardiff, South Wales, has been selected as supplier of advanced semi-conducting materials to the consortium for the development of a 150mm GaN-on-Si power electronics capability for high voltage (600V to 1200V) applications, an award which is worth up to $4M over the next five years.

GaN-on-Silicon is a key materials technology not only for highly efficient power semiconductors with applications ranging from everyday power supplies for consumer electronics to industrial motor controls and hybrid-electric vehicles, but also for radio frequency (RF) applications in next generation base station and small cell RF communication networks, as well as highly cost efficient LEDs, high speed rail and other power efficient applications.

IQE CEO and President, Dr. Drew Nelson said the announcement was "a great endorsement of IQE's recognition as a global leader in advanced semiconductor products and highlights the importance of materials such as gallium nitride (GaN) as a key enabling technology for the future.

www.iqep.com

Big ideas for biopolymers

SuPERPHA Collaborative Industrial Research Project (CIRP) Systems and Product Engineering Research for Polyhydroalkanoates (PHA)

A Consortia, led by the University of South Wales with Swansea and Bangor University, has undertaken initial research and identified that polyhydroxyalkanoates (PHAs) can be produced via a biological process utilising low cost organic intermediates and nutrients from the waste management industry and agricultural residues.

The project brings together 12 industrial partners across the waste management, process engineering, manufacturing and retail sectors, to undertake a programme of research and development. The aim is to develop and demonstrate a cost effective process for the conversion of low grade organic feedstocks to low embodied energy, bioplastic products and materials.

The production, processing and application of biopolymers within a range of industry sectors is set to increase rapidly over the coming decade. This trend is driven by legislative, economic and social considerations aimed at reducing the environmental impact of polymer based products and ensuring that products can be recovered or disposed of more effectively.

The growth of biopolymers represents economic opportunities for both manufacturers who utilise them and the companies involved in their manufacture. CIRP encourages and enables groups of companies and academic institutions to carry out industrial R & D projects in this area.

It is anticipated that advances made throughout the project will lead to the deployment of a cost effective biopolymer process for use by packaging companies and other parts of the Welsh manufacturing sector.

Blue-Chip company is the first to sign up for the Hub

Minister for Economy and Science, Edwina Hart, has welcomed Johnson & Johnson Innovation as the first company to join the Life Sciences Hub Wales in Cardiff.

The move comes as Johnson & Johnson Innovation announces the formation of a network of partnering offices across UK life science clusters; its positioning in the Hub will cover Wales and the South West of England. The offices will function as extensions of Johnson & Johnson's London Innovation Centre and will work with academics and entrepreneurs throughout the UK to identify early stage innovation and support the translation of research into new products for patients.

"Establishing these partnering offices reflects our commitment to collaborative innovation and our belief that being close to the source of innovation drives our ability to create strong networks of people who can combine ideas, resources and technologies in a new way to tackle urgent unmet medical needs," commented Patrick Verheyen, head of the Johnson & Johnson Innovation Centre, London.

"I am very pleased that Johnson & Johnson Innovation has taken a place at the Life Sciences Hub. Having such a prestigious company as the first private sector tenant at the Hub will ensure it gets off to a flying start and encourage many more companies to come to Cardiff Bay."

Edwina Hart,
Minister for Economy and Science
Welsh Government

www.wales.gov.uk

New UK virtual network launches Welsh site

The Welsh Node of the Cisco National Virtual Incubator (NVI) – a groundbreaking UK-wide virtual network- has been launched following Welsh Government support at Swansea University's eHealth Industries Innovation Centre (ehi2).

The UK has many exciting, innovative and vibrant businesses looking for collaborations but a large geographical spread sometimes makes this difficult for them to achieve. The NVI offers a digital solution by providing a free community spanning across the country through a series of communication points, known as 'nodes.' Currently there are 12 nodes situated across the UK connecting research clusters, higher education establishments and science parks.

"Collaboration is facilitated through a variety of video based technologies and use of the JANET network for research and education. This enables SMEs from various regions around the UK to collaborate more effectively, co-deploying solutions, employing remote workers, or connecting to an NVI wide broadcast event – such as the upcoming UK Investment Forum."

Akshay Thakur, Cisco Business Development Manager,

The Welsh Node based at ehi2, Swansea University, is free to join and provides a specialist communication point for the Life Science and ICT sectors.

Economy Minister Edwina Hart explained, "both Life Science and ICT are strong economic drivers for the Welsh economy and the fact that the Welsh NVI Node has come on board as a specialist communication point for these sectors demonstrates our strength in these areas.

"It is hoped it will be used by Welsh entrepreneurs, start-ups and SMEs, allowing them to tap into resources and organisations across the country to collaborate, innovate and develop new business partnerships to help them grow."

www.nvinetwork.com

Saving the old chestnut

Research scientists from Swansea University and Adnan Menderes University (Turkey) have joined forces to control insect pests of the sweet chestnut, a major export commodity for Turkey.

Chemical control methods are increasingly looked upon as unsustainable due to resource requirements, increased resistance and concerns for human health and the environment. In an effort to reduce costs and help farmers, the team has identified strains of fungi which are effective in killing larvae of the chestnut weevil (*Curculio Elephas*), one of several target pests.

The project is being led by Professor Tariq Butt of Swansea University and Professor Selcuk Hazir of Adnan Menderes University.

Professor Butt from the University's College of Science said, "the complementary expertise of the two groups has proven synergistic and could lead to extensive field trials of the fungus within the next few months."

www.swansea.ac.uk/science

Gearing up for Digital 2014

Maintaining momentum from the highly successful Digital 2013 event, 2014's offering will once again take place at the prestige Celtic Manor Resort, Newport, South Wales, and will provide a global platform for the ICT sector in Wales to discuss global trends, address related skills gaps and identify areas for future investment.

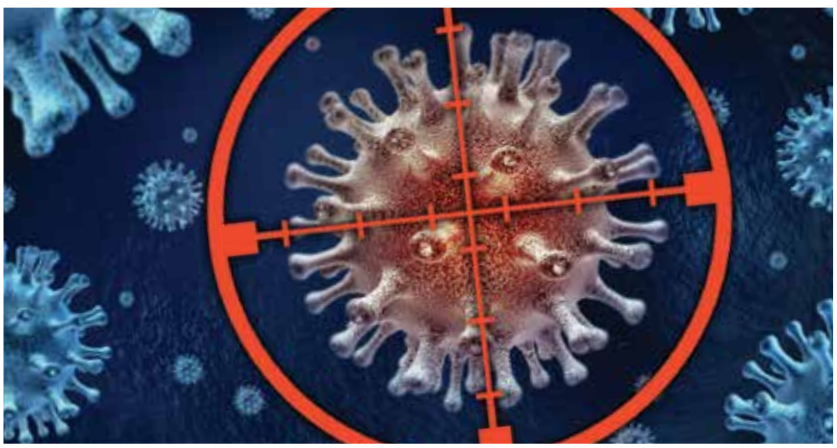
The two days, on June 2nd and 3rd, will comprise of a world-class speaker programme during the plenary sessions; as well as breakout sessions, sector workshops, an exhibition and brokerage area for more in-depth detailed discussions between delegates. One of the event's themes will be young people, their perceptions of the ICT sector, their thoughts on future sector developments and their involvement in addressing the identified skills gaps. This session will be hosted by Maggie Philbin, Well known TV personality and Founder and CEO of TeenTech CIC.

Speakers already lined up to participate at the event are globally recognised within the ICT Sector from world-renowned organisations including Microsoft, IBM, HP and BT.

www.digital2014.com

Double-sided approach may be the solution for cancer treatment

Researchers in Cardiff, South Wales, supported by funding from Cancer Research UK, are now trialling a combination of groundbreaking radiotherapy techniques and two different chemotherapy drugs before surgery in an effort to improve survival rates in patients suffering with Oesophageal cancer.



The trial, which has just recruited its first patients, will compare the two treatment plans to find out how successful each plan is and the side-effects experienced. Recent studies have shown that chemo-radiotherapy, delivered with new radiation technology and different combinations of chemotherapy drugs, may be safer and more effective than chemotherapy alone.

Oesophageal cancer is now the ninth most common cancer in adults in the UK, with around 8,000 people diagnosed each year – the equivalent of 150 cases a week. A difficulty in diagnosis means that doctors often find themselves treating this condition in its advanced stages and consequently survival rates can be low. On average, 30% of people will live for just one year after diagnosis, and only 8% will live for five years afterwards.

Run by Cancer Research UK's Wales Cancer Trials Unit (WCTU), within Cardiff University's School of Medicine, this trial involves 25 hospitals and 85 patients from Wales and England and is sponsored by Velindre NHS Trust.

Dr Tom Crosby, clinical director of Velindre Cancer Centre, who is leading the study, said, "this is a really exciting study that aims to use the most effective drugs combined with cutting edge technologies to find new avenues to treatment."

Following the trial, patients will have their tumour surgically removed and will be monitored by a research team for up to 12 months.

Dr Gareth Griffiths, director of the WCTU, explained that the results of the trial could be used to change routine practice in the treatment of the disease across the whole of the UK.

www.wctu.org.uk

Cardiff researchers reverse spread of cancer cells

Researchers at Cardiff University are developing a novel compound known to reverse the spread of malignant breast cancer cells.

The vast majority of deaths from cancer result from its progressive spread to vital organs, known as metastasis. In breast cancer up to 12,000 patients a year develop this form of the disease, often several years after the initial diagnosis of a breast lump. Recent studies have identified a previously unknown critical role for a potential cancer causing gene, Bcl3, in metastatic breast cancer.

"We showed that suppressing this gene reduced the spread of cancer by more than 80%,"

Dr Richard Clarkson,
Cardiff University European Cancer Stem Cell Research Institute

"Our next goal was to then find a way to suppress Bcl3 pharmacologically. Despite great improvements in therapy of early stage breast cancer, the current therapeutic options for patients with late stage metastatic disease are limited. There is therefore a clear unmet clinical need to identify new drugs to reverse or at least to slow down disease progression."

Dr Clarkson, Senior lecturer in the School of Biosciences joined up with researchers Dr Andrea Brancale and Dr Andrew Westwell from the School of Pharmacy and Pharmaceutical Sciences, to develop small chemical inhibitors of the Bcl3 gene.

Computer aided modelling of how the Bcl3 gene functions inside the cell allowed the group to identify a pocket on the surface of Bcl3 essential for its function. By screening a virtual compound library for chemicals that could fit inside this pocket, using state-of-the-art computer software, they identified a drug candidate that potently inhibits Bcl3.

With financial backing from UK-based Tiziana Pharmaceutical, work is now underway to progress the compound to clinical trials. The aim is to develop a therapeutic agent capable of blocking metastatic disease in breast cancer and a variety of tumour types.

www.cardiff.ac.uk

Drug resistant diseases fought by seaweed

Scientists from Cardiff and Swansea universities, are among a network of researchers involved in a four-year project investigating a new use for seaweed; fighting infectious diseases.

The £5.4m research programme is being funded mainly by AlgiPharma AS, a Norwegian biopharmaceutical company which has received grant funding from various sources including the European Union, the Norwegian Research Council and the Cystic Fibrosis Foundation of the US.

As part of the programme, researchers have found that alginates - components in the seaweed - can combat multi-drug resistant infections and these could be used in a new generation of drugs which fight off diseases and infections such as MRSA that are resistant to antibiotics.

Harnessing this knowledge, the scientists have also developed a new inhalation therapy that is being tested on cystic fibrosis patients with the aim of improving their breathing ; if proved successful this could also be used in other more common respiratory diseases such as Chronic Obstructive Pulmonary Disease which is reported to affect over one million people in the UK.

"This is a particularly exciting project that is proving we are able to derive material from the natural world with powerful abilities to modify bacterial behaviour and sputum structure, which can be applied to the development of alternative treatment approaches for challenging and hard to treat diseases. Now, more than ever in an aging population, we must to look for new ways of managing disease where conventional approaches are proving increasingly inadequate."

Professor David Thomas,
Cardiff University, School of Dentistry

Studies are also paving the way towards improved treatment of chronic non-healing skin wounds and multi-drug resistant infections, such as MRSA. These seaweed compounds are also effective against organisms that cause more benign conditions like gum disease.

Professor's prestigious Wolfson Research Merit Award

Professor Matt Jones of Swansea University, is among the 21 recipients in the latest round of prestigious Wolfson Research Merit Awards, announced recently by The Royal Society, the UK's national academy of science.

The awards, jointly funded by the Wolfson Foundation and the Department for Business, Innovation and Skills (BIS), provide universities with additional support to enable them to attract science talent from overseas and retain respected UK scientists of outstanding achievement and potential.

Professor Jones, Head of the Department of Computer Science in the College of Science, has been given the award as a platform for work motivated by his desire to understand and solve a series of complex human-technology problems with the aim of improving life for many hundreds of millions of people in the developing world.

Outlining the background to the five-year project, which is called 'Information interaction for "bottom of the pyramid" users in developing regions', Professor Jones said: "Hundreds of millions of people – in regions like India, China and South America – are getting their first taste of computing and information interaction through mobile devices. Much has been written about how empowering these devices will be for these communities, providing access to education, banking, healthcare and more.

"However, there is a problem with this vision. Most mobiles are designed with a 'first world' perspective: for people who are relatively affluent with already good access to resources like education and infrastructure such as grid power and pervasive Internet connectivity. My work addresses the situation of people who have been described as being 'at the bottom of the pyramid'."

As a human-computer interaction researcher, Professor Jones' passion has always been to explore how computer technologies can fit into people's lives effectively. Using his experiences to date, Professor Jones is now embarking on this ambitious project, which will develop and test a range of innovative devices, user interfaces and computer algorithms with the aim of transforming how such communities create, access and share information through mobile devices.

www.swansea.ac.uk/compsci

IN BRIEF

Bangor opens CLARET

A new facility has opened at Bangor University, North Wales with the help of Welsh Government funding. The first of its kind in Wales, the 'Centre for Lifetime And REliabilty Testing' (CLARET), will enable businesses to test a huge range of plastic electronics, space-related equipment and solar cells.

This new industry-standard facility will provide regional and national businesses involved in the design, manufacture or integration of opto-electronic and material technologies, with lifetime and reliability testing facilities, with access to academic expertise and business support.

From Surrey to South Wales

Stem cell regenerative therapy company ReNeuron has identified what will serve as a "one-stop-shop" location for its operations when it relocates from Surrey to South Wales.

ReNeuron, which currently employs 30, will at least double its headcount when its new location at Pencoed Technology Park, becomes operational in 2016. Welsh Government has committed a £7.8 million grant support package towards the relocation costs.

Record revenues for IQE

One of Wales's leading technology firms IQE said it is expecting to post record revenues of at least £126m. In a trading update to the London Stock Exchange, South Wales' Cardiff headquartered IQE, the leading global supplier of advanced wafer products and wafer services to the semiconductor industry, said the second half of 2013 is expected to show sequential growth.

As a result, IQE revenues for the full year 2013 is expected to be at least £126m (2012: £88m) - representing a new record and an increase of over 43% compared with the prior year.

Swansea TechHub launched

120 delegates attended the launch of Swansea's South Wales TechHub where PingTune's CEO Henry Firth spoke about setting up a tech business. TechHubs are unique environments designed to nurture an international network of like-minded and focused technology entrepreneurs with a focus on allowing technology companies to "start up faster."

Finance Wales exits GeoVS

Finance Wales' successful exit from GeoVS is the first from its portfolio of technology ventures backed by the £150 million Wales JEREMIE Fund which was launched in 2009. A spin-out of the University of South Wales, although GeoVS had successfully commercialised its innovative technology platforms which improve marine operational safety, security and efficiency, it had identified a need to partner with a larger software company in order to break into the competitive market. AIM-listed Software Radio Technology (SRT) provided the ideal partner for the acquisition and will retain the existing core team in Cardiff.

Equity investment package for Laser Wire Solutions

Laser Wire Solutions (LWS) has been boosted by a £275,000 equity investment package to develop new technologies, commercialise products and expand operations.

The company, which is based in Abertillery, South Wales, has developed a range of laser-based wire-stripping products, which are designed for use on complex and high-value wiring systems. These hi-tech products are based on technology which was originally developed for NASA's space shuttle programme.

Finance Wales supplied a £125,000 equity investment and three business angels, arranged through the Welsh angel network xénos, and one angel via the South West Angel and Investor Network, also agreed to support the company.

Paul Taylor, managing director of Laser Wire Solutions, said: "We'll use this funding package to develop our existing products and it will also spearhead our long-term expansion because we'll be able to launch some new products."

As part of the expansion, LWS has moved to larger premises and now plans to target markets with an estimated potential value of £20m. Future product development will also open up new markets as the company launches products for specific sectors.

www.laserwiresolutions.com

CNH welcomes new co-director

Professor Huw Summers, current Chair of Nanotechnology for Health and Head of the Multidisciplinary Nanotechnology Centre at Swansea University, joins the Centre's existing directors, to take CNH into its next phase of development.

Professor Summers, who is also a Senior Affiliate Member of the Methodist Hospital Research Institute in Houston, Texas, said, "I am delighted to be appointed as Co-Director at the Centre for NanoHealth. The extensive state-of-the-art equipment and facilities, combined with the breath of internationally renowned research expertise available is hard to match elsewhere."

Professor Summers is internationally recognised for his research excellence, which focuses on two areas: metrologies for cell analysis (cytometry) and the development of nanoparticle-based diagnostics and therapeutics (nanomedicine).

Vizolution solution

Santander and Vizolution have jointly been selected as finalists for the 2014 Customer Contact Innovation Awards. The firms were nominated following the introduction of Vizolution's vScreen solution into Santander's Telephone Distribution division for credit cards. The vScreen is a software platform allowing representatives to have face-to-face advice sessions with customers.

Santander has successfully used vScreen's web-based sessions to guide customers through applying for a credit card in real time with customer feedback 95% positive. Crucially this project involved a range of departments as well as contact centre agents working together to make it happen. The platform operates on the agent's standard browser without additional software or IT implementation.

Catalysis Institute partnership goes live

The School of Chemistry has teamed up with Knowledge Centre Materials Chemistry (KCMC), helping experts working on applied materials chemistry to forge closer links with businesses across the UK and beyond. The collaboration is designed to bring Cardiff's work on materials chemistry and catalysis science closer to industry leaders, product designers and developers.

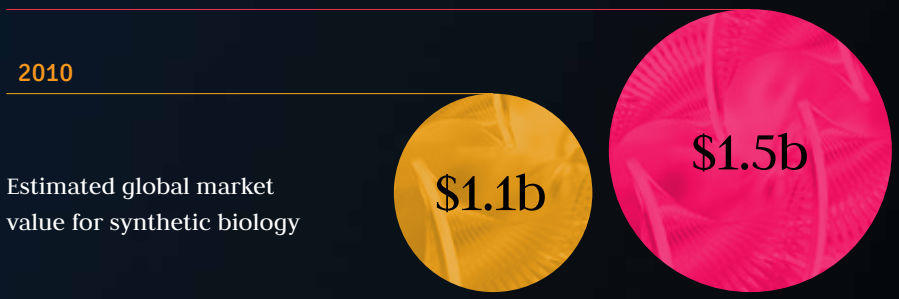
The partnership, funded through the Technology Strategy Board, is centred on Cardiff University Catalysis Institute (CCI). With its strong track record of industry collaboration, CCI will lead the Cardiff partnership with KCMC.

Funds for postgraduates

Cardiff University is set to benefit from a £350 million fund to train postgraduate students in engineering and physical sciences. It has secured a share of the UK's largest investment in postgraduate training for engineering and physical sciences. In total, the Engineering and Physical Sciences Research Council (EPSRC) will fund over 70 new Centres for Doctoral Training (CDTs) spread across 24 UK universities targeting areas vital to economic growth.

SYNTHETIC Biology

Synthetic biology is an emerging discipline underpinned by expertise from engineering and physical, life and computer sciences. It is commonly described as the design and engineering of biologically based parts, novel devices and systems as well as the redesign of existing natural biological systems. The aim is to standardise engineering-style processes for the creation of new genes to achieve reliable and reproducible biological products enabling their use in new and wide-ranging applications.



Estimated global market value for synthetic biology

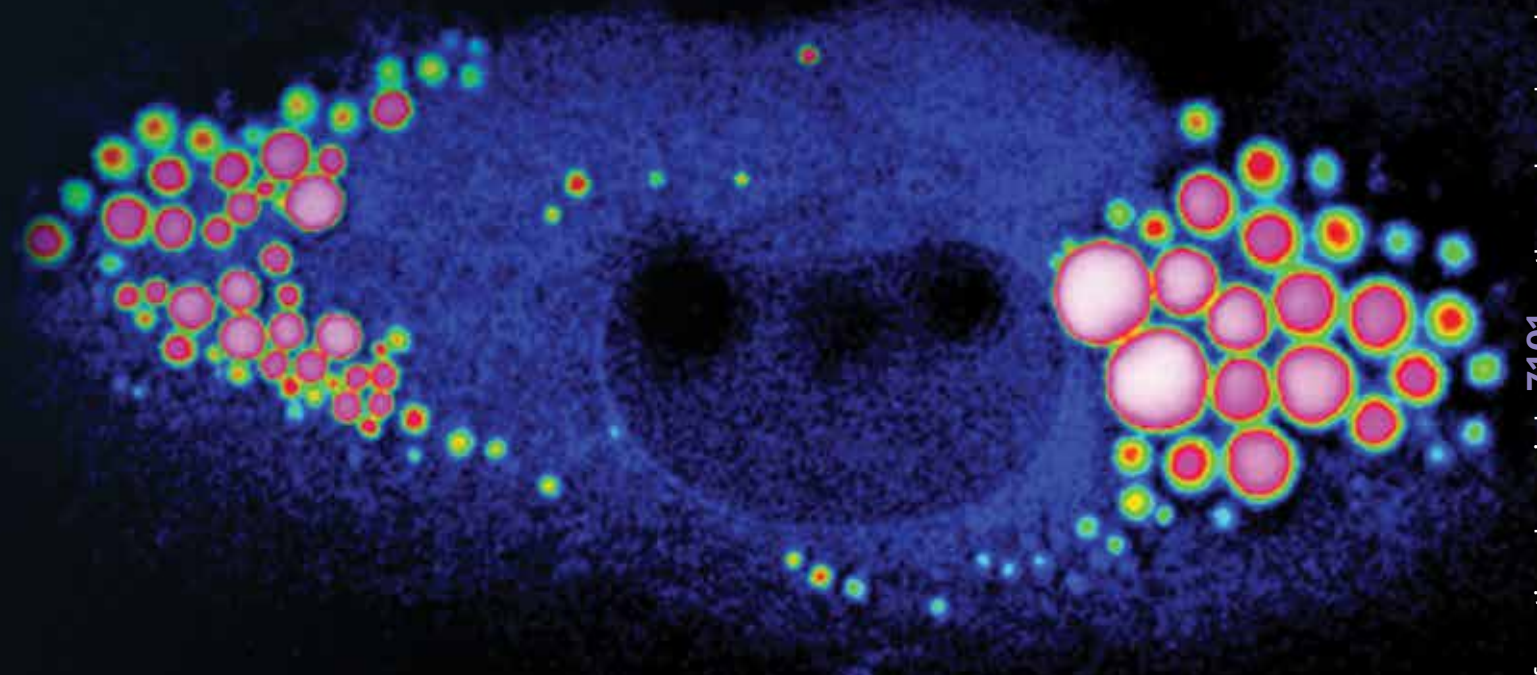
In the UK, the interest and research base in synthetic biology is growing rapidly and support from central and regional governments has allowed researchers at Welsh universities to explore this upcoming area. Swansea, Cardiff and Bangor Universities are now very much involved in the development and promotion of this technology.

Living organisms are made up of a number of key components which allow them to grow and replicate including cells, proteins and genes. The totality of the genes in an organism forms the genome and advances in molecular biology have allowed the genomes of organisms to be unravelled.

This explosion in the availability of data has led to an increased ability to engineer new genes and organisms that can be designed to meet a particular need.

The growth of synthetic biology in recent years has driven a move towards standardisation of the ways in which genes and DNA are produced to allow reproducibility and comparability of results across different laboratories. The techniques used to achieve this draw heavily on expertise from the physical sciences and engineering as well as biological understanding. In order to have reproducible parts and devices it is necessary to have a system

of standardisation and measurement of biological function. For synthetic biology, the key technologies required for this measurement are microscopy, flow cytometry, colorimetry, luminometry and fluorimetry.



Label-free Coherent Antistokes Raman Scattering (CARS) microscopy of lipids in living cells

Advances in high-performance computing and the mathematics of systems engineering are allowing the characterisation of biological parts to be expressed in terms of input and output characteristics in a similar way to the components of an electrical circuit. These characteristics can then be entered into a standard inventory or specification sheet so that a designer can understand how and where to use the part. Scientists hope that as the technology develops a wide range of standard 'bioparts' will be characterised for use in the design of multiple systems.

In common with other aspects of engineering, synthetic biology requires mathematical models of the designs and processes it makes use of. Modelling performs several functions, such as giving a fundamental description of a process or describing data in a way that allows it to be used in further simulations. It is critical to the development of synthetic biology, from describing how protein molecules bind to receptors to how groups of cells interact. It is expected that the relatively low cost and high throughput of computational modelling compared to experimental approaches will accelerate engineering design and hence innovation.

One of the aims for modelling of biological systems is the development of computer aided design environments for synthetic biology. One example of this type of BioCAD environment is clothocad . It aims to help manage and develop methods of standardising data as well as providing easily accessible tools for engineering synthetic biological systems.

Increasing the speed with which DNA and genes can be synthesised will be vital to the continued growth of the synthetic biology market. Recent developments in miniaturisation of production technologies such as microfluidics allow parallel synthesis of thousands of DNA and RNA strands. Microfluidics has also been shown to allow the behaviour of thousands of engineered cells to be monitored and tested simultaneously.

One of the main aims of synthetic biologists is to develop commercial applications that will both benefit society and lead to wealth creation and economic growth.

This field of research has applications in a wide range of areas including regenerative medicine, energy, commodity chemicals, agriculture and numerous other industrial processes.

In the area of regenerative medicine this discipline allows biologists to design cells which communicate with each other to control the way in which they grow and multiply or that respond to certain stimuli which could then be applied to control the growth and structure of biomaterials.

Crude oil has historically been the source of many of the building blocks for the chemical industries. Synthetic biology means that engineered biological systems have the potential to reduce our dependence on this finite resource using renewable sources of carbon to generate bulk chemicals.

Yeast can convert sugars into ethanol but developments in synthetic biology offer the opportunity to develop microorganisms which will produce a much greater variety of alcohols and diesel-like products. As the understanding of natural metabolic pathways in cells increases so does the opportunity to engineer these processes to produce a range of petroleum substitutes.

Synthetic biology is one of the eight emerging technologies supported by the UK government and the roadmap is directly informing its policy in this area. The UK Research Councils and the Technology Strategy Board are spending over £90 million on world leading synthetic biology research and commercialisation and a further £50 million will be invested in synthetic biology to support implementation of key recommendations from the roadmap which will help to establish multidisciplinary research centres as well as provide seed corn funding to support start-up companies and pre-companies.

> Synthetic biology has huge potential. Indeed it has been said that it will heal us, feed us and fuel us. The UK can be world-leading in this emerging technology. That is why we are backing it with further investment.
>
> **David Willetts,**
> **Minister for Universities and Science, UK**

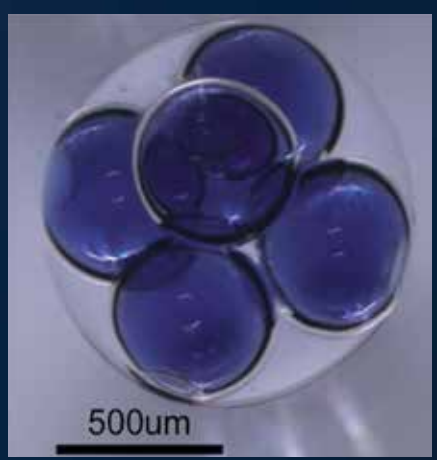
An investment of £10 million has been made by the Biotechnology & Biological Sciences Research Council (BBSRC), the Engineering and Physical Sciences Research Council (EPSRC) and the Technology Strategy Board (TSB) to establish a multi-partner Innovation and Knowledge Centre (IKC) in synthetic biology based at Imperial College London. SynbiCITE is the UK's national centre to accelerate the commercialisation of synthetic biology; it is centred at and led by Imperial College London by Prof. Richard Kitney and Prof. Paul Freemont, the centre's Directors, with a goal to create an industry based on Synthetic Biology.

Dr John Collins, acting commercial director for SynbiCITE explains that the centre treats the UK as a "cluster of expertise" and brings together eighteen University partners, including three Welsh partners, Cardiff, Swansea and Bangor, with more than thirty SMEs and seven major companies including Shell UK plc, Syngenta, Agilent, Microsoft, Procter&Gamble, GSK and LifeTechnologies, all "offering facilities, expertise and services to enable synthetic biology to become embedded in manufacturing industries."

The synthetic biology work carried out by Professor Peter Golyshin at Bangor

University focuses on two main areas. One of these is harnessing bacteria for bioremediation. Oil pollution, especially at high seas and in Polar areas poses a significant challenge for the environment and Professor Golyshin has pioneered the isolation of, and the OMICS research on, the so-called "obligate marine hydrocarbonoclastic bacteria"(i.e. naturally occurring marine microbes whose feeding requirements are limited just to hydrocarbons, i.e. the principal petroleum oil constituents). Bangor's research aims at the identification of metabolic bottlenecks in these bacteria to develop novel approaches for bioremediation. The study of mechanisms of cold adaptation in one of such bacteria, which was in particular very abundant and efficient in oil degradation after the "Deepwater Horizon" accident in the Gulf of Mexico, has resulted in establishing the microbial chassis for "cold" protein production based on E. coli that acquired the ability to grow at lower temperatures.

Another of the research areas is focused on the metagenomic mining of enzymes with unusual functions from microorgansms thriving at the limits to life, the extremophiles. These microorganisms have a great variety of interesting enzymes, however they are difficult to culture in the lab.



"Precision compartmentalised chemistry within synthetic cell-like constructs may be the starting point for future wholly synthesised artificial cells" - Courtesy Jin Li and Pr. David Barrow, Cardiff University

Metagenomics allows bypassing the issue of poor culturability of extremophiles in the lab through direct expression and selection for enzymatic activity of interest. Corresponding genes are used as "parts" in engineered metabolic circuits tailored to conduct specific biochemical reactions of biotechnological relevance. There is a strong interest in industry in establishing a comprehensive "enzymatic toolbox" (to include "extremozymes") to perform bioconversions a la carte.

Professor Jim Murray leads on the synthetic biology research at Cardiff and says, "It covers a diverse range of activities across engineering, computing, physical and biological and biomolecular sciences. We aim to increase understanding of the complex processes occurring within biological systems from whole organisms to cellular and molecular scales as well as develop techniques for the fabrication of novel devices and sensors at the interface of physical and biological systems."

Swansea University's Professor Paul Rees, explains that the researchers are, "interested in developing tools for synthetic biology for the analysis of cell population imaging data measured using flow cytometry and high-throughput microscopy." In particular, the team use multivariate analysis and machine learning algorithms to deconvolve meaningful information at the cellular level from the large data sets generated using these techniques. A key part of Swansea's approach is the development of stochastic data driven cell models which are used to deconvolve single cell information from the heterogeneous responses measured from large cell populations.

Professor Rees adds, "We are very much looking forward to working with colleagues in the other university partners and companies in the IKC. Synthetic biology is an exciting area of research and promises to hold the key to new technologies and techniques in a wide range of applications from agriculture to healthcare and we are excited to be involved in this new centre."

The global market for synthetic biology was estimated at $1.1 billion in 2010 and reached $1.5 billion by the end of 2012. Looking ahead, industry reports predict that the market will continue to grow by 41–45 percent per year for the next five years with Europe currently holding the largest share of the market. The research carried out by these Welsh universities could be crucial not only for its development as a new discipline in Wales but also for the growth of the country's economy.

> The vision is to create a dynamic centre of entrepreneurial synthetic biology at Cardiff, and we are excited to be part of the national centre at SynbiCITE and the opportunities that this provides to build further on our collaborations with industry to commercialise new products and services in this rapidly expanding area.
>
> **Professor Jim Murray**
> **Cardiff University**

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Welsh SPIRE instrument leads to noble gas discovery

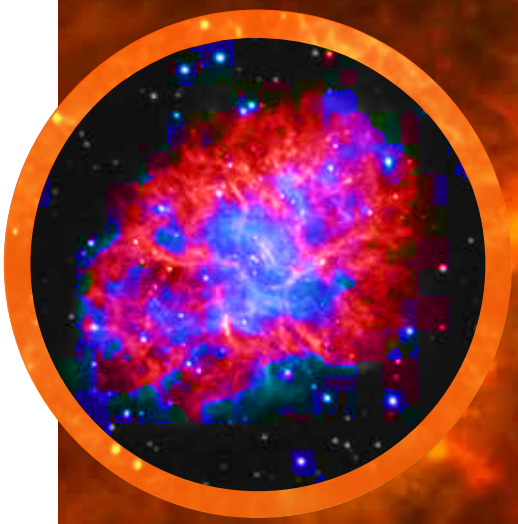
A molecule containing a noble gas has been discovered in space by a team including astronomers from Cardiff University

The find was made using a Cardiff-led instrument aboard Europe's Herschel Space Observatory. The molecule, argon hydride, was seen in the Crab Nebula, the remains of a star that exploded nearly 1,000 years ago. Prior to the discovery, molecules of this kind had only been studied in laboratories on Earth, leading astronomers to believe that the right conditions did not occur in space.

Further measurements of the Crab Nebula were made using Herschel's SPIRE instrument and it transpired that the right conditions exist there for these reactions to occur. The measurements allowed the team to infer the properties of the argon atoms and to evaluate the type (or isotope) of argon found in space.

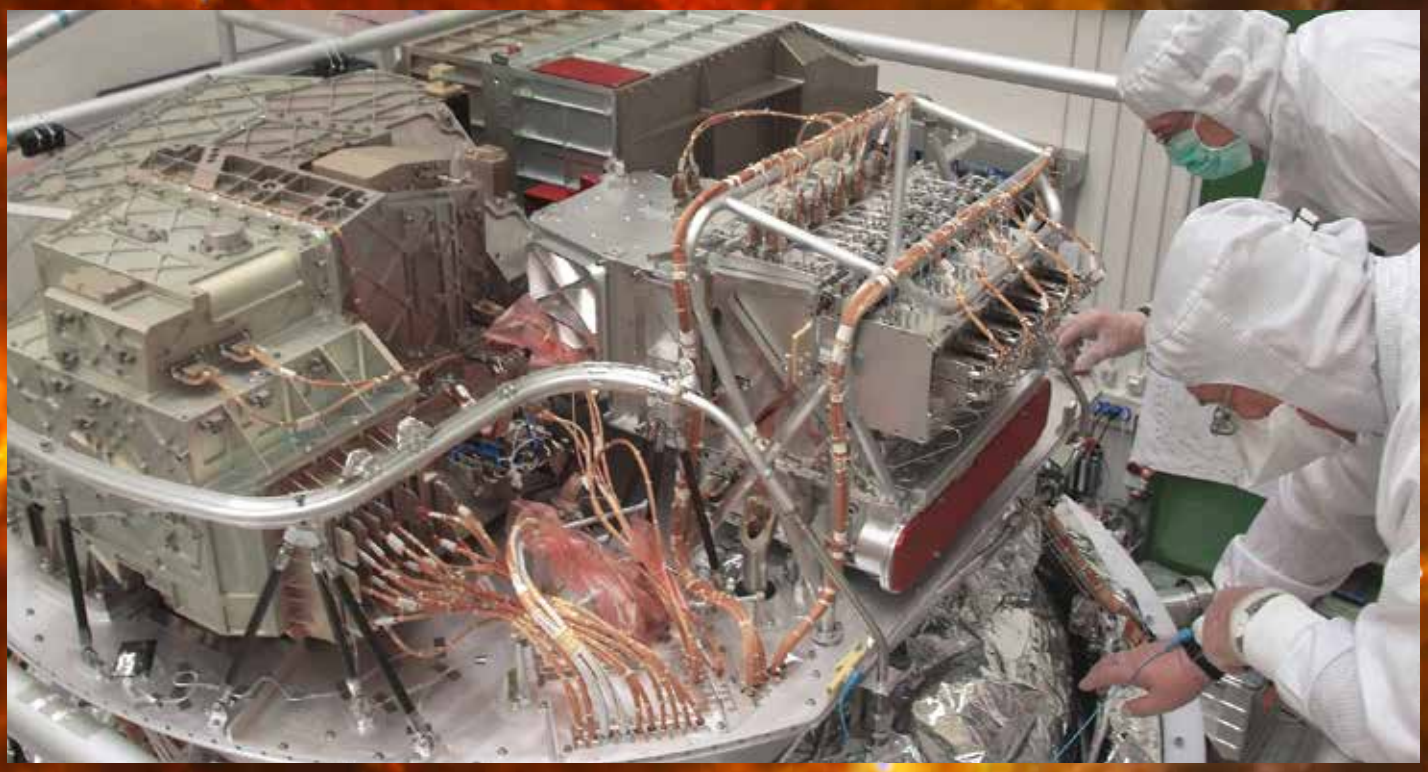
SPIRE is based on advanced technologies including detectors, cooling systems, electromechanical mechanisms and optical components, combined with specialised data processing methods. The SPIRE instrument works at wavelengths a few hundred times longer than the wavelengths of visible light. It contains a camera and an imaging spectrometer. The instrument's camera operates in three wavelength bands centred on 250, 350 and 500 μm, and so can create images of the sky simultaneously in these three sub-millimetre "colours"; the spectrometer itself covers the wavelength range between 194 and 671 μm. As molecules spin in space, they emit light of very specific wavelengths called "emission lines" and the precise wavelengths emitted are dictated by the composition and structure of the molecule. Cardiff University built cryogenic and optical components for the instrument and the development and operation of the whole instrument was led by Professor Matt Griffin, from the School of Physics and Astronomy.

The team using SPIRE to study the Crab nebula were observing the intricate network of the nebula's gas filaments to investigate how exploding stars can create vast amounts of space dust, and it was whilst examining this dust using SPIRE that they unexpectedly discovered the argon.



The Crab Nebula

> We were really concentrating on studying the dust in the filaments with SPIRE, and out pop these two bright emission lines exactly where we see the dust shining. The team had a hard time figuring out what these lines were from as no-one had seen them before.
>
> **Dr Hayley Gomez**
> **Cardiff University's School of Physics and Astronomy**



PICTURE COURTESY OF ESA

The three Herschel instruments during installation in the spacecraft. The SPIRE instrument is at the rear.

The emission lines corresponded to the first two rotational transitions of argon hydride (ArH+) at frequencies of 617.5 GHz and 1234.6 GHz, respectively. The Cologne Database for Molecular Spectroscopy (CDMS) and the Madrid Molecular Spectroscopy Excitation (MADEX) code were used to identify these lines. The results have allowed the team to determine the properties of the argon atoms and they have concluded that the type of argon seen in the Crab Nebula is different from the most common form of argon seen in rocks on Earth.

"What a great detective story," added Professor Griffin, "Here we see the excellent performance of the Herschel-SPIRE spectrometer, the expertise of the instrument team in producing the highest quality data, and the tenacity and vision of the scientists analysing it, all coming together to make an intriguing new discovery."

With unique access to new technology developed for SPIRE and other projects, the School of Physics and Astronomy is able to develop and market products through its in-house commercial arm QMC Instruments Limited.

Profile

Product
SPIRE Instrument

Applications
Observes the universe at far infrared wavelengths

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Ultravision gives surgeons better sight

Product launched by Welsh company to dispel surgical smoke and solve visibility issues during laparoscopic surgery

A South Wales company, Asalus Medical Instruments, has recently launched a revolutionary product that rapidly clears the visual field of surgical smoke produced during laparoscopic surgery and simultaneously prevents its release into the operating theatre.

The technology offers the potential to maximise the efficiency of surgery whilst minimising the risks to the surgical staff of the potential long-term health implications of chronic exposure to the smoke. Laparoscopic surgery is a minimally invasive surgery (MIS) technique for procedures performed in the abdominal cavity. Approximately six million laparoscopic procedures are performed annually worldwide and current vacuum-based solutions, more commonly used in open surgery, have proved to be largely ineffective in meeting the needs of the surgical team. This is due to the vacuum tubing being very narrow, making the process of smoke evacuation inefficient and slow. Furthermore, the repeated replacement of carbon dioxide – the gas used to inflate the abdominal cavity during the procedure – increases the risk of post-surgical adhesions and patient cooling. In addition to this, the generators used for this method are large, cumbersome and noisy which can prove a distraction for the surgical team. As a result, surgeons typically expel the smoke directly into the operating room during surgery, a process which slows surgery down and releases the smoke into the room, where it is inhaled by the operating room staff. Such chronic exposure may have long-term health implications.

approximately six million laparoscopic procedures are performed annually worldwide

The new Ultravision product uses "electrostatic precipitation" technology which has proven to be a highly effective means of removing airborne particulates from the atmosphere in industrial applications such as paper and cement manufacture. Its application in surgery was first conceived by Dr Neil Warren, Asalus' Chief Scientific Officer, who is also Director of the leading Cardiff University-based training institute, the Welsh Institute of Minimal Access Therapy (WIMAT). Although the technology has potential applications in many minimally invasive surgery (MIS) procedures, Asalus has initially focused on the use of Ultravision in laparoscopic surgery. The Ultravision system comprises a standalone generator unit and disposable peripherals: the "Ionwand" cable is introduced into the patient's abdominal cavity using a disposable trocar and catheter and the Ultravision generator delivers a low-energy current to the abdominal cavity (which is 400-1000 x less energy than electrosurgical instruments). The energy source creates negative gas ions in the abdominal cavity. The patient is the positive pole of an electrical circuit through the use of a patient return electrode which is already used in electrosurgery and is connected to the Ultravision generator. As a result of this, the negative gas ions flow towards the patient tissue and collide with the smoke particles as they are created by the electrosurgical cutting device. These smoke particles become transiently negatively charged and very rapidly migrate to the patient tissue where they are deposited. The negative charge returns to the generator via the patient return electrode and are neutralised.

Asalus completed a clinical trial at University Hospital Llandough, South Wales, as part of its regulatory requirements. In this trial, the technology was able to shorten the duration of surgery by reducing the number of pauses to surgery caused by smoke build-up in the abdominal cavity. Importantly, there was no longer any need to release the smoke into the operating room.

Dr Warren said: "Surgical smoke is a significant issue during laparoscopic surgery. Smoke rapidly builds up in the abdominal cavity, severely impairing the quality of the visual field and slowing down the procedure. The subsequent release of surgical smoke into the operating theatre is also unpleasant for the surgical team and there is a potential risk that chronic exposure may have long-term health implications."

Asalus has been awarded the CE mark for Ultravision allowing it to launch the product in the EU over the coming months and Dominic Griffiths, Managing Director of Asalus, said: "This is a significant achievement in the evolution of Ultravision and is crucial to our launch plans. The company has already received overwhelming interest in Ultravision from both the surgical community and global distributors and is looking forward to bringing Ultravision to market."

> We have developed Ultravision because we know that the current solutions used in surgery are largely ineffective in meeting the needs of the surgical team. Ultravision silently, effortlessly and unobtrusively clears the visual field of surgical smoke and prevents its release in to the operating theatre to allow best practise in laparoscopic surgery.
>
> **Dr Neil Warren,**
> **Chief Scientific Officer,**
> **Asalus Medical Instuments**

Profile

Product
Ultravision - electostatic precipitation technology

Applications
Dispels surgical smoke

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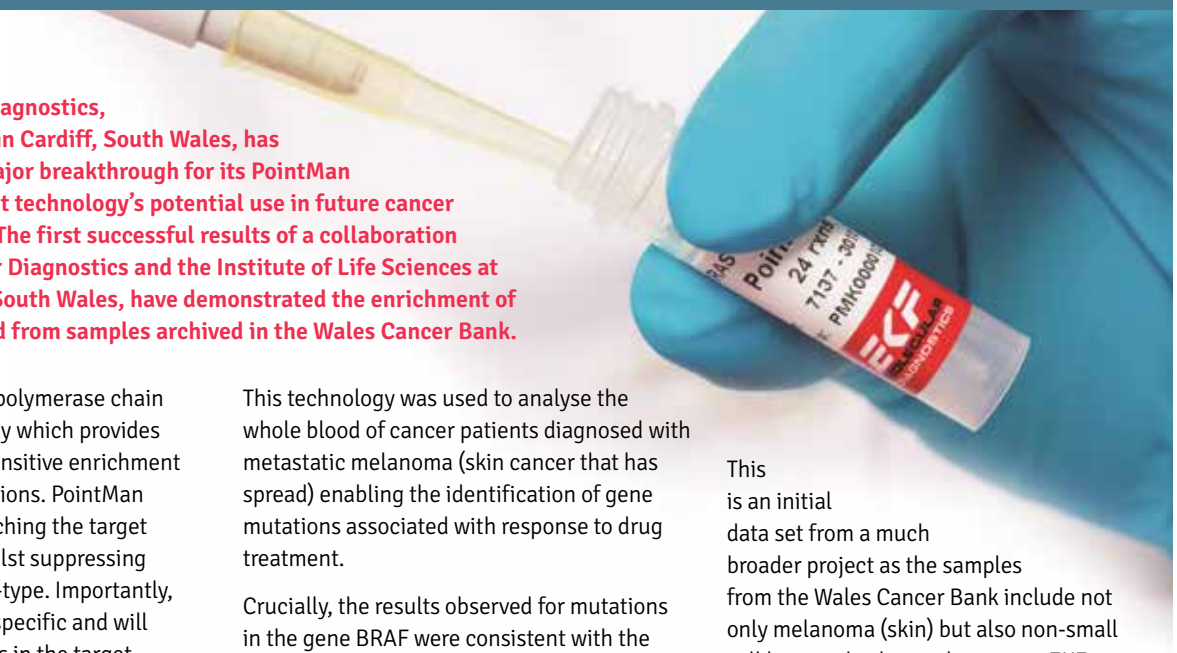
Pointing the way to a new method of cancer mutation assessment

EKF's PointMan enables blood sampling instead of tissue biopsies for cancer patient mutation status assessment



EKF Molecular Diagnostics, headquartered in Cardiff, South Wales, has announced a major breakthrough for its PointMan DNA enrichment technology's potential use in future cancer testing and treatment. The first successful results of a collaboration between EKF Molecular Diagnostics and the Institute of Life Sciences at Swansea University in South Wales, have demonstrated the enrichment of gene mutations in blood from samples archived in the Wales Cancer Bank.

PointMan, is a real-time polymerase chain reaction (PCR) technology which provides reliable and extremely sensitive enrichment for specific cancer mutations. PointMan is highly efficient in enriching the target sequence of interest, whilst suppressing amplification of the wild-type. Importantly, the method is not allele specific and will amplify any or all variants in the target sequence. This means that a particular mutation can be identified using a single reaction thereby conserving valuable sample. The resulting sample is effectively enriched for the mutation and has the potential to offer industry leading sensitivity in a wide variety of sample types. PointMan technology is considered to be extremely effective on low level mutations where other technologies, such as DNA sequencing, may often fail.

> "Once under treatment, patients can be too sick for a repeat biopsy to be taken; this initial data highlights the possibility of patient monitoring using a blood test."
>
> **Gary Dowthwaite, Product Manager, EKF Molecular Diagnostics**

This technology was used to analyse the whole blood of cancer patients diagnosed with metastatic melanoma (skin cancer that has spread) enabling the identification of gene mutations associated with response to drug treatment.

Crucially, the results observed for mutations in the gene BRAF were consistent with the formalin fixed paraffin embedded (FFPE) tissue samples. FFPE is the laboratory standard method to prepare all biopsy samples for pathology review in order to diagnose the cancer. These results have been confirmed by DNA sequencing which had failed to identify the mutations prior to sample enrichment through EKF's PointMan technology.

Dr Ricardo Del Sol, Senior Lecturer, ILS Swansea University, commented: "These results are a clear indication of the potential for PointMan to enable the use of a blood sample to assess the mutation status of cancer patients."

"This is a major step forward not just for the company but also for the future testing of cancer patients where we hope that less-invasive testing will become routine using our PointMan technology" explained Julian Baines, CEO of EKF. "Further evidence will be generated from other collaborations and I look forward to providing further updates during 2014."

This is an initial data set from a much broader project as the samples from the Wales Cancer Bank include not only melanoma (skin) but also non-small cell lung and colorectal cancers. EKF are actively working to demonstrate that a sample enriched using PointMan technology shows concordance between the tissue (FFPE) and whole blood.

This level of research will open up the opportunity for patient monitoring as well as screening for early diagnosis.

Profile

Product
PointMan DNA enrichment technology

Applications
Sensitive detection of cancer mutations

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Sheep to save humans from super bug

MicroPharm extracting antibodies from sheep to fight *Clostridium difficile*

Over the past five years, MicroPharm Limited, based in Carmarthenshire, West Wales and Public Health England (PHE) have worked to develop a systemic form of immunotherapy for use in patients with *Clostridium difficile* infections (CDI). The result is PolyCAb, ovine polyclonal antibodies directed against the two main C. difficile toxins, TcdA and TcdB. This is provided in liquid form for intravenous injection and administered when, or ideally just before, a patient with severe CDI commences specialised antibiotic therapy.

With funding from the Technology Strategy Board (the UK's innovation agency), MicroPharm and PHE are carrying out initial research and MicroPharm is now extracting antibodies from sheep to fight CDI in humans. Last year about 20,000 people in Wales and England contracted the digestive tract infection and as a result 10% of those died. Sheep have been chosen to produce the active ingredient rather than the equine immunoglobulin used initially to treat other clostridial infections. MicroPharm's research has shown that the levels of specific antibodies that can be attained in sheep are significantly higher than in horses and these antibodies are also less immunogenic than their equine counterpart, the heavily glycosylated IgGT. While it requires about five sheep to provide the same volume of antisera as a single horse, sheep are relatively inexpensive to purchase and maintain; are easy to handle; and are widely available. This is important as it may eventually be necessary to employ flocks of several thousand to meet the needs of the C. difficile programme. The primary objective of the project is to ensure that the systemic administration of PolyCAb in severe CDI is both safe and improves the patient's recovery when used as an adjunct to the present best possible standard of care.

> "Around 5% of human adults live with C.difficile in their gut and never know a thing about it. It is only when antibiotic resistant forms are allowed to multiply that the problems start
>
> **Dr Geoff Shellswell, Chief Operating Officer, MicroPharm**

"The most common time to contract a bout of C. difficile, which will cause serious problems, is when you're receiving broad spectrum antibiotics, usually in hospital" said Mr Ian Cameron, MicroPharm's Chief Executive Officer. "The drugs will knock out most other bacteria - including those which help protect against C. Diff - but because C. Diff has developed drug-resistant strains, it is left behind and can run rampant with no competition."

To conduct this research, the sheep are immunised with a minute amount of the inactivated toxins the C. difficile bacteria produces. These amounts are too small to cause any health effects in the sheep, but as they respond with a natural immune reaction, the antibodies created can be harvested from their blood.

"The process is very similar to a human blood donation and causes the sheep a little discomfort but no lasting harm whatsoever," said Dr Shellswell, MicroPharm's Chief Operating Officer. "The more technical part is then removing the unwanted parts of the blood, purifying the antibodies, and concentrating them in sufficient quantities to fight a C. diff infection in a human."

Laboratory testing has confirmed that the antibodies are active against the bacterial toxins and a phase one clinical trial is planned for late 2014, organised in collaboration with the Welsh company Simbec. Further clinical trials with patients are planned to start in 2015. Looking ahead, the product could be on sale within the next five to 10 years.

Profile

Product
Ovine polyclonal antibodies

Applications
Form of immunotherapy

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Streetkleen cleans up

Micro Bio-Digester developed in Wales to help the developing world

Designed, developed and manufactured in Wales, Streetkleen Bio's Micro Bio-Digester is the first micro scale biogas system to incorporate an integrated acidogenic pathogen reduction system. Designed for the developing world, the system turns pollutants into compost, provides liquid for irrigation and flushing water, and gas for domestic energy whilst improving hygiene.

Biogas digesters mitigate a wide spectrum of waste materials. They improve sanitation, provide high-quality organic fertilizer and reduce greenhouse gas emissions and the demand for wood and charcoal for cooking- therefore helping to preserve forested areas and natural vegetation. One of the greatest benefits of biogas to the developing world is helping to alleviate some very serious health problems.

Both human and animal wastes are loaded with pathogens including *Salmonella, E. coli O157:H7, Campylobacter jejuni, Yersinia enterocolitica, Giardia lamblia,* and several types of *Cryptosporidium*. Most of these pathogens are transmitted via the oral–faecal route and can cause diarrhoea, abdominal cramps, dehydration, fever, vomiting, and in vulnerable populations such as infants, children, the elderly, and immunocompromised persons, even death.

Even though the biodigestion process naturally reduces the pathogen load it is doubtful whether digester slurry can still harbour enough pathogens to infect humans who handle it or eat crops fertilized with it. In several experiments carried out by Streetkleen Bio using human waste as a feedstock, it was found that separating the overall digestion process into discrete acidifying and methanogenic stages and thereby isolating the acidogenic bacteria in their own tank uniquely resulted in complete eradication of live pathogens.

The Streetkleen Micro is a renewable energy system which produces 100% organic compost. The energy produced can be used for domestic purposes such as cooking, lighting and heating, and the compost as a natural fertilizer.

The liquids produced by the system will reduce water consumption and it can be run using ambient heat, supplementary solar pv, wind, or waste heat. Its unique automatic control system means that operation, and the subsequent storage of energy, does not require human intervention- a typical operator simply puts the untreated feedstock for digestion in and the treated solids and liquids will come out. The system is designed for re-use of the liquid for better digestion, mixing for better gas production, and pre-treatment thickening, sludge retention using standard components. The system's unique modularity and mobility means that it does not require any civil engineering infrastructure, any digging, or specific sites where it can be placed. It can be positioned close to the waste or feedstock or wherever the demand is and can be used as a power rental system or a mini fertilizer production unit, literally using whatever waste is being generated. These features make it easier to insulate and more efficient to operate in cold or extreme climates.

Research carried out by Streetkleen Bio shows a demand for compost, liquid, gas from over 7 billion people. Gary Downie, Streetkleen Bio's Managing Director, estimates that, "these people, especially due to the variability in oil and fertilizer prices, will need a micro system where the costs can be safely projected in the future and the main variable is feedstock which in turn depends on waste."

The modularity, mobility and minimal infrastructure costs of Streetkleen's Micro will ensure that it will be operationally robust and will satisfy the demand of the developing world by using the growing amount of material available ranging from duckweed to manure, which would otherwise be a source of pollution.

Profile

Product
Micro Bio-Digester acidogenic pathogen reduction system

Applications
Mitigation of waste materials

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Death by fungus provides solution

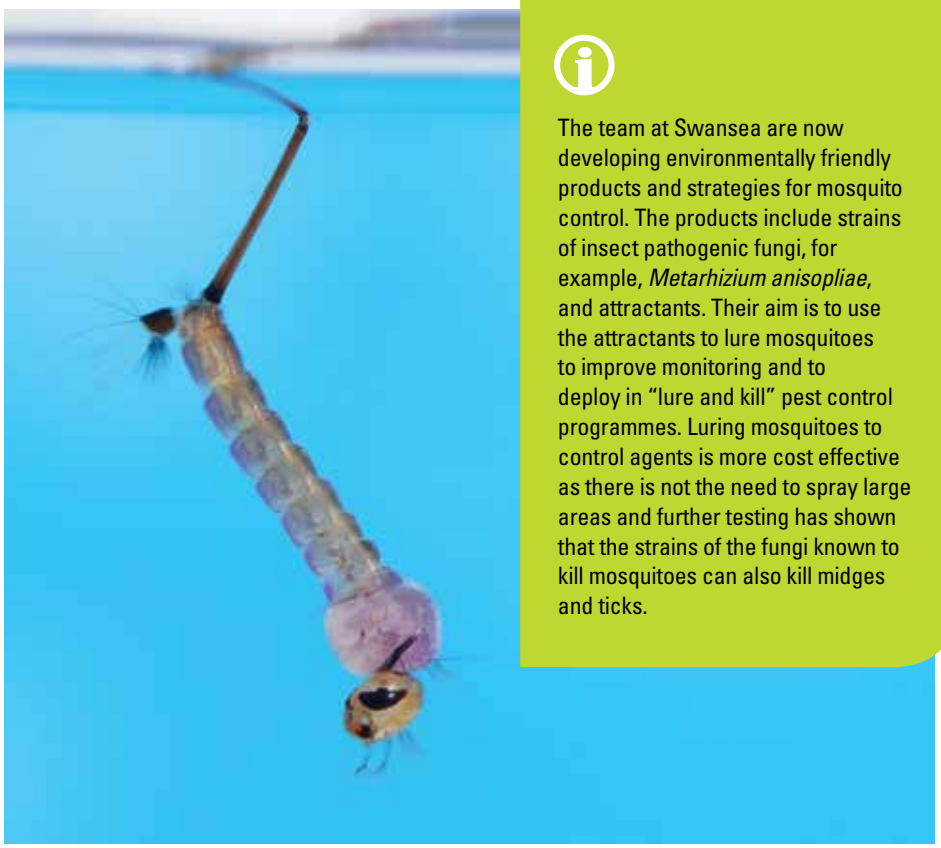
Findings of a groundbreaking study by a team of Welsh academics could have far-reaching implications for the control of mosquito larvae across the world

Professor Tariq Butt, from the Department of Biosciences at Swansea University, South Wales, has led a rigorous and thorough study into the mechanisms by which the insect pathogenic fungus *Metarhizium anisopliae* kills mosquito larvae, demonstrating that the fungus infection processes that occur for terrestrial insects do not apply to the mosquito larvae.

The research has shown that this fungus is able to kill the larvae without germinating which results in a stress related and fast 'accidental death'. It is not adapted for the aquatic environment and does not stick to the surface of the insect -instead it kills its host inadvertently when ingested. This means that the *Metarhizium* spores do not penetrate the gut or cuticle but instead produce proteases which induce stress and subsequently death to the larvae. This is a new discovery as it has always been assumed that the fungus penetrates the cuticle as it does terrestrial hosts. The fungus does not propagate in the infected larvae as it would in susceptible hosts and so the conclusion is that the death caused is therefore unintentional – hence the verdict of accidental death.

Mosquitoes are small, midge-like flies in the family *Culicidae*. Although a few species are harmless, most are considered a nuisance because they consume blood from living vertebrates, including humans. Professor Tariq Butt said, "Female mosquitoes feed on blood and in the process, some of them transmit extremely harmful human diseases, such as malaria, dengue and yellow fever. More than half the world's population is at risk to mosquito transmitted diseases."

Findings from this Swansea-led study have shown that these strains of fungi kill both adult and larval mosquito of three important genera: *Aedes* – vector of yellow fever and dengue, *Anopheles* – vector of malaria and *Culex* – vector of West Nile Virus.



The team at Swansea are now developing environmentally friendly products and strategies for mosquito control. The products include strains of insect pathogenic fungi, for example, *Metarhizium anisopliae*, and attractants. Their aim is to use the attractants to lure mosquitoes to improve monitoring and to deploy in "lure and kill" pest control programmes. Luring mosquitoes to control agents is more cost effective as there is not the need to spray large areas and further testing has shown that the strains of the fungi known to kill mosquitoes can also kill midges and ticks.

Speaking about the future application of these findings Professor Butt said, "The results from the study show that by simply casting the fungus spores on water we should be able to help to defeat troublesome life threatening colonies of mosquitoes which have been gradually moving north into Europe as the climate warms up. Trials are currently taking place in Africa and the findings would have important consequences for tackling malaria and other mosquito transmitted diseases."

"We hope that our 'accidental death' findings will stimulate much discussion on this topic and lead to some important and exciting developments which could eradicate the most dangerous animals on earth! "

The results of this study will have far reaching implications for the control of mosquitoes and other pests as well as the resulting diseases which they transmit.

Profile

Product
Mosquito attractant and *Metarhizium* fungus

Applications
Pest control

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Immune fingerprint could prove key to helping dialysis patients

Discovery by Cardiff University in South Wales could lead to groundbreaking developments for dialysis patients

A group of South Wales scientists committed to developing improved treatments for patients with chronic kidney disease have discovered a novel way of significantly accelerating the detection of bacterial infection using the patient's own immune system.

The current diagnostic tests are often delayed by days which can lead to treatment failure and sometimes even death. Dialysis patients with chronic kidney disease rely on fast and accurate diagnosis of infection so that doctors are able to administer the correct antibiotic treatment to ensure a fair chance of recovery.

Professor Nicholas Topley and Dr Matthias Eberl from Cardiff University's School of Medicine have shown proof-of-concept that a patient's unique immune responses to infection can be used to accurately detect which organism is causing infection within hours. Together with commercial partners, the Cardiff group is using these new insights, which they call 'immune-fingerprints', to inform the development of a point-of-care test.

"Infection is the biggest obstacle for any dialysis patient as it can seriously hamper their treatment and their chances of leading a normal life," said Professor Topley.

Dr Matthias Eberl from Cardiff's Institute of Infection & Immunity explained "The immune system is capable of rapid, sensitive and specific

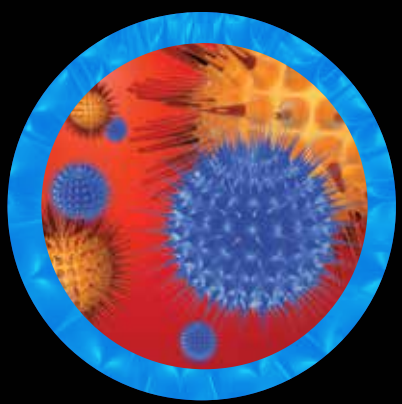
detection of a broad spectrum of microbes, which has been optimised over millions of years of evolution. A patient's early immune response is therefore likely to provide a far better insight into the true nature and severity of microbial infections than current tests, which are based on the microbiological identification of the potential pathogen (a concept introduced by Robert Koch more than a century ago)."

To test this theory, the scientists performed a detailed immunological and microbiological analysis of samples obtained from peritoneal dialysis patients with acute infection/ peritonitis (a condition in which the thin tissue that lines the inner wall of the abdomen becomes inflamed). The results revealed that each bacterial infection leaves a distinct immune signature and robustly discriminates between different types of infection.

This is the first time that scientists have attempted – or succeeded - to distinguish soluble and cellular components in defining responses to specific germs in an infected human and to translate the idea of immune fingerprints into a potential diagnostic tool.

Bacterial infections remain a leading cause of disease and death worldwide and pose a critical challenge for public health in the 21st century, not least due to the unprecedented spread of antibiotic resistance. This research provides proof-of-concept that using immune fingerprints to inform the design of point-of-care tests will help target antibiotic prescriptions and improve patient management. With the immune fingerprint test, doctors will be able to differentiate rapidly between serious and benign infections and therefore to prescribe suitable and accurate treatments.

Elaine Davies, Head of Research Operations for Kidney Research UK, said, "Kidney Research UK welcomes this publication about new evidence on how we might in future tackle this problem earlier thereby reducing the infection risk and complications for patients who are already coping with the life-threatening consequences of kidney failure."



"

Through my own experience as a transplant patient, my research in dialysis patients over the past 25 years and in talking to patient groups, I observed that conventional tests just aren't quick enough and are often inconclusive, which can be a fatal shortcoming.

We therefore decided that more needed to be done to ensure that patients had every chance of receiving a successful treatment and a healthy future, and from then on committed our research efforts to finding a new approach to identifying and targeting infection, looking to the body's own natural defences for inspiration.

Professor Nicholas Topley, Cardiff University School of Medicine

Profile

Product
Diagnostic tool

Applications
For patients with chronic kidney disease

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Coral aids bone repair

Swansea researcher looks to improve the outcome of bone grafts using sea coral

Sea coral could soon be used more extensively in bone grafting procedures thanks to new research from Swansea University in South Wales that has refined the material's properties and made it more compatible with natural bone.

Dr Zhidao Xia at the University's College of Medicine along with researchers from the UK and China found that by partially converting calcium carbonate-found in the exoskeleton of sea coral-into coralline hydroxyapatite (CHA), the refined material, called coralline hydroxyapatite/calcium carbonate (CHACC), was shown to 'considerably improve' the outcome of bone grafts in 16 patients.

The results of their clinical study showed that bone healing was observed in each of the patients after four months and that the CHACC had fully biodegraded after two years.

CHA derived from sea coral has been used for many years as a successful bone graft material; however, its use has been limited to specific bones because it does not fully biodegrade.

Researcher Dr Xia said, "Our methods have considerably improved the outcome of bone grafts by using the partial conversion technique, in which the biodegradable composition from natural coral is reserved. It works in a very similar way to commercially available CHA for conductive bone regeneration, but the better biodegradation properties are compatible with the host tissue's natural bone turnover process.

CHACC could become a promising alternative to an autograft, which uses pieces of bone from another part of the patient's body to regrow new bone in the injured area. Besides only having a limited stock, an autograft can cause discomfort, pain and long-term impairment in the area that the bone is taken from.

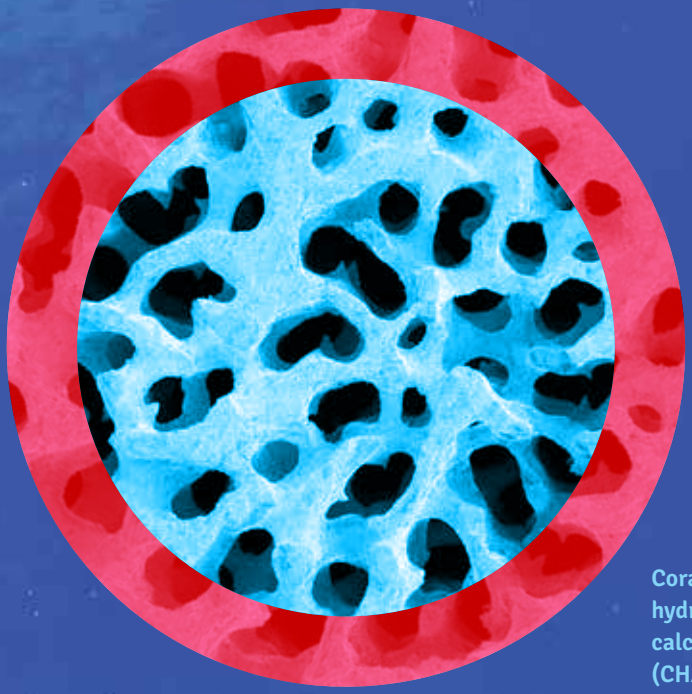
> "When biomaterials do not biodegrade and remain in skeletal tissue, they may continuously cause problems in the host. In extreme conditions, it is possible that the different mechanical properties of the artificial bone graft may cause a re-fracture or become a source for bacterium growth in infection."
>
> **Dr Zhidao Xia,**
> **Researcher,**
> **Swansea University**
> **College of Medicine**

In their study, the researchers harvested sea coral from South China and partially converted the calcium carbonate into CHA to form CHACC

They found that the CHACC composition, which contains 15 per cent of CHA in a thin layer around the calcium carbonate, has the strong, porous structure that has made CHA commercially successful, but contains significantly improved biodegrading properties to support natural bone healing.

The researchers constructed CHACC and tested its physical and chemical properties using a number of microscopic and spectroscopic techniques and the results showed that new bone formation was visible on the surface of the CHACC.

In a preliminary clinical study, 16 patients (11 male and five female) with a range of four different bone defects were surgically implanted with CHACC. Results showed there was clinical bone healing four months after surgery and the majority of the implanted CHACC degraded after 18 to 24 months in each patient.



Coralline hydroxyapatite/ calcium carbonate (CHACC)

Bone remodelling can be a complex and slow process by which old bone is continuously replaced by new bone tissue. In the case of fracture healing, the complete remodelling phase can take between three and five years depending on the individual, so a synthetic bone graft must biodegrade within a time window that relates to the natural bone remodelling cycle.

Moving forward, the researchers plan to combine the controlled growth factor delivery encapsulated in the CHACC material with stem cell technology to develop a more advanced solution which could be used on the several million people worldwide who undergo bone grafting procedures each year.

Profile

Product
CHACC composition

Applications
Bone grafting

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Drug toxicity identified by model lung

Cardiff-based researchers investigate the potential of *in vitro* lung model

Following international recognition for their ground-breaking work on developing *in vitro* human tissue-based lung models from medical waste tissues, scientists at Cardiff University's School of Biosciences Lung and Particle Research Group (LPRG) have developed the Metabo-Lung- a unique biotransformation model for toxicity testing and demonstrating cellular damage.

The Metabo- Lung advances on the science of the original Micro-Lung model which utilises normal human bronchial epithelial (NHBE) cells cultured in a filter-well bioreactor for cells to grow in the air-liquid-interface (ALI). To develop the Metabo-Lung model, Dr Kelly BéruBé and Dr Zoe Prytherch of the LPRG introduced the element of "metabolism" into their NHBE system, through co-culturing the Micro-Lung with human liver cells

This novel system enables the process of "biotransformation" to be investigated following contact with chemical substances, for example medicinal drugs and environmental pollutants. This is due to the respiratory tract's frequent exposure to elevated concentrations of environmental and man-made chemicals. The LPRG has shown that occupational, accidental or prolonged exposure to inhaled substances may result in acute or delayed injury to cells of the respiratory tract. The lung has the capability of biotransforming compounds with the aim of reducing potential toxicity. It also contributes to *in situ* activation of pulmonary toxins, for example tobacco smoke, which lead to adverse reactions such as lung and pancreatic cancers. Lung cells grown in isolation do not permit *in situ* metabolism to take place, but the primary human bronchial cells in the ALI co-cultured with the primary human liver cells enable *in vivo* metabolic activity.

Reactions in drug metabolism pathways that are of particular interest for inhalation toxicology include medicine and those which contribute to multi-drug resistance in infectious diseases and cancer chemotherapy. The actions of some drugs as substrates or inhibitors of enzymes are a common reason for dangerous drug interactions. These pathways are also important in environmental science, with drug metabolism of micro-organisms determining whether pollutants will be broken-down during bio-remediation or persist in the environment.

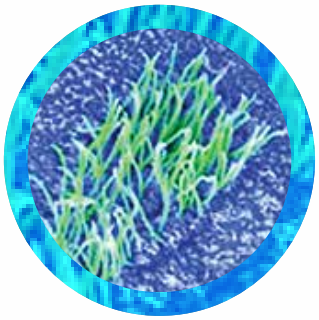
The Metabo-Lung model is a unique tool for the *in vitro* detection of toxins produced by reactive metabolites. This 21st century animal "replacement model" has illustrated that the use of metabolically competent, human-derived, primary lung and liver cells are needed to ensure realistic *in vitro* prediction of *in vivo* toxicity. Advancements with *in vitro* cell culture have given researchers a viable and economic alternative to live animal testing. Dr Kelly BéruBé, Project Director, said, "The development work now under way at the School could offer a genuine alternative to animal testing for pharmaceutical companies developing new drugs for pulmonary disorders such as asthma, chronic obstructive pulmonary disease and cystic fibrosis".

This platform is now being used earlier in toxicity testing pipelines, often to determine risk assessment and set up controls.
The combination of lower-cost and high-throughput assays can help bring products to market faster. Additionally, *in vitro* models give researchers an advantage in understanding the biological process involved in a toxic response sooner than if they were depending on the visual inspection of a live animal.

Dr BéruBé said, "the exciting potential of Metabo-Lung is already creating significant interest from major pharmaceutical companies."

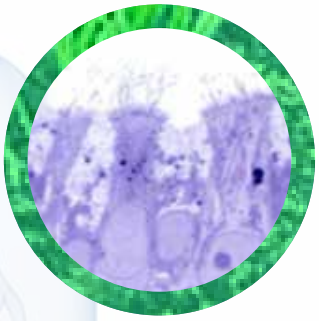
Dr Prytherch explained, "liver cells are a necessary part of the culture as they break down or bio-transform drugs into active components that behave differently from the original drug. It is these elements that need to be tested before any given product can be sold in the market place to consumers".

Cardiff's Metabo-Lung has the potential to improve current methods of testing for drug toxicity by identifying the most suitable drug candidates early in the screening process. The early identification of toxic effects would enable large cost savings and significantly reduce the need for animal testing.



Scanning electron micrograph of Metabo-Lung surface showing the cilia (pseudo-coloured green) that sweep mucous across the epithelium to keep it moist. The cilia also sweep away inhaled debris that becomes trapped in the mucous, keeping the lung environment clean.

The miniature bioreactor (held up by tweezers) that houses the Metabo-Lung. The pink solution is culture media that provides food for the cells to grow. The photograph demonstrates how numerous bioreactors may be housed in a single tray for high-through put analysis.



Light microscope image (Toludine Blue stained) of the re-grown (i.e. recycled) lung component of the Metabo-Lung demonstrating the multi-layered, mixed-cell type found in the airway epithelium of the human lungs.

Profile

Product
Biotransforming model

Applications
Toxicity testing and demonstrating cellular damage

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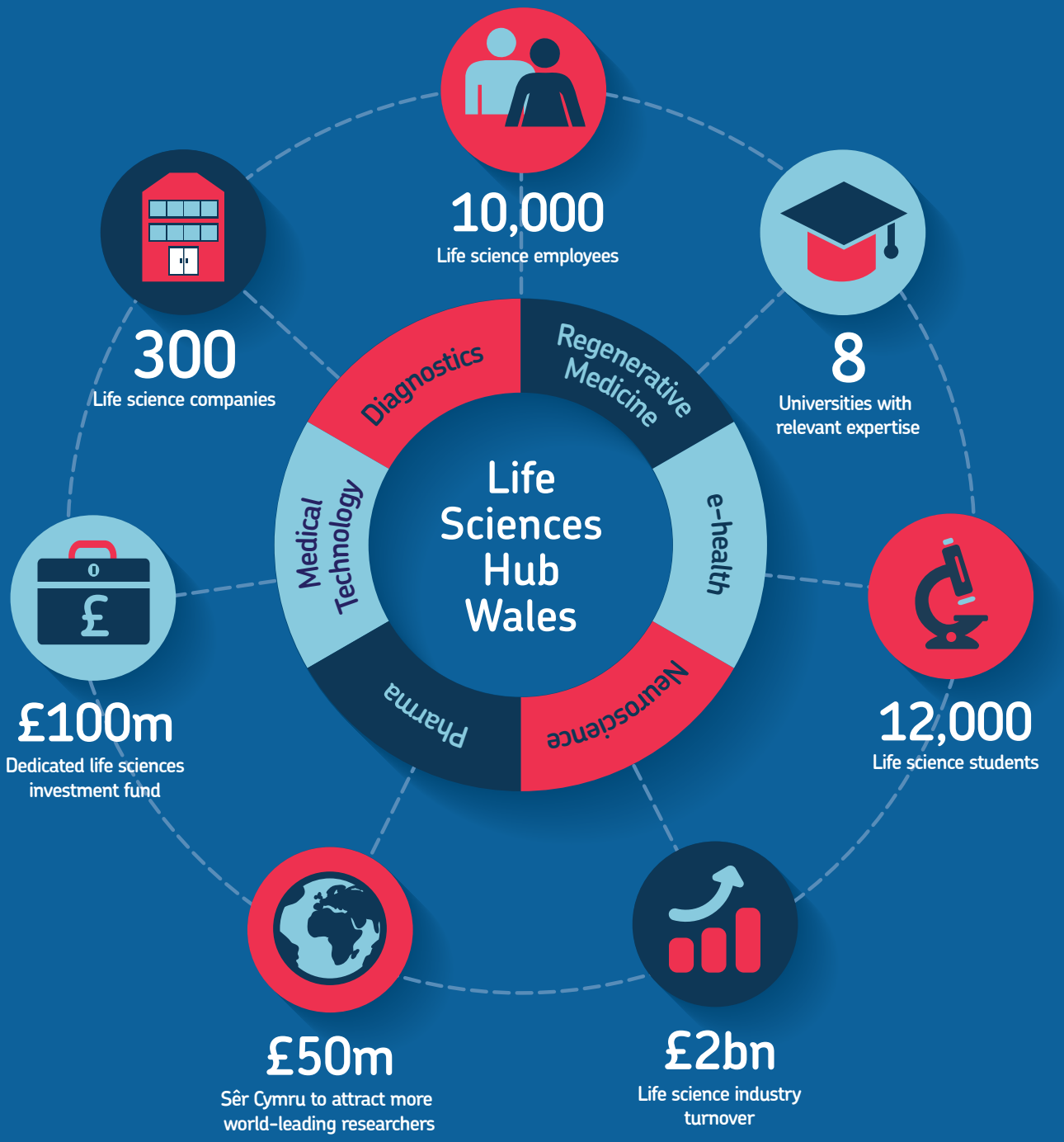

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