

BBSRC Business

Summer 2011

Connecting our science with industry, policymakers and society

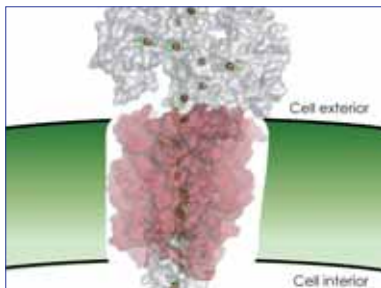
Foot-and-mouth infection 'window' raises potential for alternative to culling

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About BBSRC

BBSRC is the UK funding agency for research in the life sciences and the largest single public funder of agriculture and food-related research.

Sponsored by Government, BBSRC's budget for 2011-12 is around £445M which it is investing in a wide range of research that makes a significant

contribution to the quality of life in the UK and beyond and supports a number of important industrial stakeholders, including the agriculture, food, chemical, healthcare and pharmaceutical sectors.

In delivering its mission BBSRC invests in research and training in universities across the UK, the institutes of BBSRC and through strategic partnerships with other funders, including the

other Research Councils, charities, government departments and international agencies.

A number of institutes receive strategic funding from BBSRC. They conduct long-term, mission-oriented research and have strong interactions with their relevant industry sectors and other end users. The institutes maintain unique research facilities of national importance.

Further details can be found at www.bbsrc.ac.uk



Babraham Institute
www.babraham.ac.uk



Institute for Animal Health
www.iah.ac.uk



Institute for Biological, Environmental and Rural Studies (Aberystwyth University)
www.aber.ac.uk/ibers



Institute of Food Research
www.ifr.ac.uk



RESEARCH COUNCILS UK

BBSRC is part of the Research Councils UK partnership



John Innes Centre
www.jic.ac.uk



Roslin Institute (University of Edinburgh)
www.roslin.ac.uk



Rothamsted Research
www.rothamsted.ac.uk



The Genome Analysis Centre
www.tgac.bbsrc.ac.uk

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About BBSRC Business

BBSRC Business is a controlled circulation magazine which is distributed free of charge to end users of research and to individuals with an interest in BBSRC.

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More, regular news about BBSRC and the outcomes and impacts of BBSRC-funded research can be found at www.bbsrc.ac.uk/news

In this issue

Chief Executive Professor Douglas Kell welcomes the news that Research Councils UK (RCUK) and the Higher Education Funding Council for England (HEFCE) have announced plans to work together to ensure greater open access to published research.



Copyright TGA
Crowd-sourcing analysis of *E. coli* O104:H4 genome sequence, see page 22.

As the RCUK Champion for Information, I am delighted that RCUK and HEFCE have committed to working together on the important issue of open access. Research is essential to the growth, prosperity and wellbeing of the UK. Ensuring the widest possible access to the results of publicly funded research, both within and outside of the research community, will mean that the groundbreaking discoveries made in science and research can have a greater impact on all our lives.

Digital library launched

The consensus among UK funders of biomedicine that funding dissemination is just as important as funding the experiments themselves was integral in the development, and recent launch of UKPubMedCentral¹ – an innovative online resource that addresses the linked problems of accessing and then exploiting the biomedical literature. As I mention regularly in my blog, the US version of PubMed, upon which this new service is based, increases its list of peer-reviewed papers in biomedicine by two per minute. Clearly any individual scientist (or layperson) needs a means to prioritise those that they might wish to read, and here the UK version has now developed some important innovations, based not least on the methods of text mining.

And it would seem that the trend towards virtually universal open access publishing is (happily) now irreversible: the average annual increase in open access papers since 2000 has been 30%². I am pleased to see that in this issue of *BBSRC Business* three of the eight features are based on research that was published with open access: a simplified method to create

precursor liver cells from stem cells, which has potential to improve the testing of potential new medicines (see page 12), how genome analysis is identifying weaknesses in the important wheat pathogen *Septoria tritici* (see page 14), and a method for uncovering ‘missing heritability’ in yeast, which is being applied to the selection of robust strains for bioethanol production (see page 16).

Open science

On a wider note, ‘open science’, which includes open access to data, to the literature and so on, is being driven by the recognition that new, different and potentially better kinds of ‘e-science’ can emerge when one has digital access to such resources. The recent involvement of researchers at The Genome Analysis Centre in Norwich, which receives strategic funding from BBSRC, in the crowd-sourcing analysis of public genome sequence data relating to the recent outbreak of *E. coli* O104:H4 that centred on Germany (see page 22) shows how better use can be made of public data for health research.

¹ labs.ukpmc.ac.uk

² www.plosone.org/article/info:doi/10.1371/journal.pone.0020961



Record breaking data centre opens in Norwich

Amplify the low hum from your computer thousands of times and you will have some idea of the noise created by cooling a supercomputer with six terabytes of RAM. The Genome Analysis Centre (TGAC) has just established the largest RedHat Linux system on the planet, in a new data centre formally opened in May.

The supercomputer provides six terabytes of RAM for processing – equivalent to the capability of about 200,000 first generation MP3 players – and 600 terabytes of fast disk storage. It will enable scientists to assemble large genomes, such as wheat, that would be extremely difficult to achieve on smaller systems. The system has already broken records for its speed of processing Java-based code.

The wheat genome represents the largest and most complex set of genetic instructions

ever tackled by DNA sequencing. “The data centre will help us solve unanswered questions to help farmers increase yield and disease resistance,” said Dr Jane Rogers, Director of TGAC, which receives strategic funding from BBSRC.

BBSRC Chief Executive Professor Douglas Kell said, “So many of the research challenges facing society, not least that of providing enough sustainable, affordable and nutritious food for all, will need to be addressed by the effective manipulation of biological

data. This data centre, and the amazing computing power and storage capacity that it will provide, will equip TGAC to exploit the potential, and overcome the challenges that these mountains of data present.”



G20 endorses international wheat improvement effort



Copyright Rothamsted Research

Agriculture Ministers from the G20 group of nations have adopted the International Research Initiative for Wheat Improvement (IRIWI), which will be funded for coordination activity in part by BBSRC.

The historic agreement between the Ministers of Agriculture of the G20 in Paris on 29 June underlines the importance of increasing world agricultural production, in particular that of wheat, to resolve the urgent challenge of sustainably providing enough safe, nutritious

and affordable food for a growing global population.

Wheat is the most widely consumed crop in the world, producing over 20% of the calories and protein consumed by humans. It is also the UK's most important crop. This initiative will aim to reinforce cooperation and coordination between national and international bread and durum wheat research programmes. It will support improvements in food security, nutritional value and safety while taking into account societal demands for sustainable and resilient agricultural production systems able to adapt to anticipated climate change.

Coordination activity by IRIWI in its first four years will be supported by BBSRC, INRA (France) and CIMMYT (Mexico). IRIWI itself is supported by research and funding organisations from 10 countries which have, or intend to develop, national programmes to improve wheat germplasm. The number of partner countries is expected to increase and the coordination will ensure that information from these national programmes is available for application globally.

BBSRC Chairman elected President of the Science Council

Professor Sir Tom Blundell has been elected as the new President of the Science Council. He will lead the Council as it moves forward promoting the role of science in society, supporting professional scientists at all levels, and influencing science and innovation policy.

Sir Tom said he was looking forward to advancing the Science Council's vision for the different disciplines and professions within science to work more closely together.



Copyright Nigel Luchhurst

New Council members

The Minister for Universities and Science, David Willetts, has appointed three new members to BBSRC's highest decision-making body.

Professor Russell Foster

FRS is Professor of Circadian Neuroscience at the University of Oxford and Head of Department of the Nuffield Laboratory of Ophthalmology. Prof. Foster's research interests focus on the role of the biological mechanisms that both regulate and generate circadian rhythms and sleep. His work has important implications for understanding the relationship between health and sleep/circadian rhythm disruption.

He has significant experience of working with BBSRC, having served as chair of the Animal Sciences Committee, the Healthy Organism Strategy Panel and as a member of Strategy Advisory Board.

Prof. Foster has a strong commitment to communication and public engagement; he has published two popular science books on biological rhythms and is the new Chair of the Cheltenham Science Festival.



Dr Michael Goosey FRSC

recently retired from a senior role with Shell, following a long career in industrial research and development, with specific responsibility for Shell's research interests in bioenergy and industrial biotechnology.

Dr Goosey has significant and extensive experience in fostering and maintaining strong relationships between the research base and industry in the Americas, Europe and Asia.

He has previously been involved in a number of UK Government and BBSRC initiatives around industrial biotechnology and bioenergy; including the BIS Industrial Biotechnology Innovation and Growth Leadership Team and the BBSRC Sustainable Bioenergy Centre.



Dr Will West is Chief Executive of CellCentric Ltd. and Chairman of the BioIndustry Association's Emerging Companies Network.

CellCentric, based in Cambridge, is a biotechnology company focused on new drug discovery for epigenetic targets. The company has strong links with academia, including collaborations with BBSRC researchers and the Babraham Institute.

Dr West has a strong track record in national skills policy development. He was involved with the SEMTA sector skills committee and was part of the team behind the 2009 Bioscience Innovation and Growth Team (BIGT) Refresh and Review, which made recommendations that have since been adopted by Government.



New projects to improve food crops

BBSRC has announced the first of two tranches of projects to be funded by the £7M Crop Improvement Research Club (CIRC). These projects, funded by BBSRC, the Scottish Government and 14 companies representing plant breeders, farmers and food processors, will carry out research to improve the quality and yield of oilseed rape, barley and wheat.

The six projects will run for up to five years and focus on a range of issues including improving yield, developing pest and disease resistance, seed dispersal control (for instance, to reduce losses through pod shatter in oilseed rape), and improving traits for processing. bit.ly/mINAZD

Food security skills training

BBSRC has awarded funding to four major training programmes, totalling £12M, for industry specialists working in vital niche areas within the agri-food sector.

The BBSRC Advanced Training Partnerships will provide postgraduate level professional development in the area of agriculture and food production for a large number of industry specialists across the UK. Around 100 individuals will undertake Professional Doctorates under these schemes and several thousand Masters level CPD modules will be undertaken, with many students building up to a full Masters qualification. bit.ly/lqgKNx

Collaboration to make more of brewing by-products

New funding for research into ways of extracting valuable chemicals from the by-products of grain brewing was announced in May as part of the Integrated Biorefining Technologies Initiative (IBTI) Club, a BBSRC-led partnership with the Engineering and Physical Sciences Research Council (EPSRC) and industry.

The funding call will challenge researchers to find ways of processing these by-products to yield chemicals sustainably, which would otherwise have to be produced from fossil fuels. bit.ly/kXu8Dn

Congratulations

to the 12 members of the BBSRC community who were elected Fellows of the Royal Society earlier this year:

Professor Hagan Bayley,
University of Oxford

Professor Doreen Cantrell,
University of Dundee

Professor Alun Davies,
Cardiff University

Professor Nicolas Franks,
Imperial College London

Professor Janet Hemingway,
Liverpool School of Tropical Medicine

Professor Alejandro Kacelnik,
University of Oxford

Professor Thomas McLeish,
Durham University

Professor Mervyn Miles,
University of Bristol

Professor Mark Pagel,
University of Reading

Professor Fiona Powrie,
University of Oxford

Dr Len Stephens,
the Babraham Institute

Professor Simon Tavaré,
University of Cambridge

to **Professor Joe Brownlie**, Chair of the Institute for Animal Health's Corporate Trustee Team, and **Professor William Davies**, current BBSRC grant holder at

Lancaster University, who were each awarded a CBE, and to **Professor Ian Kimber**, co-investigator on BBSRC grant at the University of Manchester, who was awarded an OBE in the Queen's Birthday Honours list in June.

to **Professor Andrew Baker** from the University of Glasgow and **Professor Guy Rutter** from Imperial College London who received Royal Society Wolfson Research Merit Awards earlier this year.

to **Professor Dame Athene Donald** from the University of Cambridge who received a lifetime achievement award, and to **Professor Eileen Ingham** who received an award for innovation and entrepreneurship (academia and research), in the UKRC's 2011 women of outstanding achievement awards.

John Innes Centre announces collaboration with Chinese Academy of Sciences

A major collaborative venture between the John Innes Centre (JIC), which receives strategic funding from BBSRC, and institutes of the Chinese Academy of Sciences (CAS) was announced in Beijing last month.

Building on the strong associations between JIC and China that began more than three decades ago, the signing of a Memorandum of Understanding (MoU) by Professor Lu Yonglong, Director General of International Cooperation for CAS and Professor Dale Sanders, Director of the JIC, will help facilitate a programme of mutually beneficial academic exchanges over the next two years, and, once established, the subsequent development of a CAS-JIC Institute.

Prof. Sanders said, "This event is tremendously exciting for JIC. Plant and microbial science in China complements ongoing activities in the UK. There are exciting possibilities, building on traditional goodwill between JIC and Chinese

colleagues, for collaboration for the public good between JIC and CAS institutes."

UK Minister for Universities and Science David Willetts, who witnessed the signing ceremony, said, "China is a rapidly growing research nation and to make the most of this we need to look for opportunities to share knowledge and expertise. This agreement puts in place an even greater commitment to working together on areas including food security, one of the biggest challenges facing the world today."

UK delegation to Brazil strengthens research links

A new agreement was signed last month to facilitate long term collaboration between top BBSRC-funded scientists and their Brazilian counterparts. The agreement between BBSRC and CNPq – the Brazilian National Council for Scientific and Technological Development – will focus on priority areas identified by both parties: food security and bioenergy and industrial biotechnology.

A new Brazil Partnering Awards scheme, available to BBSRC grant holders, was

announced following meetings between the UK delegation to Brazil, which included UK Minister for Universities and Science David Willetts and BBSRC Deputy Chief Executive Steve Visscher, with Brazil's Minister of Science and Technology Aloizio Mercadante and representatives from CNPq.

BBSRC and CNPq will offer up to £50,000 each for bilateral interactions and £100,000 each for large consortia, over a period of up to four years.

Further links were also formed between BBSRC and FAPESP – São Paulo's State Research Council – in the form of new pump-priming awards.

Biotechnology Investment Forum fosters finance opportunities

Babraham Bioscience Technologies (BBT) held its eighth Biotechnology Investment Forum in June, showcasing new technologies pioneered by 16 biotech companies to around 50 biotechnology-focused investor groups.

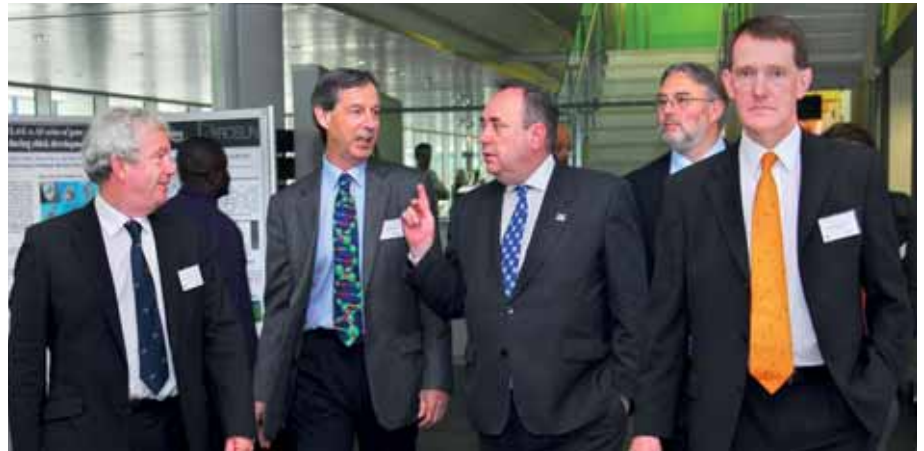
The event at Babraham Research Campus, which is supported by, and

New Roslin building opens its doors

£30M of BBSRC investment in new research infrastructure came to fruition on 29 June, as The Roslin Institute took up residence in its new purpose built centre on the outskirts of Edinburgh.

The Roslin Institute, part of the University of Edinburgh, will join partners from the Scottish Agricultural College (SAC) in the new centre which will deliver excellent science in the fields of food security and basic bioscience underpinning health, driving economic growth and providing benefits for UK society. The Roslin Institute receives around £10M a year from BBSRC in strategic funding.

Director of The Roslin Institute Professor David Hume said, "The new building is designed to maximise cooperation amongst our experts. Our new home will help us tackle complex problems ranging from fertility and reproduction through the threats of diseases



such as avian flu and tuberculosis to animal welfare and greenhouse gas emissions."

Speaking at the opening, First Minister of Scotland Alex Salmond said, "Scottish science has an international reputation for quality, and the ground-breaking work of The Roslin Institute is already famous worldwide.

(left to right) Principal and Vice-Chancellor of the University of Edinburgh Prof. Sir Timothy O'Shea FRSE, The Roslin Institute Director Prof. David Hume FRSE, Rt Hon Alex Salmond MSP, BBSRC Chief Executive Prof. Doug Kell, SAC Chief Executive Prof. Bill McKelvey OBE

This new home here at the University's Easter Bush campus gives an opportunity for further advances."

receives investment from, BBSRC, was an opportunity for companies across the UK to pitch innovative technology and business propositions for which they were seeking investment ranging from £250k to £17M. These included biomarker discovery and service companies, a bio-nanotechnology company developing treatments for inflammatory dermatological conditions, a venture developing improved drug and delivery system for ovarian cancer and technologies to tackle antibiotic-resistant infections.

"It was fabulous to have an audience so engaged with the presentations and so willing to discuss investment," said Eddie Blair, CEO of Integrated Magnetic Systems. Dai Hayward, CEO of CellAura Technologies added, "This is a higher success rate than any other investment event I've attended in the last year."

Derek Jones, BBT's Chief Executive said, "The campus plays a key role bringing together entrepreneurs and investors through events like this and we hope that the Forum will have catalysed conversations leading to the financing of early-stage bioventures. The spin off for us is that hopefully they will establish themselves at the Babraham Research Campus, where we have ongoing developments to provide more facilities for companies."

Global network to protect against animal diseases

The UK will be better protected against animal diseases like avian influenza and foot-and-mouth disease thanks to a global network of scientific research launched in May.

Increasingly, globalised movements of animals, people and food have raised the risk of animal diseases spreading to the UK, which could have serious economic, environmental and health consequences.

BBSRC will lead one of five work packages in the €1million Defra-led, EU-funded network, which will link thousands of scientists across the world. It will allow them to exchange

research, establish common goals and collaborate on developing future controls. It will also underpin early warning systems by identifying what emerging diseases are being picked up abroad.

Speaking before the launch, Agriculture and Food Minister Jim Paice said, "In this modern age of globalised trade and travel, the risk of animal disease entering the UK is greater than ever.

"Countries acting on their own just don't have the resources to research every disease, all of the time, so sharing resources like this will get us maximum protection and value for money."

Public-private investment to improve medicine production and processing

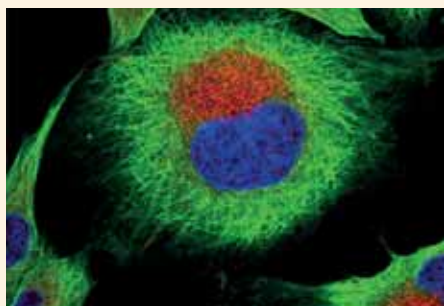
A £4M package of investment to develop research to underpin the production and processing of new types of medicines based on biological molecules was announced in June.

The funding, provided by the Bioprocessing Research Industry Club (BRIC), a BBSRC-led public-private partnership with EPSRC and a consortium of 16 industrial partners, will go to six research projects, eight PhD studentships and a Skills Development School for early stage researchers. bit.ly/iPaduB

Foot-and-mouth disease virus finding offers potential for alternatives to culling

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Research published recently in the journal *Science* shows that scientists have uncovered a window of opportunity when it is possible to identify cattle infected with foot-and-mouth disease virus (FMDV) before they become infectious and/or show signs of having the disease.



Cell infected with foot-and-mouth disease virus (red), showing the cell nucleus (blue) and other cell structures (green)

Copyright IAH

BBSRC-funded researchers have shown for the first time that the period in which cattle are infectious before they show clinical signs of foot-and-mouth disease is much shorter than previously thought.

The study, carried out at the Institute for Animal Health (IAH), which receives strategic funding from BBSRC, and the University of Edinburgh, demonstrates that diagnosis of FMDV infection is possible during the, approximately, 24 hours before the animal becomes infectious.

Researchers at IAH along with colleagues at the Department for Environment, Food, and Rural Affairs (Defra) are now assessing if this window can be exploited to reduce the number of animals that are culled during an outbreak.

Urgent need for field diagnostics

Importantly, if this short window of opportunity is to be exploited there is a need for further development of effective and efficient in-field diagnostic tools that can detect the virus as early as researchers have been able to using laboratory techniques.

What's more, similar studies could be performed for other acute viral diseases such as influenza. This would help refine our understanding of how diseases spread and choose the most appropriate measures to control an outbreak.

Dr Bryan Charleston who led the team at the Institute for Animal Health said, "Our discovery is good news and we hope that

“We now know that there is a window where, if affected cattle are detected and removed promptly, there may be no need for pre-emptive culling in the immediate area of an infected farm.”

Prof. Mark Woolhouse, University of Edinburgh

it will enable future refinement of the methods we use to control FMDV in the UK and beyond.

“That said, there are a huge number of factors involved in decisions about controlling this serious and fast-spreading virus. We have proof that it is possible to detect the virus in animals before they display signs of disease and before passing the infection on to other susceptible livestock, but there are a lot of other variables to consider before it is possible to come up with a new control strategy.

“Not least this result emphasises the need for practical tools for pre-clinical diagnosis and at present we don't have an affordable, reliable test to use on farms. We can identify infected cattle before they show signs of disease using tests in the laboratory; the next challenge is to do it in the field during an outbreak. This type of testing was successfully applied during the 2007 outbreak in Surrey on the basis of studies at IAH, including the early results of this research. We now need to develop the technology further with Defra in order to realise the potential benefits and possibly reduce the number of animals culled during an outbreak.”

Building on lessons learned

During the 2007 outbreak of FMD, preclinical testing of animals not yet showing signs of the disease was carried out every second day. This was successful in identifying infected cattle not showing clinical signs. The very early results of this project – funded by BBSRC in response to the 2001 outbreak – and other research programmes, informed the decision to take that approach in 2007. This proved an excellent example of how the close interaction between research and diagnostic laboratories at the IAH can accelerate the application of high quality science.

Professor Mark Woolhouse who led the University of Edinburgh team said, “This new information pins down the critical times for the detection and control of foot-and-mouth disease much more accurately. We now know that there is a window where, if affected cattle are detected and removed promptly, there may be no need for pre-emptive culling in the immediate area of an infected farm.

“This does make it very important that the disease is picked up quickly and farmers and others who care for livestock will continue to play a critical role. The only way we know that the disease is active is when an animal shows up with signs of the disease, which is too late. We now have an opportunity to develop new test systems which can detect infected animals earlier and reduce the spread of the disease.”

BBSRC Chief Executive Professor Douglas Kell said, “Foot-and-mouth disease has had a devastating impact on the UK in the past. This excellent research brings together top expertise in virology and epidemiology to get to the bottom of how this virus behaves. It is this thorough understanding of the causes of animal disease that will underpin future food security in the UK and ensure that we can maintain a healthy farming industry.”

The research was funded by BBSRC as part of its Combating Viral Diseases of Livestock Initiative. The initiative was launched by BBSRC in 2003 to further our understanding of damaging livestock diseases that cause significant economic, welfare and food security challenges.

Further Reading

Relationship between clinical signs and transmission of an infectious disease and the implications for control. *Science* DOI: 10.1126/science.1199884

Watch a video of Dr Charleston speaking about this research at www.youtube.com/bbsrcmedia

Next steps

- Continue detailed studies of FMDV pathogenesis to understand why animals are infectious for such a short period of time, despite the virus being readily detectable in various samples for longer periods
- Investigate how well current FMDV vaccines block transmission and, if they do, how quickly after inoculation protection occurs
- Develop improved preclinical diagnostics tests that will detect virus or virus genome in milk or air samples as well as rapid, sensitive ‘on farm’ tests to detect viral genome

Contact

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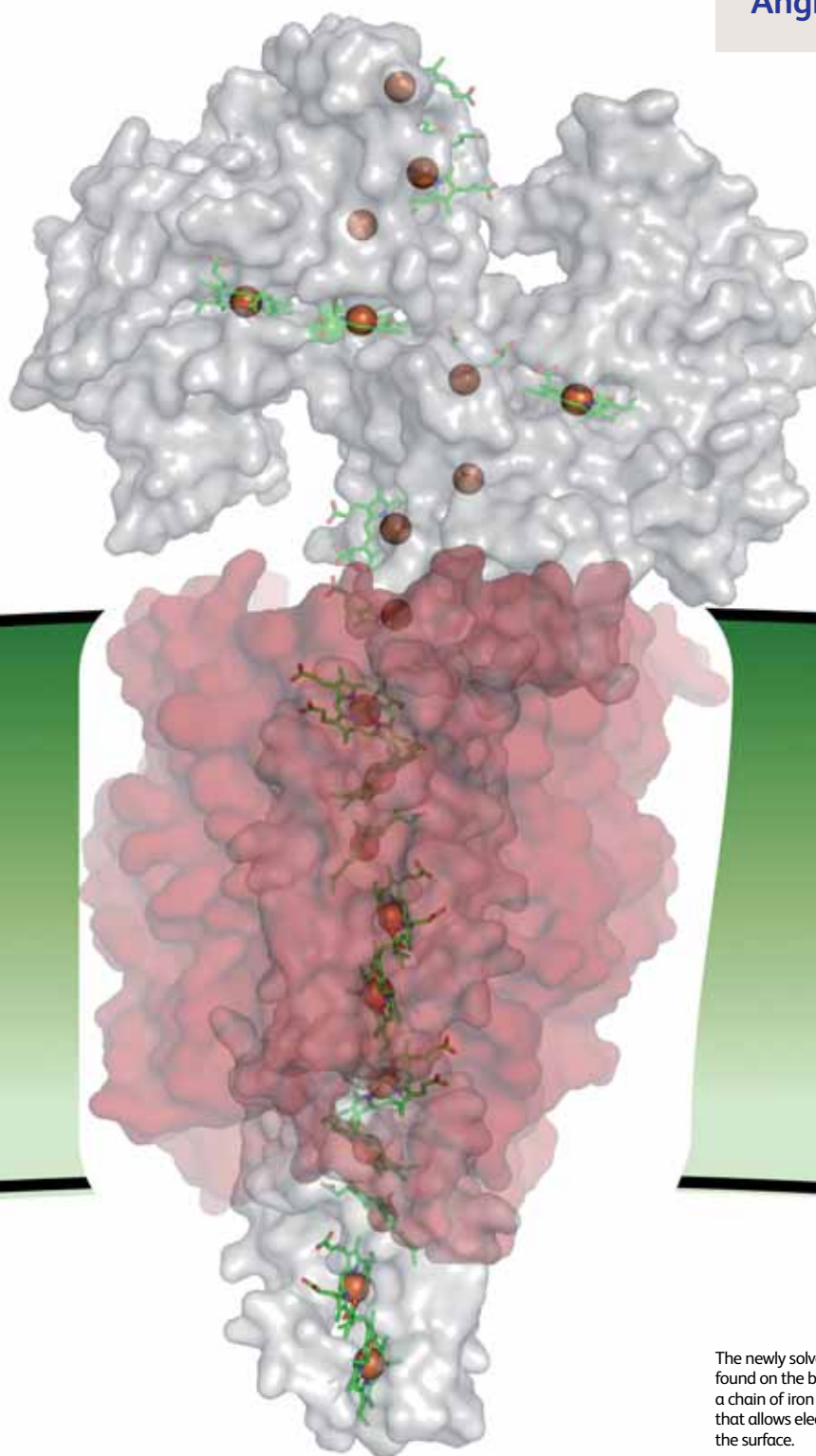
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Discovery pipeline



Discovery opens the door to electricity from microbes

Using bacteria to generate energy is a significant step closer following a breakthrough discovery by BBSRC-funded scientists at the University of East Anglia (UEA).



Cell exterior

Cell interior

The newly solved structure of an iron-containing protein found on the bacterial cell surface helps to explain how a chain of iron atoms bound by proteins form a 'wire' that allows electricity from the inside of the cell to reach the surface.

The study, which was published in the *Proceedings of the National Academy of Sciences* (PNAS), demonstrates for the first time the exact molecular structure of the proteins which enable a peculiar microorganism to transfer electrical charge.

Electrical transfer is not uncommon, it's part of respiration: all living organisms metabolise the nutrients that they consume to release energy to drive biological processes. But some do it in more unusual ways than others. Take *Shewanella oneidensis* for example, this deep sea bacterium uses iron and manganese as respiratory electron acceptors (aerobic organisms, including humans, use oxygen). Again, not so remarkable in its own right – many anaerobic bacteria share this feature – but what the UEA team discovered that really interested them was that these minerals are being used outside the cell.

'Rock-breathing' bacteria

In 2009, a team led by Dr Tom Clarke, Professor David Richardson and Professor Julea Butt of UEA, in collaboration with colleagues at the Pacific Northwest National Laboratory in the USA, demonstrated the mechanism by which *Shewanella* survives in oxygen-free environments by constructing electrical 'nanowires' that extend through the cell wall and make contact with mineral iron deposits in rock. It turns out that the bacteria can release electrical charge from inside the cell into the mineral, much like the earth wire on a household plug.

In the current study, which was funded by BBSRC and the US Department of Energy, the same team has deconstructed this nanowire apparatus. They used a technique called x-ray crystallography to reveal the molecular structure of the proteins attached to the surface of an *S. oneidensis* cell, through which electrons are transferred. This helps to explain how the nanowires are formed.

Multitasking proteins

And while they were looking at the molecular structure of the cell surface protein decaheme cytochrome, the team discovered that iron-containing 'heme' subunits of these molecules are organised in a unique, cross conformation and staggered along the length of the protein, which allows the protein to play multiple roles in electron transfer; either directly to insoluble electron 'sinks', catalyzing electron exchange with electron 'shuttle' molecules, or participating in extracellular exchange along nanowire appendages.

This arrangement provides the molecular insight into how electron transfer from the cell to insoluble substrates (such as minerals) to soluble 'redox' substrates (such as flavins) and respiratory proteins (other cytochromes) might be possible in tandem at different termini on the cell surface.

The discovery of the molecular structure means that scientists can now start developing ways to 'tether' these bacteria directly to electrodes – creating efficient microbial fuel cells or 'bio-batteries'. The advance could also hasten the development of microbe-based agents that can clean up oil or uranium pollution, and fuel cells powered by human or animal waste.

"This is an exciting advance in our understanding of how some bacterial species move electrons from the inside to the outside of a cell," said Dr Tom Clarke of UEA's School of Biological Sciences. "Identifying the precise molecular structure of the key proteins involved in this process is a crucial step towards tapping into microbes as a viable future source of electricity."

"Identifying the precise molecular structure of the key proteins involved in this process is a crucial step towards tapping into microbes as a viable future source of electricity."

Dr Tom Clarke, UEA

Further Reading

Structure of a bacterial cell surface decaheme electron conduit. Published in the online early edition of the *Proceedings of the National Academy of Sciences*, 23 May 2011. DOI: 10.1073/pnas.1017200108

Next steps

- Using the structure as a blueprint the team aims to identify which areas on the protein surface are important in attaching the microbe to mineral surfaces
- They will also use the structure to help design 'tethers' and small diffusible shuttles to optimise electron transfer between microbe and electrode
- They will obtain high-resolution structures of similar proteins to help computational modeller identify optimal routes of electron transfer through the complexes

Contact

Dr Tom Clarke,
University of East Anglia



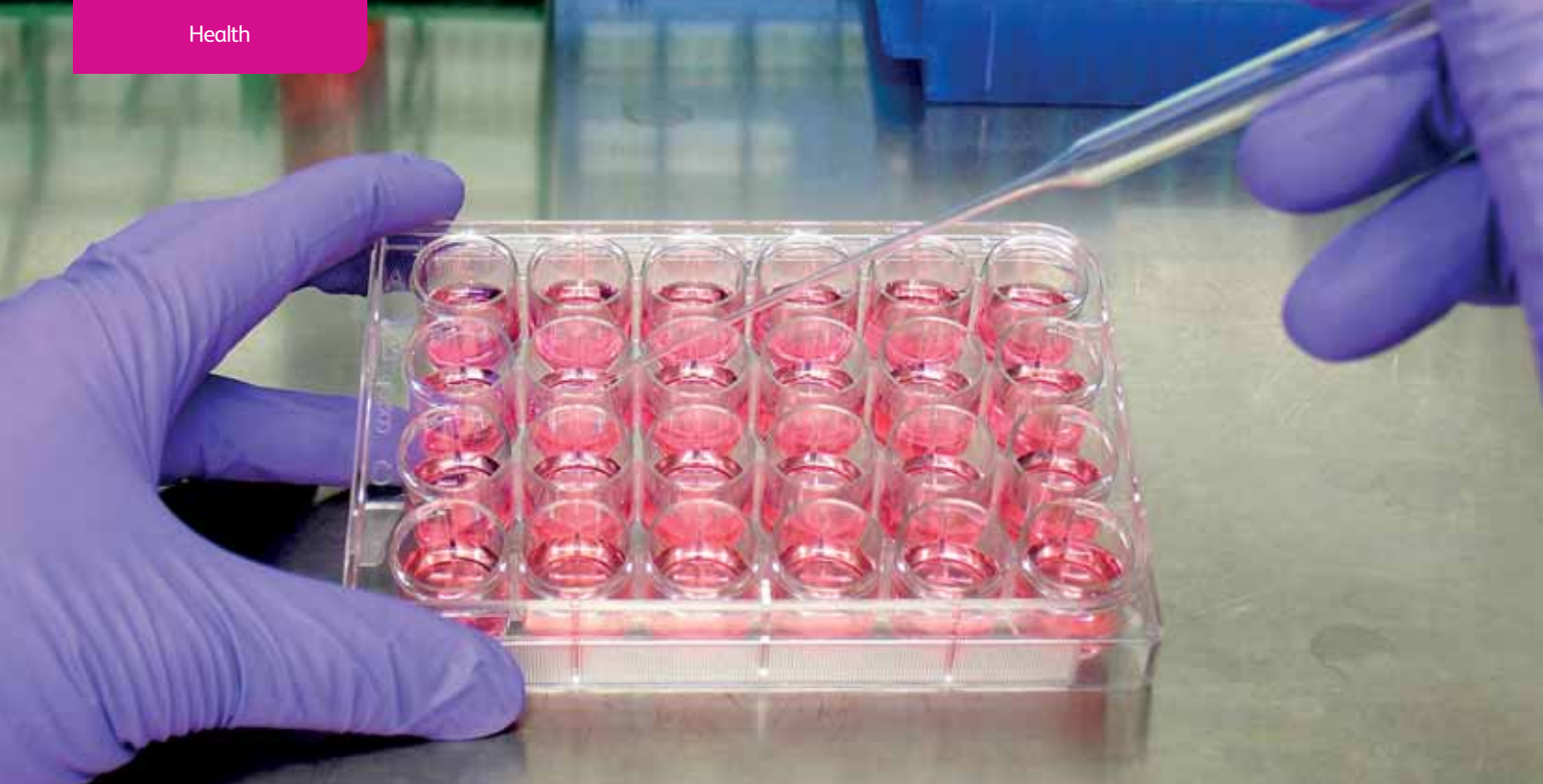
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Discovery pipeline





Lab-produced liver cells could improve drug testing

Researchers have developed a simplified method to create precursor liver cells from stem cells, which has the potential to improve the testing of prospective new medicines.

The team, led by Professor Melanie Welham and Dr David Tosh from the University of Bath, is funded by Stem Cells for Safer Medicines (SC4SM) – a public-private partnership, coordinated by the Technology Strategy Board that is investigating the potential of differentiating human stem cells into more specialised cells for use in early toxicology screening of potential new drugs. BBSRC is one of the SC4SM funding consortium that also includes the pharmaceutical companies AstraZeneca, GlaxoSmithKline, Roche and UCB as well as the Department for Business, Innovation and Skills (BIS), the Department of Health, the Medical Research Council (MRC), and the Scottish Government.

Professor Welham said, “The new method we have defined through our research is much simpler than previous procedures, so should reduce the cost of turning stem cells into precursor liver cells.”

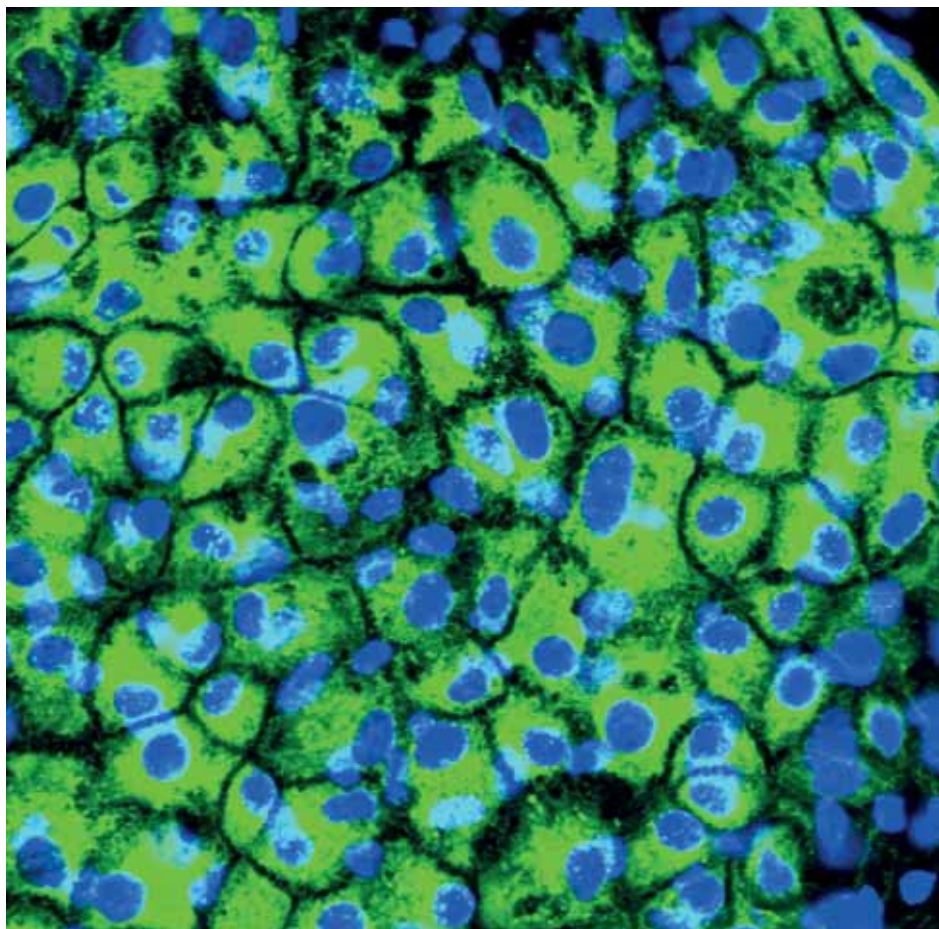
“Our team’s discovery has the potential to impact not only the way in which the safety of medicines are tested, but also on the longer-term goal of generating functional liver cells that can be used to treat those with liver failure”

Prof. Welham, University of Bath

At present the method used to develop precursor liver cells involves many different steps and a variety of biological agents. The Bath team’s new process relies on just one small molecule, called 1M which, when added to stem cell cultures, causes the stem cells to turn into precursors of liver cells. It builds on earlier BBSRC-funded research by Prof. Welham and Professor Adam Nelson at the University of Leeds to clarify the importance of glycogen synthase kinase-3 (GSK-3) as a key regulator of stem cell renewal and differentiation. As part of this research, they synthesized a number of GSK-3 inhibitor molecules, of which 1M was one.

“This new process will allow the scale on which precursor liver cells are created to be more easily increased,” says Prof. Welham.

And this could open the door to the use of such liver cells to test the safety of potential new drugs in high-throughput toxicology screening.



Precursor liver cells

Copyright: University of Bath

Is it relevant?

Even everyday painkillers are known to have toxic effects on the liver if taken in the wrong quantity, and the tests currently used don't always accurately predict what will happen in humans. Having an improved supply of liver cells would allow pharmaceutical companies to improve and strengthen the testing of drugs in physiologically relevant cells.

Dr Tosh said, "This is a significant breakthrough in the field of stem cell research and will impact on the pharmaceutical industry and the way in which medicines are tested.

"There is, however, a great deal of work still to be done. Until now our research has focused on the early stages of liver cell development and there is still a lot of research to do to expand what has been found so far and to generate fully functioning liver cells."

The funding from SC4SM supports a five-year research programme, currently just starting its third year. Now moving into phase two of the project, the research team will focus on improving the systems in the next stage of liver cell production.

The funding has supported the work of post doctoral researcher Dr Heather Bone, who has been instrumental in establishing the initial phases of this project, and has allowed Prof. Welham and Dr Tosh to create two new research posts to work with Dr Bone in phase two.

And in addition to the potential application of these cells in the field of toxicology testing, the researchers hope that their results will provide a model system in which to study liver function and disease as well as forming the basis for the development of a useful therapy for liver failure. "Our team's discovery has the potential to impact not only the way in which the safety of medicines are tested, but also on the longer-term goal of generating functional liver cells that can be used to treat those with liver failure," adds Prof. Welham.

Further Reading

A novel chemically directed route for the generation of definitive endoderm from human embryonic stem cells based on inhibition of GSK-3. *Journal of Cell Science*
DOI: 10.1242/jcs.081679.

Next steps

- Improving the efficiency of turning liver precursors into functional hepatocyte-like cells
- Refining and validating the differentiation procedure to ensure compatibility with toxicity testing
- Proof-of-concept studies to test the utility of stem cell-generated liver cells for predictive toxicology

Contact

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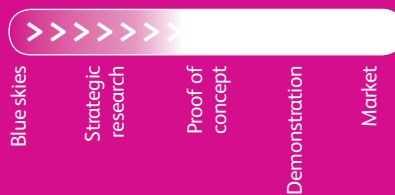



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Discovery pipeline





Identifying weaknesses in wheat stealth pathogen

Copyright, Rothamsted Research

A new study has provided insights into how an important fungal pathogen is able to evade wheat's defences. The international research team, involving UK scientists, hope that the study, which reveals the fungus's complete genome sequence, will enable them to breed resistant crop plants or improve the use of pesticides.

“This work illustrates the power of sequencing the genomes of plant pathogens in identifying key targets for efficient plant protection.”

Professor Maurice Moloney, Rothamsted Research

The genome sequence was produced by an international consortium of researchers including scientists at Rothamsted Research in the UK. The scientists, who were funded by BBSRC and others, are already using the fungus's genome sequence to find ways to control the disease in order to help meet the challenges of ensuring global food security.

The consortium has sequenced the genome of a fungus called *Septoria tritici* (sexual name *Mycosphaerella graminicola*), which causes leaf blotch disease in wheat. The disease kills cells in the plants leaves leaving large dead blotches which are unable to absorb energy from the sun. This significantly reduces yields and takes a serious toll on wheat crops globally and in the UK; annually a 5-15% reduction in grain

yield is incurred in each wheat field solely as a result of these infections.¹

The enemy within

M. graminicola attacks wheat plants by stealth. There is normally a period of about a week between when a plant first becomes infected and when the characteristic blotches of the disease appear on the leaves. During this time it appears that the plant fails to recognise it has become infected and so is unable to activate its defences to fight back. Professor Kim Hammond-Kosack of Rothamsted Research who led the study in the UK said, “Studying the fungus's genome will help us to understand how the pathogen is able to go undetected and maybe reveal a chink in its armour that we can exploit.”

¹ Hardwick et al. (2001) Plant Pathology 50, 453-462

The genome sequence reveals that *M. graminicola* has very few genes which produce enzymes able to breakdown plant cell walls compared with other fungi that specialise in infecting plants. Plants often use the presence of the sugars and proteins released when a cell is broken down as a cue for turning on their immune responses, so the researchers think that the unusually low numbers of genes producing enzymes for breaking down plant cells may be crucial to the fungus's stealth approach.

The team from Rothamsted² have already started on work using the genome to look for potential weaknesses in the fungus's defences. Collaborating with researchers at Wageningen University in the Netherlands, they have identified a protein in the fungus which is important in keeping it hidden. This research was published recently in *Plant Physiology*.

Spotting the Achilles' heel

Rothamsted's Dr Jason Rudd said, "We were able to use the information in the genome sequence almost immediately to look for a potential Achilles' heel. We singled out a protein that helps keep the fungus camouflaged and protects it from the plant's defences. When we generated a mutant strain of the fungus that didn't contain the gene for this protein, the infected wheat

plants produced strong immune responses and didn't develop the characteristic leaf blotches. Our next step is to use these and similar findings to help farmers combat this disease out in the field in order to reduce wheat losses."

Director and Chief Executive of Rothamsted Research Professor Maurice Moloney commented, "Rothamsted Research is proud to be part of the team that has sequenced and analysed the *M. graminicola* genome. This fungal pathogen causes one of the most pernicious plant diseases and accounts for significant losses annually in wheat yields throughout the world. This work illustrates the power of sequencing the genomes of plant pathogens in identifying key targets for efficient plant protection."

BBSRC Chief Executive Professor Douglas Kell said, "Genome sequencing is an important tool in the fight to ensure global food security. Determining the sequence of a destructive crop disease like this is now so quick and affordable that it can be viewed as a research tool rather than a project in itself. This is especially true when the complementary talents of researchers in different countries can be brought to bear. As in this project, this information can be put to immediate use in finding new ways to combat plant disease."

² Dr John Antoniw and Dr Hans Cools also contributed to the work at Rothamsted Research.



Septoria leaf blotch disease

Further Reading

Finished genome of the fungal wheat pathogen *Mycosphaerella graminicola* reveals dispensome structure, chromosome plasticity and stealth pathogenesis. *PLoS Genetics* DOI:10.1371/journal.pgen.1002070

Analysis of two *in planta* expressed LysM effector homologues from the fungus *Mycosphaerella graminicola* reveals novel functional properties and varying contributions to virulence on wheat. *Plant Physiology* DOI:10.1104/pp.111.176347

Next steps

- Determine the full range of genes coding for secreted proteins produced by the fungus during stealthy infection
- Explore the functions of these proteins during the interaction with wheat cells
- Sequence additional *M. graminicola* isolates with different disease resistance breaking abilities

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Professor Kim Hammond-Kosack and Dr Jason Rudd, Rothamsted Research



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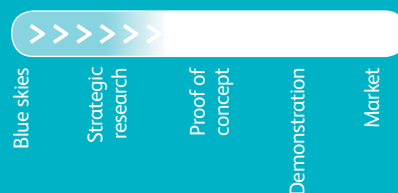


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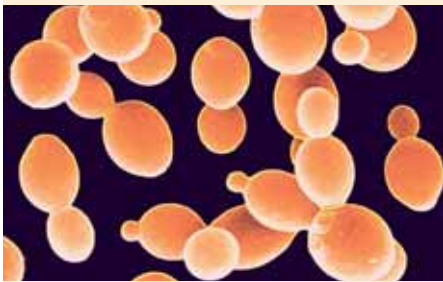


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Discovery pipeline



Solving the genetics jigsaw puzzle



Coloured scanning electron micrograph of a strain of *Saccharomyces cerevisiae*, often referred to as baker's yeast.

“It’s a whole new way of looking at things: instead of looking at changes in the genomes of individuals we are directly detecting changes within a population.”

Dr Gianni Liti, University of Nottingham

A method which could help pinpoint the ‘missing pieces’ of the genetic makeup underlying complex traits, such as height, skin colour and diseases including cancer, diabetes and heart disease, has been developed by researchers at the University of Nottingham.

Despite huge advances in recent years, one of the central challenges of modern genetics is to identify all the genes involved in complex traits and how they interact to bring about variation within a population.

So-called ‘mapping’ studies, which identify areas of a genome (loci) that are associated with specific traits, for example those that influence disease risk, tend to leave many questions unanswered. Despite the large numbers of loci that have been detected, the effects are almost all modest, and explain only a small portion of the variability.

According to geneticist Dr Gianni Liti from the University of Nottingham, the problem is largely one of ‘missing heritability’: “Mapping studies typically detect only a fraction of the loci underlying heritable traits,” he says. “And of those trait loci that are found, the association peaks generally span a large region of the genome, and do not point to the mechanism responsible for the association.”

In a recently published study, Dr Liti and colleagues at University of Nottingham, the Wellcome Trust Sanger Institute and the Universities of Gothenburg and Toronto have developed a highly sensitive method to detect trait loci, in some cases down to the level of single genes.

Finding all the pieces

Working with yeast – a model organism – Dr Liti and his team crossed two different strains, one that was heat tolerant and one that was heat sensitive. After multiple rounds of ‘intercrossing’ they had generated a pool of 100 million cells with a variety of genetic backgrounds.

The team then selected for heat tolerant individuals by growing the resulting pools of cells asexually at 40°C and used next generation sequencing methods to assess changes in the frequency of beneficial ‘alleles’ over a period of 12 days.

“We mapped 21 loci with significant changes in genetic background in response to selection. This is several times more than found with traditional linkage methods,” says Dr Liti. “Nine of these regions contain two or fewer genes, yielding much higher resolution than previous genomic linkage studies.”

According to Dr Liti, there are two reasons for the enhanced sensitivity of their new method. Firstly, the multiple rounds of intercrossing introduce recombination between the genomes of the mating cells, which in turn increases the mapping resolution by stretching the length of the entire genome and reducing the linkage between individual loci. Secondly, by applying a selective pressure



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and monitoring changes over time the team was able to detect alleles with minor fitness effects, which had risen in frequency to become detectable.

Dr Liti explains, "Our dynamic monitoring means that we are more likely to find all the pieces in the puzzle, even the very small ones. This approach was only possible because of recent advances in next generation sequencing.

"It's a whole new way of looking at things: instead of looking at changes in the genomes of individuals we are directly detecting changes within a population."

And because they can pinpoint trait genes in yeast, they can also look at how they interact.

Building a complete picture

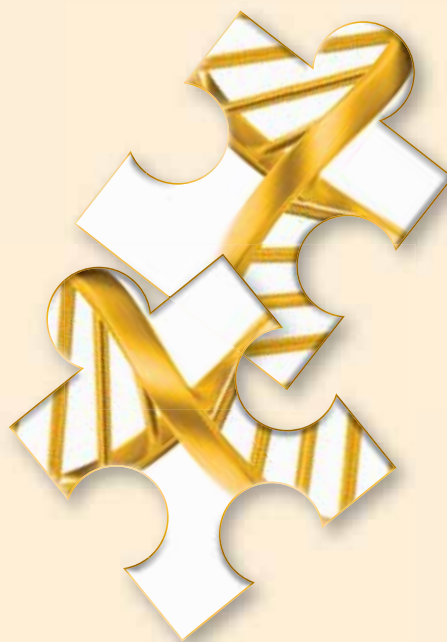
"One of the good things about yeast is that we can engineer variation into the population to experimentally measure the effect on the phenotype and how trait genes interact with each other," says Dr Liti. "Once we can quantify the total genetic basis of a trait and the contribution from the environment, we will be in a position to make predictions about an organism's biology from its genome sequence."

This could have important implications for the study of human diseases like type 1 diabetes where it is not certain what all the genetic factors are. Dr Leopold Parts and Professor Richard Durbin at the Wellcome Trust Sanger Institute who, together with Dr Liti's team, developed the approach and analysis methods are now studying the implications of these findings on understanding the genetic makeup of human disease.

The possibilities are endless

Back in Nottingham, Dr Liti, together with Professor Edward Louis, is looking to use the method to generate robust yeast strains for ethanol production, as part of a BBSRC Sustainable Bioenergy Centre (BSBEC) programme. They hope to be able to select strains that are better at overcoming pH and temperature inhibition during the fermentation process as well as those that are better able to metabolise xylose and cellulose sugars found in waste plant material.

"Our method can be applied to any selectable trait, including ones that do not affect fitness. For example, cell sorting to select for cell size, GFP expression on specific promoters or washing the plate to detect cell adhesion traits," says Dr Liti. "A similar approach could also be applied to other model genetic systems, including *Drosophila* and *C. elegans*, that are amenable to crossing in bulk and large experimental population sizes."



Further Reading

Revealing the genetic structure of a trait by sequencing a population under selection. *Genome Research* DOI: 10.1101/gr.116731.110

Next steps

- Generate a very large diploid population with sequenced genomes to establish the budding yeast as a model for human genome-wide association study populations
- Dissecting the genetic architecture of multiple biotechnologically relevant complex traits
- Extrapolate this knowledge to make predictions, based on population genomics data, of the standing variation in natural populations

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Discovery pipeline



Blue skies

Strategic research

Proof of concept

Demonstration

Market



Cocoa chemical could promote good gut health

Regular cocoa drinkers may take heart from a recent clinical trial where researchers at the University of Reading have shown that eating flavanols – phytochemicals found in cocoa powder – can stimulate the growth of ‘good bacteria’ in the human gut.

“We were particularly pleased to observe the increase in growth of *Lactobacillus* species in response to cocoa flavanols...
...most currently accepted prebiotics do not elicit changes in lactobacilli.”

Dr Jeremy Spencer, University of Reading

They make up about 95% of the cells in our bodies, play an important role in food digestion, produce vitamins, and help fight infection and disease – yes, life would be very different without gut bacteria.

And, like in your average fairy tale, it is a case of good triumphing over evil as the gut ‘microbiota’ have pathogenic properties in addition to their health-giving ones: they can produce toxins and carcinogens, cause infections and have been implicated in conditions including diabetes and obesity, inflammatory bowel disease and cancer.

Balance, therefore, is key to a healthy gut. In recent years there has been growing interest in both probiotics (live microorganisms that are added to foods such as yogurts) and prebiotics (non-digestible food ingredients that stimulate the growth or activity of certain bacterial species) as a way to alter the gut microbiota to a more healthy composition.

Most of the prebiotics on the market are long-chain carbohydrates (fructooligosaccharides and galactooligosaccharides), but scientists and food manufacturers are on the lookout for other potential beneficial supplements that may stimulate the microbiota in different ways.

Dr Jeremy Spencer at the University of Reading is leading a research project, funded through the BBSRC’s Diet and Health Research Industry Club (DRINC), to examine the impacts of industrial processing on the levels of flavanols in foods such as cocoa.

“We know that some flavanols in cocoa, such as epicatechin, are absorbed in the small intestine and studies have shown that these compounds have direct benefits for cardiovascular health,” he says. “But the majority of flavanols in pure cocoa are not absorbed. Instead they pass to the large intestine where, we believe, they may influence the growth of the microbiota.

Yet there has been very little research regarding the ability of these flavanols or other phytochemicals to influence the growth of beneficial intestinal bacteria to date.”

Drink to your health

In a randomised, controlled, double-blind trial, Dr Spencer and colleagues examined the effects of a drink containing either high or low levels of cocoa flavanols on the gut microbiota of healthy human volunteers. They found that the populations of beneficial bacteria in the gut (bifidobacteria and lactobacilli) increased, and potentially harmful populations of clostridia bacteria decreased in the participants who consumed the high flavanol drink, compared to volunteers in the low flavanol group.

It's the first time that the consumption of cocoa flavanols has been shown to have a potential prebiotic effect.

“We were particularly pleased to observe the increase in growth of *Lactobacillus* species in response to cocoa flavanols,” says Dr Spencer. “This bacterial group is associated with beneficial effects in the gut, including an ability to prevent the growth of pathogenic organisms, and most currently accepted prebiotics do not elicit changes in lactobacilli.”

According to Dr Spencer, lactobacilli may be better equipped to use flavanols as an energy source compared to their bacterial competitors in the gut.



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The team also observed that the high flavanol drink led to a significant decrease in a group of clostridia bacteria that includes *Clostridium perfringens*, a known pathogen that has been implicated in the progression of colon cancer and the onset of inflammatory bowel disease.

The benefit's in the bean

But before rushing home to guzzle a nice hot cup of cocoa, it's worth pointing out that the concentration of flavanols in processed cocoa is much lower than the pure cocoa extracts tested in this study.

As part of his wider DRINC-funded project, Dr Spencer is looking at the broader health benefits of flavanols, and is working with manufacturers to identify ways to optimise processing to prevent flavanol loss. This is because conventional processing (drying, fermentation, roasting and alkaline treatment) drastically reduces the amount of flavanols – up to 98% in the case of epicatechin.¹

“Ultimately, our goal is to develop future strategies to maximise flavanols in our foods, whether by optimising industrial processing conditions or extracting the active ingredients that can be added to other foods or used as supplements,” says Dr Spencer.

But interestingly, the team has discovered that whilst the roasting of cocoa does lead to flavanol losses, it does not significantly reduce the prebiotic effect.

Dr Spencer believes that this is because, during roasting, flavanols participate in ‘Maillard reactions’, forming new complexes which also promote the growth of ‘good bacteria’. Such chemistry has long been known to be important for flavour and aroma development in cocoa but now it seems that these by-products may also contribute to beneficial effects in our gut.

“We observed a prebiotic effect with just 500mg of flavanols in our study. The news for flavanols is now particularly good because, as well as the cardiovascular benefits, we also have a prebiotic effect at amounts that are achievable through a moderate dietary intake of cocoa, apples, red wine and green tea,” he says.

¹M.J. Payne *et al.* *Journal of Agriculture and Food Chemistry*
DOI:10.1021/jf102391q

Further Reading

Prebiotic evaluation of cocoa-derived flavanols in healthy humans by using a randomised, controlled, double-blind, crossover intervention study. *American Journal of Clinical Nutrition*
DOI: 10.3945/ajcn.110.000075

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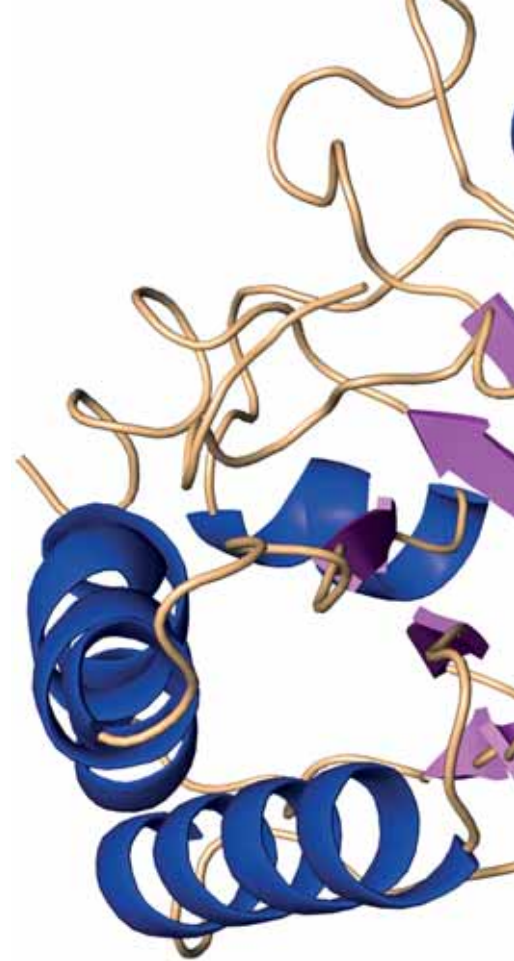
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Discovery pipeline



Bacterial enzyme discovery could catalyse large scale sustainable biofuel production



Scientists funded by the BBSRC-led Integrated Biorefining Research and Technology (IBTI) Club have identified a bacterial enzyme which could be used to make biofuel production more efficient.



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The research, which was carried out by teams at the University of Warwick and the University of British Columbia in Canada, could make sustainable sources of biofuels more economically viable. The findings of the study were published recently in the American Chemical Society's journal *Biochemistry*.

Fast-growing woody plants and the inedible by-products of crops could both be valuable sources of biofuels. But they remain a largely untapped energy source due to difficulties in extracting fermentable sugars at an industrial scale. This is largely down to lignin – a major component of plant cell walls – which is

important in making plants sturdy and rigid but, because it is difficult to breakdown, means that fermenting these materials to produce bioethanol does not give a yield large enough to be economically viable. Using an enzyme to break down lignin would allow more fuel to be produced from the same amount of plant biomass.

In this study the research team, who were also supported by the Engineering and Physical Sciences Research Council, have identified two enzyme genes in the soil-dwelling bacterium *Rhodococcus jostii*, which could be important in lignin degradation. This is the first time that lignin peroxidase genes have been identified in a bacterium.

Shedding light on novel enzymes

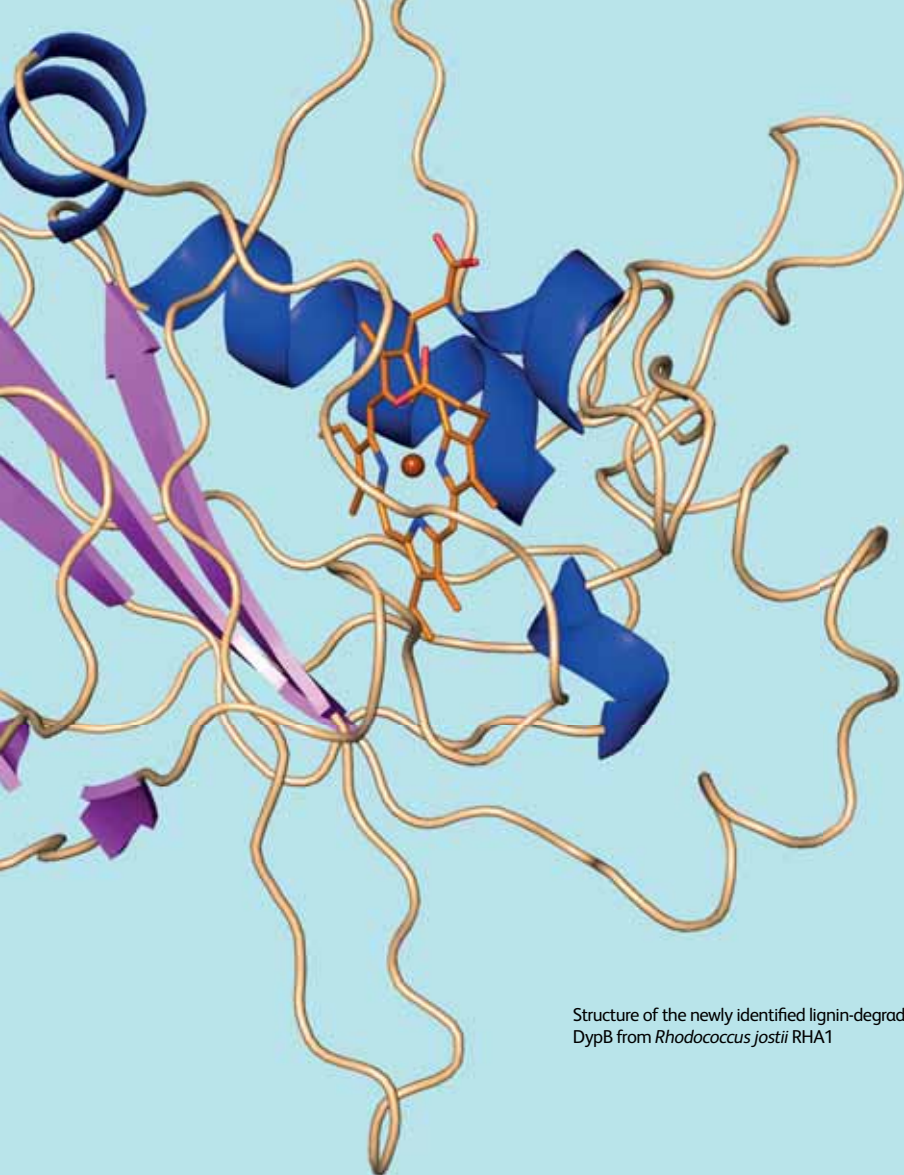
Lignin-degrading enzymes are common in wood-rotting fungi. Yet despite being studied for 25 years, these fungal enzymes have not translated to a commercial process for lignin breakdown, in part because of inherent difficulties in fungal genetics and protein expression. And while there have been reports of soil-dwelling bacteria that can

also metabolise model lignin compounds, no bacterial lignin-degrading genes have been identified and no bacterial lignin-degrading enzymes have been characterised, until now.

Having first confirmed lignin-degrading activity in *Rhodococcus jostii*, using a novel assay developed by Professor Timothy Bugg and colleagues from the University of Warwick¹, the team set about analysing the bacterium's genome to identify two peroxidase genes (*DypA* and *DypB*) which shared sequence similarity with known peroxidase genes from other microbes.

"When we tested mutant *R. jostii* strains – those with the *DypB* gene removed – we were able to show that lignin degradation activity was greatly reduced," Prof. Bugg explains. "Furthermore, we demonstrated that purified DypB protein extracts from *R. jostii* could oxidise Kraft lignin (a by-product of the paper-making industry) and wheat straw lignocellulose."

¹M. Ahmad *et al.* *Molecular BioSystems*
DOI: 10.1039/B908966G



Structure of the newly identified lignin-degrading enzyme DypB from *Rhodococcus jostii* RHA1

Scaling up

Rhodococci are well-known for their abilities to degrade a wide range of organic compounds and pollutants which, combined with their robust growth and exceptional stress tolerance, has led to their use in a wide range of applications. And, with a fully-annotated genome sequence now available, the possibility of modifying this bacterium raises the prospect of producing enzymes which can break down lignin on an industrial scale.

“For biofuels to be a sustainable alternative to fossil fuels, we need to extract the maximum possible energy available from plants. By raising the exciting possibility of being able to produce lignin-degrading enzymes from bacteria on an industrial scale, this research could help unlock currently unattainable sources of biofuels,” says Prof. Bugg.

“By making woody plants and the inedible by-products of crops economically viable, the eventual hope is to be able to produce biofuels and renewable chemicals that don’t compete with food production.”

The team at Warwick have been collaborating with colleagues at the University of British Columbia, led by Professor Lindsay Eltis,

who determined the genome sequence of *Rhodococcus jostii* RHA1, and have been working to unravel the structure of the enzyme. With the aid of the crystal structure, it may be possible to use directed evolution to enhance the catalytic activity of the enzyme, and confer thermostability.

“We suspect that DypB is one of a group of lignin-metabolising enzymes present in bacteria, so we hope to find a wider set of enzymes that could be used for biotechnology,” says Prof. Bugg. “We also hope to find similar enzymes from thermophilic bacteria [those that live in very hot environments, such as near volcanic vents] that would be better suited to use in industrial biorefinery processes, which often operate at a high temperature.”

BBSRC Sustainable Bioenergy Champion Duncan Eggar said, “Burning wood has long been a significant source of energy. Using modern bioscience we can use woody plants in more sophisticated ways to fuel our vehicles and to produce materials and industrial chemicals. This must all be done both ethically and sustainably. Work like this, which develops conversion processes and improves efficiencies, is vital.”

Reprinted with permission from J.N Roberts et al, Vol 50 *Biochemistry*, Copyright 2011 American Chemical Society

Further Reading

Identification of DypB from *Rhodococcus jostii* RHA1 as a lignin peroxidase, *Biochemistry* DOI: 10.1021/bi101892z

Characterization of dye-decolorizing peroxidases from *Rhodococcus jostii* RHA1 *Biochemistry* DOI: 10.1021/bi200427h

Next steps

- Identify novel lignin-degrading bacteria, including thermophilic bacteria
- Identify a wider range of lignin-metabolising enzymes from lignin-degrading bacteria
- Apply lignin-degrading enzymes to the production of renewable chemicals from lignin and lignocellulose

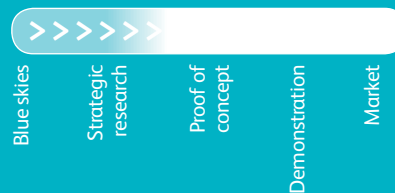
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Discovery pipeline



Blue skies

Strategic research

Proof of concept

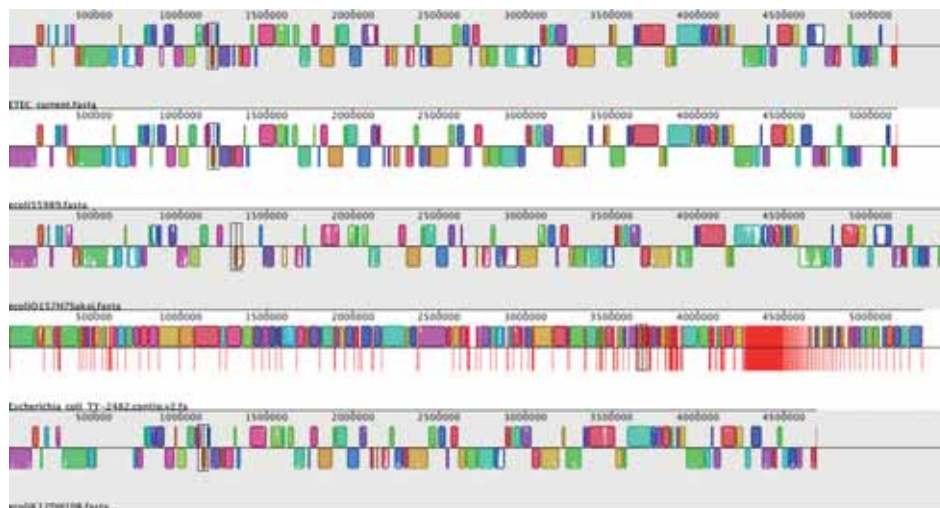
Demonstration

Market

The Integrated Biorefining Technologies Initiative (IBTI)

club aims to provide a means to combine relevant academic expertise to work on innovative, multidisciplinary, scientific areas of relevance to industry. An integral feature of the club’s operation will be the delivery of efficient mechanisms to facilitate the dissemination of research outcomes to club members and support effective networking and community building between academic groups and the companies involved.

www.bbsrc.ac.uk/ibtclub



A comparison between different *E. coli* strains including O157:H7, responsible for a previous food poisoning outbreak in the UK. The coloured blocks represent regions of the genome sequence in common with other *E. coli* strains. *E. coli* O104:H4 is second from the bottom, red lines on this sequence show where the sequence is still in pieces that need to be joined before we can make sense of the genes in these regions.



Keith Brofsky/Photodisc. Copyright Thinkstock, 2011

One of the crowd in *E. coli* outbreak analysis

Scientists from The Genome Analysis Centre (TGAC), which receives strategic funding from BBSRC, have identified several genes that may be key factors in the recent outbreak of *Escherichia coli* strain O104:H4.

The strain has been implicated in a number of hospitalisations and deaths, particularly in Germany; the outbreak has also had a high economic impact on the fresh vegetable market across the EU.

TGAC is contributing to the ‘crowd-sourcing’ analysis of the genome sequence, which is involving an unprecedented level of scientific cooperation across the globe, via the internet, in order to uncover what is making it so deadly. This approach was made possible by the public release of genome sequence data from BGI, China at the beginning of June.

Compare and contrast

Many antibiotic resistance genes have been found in this draft sequence, as well as at least part of a gene known to be involved in attachment and uptake into human cells. There are several other genetic factors that, taken together, are likely to contribute to this organism’s serious impact on human health. Several of these implicated genes are found in key areas of the genome which may have been gained from other *E. coli* strains.

Genes for outer cell structures, known as pili, have been found that could potentially be involved in attachment to vegetable skins or plastic packaging. In addition, this bacterium has a number of genes associated with survival under stress conditions, which could improve its tolerance to adverse conditions such as acid, heavy metals, low oxygen and UV light.

TGAC’s Microbial Genomes Project Leader Dr Lisa Crossman said, “By studying the genetic factors involved in the survival of this bacterium on surfaces, we hope to get an angle on how this organism has been able to get a foothold in the global food chain.”

So far the analysis has identified that the most closely related *E. coli* strain is one that was isolated several years ago in the Central African Republic and was linked with serious diarrhoea. However, the new outbreak strain is believed to have gained genes from a different *E. coli* strain not previously involved with food poisoning, which now allows it to induce life-threatening haemorrhagic uraemia symptoms.

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Discovery pipeline



Blue skies

Strategic research

Proof of concept

Demonstration

Market

July

11-14 July

BBSRC will be attending 'the science of ageing – global progress', the annual meeting of the British Society for Research on Ageing

www.bsra.org.uk

15-16 July

BBSRC/Age UK sponsored workshop on ageing and muscle mass, Liverpool

www.liv.ac.uk/ageing-and-chronic-disease/workshop-july

19 July

Deadline for applications to BBSRC's modular training for industry scheme

www.bbsrc.ac.uk/mti

28 July

Deadline for applications to BBSRC's industrial CASE award scheme

www.bbsrc.ac.uk/industrial-case

September

13-14 September

The science behind food and sustainability, Sheffield

shine.sheffield.ac.uk/conference

17-20 September

6th international chick meeting, Roslin Institute, Edinburgh

www.roslin.ed.ac.uk/chick6

October

11 October

Innovate 2011, Business Design Centre, London

ktn.innovateuk.org/web/innovate-2011

November

30 November-01 December

bioProcessUK conference 2011: advancing next generation therapies, Glasgow Science Centre

www.bioprocessuk-annualconference.org

Cereals 2011

BBSRC attended Cereals last month, the leading technical event for the arable industry. In addition to our exhibition stand, where some of the 26,900 visitors could find out more about our role as the major UK funder of crop science research, we hosted two networking events for policymakers, researchers and representatives from the agriculture industry.

The first event provided an opportunity for end-users to hear from leading scientists in the fields of bioenergy, disease control in arable crops and improving wheat and oilseed rape and to make new connections. The second, held jointly with Rothamsted Research and the John Innes Centre and hosted by NFU Deputy President Meurig Raymond, provided an introduction to the newly appointed Directors of these two



Rothamsted Research Director Professor Maurice Moloney (speaking) with (left to right) BBSRC Director of Communications and Information Management Paul Gemmill, NFU Deputy President Meurig Raymond, and BBSRC Council member Jim Godfrey

centres, which both receive strategic funding from BBSRC, and a discussion on how their emerging strategies will produce excellent science and agricultural research that will benefit farmers and the wider agricultural community.



John Innes Centre Director Professor Dale Sanders (right) in conversation



NFU Deputy President Meurig Raymond (centre) in conversation

Find us on YouTube



Modelling bumblebee pollination

BBSRC-funded researchers are engaged in a number of activities to investigate the decline in pollinating insects such as bees. Among them are lab-based experiments to find out what cues bees use when visiting flowers.

bit.ly/hi001e



Eradicating rinderpest

As the World Reference Laboratory for rinderpest, staff at the Institute for Animal Health, an institute of BBSRC, have played an important role in eradicating the disease, which has helped to reduce famine and poverty in rural communities and increase agricultural production throughout the developing world.

bit.ly/fPQVeo



Global Food Security (GFS) at Oxford Farming Conference

BBSRC represented the GFS Partnership at Oxford Farming Conference in January. Watch BBSRC's Director of Research Professor Janet Allen, speaking about food security research – an important issue that was represented at this year's conference.

bit.ly/hMpzdT



The Age of Bioscience

In this, our strategic plan 2010-2015, BBSRC continues to move UK bioscience forward to exploit new and exciting ways of working and thinking. We will ensure that UK bioscience stays world-class and delivers significant social and economic benefits.

bit.ly/dOX5tB

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