

MICROBIOLOGY TODAY

QUARTERLY MAGAZINE OF THE SOCIETY FOR GENERAL MICROBIOLOGY

39:3 AUG 2012



HARRY SMITH MEMORIAL ISSUE

Widely distributed throughout the body, including CSF¹

Oral levels comparable to i.v. levels²

Rarely implicated with *C.difficile*³

Effective against serious infections including:

- *H. influenzae*^{1,2}
- Typhoid^{1,2}
- MRSA⁴
- VRSA⁵
- *Neisseria*^{1,2}
- *Legionella*^{1,2}
- *Rickettsia*^{1,2}
- *C.difficile*⁶⁻⁹
- *E. coli*¹



CHLORAMPHENICOL CAPSULES

respiration and death within a few hours of the onset of symptoms. **Overdose:** Stop chloramphenicol immediately if signs of adverse events develop. Treatment is mainly supportive. If an allergy develops, oral antihistamines may be used. In severe overdosage e.g. Gray Baby Syndrome, reduce plasma levels of chloramphenicol rapidly. Resin haemoperfusion (XAD-4) has been reported to substantially increase chloramphenicol clearance. **Pack size and Price:** 60 capsules £377.00 **Legal Category:** POM. **Market Authorisation Number:** PL17736/0075. **Market Authorisation Holder:** Chemidex Pharma Limited, 7 Egham Business Village, Crabtree Road, Egham, Surrey TW20 8RB, UK. **Date of preparation:** April 2012. See Chloramphenicol Summary of Product Characteristics for full prescribing information.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Essential Generics on 01784 477167.

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PIP: 106-5796

AAH: CHL600B

ALLIANCE: 065995

MOVIANTO: CHL25060



COVER IMAGE

Prof. Peter Owen,
Microbiology Department,
Mayne Institute, Trinity
College Dublin

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MANAGING

EDITOR & DESIGN

Ian Atherton

EDITORIAL ASSISTANT

Yvonne Taylor

ADDRESS

Society for
General Microbiology,
Marlborough House,
Basingstoke Road,
Spencers Wood,
Reading RG7 1AG
tel. 0118 988 1800
fax 0118 988 5656
email mtoday@sgm.ac.uk
web www.sgm.ac.uk

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Society for General
Microbiology (SGM)

ISSN 1464-0570

PRINTED BY

Latimer Trend & Co. Ltd,
Plymouth, UK

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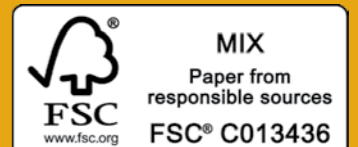
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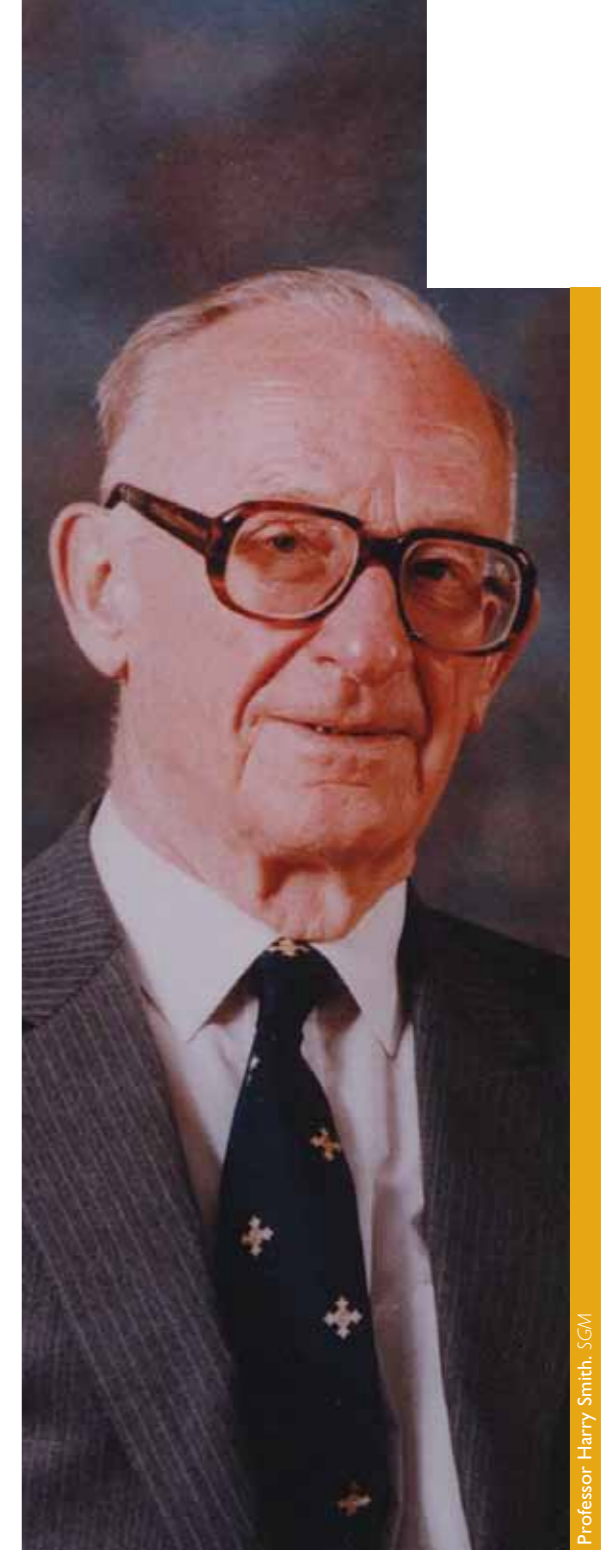
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Welcome to the August issue of *Microbiology Today* dedicated to the memory of the late Professor Harry Smith CBE FRS.

THE SAD NEWS of Professor Harry Smith's death reached me by text message via Ian Henderson while I was at a conference in Mexico in December 2011.

While I had never met Harry personally, it was clear to me that as a Society we needed to mark his death, not only as a Past President of the Society, but also for the wide range and depth of influence Harry's work had on modern microbiology. At the February meeting of SGM Council it was agreed that we should mark Harry's passing with a special issue of *Microbiology Today* and, rather than have an issue of personal tributes to him, create an issue which celebrated his outstanding contribution and influence across the microbiological world. So here, with the help of the *Microbiology Today* Editorial Board, and additional input and suggestions from Nigel Brown and Ian Henderson, we have put together an issue that hopefully covers the breadth of interest and influence Harry had in microbiology.

We have an article covering Harry's influence on the development of microbiology at the University of Birmingham, and especially the career of the author Charles Penn, in addition to a contribution from Ian Henderson and Mark Pallen showing how the foundations set by Harry have led to the formation of the new Institute of Microbiology and Infection at Birmingham. Three



Professor Harry Smith, SGM

articles cover Harry's work and its legacy. Jeff Cole and Chris Tang discuss his contribution to *Neisseria* research and *in vivo* pathogen biology. Les Baillie's article is a tour de force on the seminal work Harry and his laboratory carried out on anthrax. Finally, the tributes to Harry's work is rounded up by Clive Sweet's discussion of his contributions to influenza research and in particular, again, the *in vivo* work carried out using the ferret model.

What is clear from all these articles is that Harry was a character who was universally respected across the world for his outstanding and influential contributions to our science, and he will be sadly missed.

The theme of the next issue of the magazine (November) will be 'Antimicrobials'.

PAUL A. HOSKISSON, Editor (email paul.hoskisson@strath.ac.uk)



NEW HONORARY MEMBER PROFESSOR ANNE GLOVER



Anne Glover

Anne obtained a BSc in Biochemistry at Edinburgh in 1978 and then studied at Cambridge where she obtained a Doctorate in Molecular Microbiology. Her research has been varied and has included the development of biosensors to detect environmental pollution and, more recently, how we respond to stress at the molecular level. In 1999, she commercialized some of her biosensor technology into a successful company which diagnoses environmental pollution and provides solutions for its clean-up.

Anne has played major roles in UK research councils in the setting of strategic priorities and budgets for science and has been a partner in several European research initiatives. In 2006, she was awarded a CBE in recognition of her services to environmental sciences. In 2008, she was made a Woman of Outstanding Achievement in Science, Engineering and Technology (SET), and has worked hard to raise the profile of women in SET and to ensure that not only are women recruited into careers in SET but that they are supported to remain in the profession.

Anne was awarded the Proctor and Gamble Award for applied microbiology in 2012 and has received Honorary degrees from Edinburgh Napier University, the Open University, the Scottish Agricultural College, Glasgow Caledonian University and Strathclyde University. She also received a special recognition award from the Scottish Life Science community in 2012. She has a strong interest in how science, engineering and technology can contribute to the developing world and chaired the UK Collaborative on Development Sciences 2009–2011.

Anne joined the European Commission on 1 January 2012 as the first Chief Scientific Adviser to the President. Prior to that, she was the first Chief Scientific Adviser for Scotland (2006–2011).



MICROBIOLOGY TODAY EVOLVES

Look out for the November issue of *Microbiology Today*. New features, new design and new content!

News of Members

Congratulations to:

LORNA CASSELTON, Emeritus Professor of Fungal Genetics, Plant Science, University of Oxford, on the award of a CBE in the 2012 Queen's Birthday Honours for services to fungal genetics and international science.

ANDREW LOVERING, School of Biosciences, Birmingham, who has been awarded the American Society for Microbiology 2012 ICAAC Young Investigator Award for his crystallographic research into the enzymes that build and modify bacterial cell walls.

MERVYN BIBB, John Innes Centre, who has been awarded the Heatley Medal and Prize by the Biochemical Society.

The Society notes with regret the deaths of:

EMERITUS PROFESSOR LENNART

PHILIPSON, Karolinska Institutet, Stockholm, Sweden (member since 1963).

PROFESSOR COLIN KAPLAN (member since 1954). Colin was born in 1929 in South Africa where he trained as a doctor, but he spent most of his professional life in the UK, holding posts at the London School of Hygiene and Tropical Medicine and University College Hospital Medical School. In the 1950s, at the Lister Institute of Preventive Medicine, he improved a method of making freeze-dried smallpox vaccine – a method used widely in the WHO's smallpox eradication campaign.

Following consultancy work for WHO in India and further work on rabies, he took up the Chair of Microbiology at Reading in 1968. It was at the beginning of this tenure that, together with Peter Wildy, he founded JGV. He retired in 1986. A full obituary is available online at http://vir.sgmjournals.org/content/93/Pt_9/1851.full

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THE LATEST ON SOCIETY ACTIVITIES

PEOPLE

SUPPORTING THE PROFESSIONAL DEVELOPMENT OF SGM MEMBERS



Marieke Hoeve

MICROBIOLOGY OUTREACH PRIZE WINNER ANNOUNCED

Congratulations to **DR MARIEKE HOEVE**, The University of Edinburgh, who has been awarded the SGM Microbiology Outreach Prize 2012 (sponsored by Yakult).

Marieke has developed and delivered a variety of exciting outreach activities during the last 4 years, including hands-on activity stands for the Edinburgh International Science Festival, and has led biology workshops at primary schools. In 2009 she was awarded an Edinburgh Beltane Public Engagement Fellowship with which she created MicroMania, a science card game for children (age 8–12).

Marieke will be presented with her prize during the SGM Autumn Conference at the University of Warwick and will give a talk on 4 September 2012 where she will discuss the gains and pains of participating in science communication as an academic researcher.

HARRY SMITH VACATION STUDENTSHIP

The SGM Vacation Studentships will be renamed **HARRY SMITH VACATION STUDENTSHIPS** from 2013 onwards in recognition of Harry's well-known support of microbiologists and microbiology students at the start of their careers. The scheme offers supervised research experience in microbiology to undergraduate students in the summer vacation before their final year.

FREE PLACES FOR SGM MEMBERS AT THE STANDING UP FOR SCIENCE MEDIA WORKSHOP

The Voice of Young Science *Standing up for Science* media workshops encourage early-career researchers to get their voices heard in public debates about science. The 1-day workshop involves a series of panel discussions with fellow scientists, science journalists, press officers and the Sense about Science team. The workshop aims to confront misconceptions about how the media works and discuss participants' concerns about speaking to the public. Four workshops are held each year (the next one is on 16 November 2012 in Glasgow) and SGM members are eligible for free places (look out for announcements on the SGM website or contact Laura Udakis at the SGM Press Office – l.udakis@sgm.ac.uk).

SGM member **DR LENA CIRIC**, University College London, attended a workshop on 25 May in London. *'I attended the workshop because I believe talking to the public about the science we do is very important and using the media to do this gives access to a*



Lena Ciric

wide audience. For me, the most interesting aspect of the workshop was talking to science journalists. It gave an insight into what they are looking for from a science story – and it was also interesting to learn about what goes on behind the scenes in the world of media! To practice communicating with non-scientists, the journalists advised us to talk to our friends and family about science. They said that you should be yourself, talk in simple and clear terms, and it is OK not to know everything. Attending the workshop has highlighted how important it is to communicate the science that I do to the public and has made me think more about the bigger picture. It's important to think about why we do what we do and how it benefits society – and then communicate this. I now feel much more confident about doing this.'

Annual General Meeting

The AGM of the Society will be held at the Autumn Conference at the University of Warwick on Tuesday 4 September 2012, 12:35–13:00, in the Warwick Arts Centre Theatre.

AGENDA

1. Introduction by the President
2. Minutes of the 2011 Annual General Meeting
3. Matters arising from the Minutes
4. Report of the Treasurer
 - (a) Receiving of the Annual Accounts
 - (b) Appointment of Auditor
 - (c) Approval of membership subscription rates
5. Announcement of new President
6. New Members of Council and Divisional Committees
7. New Council Committees, Chairs and Members
8. Special resolution to amend Articles of Association
9. Any other business

DR SIMON FESTING Company Secretary

Supporting papers can be downloaded from www.sgm.ac.uk/about/objectives.cfm

GRANTS

MAKE THE MOST OF YOUR MEMBERSHIP

SCIENTIFIC MEETINGS TRAVEL GRANTS – INVITING APPLICATIONS FROM CAREER RETURNERS

The Scientific Meeting Travel Grants scheme provides funds to support members in the early stages of their career to present work at scientific conferences, or to attend a short course, in the UK and overseas. SGM has extended this scheme to welcome applications from postdoctoral scientists who are funded by a career returner scheme (Daphne Jackson Fellowship, Wellcome Trust Career Re-entry Fellowship, or similar scheme) in a microbiological post in the UK or Ireland at the date of application. Up to £500 is available as a contribution towards the costs of the proposed activity. Applications are accepted throughout the year (but must be made in advance of the conference or course).

Full details of the scheme, including eligibility criteria and an application form are available at www.sgm.ac.uk/grants/smtg.cfm. Enquires to grants@sgm.ac.uk

UPCOMING DEADLINES

31 AUGUST 2012

Postgraduate Student Conference Grants | Undergraduate Student Conference Grants | Technician Conference Taster Grants | Retired Member Grants for the SGM Autumn Conference, University of Warwick, 3–5 September 2012 (see p. 152).

21 SEPTEMBER 2012

President's Fund for Research Visit Grants | Elective Grants | Infection Training Support Grants | International Development Fund | Watanabe Book Fund

9 NOVEMBER 2012

Postgraduate Student Conference Grants | Undergraduate Student Conference Grants | Technician Conference Taster Grants | Retired Member Grants for the SGM Irish Division Conference, University College Cork, 14–16 November 2012 (see p. 152).

Heatley-Payne and Hayes-Burnet Award schemes revised

The Heatley-Payne and Hayes-Burnet Awards, offered jointly with the American and Australian Societies for Microbiology, respectively, support the reciprocal exchange of one early-career society member (within 5 years of being awarded their PhD) to present their research at the other Society's main annual conference and visit a research laboratory in that country. The awards recognize the scientific excellence of the recipient's current programme of research and scholarly activity, and enable them to raise their profile in the scientific community and initiate collaborations. See Gradline (*Collaborate or stagnate*, p. 171) for a summary of the scheme benefits and profiles of previous recipients.

For 2013, the rules and application processes for these awards have been revised. Full details and an application form are available at www.sgm.ac.uk/grants. Enquires to grants@sgm.ac.uk. Closing date for applications: **30 November 2012**.

2012. 299 pages, illustrations, index. Paperback. (978-1-55581-540-0) or E-book (978-155581-847-0)

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THE USE OF MOBILE DEVICES is escalating, with more and more people accessing information on the move. SGM has responded to this by launching mobile-optimized sites for the Society's four journals, *Microbiology* (<http://m.mic.sgmjournals.org>), *Journal of General Virology* (<http://m.vir.sgmjournals.org>), *International Journal of Systematic and Evolutionary Microbiology* (<http://m.ijs.sgmjournals.org>) and *Journal of Medical Microbiology* (<http://m.jmm.sgmjournals.org>), using HighWire's Mobile Web interface.

Readers accessing the main journal sites on a mobile device are redirected automatically to the simplified mobile sites. This does not apply to the iPad, which has a large-enough screen to view the main sites with their full functionality. The branding of the journals is carried through to the mobile sites by the use of the standard journal colours and logos.

The current issue, the entire back content (archive) and Papers in Press (papers published ahead of print) pages can be accessed from the home page and via a navigation bar on other pages. A graphic of the cover of the latest issue on the home page also links to the table of contents of that issue. Within a table of contents, there are bars for each of the contents categories, which expand to give the titles of papers in that



SGM journals go mobile

category. The titles link to the abstract, full text and PDF versions of an article, which are also optimized for viewing on a small screen. As for the full-text papers on the main sites, inter-article links enable quick navigation between the paper sections, and figures and tables can be opened in new windows. Each paper also has an 'Email this article' feature. Articles have links to the previous and next articles in the issue, facilitating quick browsing, and a link back to the table of contents.

A simplified search page can be accessed from the home page of each mobile site, as can a drop-down menu enabling quick access to the mobile sites of the other three SGM journals.

Currently, users belonging to an institution that subscribes to the journal will only be able to access content that is behind access controls if they are within the institution IP area. However, a mobile voucher service will shortly be set up enabling mobile devices to be linked with an institution's subscription. This will enable access to the embargoed content when the user is not on the institution's network.

The mobile sites will make the content of the SGM journals more widely accessible and help readers keep up to date with the latest research. Why not try out the websites today by scanning the QR codes above with your smartphone?

MELANIE SCOURFIELD is Managing Editor of *Journal of Medical Microbiology* (email m.scourfield@sgm.ac.uk)

To find out more about the SGM journals, meet the Editors on the SGM YouTube channel (www.youtube.com/user/SocGenMicrobiology).

SGM JOURNAL MICROSHORTS

Quicker diagnosis for GBS infection

A more accurate, faster diagnostic test for group B streptococcal infection in babies has been developed by Health Protection Agency researchers. The new test could allow better treatment and management of the disease and reduce the risk of mortality among newborns. group B *Streptococcus* (GBS) infections, caused by the bacterium *Streptococcus agalactiae*, are the most common cause of meningitis, septicaemia and pneumonia in infants. The new test detects the presence of the *cyB* gene in *S. agalactiae* in samples of blood or spinal fluid in less than 2 hours. GBS bacteria live harmlessly in the genital tract of women and are carried by 20–30% of pregnant women. The bacteria can be transmitted from mother to newborn during delivery. The authors believe that more rapid diagnosis of GBS will mean that antibiotic treatment can start sooner, reducing the risk of infant mortality.

JMM doi:10.1099/jmm.0.042879-0

Hitchhiking microbes

A rare and unusual novel species of yeast has been identified at three separate locations across the world, according to Canadian scientists. The findings suggest a link between the distribution of specialized microbes and human migrations. The novel strain of yeast has been named *Saccharomycopsis fodiens* and was isolated from flower-associated beetles in three geographically distinct locations in Eastern Australia, Costa Rica and the Galapagos islands. The authors say that the collection sites for *S. fodiens* are compatible with the hypothesis that ancient Polynesians migrated southward from Taiwan and then eastward across the Pacific and eventually South America. They travelled carrying sweet potato plants, whose flowers carry similar insects and yeasts. The findings should allow testable hypotheses to be formulated about the influence of human migrations on the global distribution of micro-organisms.

IJSEM doi:10.1099/ijms.0.043109-0

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tel. 0131 650 6443; email nigel.brown@ed.ac.uk
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tel. 0113 343 5632; email m.harris@leeds.ac.uk
- **Prof. Ian R. Henderson** Division of Immunity & Infection, University of Birmingham Medical School, Edgbaston, Birmingham B15 2TT
tel. 0121 414 4368; email i.r.henderson@bham.ac.uk
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tel. 0141 548 2819; email paul.hoskisson@strath.ac.uk
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tel. 0115 823 1094
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tel. 01223 336850; email js@mole.bio.cam.ac.uk

Vaccine-producing algae

Algae have been successfully used as factories to produce complex proteins for a potential malaria vaccine. Scientists from the University of California San Diego published their achievement in the May issue of the journal *PLoS ONE*. The researchers harnessed algae to generate and fold three-dimensional proteins from the *Plasmodium falciparum* malaria parasite into their natural form. The harvested proteins stimulated the production of antibodies in mice which attack the malaria parasite, preventing its reproduction. Traditionally, these proteins are difficult and prohibitively expensive to manufacture, artificially or in animal cells. The genetically selected algal strain that was used, *Chlamydomonas reinhardtii*, is easy and inexpensive to grow, providing an opportunity to mass-produce the complex *Plasmodium* proteins. Such proteins could be used to immunize humans to prevent infection and transmission of the malaria parasite between humans and the mosquitoes which carry it.

PLoS ONE – doi:10.1371/journal.pone.0037179

Rebecca Gladstone, University of Southampton

Cyanobacteria with bones

The first cyanobacteria that can form internal hard bone-like structures have been discovered. Scientists from the Centre National de la Recherche Scientifique in France have discovered cyanobacteria that form calcified structures inside the cells, rather than outside as other cyanobacteria do. '*Candidatus* Gleomargarita lithophora' was isolated from a biofilm in an alkaline lake in Mexico and belongs to an ancient cyanobacterial order. The calcified granules significantly increase cell density and might act to help them sink as an adaptation to life at the bottom of the lake. The researchers suggest that the cyanobacterium might itself influence the biomineralization process because the chemical composition of the granules (calcium, strontium, barium, carbonate and magnesium) is different from that of the surrounding medium. The group highlight that the cyanobacterium is not likely to form microfossils; however, the carbonates enriched in barium and strontium might have left signatures in the fossil record and may potentially help us understand the gap in their record.

Science – doi:10.1126/science.1216171

Paola R. Gomez-Pereira, National Oceanography Centre, Southampton

Chlamydomonas reinhardtii algae. AMI Images / Science Photo Library



Plant perfumes elicit microbial attraction

Maize crops have been shown to emit chemical signals which attract growth-promoting microbes to live amongst the plant's roots. Further research could prove invaluable to improving crop yields, which would help meet the increasing demands on food production created by the growth of the world's population. The common soil bacterium *Pseudomonas putida* and maize plants are known to participate in a relationship in which both parties benefit. To understand this further, scientists from Rothamsted Research and the University of Sheffield, analysed bacterial genes expressed in response to the presence of benzoxazinoids (BXs). These molecules are considered toxic and are known to be released by the plant as a defence mechanism. The researchers found that BXs released in the soil affect *P. putida* genes associated with movement, encouraging migration of the bacteria towards the roots. The presence of *P. putida* is beneficial to the plants since they increase the availability of nutrients, including iron and phosphorus, defend against harmful bacteria and additionally detoxify the root system by breaking down the toxic BXs. The research helps to improve our current understanding of growth strategies and mechanisms for the maintenance of good plant health.

PLoS One – doi:10.1371/journal.pone.0035498

Avika Ruparell, Unilever

Non-coding RNA may detect infection

Non-coding RNA (ncRNA) offers further clues to how pathogens interact with the human host. Patients with diseases like cancer, autism and Alzheimer's have been found to have mutations in their ncRNA. A new study shows that monitoring the increase, or decrease, of certain ncRNA molecules within a virus-infected cell could help detect diseases. Scientists at Tel Aviv University used a deep sequencing technique to analyse millions of human genome sequences. They developed new software to profile ncRNA of virus-infected cells. Further experiments, comparing HIV-infected cells and uninfected cells, showed that infected cells had different ncRNA profiles. The researchers could successfully discriminate between infected and non-infected cells with 100% accuracy. Even though ncRNA does not translate into proteins, the work suggests that it has crucial cellular functions and is involved in viral infection. This new finding, described as the 'Achilles heel' of disease, could lead to alternative virus treatments that target both coding and non-coding genetic material.

Nucleic Acids Research – doi:10.1093/nar/gks228

Rebecca Way, University of Aberdeen

'Barcodes' predict viral infection impact

Scientists are using protein signatures to formulate 'barcodes' for different viral diseases. Viral infections alter the balance of proteins in host cells causing some to be over-produced and others to be suppressed, which is a function of virus type.

Researchers from the University of Leeds used labelling techniques in conjunction with mass spectrometry to identify the cellular proteins most affected by infection with different strains of influenza virus and human respiratory syncytial virus (HRSV). From this they could assign a typical host protein profile to each virus. Since flu viruses frequently mutate, this newly developed method may be used to rapidly determine a mutant strain's impact on the host by comparing its 'barcode' with those of viruses that are already known. The swine flu 'barcode' in pulmonary cells was found to be similar to that of seasonal flu – a finding which may have informed predictions of the severity of the 2009 swine flu pandemic. Ongoing research focuses on how the more virulent avian flu barcode differs from other flu strains. While the research has focussed on respiratory viruses the method could also be extrapolated to others, particularly those causing highly pathogenic tropical diseases that are prone to sudden outbreaks and are often fatal.

Proteomics – doi:10.1002/PMIC.201100470

Tom Kennedy, Department of Agriculture, Ireland

Immune response helps bacteria infect host

Scientists at National Jewish Health have shown that *Listeria monocytogenes* can subvert the host immune response to help the bacterium successfully infect. *L. monocytogenes* infection is generally caused by eating contaminated foods (most commonly soft cheeses and pâtés). In most healthy adults, infection causes only mild symptoms, but it can be life-threatening in immunocompromised groups, and infection during pregnancy can cause miscarriage. When *L. monocytogenes* infects the host it triggers the innate immune response to help protect cells against invading bacteria, including the production of nitric oxide which triggers several defence mechanisms. The researchers found that when the bacteria are already inside cells nitric oxide can actually help the bacteria survive and spread – increasing the number of infected cells. Once inside a cell *L. monocytogenes* spreads directly from cell to cell by forming small bacteria-filled buds from the cell membrane which are absorbed by neighbouring cells into vacuoles. Nitric oxide was found to delay the cellular response to destroy these vacuoles, buying the bacteria time to escape into the cell interior. The researchers hope that knowledge of this mechanism will help provide targets for possible drug interventions to reduce severe food-borne infection.

Immunity – doi:10.1016/j.immuni.2012.03.011

Emma Trantham, University of Bristol



Listeria monocytogenes bacterium. James Cavallini / Science Photo Library

FORTHCOMING SGM CONFERENCES

AUTUMN 2012 | WARWICK | 3–5 SEPTEMBER

There is still time to register for the SGM Autumn Conference 2012 at the University of Warwick

Symposia

The dynamic genome | Next-generation sequencing – enabling new technology | The concept of species | Designer microbes | Molecular motors | *Streptococcus* in health & disease | Developing winning ways and competitive success

Registration

Register online at www.warwick2012.org.uk or complete (and return) the downloadable PDF. Registration fees include: refreshments, lunch, drinks receptions, the abstracts book, exhibition entry and all conference literature. Specially discounted rates are available for SGM Associate/Postgraduate Student Associate Members.

SPRING 2013 | MANCHESTER | 25–28 MARCH

Keep your diary clear for the SGM Spring Conference 2013 which will be held at Manchester Central, Manchester, UK.

Confirmed symposia include:

Viruses and human cancer: causes to cures | RNA – so much more than a genome | Metabolic interactions at the host–pathogen interface | Co-infections and co-colonization | *Streptomyces* | Next-generation antimicrobials | Bacterial–fungal interactions | Antimicrobials: resistance, emergence & communication.

We are also proud to announce that the **2013 SGM Prize Medal Lecture** will be delivered in Manchester by **HARALD ZUR HAUSEN**, winner of the 2008 Nobel Prize in Physiology or Medicine 'for his discovery of human papilloma viruses causing cervical cancer'.

OTHER SGM-SPONSORED MEETINGS

European Microscopy Congress

16–21 September 2012
Manchester Central
Conference Centre

The Molecular & Cellular Biology of Human Papillomaviruses (HPV UK)

9–11 November 2012
Rydall Hall, Ambleside,
Cumbria



NEWS FROM THE IRISH DIVISION

Marine Microbiology & Biotechnology; Biodiscovery, Biodiversity and Bioremediation

University College Cork, Ireland, 14–16 November 2012 – www.ucc.ie/en/mmbiotech2012/

'Marine biotechnology' has become an umbrella term for a plethora of diverse research activities aimed at providing sustainable food and energy sources, protecting environmental and human health and facilitating the development of novel industrial products and processes. Against this background, SGM Irish Division are hosting a joint SGM/FEMS Marine Microbiology & Biotechnology Autumn conference. The meeting will focus on three central themes within marine biotechnology research, in which microbiology is a core discipline; biodiscovery, biodiversity and bioremediation. The broad scope offered within these themes is intended to promote interactions between diverse research groups and to highlight overlapping research interests.

Confirmed international speakers include: **Marcel Jaspers** (marine symbiont bioactives), **Jan Roelef van der Meer** (marine microbial biosensors), **Jeroen Raes** (systems biology, phylogeography), **Jeanette Andersen** (Arctic sampling & biodiscovery), **Chantal Compere** (biofilms & biofouling), **John McGrath** (marine phosphate recycling), **Julian Marchesi** (sea floor microbial ecology) and **Ute Henschel** (bioactives from marine sponges).

Abstracts for poster presentations will be accepted until **Friday 5 October 2012**. Discounted registration fees are available for SGM and FEMS members.

DIVISION COMMITTEE ELECTION RESULTS

We are delighted to welcome new members to the Division Committees. Their term of office will start in September 2012.

VIROLOGY DIVISION

Microbial diversity & evolution –

Janet Daly *University of Nottingham*

Fundamental microbiology –

David Evans *University of Warwick*

Translational microbiology –

Catherine Adamson *University of St Andrews*

Infectious disease –

Kevin Brown *HPA Colindale*

Michelle West *University of Sussex*

PROKARYOTIC MICROBIOLOGY DIVISION

Microbial diversity & evolution –

Julian Marchesi *Cardiff University*

Translational microbiology –

Sandra McFarlane *University of Dundee*

EUKARYOTIC MICROBIOLOGY DIVISION

Microbial diversity & evolution –

Ursula Bond *Trinity College Dublin*

Translational microbiology –

Elinor Thompson *University of Greenwich*

Infectious disease –

Donna MacCallum *University of Aberdeen*

Justin Pachebat *Aberystwyth University*

IRISH DIVISION

Jakki Cooney *University of Limerick*

Gerard Fleming *NUI Galway*

Jarlath Nally *University College Dublin*

Vincent O'Flaherty *NUI Galway*



WWW.SGM.AC.UK/MEETINGS — DELIVERING MODERN MICROBIAL SCIENCE

SCIENTIFIC MEETINGS COMMITTEE

- **Scientific Meetings Officer**
Dr Evelyn Doyle
evelyn.doyle@ucd.ie
- **Deputy Scientific Meetings Officer**
Prof. Mark Harris
m.harris@leeds.ac.uk
- **Education Division**
Dr Sara Burton
s.k.burton@exeter.ac.uk
Dr Beatrix Fahrert
fahrertb@cardiff.ac.uk
- **Eukaryotic Microbiology Division**
Prof. Peter Sudbery
p.sudbery@sheffield.ac.uk
Prof. Mick Tuite
m.ftuite@kent.ac.uk
- **Irish Division**
Dr Kevin Kavanagh
kevin.kavanagh@AUG.ie
Dr Steve Smith
sgsmith@tcd.ie
- **Prokaryotic Microbiology Division**
Dr Nick Dorrell
nick.dorrell@shmt.ac.uk
Prof. Mark Stevens
mark.stevens@roslin.ed.ac.uk
- **Virology Division**
Dr Paul Duprex
p.duprex@qub.ac.uk
Prof. Wendy Barclay
w.barclay@imperial.ac.uk
- **Chief Executive Officer**
Dr Simon Festing
s.festing@sgm.ac.uk
- **Head of Membership Activities**
Dr Jane Westwell
j.westwell@sgm.ac.uk
- **Scientific Conferences Managers**
Claire MacLean
meetings@sgm.ac.uk
tel. 0118 988 1832
fax 0118 988 5656
- Susan Wong
s.wong@sgm.ac.uk
tel. 0118 988 1839
fax 0118 988 5656

HARRY APPOINTED ME to a 1-year postdoc vacancy in 1974 after we met at the Beckenham research labs of the Wellcome Foundation (one of the progenitors of GSK) where he was a consultant and I was a humble graduate researcher, working towards a PhD. I had stood in for my supervisor at a research meeting, and he made one of his snap judgments that I was OK, an impression that, characteristically, he never went back on over the following decades. The fact that I left a permanent job in industry to join his group on a 1-year externally funded vacancy also won his approval, although family considerations also contributed to this decision.

Over the next decade Harry mentored me in the development of a mainstream academic research career with fellowships and ultimately a 'New Blood' lectureship. His approach was to identify opportunities and use his influence to ensure success, which for me and others encouraged to branch out was a terrific opportunity. When

CHARLES PENN

it came to a senior Wellcome Trust fellowship he made it clear he would support me only as an independent PI with my own research interest, so I dropped out of his *Neisseria* project and embarked on spirochaete research, with the main focus on the syphilis pathogen.

The pay-off for Harry's support was loyalty and hard work in the cause of high-quality academic research on his terms. He was dismissive of any engagement in commercial contract work, which he called 'hick' research, and he would not tolerate it in his department. He was very reluctant to accept my diversion into university politics, representing the research staff community, which he saw as a competing call on my time, tempting me away from the laboratory. I only won that argument by undertaking to put in extra hours in the laboratory to compensate. He was in fact generous and accommodating in allowing me complete flexibility in organizing my working hours, mainly in the afternoons and evenings, so that my wife could develop her own career while our children were small. Others were not so lucky; one hazard well known among the research staff was to give him any inkling of itchy feet: this was taken as a lack of commitment and a slur on the reputation of his laboratory, if not a personal affront, and it was expected that the miscreant would be gone within weeks whether or not the competing position materialized.

Harry's most visible achievement on campus at Birmingham was the Microbiology building, completed

in the early 1970s and ensuring his freedom to run his ship independently without having to rub along with colleagues in other departments of biology. However, although 'core' funding appeared to flow directly to the department (I was too junior to know the full details), we had to compete with other departments for funding of large equipment items, by bidding to Faculty Board and arguing the case at Board meetings. The arguments were robust and aggressive and sometimes seemed to me, listening in as the research staff representative, to descend to a level of personal abuse – but I was naive and impressionable perhaps about what makes the world go round. Clearly Harry was in his element in these encounters – his competitive approach often being effective.

Harry's academic career perhaps peaked with his election to the UK's scientific elite, the Royal Society, in 1979 – he referred to it as 'the Royal' – and he was obviously immensely proud of this achievement. However,

at a day-to-day level his approach to research was sometimes idiosyncratic. Often he would come up with an idea with an unexpected angle, sometimes leading to the emergence of a personal research niche. He would then appear to set out to prove that he was right, rather than to test the hypothesis objectively and discard it if it didn't stand up. Usually he was indeed right, but when things didn't go his way, a favourite phrase was that it would 'come right' if we repeated the experiment a few more times. He was also wary of competition, sometimes to the point of avoiding approaches that he knew were being followed by able competitors and preferring to find a different path. Those were times when SDS-PAGE was being refined as an extremely powerful tool in protein analysis, and in the *Neisseria* field it was revealing superb biological insights into the roles of pilus and outer-membrane protein variation. However, Harry decided we would plough our own furrow and do things differently, and I vividly remember his coming to the laboratory one day and finding us looking at an SDS-PAGE gel. He was furious – 'I thought I told you not to run any more gels'!

Harry had many commitments outside the university, some of them arising from his time at the Military Research Establishment (MRE) at Porton Down. He was well connected both in UK and US defence-related microbiology, and sometimes had to phone or talk in person to his contacts about secret matters. He was obsessive

Background The University of Birmingham campus at Edgbaston. iStockphoto / Thinkstock

Charles Penn presents a personal view of Harry Smith and his legacy at Birmingham.



The University of Birmingham campus at Edgbaston. University of Birmingham

Harry Smith in Birmingham: past recollections and ongoing development

about security and had his office door sound-proofed, even though the outer departmental office was occupied by his and the department's secretary and constantly busy with comings and goings – hardly eavesdropper-friendly! Closer to home, but nevertheless secret for the rest of his life was his involvement in an internal enquiry after the smallpox case in the Medical School, where he solicited advice from experts at MRE and was a key architect of the University's defence strategy – or so it appeared from occasional unguarded comments to his colleagues.

Harry's influence was formative in the development and expansion of the SGM, and he served as both Treasurer and, in 1975, as President. This involvement also led to his presiding role at the 1986 International Congress of Microbiology held in Manchester

long outlived Harry's term as Head of the Microbiology Department, not only through the impact of his own work, but also in the legacy of associates, expertise and infrastructure that attracted the attention of recruits to Birmingham long after Harry's 'official' retirement (he continued to be involved in research through collaborations and co-supervisions for many years afterwards). Harry's successor as Professor of Microbiology, Nigel Brown, recognized the strength and reputation of pathogen microbiology in Birmingham although it was not his field, and supported the continuation of this research thread which has since expanded again. High-impact recruits to Birmingham as well as 'home-grown' experts in the pathogen biology tradition include Del Besra, Jane McKeating, Mark Pallen, Ian

“The breadth of expertise and international stature [at Birmingham] reflect the broadening of Harry's focus on the pathogen in vivo and its molecular determinants of virulence.”

where he built on many international connections and forged new ones. He was in some ways at his best in this kind of role, energetic and focussed on ensuring that everything was in place and all contingencies allowed for, including personal oversight of the finances. Undoubtedly, this role contributed to major international recognition for Harry and his home university as a centre for academic pathogen biology. The engagement of Birmingham academics with the SGM has continued to be significant, with two past and one present General Secretary currently on campus (Jeff Cole, myself and currently David Blackburn), and Ian Henderson, until recently Scientific Meetings Officer.

The University's reputation for excellence in pathogen biology has

Henderson, Laura Piddock, Mark Webber, Robin May, Tim Mitchell and many others. The breadth of expertise and international stature of this group reflect the broadening of Harry's focus on the pathogen *in vivo* and its molecular determinants of virulence, to embrace today molecular microbiology and pathogen genomics on a broad front. The recent establishment of the Birmingham Institute of Microbiology and Infection underlines the University's ongoing commitment to what is now perhaps the predominant sector in molecular microbiology nationally and internationally.

CHARLES PENN, School of Biosciences, University of Birmingham, Edgbaston, Birmingham B15 2TT (email c.w.penn@bham.ac.uk)



The University of Birmingham campus at Edgbaston.

THE LAST 12 MONTHS have seen bacteriology at the University of Birmingham flourishing, benefiting from substantial investments by the University and external sources. The new Institute of Microbiology and Infection (the IMI) will open its doors later this year, co-locating bacteriologists from our colleges of Medical and Dental Sciences and Life and Environmental Sciences together at the heart of the campus to create one of the largest bacteriology research centres in the UK. This will extend our global reach and energize our research, teaching and outreach efforts through a wide range of academic activities and initiatives. With funds from the NIHR and Ministry of Defence, we have established a Surgical Reconstruction and Microbiology Research Centre, enhancing our capacity in bacterial genomics and academic clinical microbiology. Thanks to significant investment from the University and the Wolfson Foundation, we have established the Birmingham Interdisciplinary Centre for Antimicrobial Drug Discovery to drive forward the search for new antimicrobials. These investments place the University of Birmingham firmly on the global map for bacteriology research.

MARK PALLEN & IAN HENDERSON

Pride in a century-long tradition of microbiology in Birmingham



The University of Birmingham has developed into one of the great centres for microbiology research. As the new Institute of Microbiology and Infection opens its doors, how has the legacy of Harry Smith been built upon?

However, these successes are built on a solid foundation. Bacteriology in Birmingham stretches back to the very foundation of our university, as illustrated by the cutting from 1898 (left), and builds on the legacy of the late Professor Harry Smith. This tradition encompasses:

- nearly half a century of research into the pathogenesis of bacterial infections, a research theme pioneered by Harry Smith;
- four decades of research into antimicrobial chemotherapy and resistance, initially Edward Lowbury, Alasdair Geddes and Laura Piddock, and more recently Peter Hawkey and Mark Webber;
- over a quarter of a century of model-organism biology with Jeff Cole, Chris Thomas, Pete Lund and most notably Steve Busby;
- significant achievements in biotechnology (Lynn Macaskie, Chris Thomas, Tim Dafforn, Tim Overton, Ian Henderson and Adam Cunningham), resulting in several patents and spin-out companies.

The university has continued to build on this tradition. Around 10 years ago, our microbiology community received an injection of fresh talent with the arrival of Gurdyal Besra (a world authority on tuberculosis), Mark Pallen (a clinical microbiologist with interests in bacterial pathogenomics), Peter Hawkey (a clinical microbiologist with expertise in antibiotic resistance and epidemiological typing) and Ian Henderson (an expert on bacterial protein secretion and outer-membrane biogenesis).

The intervening decade has provided a continuous record of outstanding achievement for microbiology in Birmingham, both in attracting external funding and in

Background *E. coli* cells bound to the surface of rocket salad leaves.

producing high-impact publications (over two dozen in the *Nature* stable of journals, over 20 in *PNAS* and a recent *NEJM* paper).

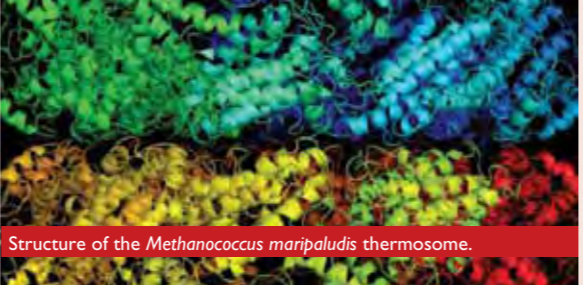
During the last 10 years, externally funded fellowships, twinned with university funding, have resulted in the appointment of a string of early-career academics: Klaus Fütterer, Robin May, Luke Alderwick, Apoorva Bhatt, David Grainger, Katie Hardy, Jan-Ulrich Kreft, Andy Lovering, Tim Overton and Mark Webber. More recently we have recruited Tim Mitchell, an expert on pneumococci to a Chair in Global Infection. Through the pioneering Birmingham Fellows scheme (www.birmingham.ac.uk/birminghamfellows), we have appointed two world-class early-career microbiologists (Vassily Bavro and Anne-Marie Krachler). *The University of Birmingham continues to build on the success of its bacteriology portfolio; through a new round of the Birmingham Fellows scheme we are actively seeking creative individuals who want to make a difference in bacteriology and we warmly encourage individuals with external fellowships to join our family.*

Our current research spans a spectrum of interest that runs from the fundamental science of model organisms to translational research on pathogens of medical importance. Current research strengths include:

- cell envelope biosynthesis in bacteria as diverse as mycobacteria, *E. coli* and pneumococci (Besra, Alderwick, Bhatt, Henderson, Lovering, Mitchell);
- bacterial protein secretion (Henderson, Pallen);
- molecular basis of microbial pathogenesis and host response (Penn, May, Krachler, Henderson, Pallen, Cunningham);
- bacterial transcription and nucleoid structure (Busby, Grainger, Pallen);
- high-throughput sequencing/bacterial pathogenomics (Pallen, Loman, Henderson);
- molecular basis of antimicrobial action/resistance (Piddock, Webber, Hawkey, Bavro).

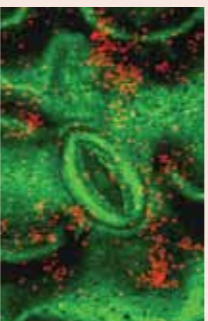
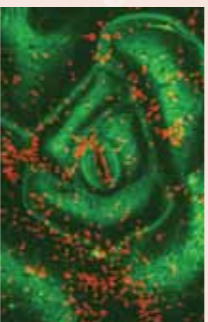
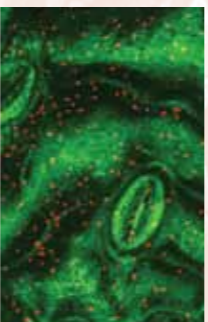
A cadre of our microbiology staff sit at the interface between academic and clinical activities, including medics and clinical scientists. We benefit from collaborations with medical microbiologists in local NHS Trusts and with the Health Protection Agency, providing opportunities for translational research that make an impact on patients' lives. Further opportunities to create impact arise through our existing network of industrial partners with translational research spanning the areas of bioprocessing to vaccine development, and renewable energy sources to development of novel antimicrobials.

Microbiology is taught across a range of degree programmes and features in the training of medical and dental students. In any one year, several thousand University of Birmingham students will have been exposed to microbiology teaching. Indeed, bacteriology teaching is a core theme in many of our degree programmes and remains amongst the most popular subjects with our students.



Structure of the *Methanococcus maripaludis* thermosome.

“Bacteriology teaching is a core theme in many of our degree programmes and remains amongst the most popular subjects with our students.”



Enterotoxigenic *E. coli* cells bound to the stomatal/epicuticular surface of rocket salad leaves.

However, the University of Birmingham is more than a work place for the bacteriology community. The Institute is located in a campus environment, providing a host of social, eating and sporting facilities. Our postgraduate and postdoctoral students benefit from a social agenda, including hiking trips on the Malvern hills, paintballing, swinging through trees for fun and singing karaoke! Students and staff often congregate in the adjacent bar for scientific discourse on a Friday evening and, as per local tradition, Balti's at the local curry houses are a frequent event. While these activities contribute to a sense of community amongst our researchers, they have the tangible benefit of enhancing internal collaborative relationships and developing new directions in research.

We have ambitious plans for bacteriology research at Birmingham. Our mission is to create an Institute that becomes a destination for industry, an aspiration for our peers and a home for our students.

TRANSLATIONAL MICROBIOLOGY AT BIRMINGHAM

From *E. coli* in our food or superbugs in our hospitals to TB resurgent in our communities, microbiologists at the University of Birmingham are finding new ways to fight our most fearsome microbial adversaries.

In May 2011, a lethal outbreak of *E. coli* infection erupted in the heart of Europe, reminding us that pathogenic micro-organisms can devastate even the most advanced societies. The outbreak

strain infected more than 4,000 people and resulted in more than 50 deaths, mostly in previously healthy individuals. But what kind of strain was this, where had it come from and why was it so virulent?

To answer these questions, Birmingham's Professor Mark Pallen worked with groups in Hamburg and China to spearhead a pioneering 'open-source genome analysis' of a bacterium from the outbreak. As Mark says, *'This project drew on a remarkable combination of rapid DNA sequencing, speedy data release and crowd-sourced analyses, powered by social networking tools. Instead of all the computer-based work being done in a single research centre, DNA sequences were released on to the internet, which triggered a flurry of analyses by bioinformaticians across the globe. Within a week, more than 20 entries had been filed on a collaborative website, revealing the strain's identity and evolutionary origins and priming the development of a new laboratory test specific to this strain.'*

The emergence of resistance to antibiotics is another pressing problem, whether in hospital infections or community-acquired infections such as tuberculosis. A team led by Professor Laura Piddock is exploring the factors driving the emergence of antibiotic resistance and the molecular mechanisms involved. *'Twenty-first century medicine is very different from when antibiotics were developed 60 years ago,' she explains. 'The infections we are seeing now are unlike those we encountered even 25 years ago because we have more sophisticated medical techniques. If we want effective cancer or transplant treatments, we have to be able to treat the infections these patients get with antibiotics that work. We are working to understand how bacteria develop resistance to drugs in the hope that we can prevent this happening in the future. We strive to raise public awareness about the need for urgent action in this area through the Antibiotic Action initiative.'*

So, how can we find new antibiotics? One way forward is to gain a better understanding of what makes microbes tick, in the hope of discovering new vulnerabilities open

to attack. Professor Ian Henderson, who is working on outer-membrane biosynthesis in *E. coli*, explains, *'I hope our work will lead to novel strategies for combating infectious diseases and to the identification of new treatments for bacterial infections. This progress is made possible by exploiting our strengths in disciplines from structural biology to chemistry. It is a collaborative endeavour to tackle one of the greatest threats to human health today.'*

In the group of Del Besra, Bardrick Professor of Physiology and Chemistry in the School of Biosciences, scientists are unpicking how the mycobacterial cell wall is made. *'By working out what enzymes the bacterium uses, we hope to be able to develop drugs that actually target some of those enzymes, resulting in better and more cost-effective treatments',* he explains. *'In a sense, we treat the enzyme as a lock and we try to design a key that fits it.'*

An alternative is to adopt an empirical strategy, screening compounds for antimicrobial activity without worrying, at least at first, about how they work, so long as they are effective. Del points out, *'We are one of very few centres in the world with the combination of cutting-edge, high-throughput screening technology and a detailed understanding of how the bacterium works, so we are very well*

placed to make these breakthroughs in drug discovery.'

Birmingham microbiologist Professor Chris Thomas is trying yet another approach to the creation of new antibiotics – a method called mutasynthesis. This line of attack exploits the pathways that naturally occur in micro-organisms to produce antibiotics, but feeds them unusual compounds, so that the microbes produce antibiotics with novel properties.

In closing, Professor Pallen explains, *'We are fortunate in Birmingham in having such a concentration of talent and technology on the same campus, attacking the problem of infection from so many different angles. It is clear that we are making our mark on global efforts to rid humanity of the scourge of infection. Together, we can make a difference.'*

Follow the IMI on:

- <http://imicrobham.blogspot.com/>
- <https://twitter.com/#!/imicrobham>
- www.bham.ac.uk/imicrobham

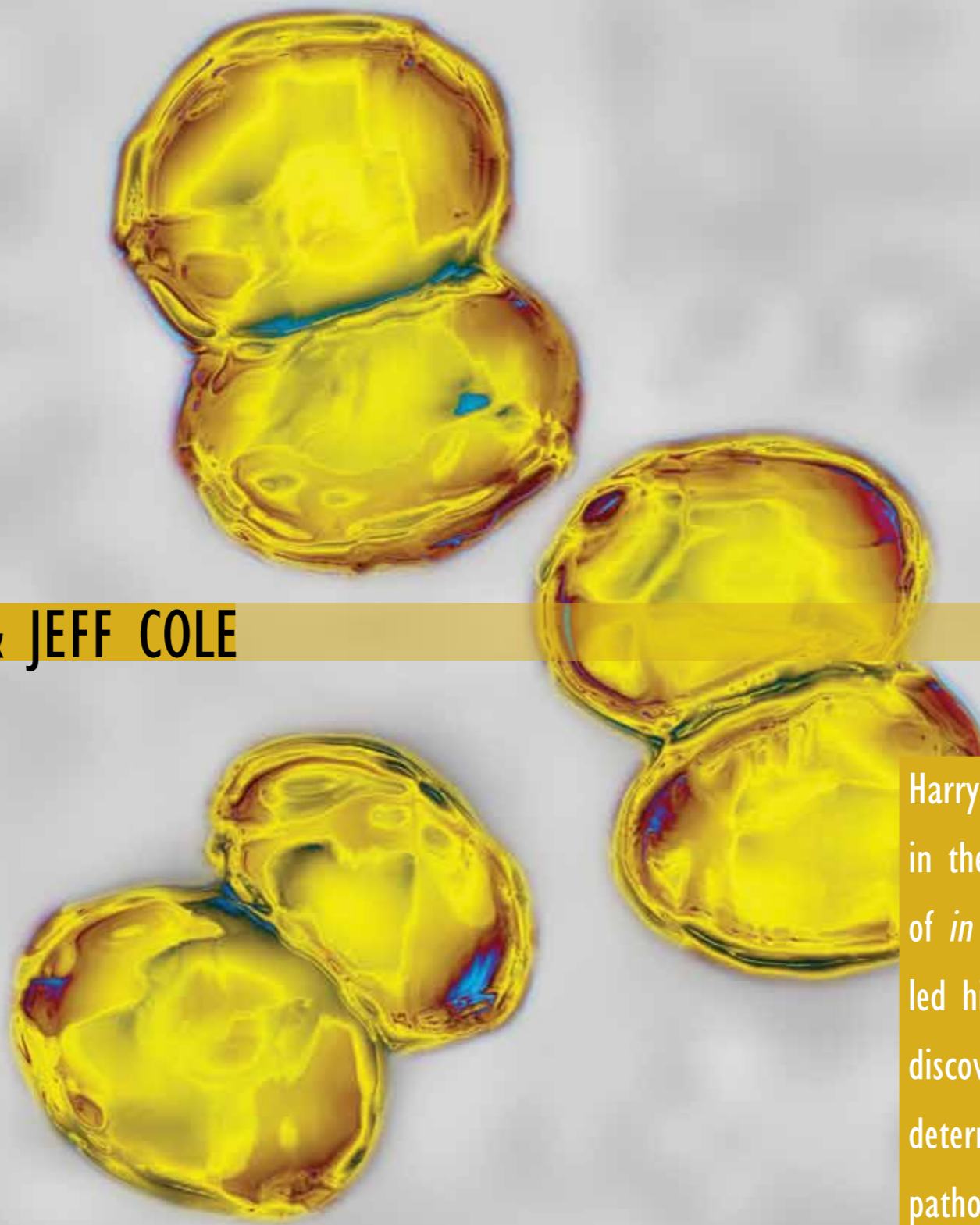
Structure of Bd1817, an HD-Gyp domain protein from *Bdellovibrio bacteriovorus*.



CHRISTOPH TANG & JEFF COLE

HARRY SMITH left Northampton Grammar School when he was 15 to work as a trainee pharmacist, and he won a scholarship to study pharmacy at University College Nottingham. He graduated with a first class degree in Special Chemistry, and was then appointed as an assistant lecturer. His PhD in chemistry involved the first chemical synthesis of a dinucleotide, the building blocks of DNA. His external PhD examiner was the famous chemist Lord Todd who recommended Harry for a position at the Chemical Defence Establishment, Porton Down. At Porton Harry started work on bacterial virulence, initially on the virulence-enhancing activity of mucin. His was the first group to study bacteria isolated directly from infected animals. This approach was so far ahead of the pack that it gained full recognition only in the 1990s. His seminal contributions included demonstrations that bacteria can live inside cells of the human body, and that they can exploit components of human tissue for their survival and growth. Even his critics now accept that he was correct, and his final contribution to a scientific meeting was at the Pathogenic *Neisseria* Conference in Cairns in 2006 when he thanked opponents for their rather belated acknowledgement.

Harry was the guru of microbial pathogenicity. He was the first person to identify a chemical within the human body that is exploited by *Bacillus anthracis* to enhance its



Coloured TEM of *N. meningitidis* bacteria.
James Cavallini/Science Photo Library

Molecular mimicry and microbial physiology in neisserial pathogenicity

Harry Smith's belief in the importance of *in vivo* studies led him to the discovery of the key determinants in the pathogenesis of two *Neisseria* species in humans.

pathogenicity (see the article by Les Baillie on p. 163). This led to his life-long mantra that mechanisms of pathogenesis can be discerned only by studying bacteria *in vivo*, not in a laboratory shake flask. It was this mantra that focused his research into the mechanism of pathogenicity of the obligate human pathogen *Neisseria gonorrhoeae*.

The genus *Neisseria* includes a range of bacteria associated with the human body. No adverse symptoms have been reported due to commensal species such as *N. cinerea* and *N. lactamica*. In contrast, the pathogenicity of two species, *N. gonorrhoeae* and *N. meningitidis*, is well documented by references dating back to biblical times, even when the cause of gonorrhoea was of course unknown. The two pathogens occupy contrasting niches within the human body. Meningococci typically reside in well-aerated regions of the upper respiratory tract, but gonococci are surrounded by obligate anaerobes and lactobacilli that reduce the limited amounts of available oxygen to hydrogen peroxide. Despite their different ecological niches, the respiratory capacity of gonococci is extremely high, comparable to that of aerobic bacteria. This enables them to minimize oxidative damage from reactive oxygen species generated both from their own respiratory metabolism and by other bacteria that share their natural environment. As gonococci *in vivo* are

surrounded by anaerobic, fermentative bacteria, they have evolved the ability to survive even where the supply of oxygen is extremely limited. Central to this survival is the ability to catalyse a truncated denitrification pathway in which nitrite is reduced via nitric oxide to nitrous oxide.

Harry was always meticulous in assigning credit where it was due. The origin of his interest in gonococcal pathogenicity was the seminal paper by Ward & Watts (1971), who reported that gonococci *in vivo* are resistant to complement-mediated killing, whereas those grown in the laboratory are serum-sensitive. Sixteen years of research culminated immediately before his retirement in 1988 in the demonstration that gonococci exploit the host-derived nucleotide, cytidine monophospho-*N*-acetyl neuraminic acid (CMP-NANA) to evade killing by the body's natural defence mechanisms. CMP-NANA is the nucleotide that delivers sialic acid to blood group antigens and other human cellular components. In the gonococcus, the target receptor is the terminal galactose residue of the lipo-oligosaccharide antigen that terminates with the tetrasaccharide lacto-*N*-neotetraose. Exactly the same tetrasaccharide on transferrin is sialylated by CMP-NANA in human blood. This was a beautiful example of molecular mimicry in which the pathogen decorates a potential antigen on its surface with a host-derived disguise. Subsequently, other colleagues, including Virginia Clark (Cornell) and Rick Rest (Pennsylvania), showed that gonococcal serum resistance is enhanced by growing gonococci in oxygen-limited cultures, reinforcing Harry's emphasis that it is essential to understand microbial physiology *in vivo* if one is to understand mechanisms of microbial pathogenicity. More recently Mike Apicella (Iowa) reported that gonococci can even form biofilms in which the supply of oxygen is restricted.

While attempting to identify the small molecule from human blood responsible for serum resistance, Harry noticed that there was a second factor that increased the resistance-inducing activity. The effects of this 'enhancer' molecule were small, suggesting that they were indirect, rather than direct. The molecule was finally identified as lactate, which 30 years earlier had been reported by Steve Morse and colleagues to be the preferred source of carbon and energy for gonococcal growth. The key role of lactate in gonococcal pathogenicity was confirmed by Ann Jerse (Uniformed Services University) by showing that a lactate permease mutant is severely compromised in growth and pathogenicity.

Harry was pivotal in extending these studies to the related pathogen *N. meningitidis*. Similar effects on serum resistance were observed upon adding lactate to bacteria grown in the presence of glucose. However, he was able to show that in this case the effect was direct as lactate metabolism is intimately linked with the biosynthesis of sialic acid in the meningococcus: additional lactate enhances expression of capsule polysaccharide (a homopolymer of sialic acid) and sialylation of lipopolysaccharide, both promoting serum resistance. Harry's final paper was

“Mechanisms of pathogenesis can be discerned only by studying bacteria in vivo, not in a laboratory shake flask.”



his review of 2007, summarizing work on the effects of lactate on the gonococcus and meningococcus, again highlighting the importance of metabolism to the behaviour of microbial pathogens *in vivo*.

CHRISTOPH TANG is Glaxo Professor of Cellular Pathology at the Sir William Dunn School of Pathology, South Parks Road, Oxford OX1 3RE (email christoph.tang@path.ox.ac.uk)

JEFF COLE is a Professor at the School of Biosciences, University of Birmingham, Birmingham B15 2TT (tel. 0121 414 5440; email j.a.cole@bham.ac.uk)

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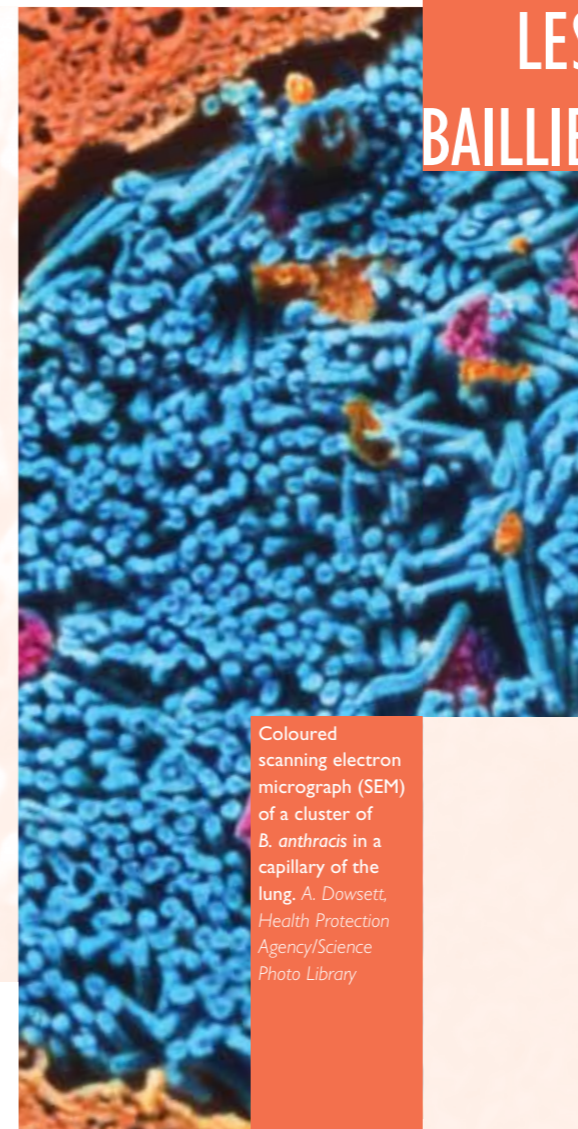
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Despite its low level of infectivity in humans, *Bacillus anthracis* has become the pathogen of choice for bioweapons. This is due to the production of a tripartite toxin, the central role of which in anthrax was discovered by Harry Smith.



Coloured scanning electron micrograph (SEM) of a cluster of *B. anthracis* in a capillary of the lung. A. Dowsett, Health Protection Agency/Science Photo Library

ANTHRAX has many claims to fame, not least that it is the only bacterial disease to have a heavy-metal group named after it! It is caused by a Gram-positive, spore-forming bacterium, *Bacillus anthracis*, which can be considered as the problem child of a group of predominantly soil-dwelling bacteria. As a human pathogen one could argue that it is not particularly successful; although it is able to infect domestic animals such as cattle and sheep, its natural infectivity for humans is thought to be comparatively low. It lacks the ability to spread from person to person and relies on killing the host to return to the environment. Indeed, an analysis of the genetic diversity of the organism, or rather lack of it, suggests that the bacterium spends the bulk of its time as a dormant spore waiting for the next grazing victim to chance along. So, if it is such a poor pathogen why is it considered the principal



LES
BAILLIE

***Bacillus anthracis:* despite what you have heard it's not all bad**

biological warfare agent? The answer lies in the organism's ability to form heat-resistant spores capable of surviving explosive dissemination, which can be incorporated into a bomb and are capable of initiating infection via the aerosol route.

ROUTE OF INFECTION

The route of infection plays a central role in the utility of the organism as a weapon. The traditional means by which the bacterium gains entry into a new host includes access via broken skin and across the lining of the gut wall as a consequence of eating under-cooked meat from an animal that has died of the disease. Such an undertaking sounds extremely foolhardy until you realize that in some parts of the world a dead animal is an important source of protein and that the ability to diagnose the cause of an animal's sudden demise is lacking. Natural human infection is primarily associated with the handling of spore-contaminated animal products, such as contaminated meat and animal hides. For example, in recent years there have been two cases of fatal infection in the UK caused by bongo drums made from animal skins imported from anthrax-endemic areas. It might surprise you to learn that there is currently an anthrax epidemic in the UK amongst intravenous drug users due to the contamination of a shipment of heroin with anthrax spores. Its source is unknown, but as you might imagine the injection of anthrax spores directly into the human body is ill-advised and to date has resulted in 47 confirmed cases, of which 13 have been fatal.

ANTHRAX AND BIOTERRORISM

The primary route of infection in the context of a bioterror event would be via the lungs as a consequence of inhaling an aerosol of spores. The lung is not the primary site of infection, rather it is the means by which the spores enter the body. Spores which penetrate deep into the lungs



A culture of *B. anthracis* isolated from a burial site of a cow that died of anthrax in north-east Turkey. The circular zone of clearing represents lysis caused by a diagnostic bacteriophage called gamma.
L. Baillie

are taken up by alveolar macrophages and transported to the regional lymph node where they undergo germination and subsequently escape from the macrophage to establish a systemic infection which, if left untreated, will kill the host within 4–5 days. The central role of a tripartite toxin, discovered by Harry Smith and colleagues at Porton Down, in the pathology of the disease will be discussed below.

It has been estimated that an aerosol spore attack against a major US city with around 1 kg of material could result in between 50,000–125,000 deaths, which probably explains why anthrax has been weaponized by a number of states, including the UK, USA, Japan and the former Soviet Union. Unfortunately, the potential of anthrax to invoke physical and psychological terror has been recognized by terrorist groups. Even a small-scale release has the potential to cause considerable harm and disruption as was amply demonstrated during the US postal attacks in 2001.

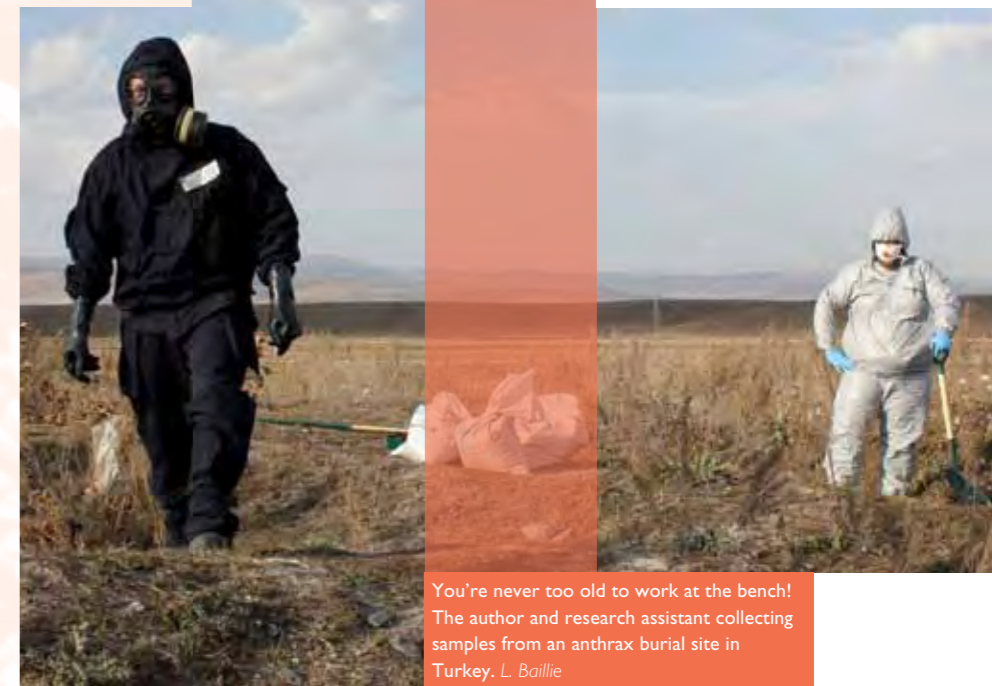
It was this event, and the billions of dollars subsequently made available by the US government, which stimulated a massive expansion of research into the biology of *B. anthracis*. A recent scan of the online biomedical literature (Pubmed) using the search term '*Bacillus anthracis*' yielded 3,145 entries since 2001 in contrast to 1,297 papers in the preceding 115 years (1886–2001). Indeed, the latter half of the 19th century saw a revolution in the study of infectious diseases and a strong case can be made that this organism underpinned the establishment of the current disciplines of microbiology and immunology.

A BRIEF HISTORY OF ANTHRAX RESEARCH

Anthrax was the first disease of man (Woolsorter's disease) and animals shown to be caused by a micro-organism, and it played a pivotal role in enabling Robert Koch to establish his postulates in 1877 by proving that *B. anthracis* (named by Cohn in 1872) was the cause of anthrax. Subsequent researchers such as Greenfield and

Pasteur in the early 1880s went on to demonstrate the feasibility of employing an attenuated strain of *B. anthracis* as a vaccine to protect livestock, thus establishing history's second bacterial vaccine. At the turn of 20th century, Metchnikoff employed *B. anthracis* to characterize the ability of macrophages to kill microbes and helped establish the field of immunology.

During the 20th century the scientific fruits of these early endeavours, particularly the development and extensive use of animal vaccines, saw the status of the organism reduced to that of an exotic disease responsible for occasional outbreaks in animals and of rare secondary infections in humans. As a consequence, little research was carried out into the biology of the organism outside the confines of military laboratories. Until the pioneering work of Harry Smith and colleagues at the Microbiological Research Establishment, Porton Down in the 1950s the mechanisms by which the pathogen killed its host had remained an enigma for 70 years. Working with guinea pigs, Harry and James Keppie observed that while treatment with streptomycin effectively killed the bacteria, they were unable to save the animal if



You're never too old to work at the bench!
The author and research assistant collecting samples from an anthrax burial site in Turkey.
L. Baillie

infection had progressed beyond a certain stage, suggesting that other factors, such as the accumulation of a lethal toxin, may be responsible. A toxin was subsequently isolated and was shown to be tripartite in nature, comprising two biologically active subunits, lethal factor (LF, a metalloprotease) and edema factor (EF, a cyclic AMP modulator), and a third non-toxic, cell-binding component called protective antigen (PA). The role of PA is to transport LF and EF into host cells. This protein owes its name to its ability to confer protective immunity when administered as a vaccine and is the principal immunogen of the current UK and US licensed human vaccines. It was the identification of the central role of the toxin in the pathology of the disease that underpinned the massive expansion of research that occurred at the beginning of this century.

In addition to reawakening interest in bacterial toxins, Harry's work showed that bacterial pathogenicity factors could be identified by directly characterizing the interaction between the bacteria and the infected host. At the time, the study of pathogenicity was not a popular area of microbiology due in part to the technical and ethical challenges faced when working with animals and to the lack of experimental tools with which to interpret the data. Indeed, it was this lack of tools which was to hamper meaningful research in this area for many decades and thus it could be argued that Harry was ahead of his time.

If I had to identify one area in which Harry contributed to the field of anthrax research I would have to say it was in the discovery of the toxins, a discovery that has been the basis of my research for over 20 years. Thanks Harry!

LES BAILLIE is Professor of Microbiology at Cardiff School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Redwood Building, King Edward VII Avenue, Cardiff CF10 3NB (tel. 0292 087 5535, email bailliel@cardiff.ac.uk)

“It was the identification of the central role of the toxin in the pathology of the disease that underpinned the massive expansion of research that occurred at the beginning of this century.”



Influenza research at

I JOINED HARRY in 1970 on a project with Dr John Stephen to produce a purer influenza vaccine. At the time there was concern that contaminating egg protein contributed to the unpleasant effects of the vaccine and the aim was to use antibodies, insolubilized by a method developed by John, to hook out the virus from the egg-grown soup. After washing to remove contaminants from the antibody 'immunosorbent', the virus could be eluted in a much purer form. While scientifically successful, it did not work on an industrial scale, although the procedure was later used by Wellcome to produce their tetanus toxoid vaccine. As part of this funding we also pursued Harry's hypothesis that viruses grown *in vivo* would be different to those grown *in vitro* by using ferret-grown virus to immunize ferrets. Although there was much

scepticism about this approach at the time it is now well established that influenza virus grown in some tissues is antigenically and biologically different to that grown in other tissues. To give just two examples: virus grown in tissues without trypsin-like enzymes is non-infectious and avirulent due to lack of cleavage of the haemagglutinin (HA); host sugars on the HA can alter antibody binding and virus virulence.

THE FERRET INFLUENZA VIRUS MODEL

Funded by the MRC, Harry embarked on a wide-ranging programme to examine the factors that determine the pattern of influenza virus infection in adults and the young, and the signs, symptoms and severity of disease. To do this, Harry together with Dr Geoffrey Toms and myself, used his classical approach developed from studies of bacterial pathogenicity to compare virulent and attenuated strains of virus in both animals and organ cultures of relevant tissues, the latter allowing studies of virus replication under conditions nearer to those *in vivo* than afforded by conventional tissue culture. The results of these studies over 20 years are too numerous to mention in detail here. To summarize, we explained the mechanisms underlying why influenza in adults

Birmingham

Whilst Harry Smith is quite correctly recognized as the 'guru' of microbial pathogenicity, renowned for pioneering studies of how bacteria survive *in vivo*, it should not be forgotten that he also carried out innovative research with influenza virus.

is predominantly an upper rather than lower respiratory tract infection while it can produce a severe lung infection in neonates, including the possible relationship of influenza in babies to cot death or sudden infant death syndrome (SIDS). Why influenza virus was limited to the respiratory tract and did not spread to other organs was also explained. My particular interest was how constitutional symptoms such as fever, headache, backache, muscle pain, etc., were produced in an infection that was limited to the respiratory tract. The clue came when we observed that the timing of the nasal inflammatory response in ferrets, which comprised predominantly phagocytes not lymphocytes as others had suggested, correlated with the onset of fever. We subsequently showed that the nasal phagocytes release pyrogenic cytokines and clinical studies by

others demonstrated that such cytokines induced all the constitutional symptoms of influenza. However, levels of pyrogenic cytokines induced in ferret nasal phagocytes *in vivo* did not correlate with levels of fever, neither did the levels of these cytokines stimulated by influenza virus in human phagocytes, suggesting that more than one cytokine might contribute. The virion HA and/or neuraminidase (NA) induced these cytokines, but interestingly they were only pyrogenic when presented on a virus-like particle, explaining how killed whole-virus vaccines induce the symptoms of influenza while subunit vaccines do not. Importantly, from the clinical point of view, fever was demonstrated to be a host defence mechanism such that treating infected ferrets with sodium salicylate prolonged and increased virus shedding, suggesting that treating influenza with antipyretic drugs is probably detrimental.

CYTOKINES AND SYMPTOMS

The work was continued after Harry's retirement in 1988 by myself, collaborating with Harry. The same approach of comparing virulent and attenuated viruses was used to examine the mechanisms underlying virus-induced cell death by apoptosis

“Many countries have now stockpiled Tamiflu to treat patients in the event of a pandemic.”

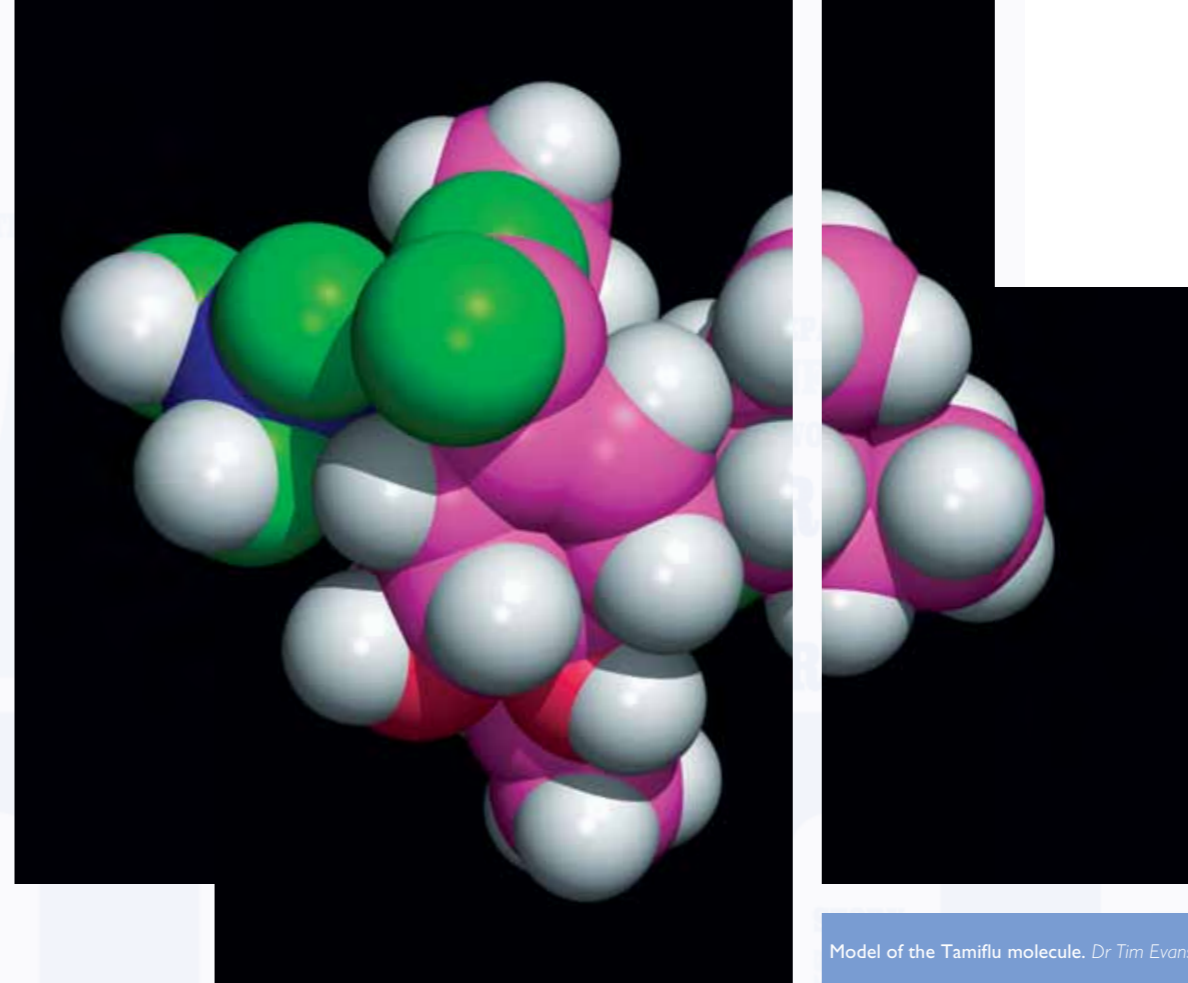
and the link between apoptosis, pro-inflammatory cytokines, and influenza morbidity and mortality. These studies demonstrated that the relative interaction of the virus HA with its sialic acid receptor was a major factor influencing not only infectivity but also apoptosis, and the viral NA played an indirect role in apoptosis induction at virus entry by removing sialic acid from the HA, thereby increasing receptor binding. However, other viral proteins were also involved, since fusion proteins between PB2, NS1 and M and herpes simplex virus VP22 induced apoptosis when expressed in cells. VP22 was used so that expressed proteins would transfer from cells originally transfected to others.

Generation of recombinant viruses by reverse genetics confirmed these results, although the combination of genes required appeared to be strain-specific, highlighting the difficulty of predicting the virulence of new strains that arise in nature.

Although apoptosis is by definition a non-inflammatory response, we showed that expression of pro-inflammatory cytokines and chemokines, such as CCL2 and CCL5, was upregulated during influenza virus infection of bronchiolar cells. However, if cell death was inhibited by the caspase-8 (Z-IETD-fmk) and pan-



Tamiflu capsules to be taken orally. Jan Van De Vell/Reporters/Science Photo Library



Model of the Tamiflu molecule. Dr Tim Evans/Science Photo Library

caspase (Z-VAD-fmk) inhibitors, then expression of some cytokines was increased, suggesting that apoptosis dampens the inflammatory response to reduce damage whilst still stimulating the immune response. Reduced cytokine release was associated with fragmentation of the Golgi body.

TAMIFLU

The establishment of the ferret model of influenza virus infection, where both respiratory infection and constitutional symptoms can be measured reproducibly, allowed assessment of the efficacy of antiviral compounds. There is much concern that while vaccines are important for protecting against seasonal influenza, it will not be possible to generate and manufacture new vaccines rapidly enough to protect against future pandemic strains such as avian H5N1 and A/H1N1pdm09 ('swine flu'). Consequently, much research has been directed at identifying new anti-influenza virus antivirals. The NA cleaves terminal sialic acid residues from glycoproteins, glycolipids and oligosaccharides, and is required for elution of newly synthesized virions from infected cells. The enzyme active site is conserved among all influenza A and B viruses. We examined two NA inhibitors, GS4116 and GS4071, designed by Gilead Sciences Inc., together with their ethyl ester prodrugs for oral bioavailability in our ferret model, but only GS4071 and its prodrug showed good bioavailability. It was then shown to reduce peak virus titres in nasal washings and eliminated constitutional responses, including fever, nasal signs (sneezing, nasal discharge, mouth breathing) and decreased activity. On the basis of the lack of toxicity in various animal species together with these studies in ferrets (and mice), the compounds were clinically trialled by Roche as oseltamivir and subsequently marketed as Tamiflu. Many countries

have now stockpiled Tamiflu to treat patients in the event of a pandemic. In other studies, the cyclopentane NA inhibitor BCX-1812, now known as Peramavir (BioCryst Pharmaceuticals), was also active in ferrets, but its poor bioavailability in humans has hindered its clinical development. However, it is currently undergoing phase 3 clinical trials administered via intramuscular or intravenous routes.

While Harry was not always an easy person to get along with, he was always helpful and supportive of his research colleagues. He was totally dedicated to his research to the extent that when external funding was not forthcoming for PhD students he contributed his personal money to keep the projects going. I shall always be extremely grateful to him for that.

CLIVE SWEET is an Honorary Senior Research Fellow in the School of Biosciences, College of Life and Environmental Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT (tel. 0121 628 1247; email c.sweet@bham.ac.uk)

FURTHER READING

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Publications are one of the key indicators of success as a researcher (and an important part of your CV when applying for research positions). This article explores two aspects of publishing your research – choosing the best journal to submit your manuscript to and the advantages of collaborating to boost your publication number.



Publish or perish

The accepted method of communicating your research to fellow scientists is by publishing it in a peer-reviewed scientific journal. The process of getting a paper published involves several steps – writing the paper, submitting it and dealing with editors' and reviewers' comments. How you do each of these impacts on whether your paper is published or not and how long it takes.

In this article Karen McGregor gives an overview of the factors that may influence your decision of which journal to submit your paper to. Do also seek advice from colleagues who have experience as authors, reviewers and journal editors. Remember, sending your manuscript to an inappropriate journal can potentially slow publication by many months, or result in rejection, meaning you have to start the submission process all over again.

The two most important questions to ask are:

- will they accept my paper?
- who will read my paper?

Scope of the journal. There are many (hundreds) of journals to choose from, ranging from general science to highly specialist in your field of interest. Papers submitted to more general journals will only be accepted if the findings have impact to workers outside your field of interest. More specialist publications may give you space to describe fine details of the method, or give a more extensive analysis of the results.

Citation metrics. There are a number of systems that attempt to measure the quality and impact of a journal (impact factor, Eigenfactor and article influence score). These measures may help guide your choice – generally journals with higher scores are read by more people and viewed as more desirable to publish in – but don't use this as the sole basis for your decision. Do remember that there are many examples of microbiology articles published in *Nature* or *Science* that have been cited less times than articles in the specialist microbiology journals.

Speed of publication. This may be particularly important in the early stages of your career – it gets you and your research seen quicker by the scientific community (and starts building citations sooner). For articles published in a journal look at the dates of submission, acceptance and publication as a guide for when your article might be published. Check whether the journal offers advance online publication of accepted papers.

Appropriate to your field of research. As well as looking at the articles published by the journal to see if they are on similar topics to

USE JANE TO HELP YOU PICK A JOURNAL FOR YOUR PAPER

Go to www.biosemantics.org/jane/, enter the manuscript title or abstract and click 'Find journals'. Jane (Journal/Author Name Estimator) will compare your input to the contents of Medline to identify journals that publish similar work. It gives you a list of journals together with their article influence score (a value greater than one indicates that each article in the journal has above average influence, i.e. it is likely that someone will read it).

your paper, look at the editorial board (do you see names you recognize?).

Appropriate to your paper format. Check that the journal publishes the type of paper you want to write (e.g. review, note, case report, short communication). Check whether there are length restrictions, or limits on the number of figures that can be included and if they accept supplementary information.

Requirements of your funding body. Does your funder require you to publish your work as open access – if so, you need to check whether the journal offers this service.

FIND OUT MORE ABOUT GETTING PUBLISHED

How to get published. Presentations from the SGM Spring 2011 Conference – www.sgm.ac.uk/news/videoportal.cfm

Getting published. *Microbiology Today*, May 2008 – www.sgm.ac.uk/pubs/micro_today/pdf/050807.pdf

Search for and view the Eigenfactor and article influence scores for any journal – www.eigenfactor.org

Publishing your research. Vitae – includes links to other resources – www.vitae.ac.uk/researchers/1298/Publishing-your-research.html

Collaborate or stagnate

Collaborating with other laboratories and researchers can bring many benefits (indeed many funding schemes now require submissions from multiple labs working in collaboration). In terms of publications, you can more readily generate data for publication if there are more of you working on the project. If you are in a small research group, collaboration can allow you to generate competitive research at a level that is required for publication in good journals. Having input from a diverse group of people (potentially with different skills and expertise) is a good way to generate new ideas and technologies – it can take you to places that you would never otherwise think of going with your research.

To help early-career researchers (within 5 years of being awarded their PhD) raise their profile and initiate collaborations SGM, together with the American and Australian Societies for Microbiology, offers annual awards to support the reciprocal exchange of one Society member between countries – the Heatley-Payne Award for a UK-based researcher to travel to the US, and

the Hayes-Burnet Award to travel to Australia. The Award recipient will present their research at the other society's main annual conference and visit a research laboratory for a period of 1–3 weeks to establish a new, or strengthen an existing research collaboration. The visit can be used to learn a new technique or to carry out a defined piece of research. During the visit the recipient will deliver a research seminar to members of the department.

The eligibility criteria, rules and application forms for each scheme are available from the SGM website (www.sgm.ac.uk/grants). The closing date for applications to these schemes for 2013 is **30 November 2012**

Previous recipients of these awards talked to Karen McGregor about their experiences and the benefits they gained as a result of receiving the award:

HEATLEY-PAYNE AWARD

UK recipient (2011)* – Daniel Tromans, University of East Anglia and John Innes Centre

Attended – ASM General Meeting, New Orleans

Visited – David Newman, National Cancer Institute, Frederick, Maryland

Dr Newman gave a seminar at my department not long after I started my PhD. After the seminar I spoke to him about a potential visit to his laboratory and he agreed. My PhD was investigating the natural product pacidamycin, a secondary metabolite produced by *Streptomyces* with activity against *Pseudomonas aeruginosa* and Dr Newman's lab was using a number of techniques for natural product extraction that I was keen to learn. My visit was designed to increase my understanding of the techniques available for my work and to allow me to develop a more comprehensive view of natural product research. Following this visit I was able to share this knowledge with members of my home laboratory.

The ASM general meeting was fantastic – I really enjoyed the breadth of research being discussed and I got to speak to a number of prominent researchers in my field, as well as meeting fellow PhD students from some of the most prestigious research institutes in the US.

Receiving this award has improved my confidence in writing applications for funding and increased the impact of my CV – which I hope will help me next year when applying for post-doctoral positions.



Daniel Tromans



Joseph Hyser

US recipient (2012) – Joseph Hyser, Baylor College of Medicine

Attended – SGM Spring Conference, Dublin

Visited – Stephen Griffin, Leeds Institute of Molecular Medicine

The primary goal of my visit was to be trained to perform the viroporin inhibitor screening assay developed by Dr Griffin. To maximize the benefit of the training we had spent a long time prior to the visit identifying a small library of compounds to screen. This preparation paid off as during my visit I identified several compounds that appear to block rotavirus NSP4 viroporin activity. I will continue the evaluation of these compounds in my own laboratory with a collaborative publication already being planned on this work. This award has given me the opportunity to share my work with a new and diverse group of researchers as well as establish new professional relationships, both with researchers I met at the conference and those in Leeds. It has been a very memorable experience, full of outstanding scientific (and social) interactions and I highly recommend early-career researchers to consider applying for this award.

UK visit host – Stephen Griffin, Leeds Institute of Molecular Medicine

Hosted – Joseph Hyser, US recipient 2012

My laboratory was fortunate enough to benefit from this award this year by hosting the visit by Joseph Hyser. Our labs had previously interacted by email, but the opportunity for one-to-one communication and exchange of ideas has been massively enabling to both of us and has laid the foundation for a long-term, productive and enjoyable collaborative relationship.

I believe it is very difficult to do competitive science nowadays without collaborating – of the papers published by my lab in the last 5 years, only about 20% had no input from another laboratory. I would actively encourage other group leaders to take advantage of opportunities offered to host a visit and if approached by potential visitors from the US or Australia would advise them to apply for this award from their own microbiology society.

HAYES-BURNET AWARD

UK recipient (2010)* – Amanda Rossiter, University of Birmingham

Attended – Australian Society for Microbiology Annual Scientific Meeting, Sydney

Visited – Mark Schembri, University of Queensland, Brisbane

I became aware of the SGM Hayes-Burnet award during the third year of my PhD studies. I liked the collaborative nature of this award, and contacted Mark Schembri, University of Queensland, who my supervisor had met previously. I submitted my application and was thrilled to be selected as the award winner that year.

The aim of my research visit was to apply what I had learnt from my PhD studies on the enteric pathogen enteroaggregative *Escherichia coli*, to investigate whether similar principles were necessary for the pathogenesis of the urinary tract pathogen uropathogenic *E. coli*, on which Professor Schembri is an expert. The visit proved to be very successful – it resulted in a collaborative publication and formed the basis for a significant part of my PhD thesis which I submitted in 2011. I have maintained the collaboration with Professor Schembri and we have extended the initial work to other aspects of microbial pathogenesis.

The experience of travelling to Australia and working within another research laboratory was an amazing opportunity offered by the SGM. The award has enriched my academic standing and, most importantly, highlighted the rewards of – in fact the necessity of – initiating independent collaborations. I am currently working as a Research Fellow at the University of Birmingham and hope to draw from lessons learnt as a result of this experience to aid in fulfilling my longer-term career aspirations of leading an independent microbial pathogenesis research group.



Amanda Rossiter



Jeff Butler

Australian recipient (2010) –

Jeff Butler, WHO Collaborating Centre for Reference and Research on Influenza, Melbourne

Attended – SGM Spring Conference, Edinburgh

Visited – Rod Daniels, WHO Influenza Centre, MRC National Institute for Medical Research, Mill Hill

Receiving this award and visiting the laboratory in the UK was the first step of what has become an on-going collaboration between our groups to investigate the effect of novel amino acid changes within influenza viral proteins. The opportunity to meet the scientific leaders in my field and discuss my research data provided me with invaluable insight regarding future research directions for my project. The award is highly regarded by microbiologists, both in Australia and the UK and it added significant value to my CV – it even helped me secure my next job.

**In 2010 and 2011, the SGM awards were granted to PhD students. The eligibility criteria were changed in 2012 to members who are within 5 years of being awarded their PhD (in line with the American and Australian schemes).*

OTHER SGM INITIATIVES TO SUPPORT EARLY-CAREER MEMBERS IN ESTABLISHING COLLABORATIVE PROJECTS**Scientific Meetings Travel**

Grants – funds to support conference attendance in the UK and overseas. Giving a presentation at a conference will showcase your work to other researchers and raise your profile. Use your time at the conference to network with researchers and identify potential collaborators. Choose you conference wisely to maximize your targeted networking opportunities. Applications should be submitted in advance of the conference. www.sgm.ac.uk/grants/smtg.cfm

President's Fund for Research

Visit Grants – funds to support a 1–3 month visit to another laboratory to carry out a defined piece of laboratory-based research. Two rounds of applications per year. Next closing date is **21 September 2012**. www.sgm.ac.uk/grants/pfrv.cfm

Applications to these schemes are invited from PhD students and researchers in their first postdoctoral position (in a country in the EU), new graduate scientists or lecturers (within 3 years of first appointment in the UK or Ireland).

FIND OUT MORE ABOUT WORKING COLLABORATIVELY

Vicens, Q. & Bourne, P.E. (2007). Ten simple rules for a successful collaboration. *PLoS Comput Biol* 3(3), e44 (www.ploscompbiol.org/article/info:doi/10.1371/journal.pcbi.0030044)

The Collaborative Researcher. Vitae 2-day course; places are free, but you will need to cover your own travel expenses (www.vitae.ac.uk/researchers/342411/The-Collaborative-Researcher.html)



During what seems like the only week of summer weather the UK has experienced this year, SGM welcomed over 4,000 visitors to its stand in the Great Pavilion at the RHS Chelsea Flower Show. The theme was *The New Green Revolution*, highlighting beneficial interactions between microbes and plants. In a space designed to make visitors feel they had entered the underground world of plant roots, acetate displays, interactive animation and video screens, and material for inspection by microscope and hand lens focussed on mycorrhizal fungi and root nodules, raising awareness of plant-microbe interactions in the context of food security.



"The Chelsea Flower Show provides a novel and wide-ranging audience among whom to spread the message of the importance of microbes in the soil and the rhizosphere. While most visitors to the SGM stand were intrigued to discover the breadth of this microbial activity, I was pleasantly surprised by how many horticulturalists were already well informed about the role of microbes in the soil. However, best of all was seeing children getting excited by seeing the little "beasties" for themselves." **Colin Harwood**



SGM AT RHS CHELSEA

MAY 2012

MICOBIOLGY TODAY AUG 2012 174

MICOBIOLGY TODAY AUG 2012 175



Building on the work of the SGM *Position Statement on Food Security and Safety*, Professor Nigel Brown (Chair) said 'In the long term, we hope that research aimed at a fuller understanding of the role of soil micro-organisms will allow us to produce healthy crops in a wider range of locations, such as in poor soils or drought areas, and that the results of this research will be widely implemented to solve the problems of food shortage and climate change'.

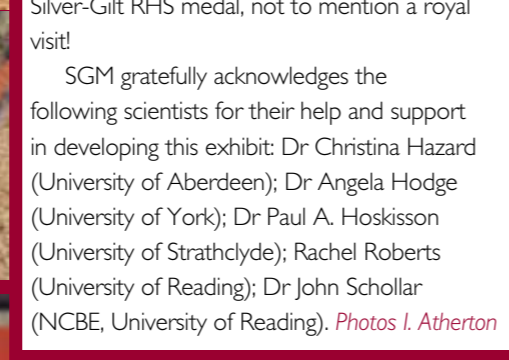
The hard work of the team behind the exhibit was rewarded with a prestigious Silver-Gilt RHS medal, not to mention a royal visit!

SGM gratefully acknowledges the following scientists for their help and support in developing this exhibit: Dr Christina Hazard (University of Aberdeen); Dr Angela Hodge (University of York); Dr Paul A. Hoskisson (University of Strathclyde); Rachel Roberts (University of Reading); Dr John Schollar (NCBE, University of Reading). *Photos I. Atherton*



"It was delightful to find some microbiology amongst the flowers at Chelsea. SGM's display brought microscopy, plants and microbiology together in a really interesting and ingenious way. Plants grew along the top of the display, showing their root nodules through Perspex pots, and visitors to the stand could also look at the nodules up close under the microscopes. Lovely publicity material, cheerful and informed presenters – spreading the microbiology message! Great!" **Joanna Verran**

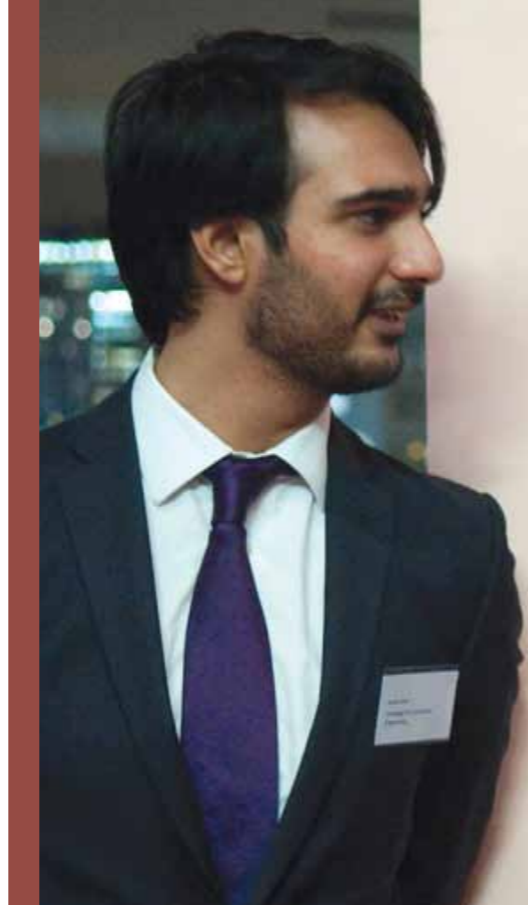
"Raising the awareness of micro-organisms, the influences and the roles they play in soil and how they interact with plants with visitors to the SGM stand was a great experience. Seeing the astonishment on the faces of the visitors as we made them aware that lots of the processes they rely on in their gardens and allotments are down to micro-organisms was lots of fun." **Paul Hoskisson**



The Campaign for Science and Engineering (CaSE) is an important non-governmental group that raises scientists' voices in the political sphere. In this interview, Oxford biology graduate and CaSE Director Imran Khan explains why his organization matters.

Q Why was CaSE originally set up and what was its remit?

A CaSE was originally founded in 1986 as 'Save British Science' (SBS) by a group of scientists who were concerned about cuts to research. 1,500 of them pitched in together to buy a full-page advert in *The Times* calling on the then Prime Minister, Margaret Thatcher, to address the crisis in British science funding. The advert generated a huge amount of media interest and led to meetings at the highest levels of government, so the instigators kept the initial group together and the rest, as they say, is history.



Q How has CaSE evolved over time?

A The most obvious change has been the switch from SBS to CaSE. In the mid-2000s, the organization recognized that British science, although still in need of support, was no longer in crisis. So our name was changed to CaSE, reflecting that we now have a slightly different remit.

We've also expanded our focus beyond issues of research funding, as important as they are. We now campaign for the scientific angle on everything from education to immigration, as well as looking at issues like social and gender diversity within science and engineering.

A longer-term aim is to improve scientific representation in politics and government, both by helping politicians understand what the issues facing scientists today are, but also by encouraging scientists themselves to get more involved – and perhaps even consider running for elected office.

A big change has been our support base. Originally, we relied on donations from individual researchers. We still have that as a focus, but over the years we've moved towards looking to organizations for support. We now gather funds from over 100 bodies ranging from universities, companies, charities – and indeed societies like SGM – who enable us to be independent and speak out in the interests of the sector as a whole.

Q What was the rationale behind expanding the campaign to include engineering and does the organization also campaign on behalf of the other STEM subjects – technology and maths?

A We definitely see all STEM subjects as within our remit, but I suppose that within STEM there is a slight distinction between science and maths on one side, and engineering and technology on the other. They do have huge amounts in common, but there are different National Academies for science and engineering, for instance. It's useful that we're able to emphasize that we're passionate about

the importance of both, and don't favour one side. I think this approach helps policy-makers understand who we are and where we're coming from, which can only be a good thing.

Q What is your role and what projects are currently important to you?

A We're here to raise the political profile of science and engineering. We want to get political decisions that properly reflect the national importance of these subjects.

In the current climate, often that comes back to funding – there's a real worry that stagnation in research funding could continue, particularly if the economy doesn't pick up. A big part of what we're doing is trying to make the argument that unless we see investment in science, the long-term prospects for the UK's scientific excellence are dire.

Additionally, we've seen major reforms to schools, immigration and higher education since the coalition government came in. In

our view, many of these were made without proper consideration of their effect on science and engineering, so we're still trying to argue that retrospective action is needed to repair the damage. For instance, we've had success in saying that the Home Office needs to exempt scientists from new visa restrictions, and that the Higher Education Funding Council for England (HEFCE) needs to delay changes to the funding mechanism for university science and engineering departments.

Q What are the barometer issues in science policy in the coming years?

A The flashpoints will be the next Spending Review – which will see every penny of public spending reviewed, and probably take place in late 2013 or early 2014 – and the next General Election in 2015, when all parties will be setting out their priorities. We have to make sure that science is in the minds of all the main players for those two events.

Q What is 'science policy'? What does it mean to you – and how is it useful to microbiologists?

A There are two types of 'science policy'. One is 'science for policy' – in other words, how you use scientific evidence to create good public policy. This includes everything from food regulation, epidemic contingency planning, energy policy, and whether or not embryo research should be allowed. It's mainly concerned with how we translate the work being done by scientists into the way in which the UK (and indeed the world) is run.

The other type is 'policy for science', and this is what CaSE concentrates on. It's the process of creating and changing public policies which affect science. Funding and education are obvious examples; without them we wouldn't have a science establishment in the UK. It also includes issues such as the structure of academic publishing and libel reform.

Q How do you determine your priorities – and how do you bring your influence to bear?

A Our priorities are very much driven by the interests of our members as a whole. When we try and speak for everyone from microbiologists to Rolls Royce and Google, we have to concentrate on what will affect them all. Inevitably, it tends to be the cross-cutting issues which we work on, but we do rely on direct feedback from our members in deciding where to focus – for instance, what impact visa rules are having on a university's ability to attract

top talent, and thus what specific changes to the rules we would like the Government to make.

Q How does the UK's science base look today? In these straightened economic times, are you hopeful for the future, or pessimistic?

A There's no reason why UK science can't continue to lead the world for decades to come. Our research base is currently one of the best in the world. In terms of quality of output we beat almost every other nation, other than the USA. When you take into account value-for-money, we're way ahead of even the Americans – so there's a lot to be optimistic about. On other measures we're not doing so great. Every year the UK spends approximately 1.8% of its overall wealth on research and development (that figure includes private as well as public spending) – but the figures for competitor nations like Germany, the USA and South Korea are 2.7, 2.8 and 3.4%, respectively. We need to improve that if we are to turn ourselves into a genuine knowledge economy that's more focused on science.

Q How can scientists contribute to science policy?

A My first bit of advice is to engage with your local MP. Out of 646 elected Parliamentarians, only one has had a research career (Dr Julian Huppert) – compared to 86 lawyers, for instance. This means that we can't expect politicians to understand the issues facing our sector unless we communicate properly, so it's up to us to engage with MPs. Inviting your local MP to visit your lab or institution can be a great first step for both of you, and is the kind of thing CaSE is happy to help facilitate.

Electron micrograph of the H5N1 influenza virus. Reproduced with permission from Nature Publishing Group

Ferreting out the facts behind the H5N1 controversy

IN THE SUMMER of 1974, in response to serious concerns about the safety of the then nascent field of recombinant DNA technology¹, Paul Berg, chairman of the US National Academy of Science's Committee on Recombinant DNA Molecules Assembly of Life Sciences, submitted a letter to *Science*² calling for a voluntary moratorium on certain recombinant DNA experiments which the committee deemed to be potentially dangerous. The now infamous Berg Letter also called for the establishment of 'an international meeting of involved scientists from all over the world ... to further discuss appropriate ways to deal with the potential biohazards of recombinant DNA molecules'.

The meeting, held the following February at the Asilomar Conference Centre, California, marked an important milestone in the history of modern molecular biology³. On the final day of the conference, participants (which included lawyers and assorted members of the media, as well as the scientists) agreed that the moratorium should be lifted, and the research allowed to continue, albeit under stringent restrictions⁴.

The recommendations resulting from Asilomar, issued in July 1976, proved remarkably effective; informing the official US guidelines on research on recombinant DNA technology to this day.

Four years after this landmark meeting, when the dust had finally settled on the recombinant DNA controversy, Donald S. Fredrickson, the then director of the National Institutes of Health (NIH), published a history of the guidelines, concluding with the following prophetic statement: '*Faced with real questions of theoretical risks, the scientists paused and then decided to proceed with caution ... Uncertainty of risk, however, is a compelling reason for caution. It will come again in some areas of scientific research, and the initial response must be the same. After that, the lessons learned here should help us through the turbulence that is sure to come.*'

Fredrickson was right, it has come again and yet again we find ourselves caught up in the turbulence surrounding so-called dual-use research of concern (DURC) – that which has the potential to cause harm as well as good. This time the controversy is focused on the laboratory adaptation

ROY D. SLEATOR

*I had a little bird,
Its name was Enza,
I opened the window,
and in-flew-enza.*

Children's Rhyme, 1918

Recent recommendations by the National Science Advisory Board for Biosecurity (NSABB) to redact key methodological details of two studies involving mammal-to-mammal transmission of the H5N1 (H5) subtype influenza viruses, have led to a temporary moratorium on all research involving live H5N1 or H5 HA reassortant viruses shown to be transmissible in ferrets. What events led to this impasse and what will be the impact?

of avian H5N1 (H5) subtype influenza virus. Specifically, studies enabling the virus to move from mammal-to-mammal by respiratory transmission, and subsequent recommendations by the National Science Advisory Board for Biosecurity (NSABB – a Governmental advisory body set up to inform the research community about research involving agents that pose potential threats to national security and/or public health) to redact key manuscript details in an effort to prevent the studies from being easily replicated by individuals of 'nefarious intent'.

THE STORY SO FAR ...

In October 2011, the NSABB was asked to review two papers – one by Ron Fouchier and colleagues of the Erasmus Medical Center in Rotterdam, the other by Yoshihiro Kawaoka and his team at the University of Wisconsin (both currently under review by *Science* and *Nature*, respectively). The concerns arose from the DURC potential of the reported studies, specifically the adaptation of the highly pathogenic avian influenza A/H5N1 virus to infect mammalian hosts (ferrets), such that it could potentially be transmitted via respiratory droplets (or aerosols). Despite regular human contact with animal reservoirs (poultry) for at least 50 years, H5 strains which cause sustained human disease have, as yet, failed to emerge. However, notwithstanding, the NSABB felt that the mutations created by Fouchier and Kawaoka may expedite such a zoonotic shift – leading to a virus that is more easily transmissible between humans and a potentially catastrophic pandemic. While NSABB recommended that the general conclusions of both papers be published, the manuscripts should not report the methodological details necessary to

replicate the reported experiments (NIH Press Release, www.nih.gov/news/health/dec2011/od-20.htm). The US Government, accepting the NSABB recommendations, relayed the imprimatur of redacted publication to the researchers and the associated scientific journals. Both parties reluctantly agreed, with the proviso that the Government devise an equitable process for sharing the details of the experiments with 'responsible' scientists and clinicians.

However, while the compromise went too far for many, it simply was not enough for others – a feeling crystallized by an editorial in *The New York Times* on 8 January 2012 entitled '*An engineered doomsday*' – calling for the newly constructed H5N1 constructs to be destroyed. Against this background of heightened public interest and fear, Fouchier (the lead author of the *Science* paper) and Kawaoka (of the *Nature* paper), along with 37 other prominent influenza researchers, published a letter in both *Nature*⁵ and *Science*⁶ calling for a voluntary 60-day moratorium on all experiments involving '*live H5N1 or H5 HA reassortant viruses already shown to be transmissible in ferrets*'. This latter



Scenes like this at the Naval Training Station, San Francisco, with rows of infected patients, were common during the 1918 flu pandemic. History must not be permitted to repeat itself, through ignorance or neglect. *US Naval Center*

day Berg letter also called for an Asilomar-like meeting in which 'the scientific community comes together to discuss and debate these issues'. The World Health Organization convened this meeting in Geneva on 16–17 February 2012. Attended by the lead researchers of the two offending studies, representatives of *Science* and *Nature*, bioethicists and directors from several WHO-collaborating laboratories specializing in influenza, the Geneva symposium reached consensus on two important issues:

1. The temporary moratorium on research with newly modified H5N1 viruses must continue, while allowing research on naturally occurring H5N1 influenza virus to proceed;
2. Delayed publication of the entire manuscripts would have more public health benefit than urgently publishing the incomplete story.

'MORE SINN'D AGAINST THAN SINNING'

This is not the first time the influenza community has faced the DURC issue. In 2005, a similar controversy erupted around the recreation of the infamous 'Spanish flu'; the 1918 pandemic virus which claimed the lives of an estimated 50–100 million people – approximately twice the number killed during the previous 4 years of World War I. Following the discovery in the 1990s of partially degraded samples of the 1918 virus in the lung tissue of US soldiers who had succumbed to the 'Spanish flu', researchers were able to salvage and amplify the viral RNA. With the 1918 influenza virus coding sequence to hand, Tumpey and colleagues⁷ used a reverse genetics approach, i.e. taking an existing contemporary influenza virus of lesser virulence and, one by one, swapping its genes with those from the 1918 pandemic strain – thereby creating (or recreating) a live version of the extinct 'Spanish flu'. While the NSABB was also convened in this instance, their recommendations were far less punitive than those handed down to Fouchier and Kawaoka – the Tumpey paper was published in full. Indeed, several other high-profile influenza-related studies have apparently flown below the NSABBs radar, many of which arguably pose a similar if not greater threat than that of the Fouchier and Kawaoka studies. In 2006, for example, both *Science* and *Nature* carried reports of specific mutations enabling the H5 viral haemagglutinin to bind to human as opposed to avian tissues. In January of this year, a report by Chen *et al.*,⁸ published in full in the journal *Virology*, bears an uncanny resemblance to the works of Fouchier and Kawaoka; describing mutations in an H5N1 virus which confer air-borne transmissibility between ferrets. Furthermore, several recent studies have been published which describe mutations that enable transmission of other potentially pandemic strains between ferrets or that increase the virulence potential of currently circulating virus strains.

Echoing Fredrickson's post-Asilomar assertion that we pause and proceed with caution, let us consider for a moment where the true risks lie. At the heart of the controversy is the assertion that the case fatality rate

for human H5 infections is in the range of 50–80%. Derived from a list of H5 cases confirmed under WHO guidelines; the list tallies 573 cases in 15 countries with a ~60% mortality rate. However, a literature search reveals seropositivity in humans resulting from H5 infections to be in the order of 0.2%–5.6%, at least an order of magnitude lower than that reported by the WHO. Thus, it is entirely likely that the case fatality rate for H5N1 in humans is significantly lower than previously reported. Moreover, ferrets are not humans; as a model organism they are more susceptible to infection with influenza viruses and are also more likely than humans to exhibit disseminated, multiorgan disease, including neurologic sequelae resulting from virus replication in the brain. Furthermore, passage of the virus in ferrets, the approach taken by Fouchier and Kawaoka, is more likely to tailor viral pathogenesis specifically to that host rather than human. Indeed, virus passage in a non-human host has frequently been used to reduce viral virulence in humans, and has been successfully applied to the generation of several attenuated viral vaccines, including poliovirus. Rather than engineering a hypervirulent H5N1 variant for humans, the Fouchier and Kawaoka studies may in fact have led to an attenuated human variant – though this is simply unknowable from the available data. In any case, viable vaccine candidates for H5 viruses do exist and available influenza medications have been shown to be effective against H5 strains.

PUBLISH OR PERISH

Thus, perhaps our fears should focus more on the consequences of forced scientific censure, rather than the unlikely worst case scenarios (be they real or imagined) resulting from a full disclosure of the facts. Playing devil's advocate, let us consider for a moment a scenario in which the NSABB had blocked, or redacted, publication of the Tumpey 2005 influenza paper⁷; would the world be a safer place?

The answer is quite simply no! In this scenario, we would not know that the 1918 virus is sensitive to the seasonal flu vaccine as well as to the common flu drugs amantadine (Symmetrel) and oseltamivir (Tamiflu), and so poses no serious pandemic threat at this time⁹. Without the Tumpey paper⁷, we would still be living in fear of 'nefarious intent' and the potential for 'Spanish flu' to be used by bioterrorists. Blocking publication of the Fouchier and Kawaoka studies does not make the world a safer place – just a less enlightened one.

ADDENDUM

On 30 March 2012, following 2 full days of deliberations, the NSABB reversed its controversial decision to block publication of the *Nature* and *Science* papers.

On 20 April, the US government, in a statement delivered by Francis Collins of NIH, formally accepted the revised recommendations of the NSABB; moving the controversial H5N1 manuscripts another step closer to publication.

On 2 May, *Nature* finally published the 11-page study, by the Kawaoka group¹⁰; elegantly describing how stitching a mutated version of a key viral protein (haemagglutinin) from the H5N1 bird flu virus onto the human H1N1 virus results in a hybrid strain capable of binding more strongly to mammalian cells and copying itself at high enough levels to be readily transmitted via respiratory droplets.

The *Science* paper of Russell *et al.*, (*Science* 336, 1541–1547; www.science.org/content/336/6088/1541. full) was published as *Microbiology Today* went to press.

ROY D. SLEATOR, Department of Biological Sciences, Cork Institute of Technology, Rossa Avenue, Bishopstown, Cork, Ireland (tel. +353 21 433 5405; email roy.sleator@cit.ie).

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Humans have always made use of data encryption to communicate important messages. Can modern-day forms of digital encryption, such as QR codes, be used to educate the peer group who are most at home with new technology about sexually transmitted infections?

B. CHERIE MILLAR & PETER J.A. MOORE

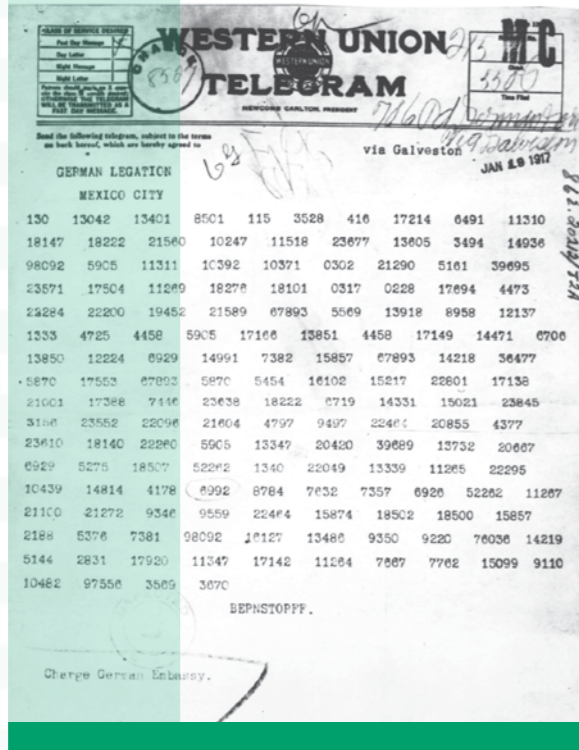
Deciphering infectious diseases

AN ENCRYPTED TELEGRAM was sent in January 1917 by German Foreign Minister Arthur Zimmermann via the German Ambassador in Washington DC, Johann von Bernstorff, to the German Ambassador to Mexico, Heinrich von Eckhardt, offering US territory to Mexico in return for joining the German cause. Fortunately, the British codebreakers intercepted and deciphered the coded telegram, which thus drew America into the Great War and altered the course of world history.

The use of codes and encryption in history has generally been for devious motive. We can see from the Zimmerman telegram how encryption was used to mask the true intent of the German Empire in the course of World War I. The use of codes and ciphers dates back to much earlier times. The ancient Egyptians used non-standard hieroglyphs on monuments as early as ca 1900 BC. In so doing, the Egyptians successfully captured the attention of the viewer by creating unusual codes which aroused curiosity. Other numerous examples of encryption have included its exploitation for political and religious gain.

And with codemakers come codebreakers.

Zimmermann telegram (right), and decoded message (below), as received by the German Ambassador to Mexico, 19 January 1917. Record Group 59: General Records of the Department of State, 1756–1979. National Archives and Records Administration (ARC Identifiers 302025/302022). www.archives.gov/education/lessons/zimmermann/



RECEIVED TELEGRAM RECEIVED.
 FROM 2nd from London # 5747.
 "We intend to begin on the first of February unrestricted submarine warfare. We shall endeavor in spite of this to keep the United States of America neutral. In the event of this not succeeding, we make Mexico a proposal of alliance on the following basis: make war together, make peace together, generous financial support and an understanding on our part that Mexico is to reconquer the lost territory in Texas, New Mexico, and Arizona. The settlement in detail is left to you. You will inform the President of the above most secretly as soon as the outbreak of war with the United States of America is certain and add the suggestion that he should, on his own initiative, ^{invite} ~~invite~~ Japan to immediate adherence and at the same time mediate between Japan and ourselves. Please call the President's attention to the fact that the ruthless employment of our submarines now offers the prospect of compelling England in a few months to make peace." Signed, ZIMMERMANN.

Below
Cipher – original contemporary digital artwork by Peter J.A. Moore.



MMXXI

However, encryption also serves as a means of protection, as well as abbreviation. The 21st century has become live to the need for protection of financial assets through electronic banking and we can all subscribe to the sophisticated methods of encryption that are now part of everyday life and the consequences when such systems fail in terms of financial fraud, as well as the theft of personal information and identity.

Non-devisive use of encryption techniques has allowed for encryption to serve as a means of abbreviation of large amounts of information. Such a novel employment of encryption can serve a philanthropic purpose.

QR codes, as illustrated in the artwork *Cipher*, were first developed by DensoWave company in the early 1990s and aided the Japanese car manufacturer Toyota to track vehicles during the production process. 'QR code' is a registered trademark of DensoWave Inc. (www.denso-wave.com) in Australia, Europe, Japan and the US, but this does not apply to the pattern image. They are different to simple one-dimensional barcodes, in that they carry information in two dimensions, as well as storing significantly more data, with a

maximum of 7,089, 4,296, 2,953 and 1,817 characters, relating to numeric, alphanumeric, binary (8-bit) and Kanji (full width Kana), respectively. They are also highly pragmatic, in that the codes are largely dirt- and damage-resistant and are readable in any direction.

What makes QR codes highly practical in a emerging world of digital literacy and adoption, is their ability to be generated, as well as be read by almost anyone. QR codes can be generated with the aid of several free online QR code generators (e.g. www.qrstuff.com) and can be adapted for various applications, including the use of free text, as well as simple links to websites and hence further information. Adoption of QR codes within healthcare has been slow. A recent Medical Marketing survey of November 2011, described that 65% of physicians surveyed were unaware of this mobile information resource. Furthermore, in October 2011, the *Journal of the American Medical Association* (JAMA) began incorporating QR codes on at least one study in every issue, which directs the reader to a video of the study's author, discussing their work.

Although technological innovation may change and develop through time, the human psyche does not. The marvelment of things unknown still captures the human's attention. In this way, we can indeed learn some valuable lessons from the early Egyptians of how to capture the curiosity of man through encryption and code. Like this early civilization, the employment of unusual 21st century hieroglyphs, namely the QR code, offers a whole new medium of communication and potentially opens up novel conduits of communication to both the donor, as well as the recipient of such information. In an increasingly busy world, with continued pressures on time, a modality which offers quick yet reliable information delivered through an electronic data-driven means is surely attractive to healthcare professionals with an important message to be heard. Infectious diseases specialists should now exploit this new technological medium to educate those peer groups who fully embrace such technological innovations. One example may be the use of QR codes to promote awareness of sexually transmitted diseases among the young, who are undoubtedly the biggest proponents of digital communications technology.

The artist of the digital picture *Cipher* is Peter J.A. Moore, a 5th-form Grammar School pupil at Ballymena Academy, Co. Antrim. Peter is interested in contemporary digital art and design, both for its aesthetic and functional qualities. *Cipher* was conceived by the artist during a period of vocational research during the summer of 2011, under the supervision of Dr B. Cherie Millar at the Department of Bacteriology, Belfast City Hospital, Belfast. During this period, the young artist reported on the emergence of increased antibiotic resistance in Gram-negative, as well as Gram-positive pathogens, following γ -radiation exposure, equivalent to those doses received by cancer patients undergoing clinical radiotherapy for the treatment of their disease [Moore, P.J.A., Goldsmith, C.E., Coulter, W.A., Millar, B.C., Matsuda, M. & Moore, J.E. (2012).

Exposure to sublethal clinical radio-therapeutic doses of ionizing γ -radiation gives rise to mutants of Gram-negative and Gram-positive clinical pathogens with increased antibiotic resistance. *J Med Microbiol* 61, 302–304].

Cipher hangs in the Northern Ireland Public Health Laboratory, Department of Bacteriology, Belfast City Hospital. Its mission is to evoke the aesthetic, as well as curiosity. It is a digital gateway to knowledge relating to (left to right and top to bottom) salmonellosis, H1N1 influenza, cryptosporidiosis, campylobacteriosis, SARS, aspergillosis, MRSA infection, HIV infection, malaria, cholera, Ebola virus infection and anthrax. Through the viewer's quest to fulfil their curiosity of the hidden QR codes, the viewer of this work and decipherer of these codes inadvertently uses modern technology to discover their hidden messages, which refer the reader to sentinel web resources at the CDC. Employment of new and emerging digital media forms, such as QR codes, may introduce technology-savvy readers to educational messages relating to infectious diseases, for example sexually transmitted diseases, within the peer group who are the most familiar and biggest users of such technology.

B. CHERIE MILLAR is Clinical Scientist in Molecular Microbiology at the Northern Ireland Public Health Laboratory, Department of Bacteriology, Belfast City Hospital, Lisburn Road, Belfast BT9 7AD (tel. 028 9026 3554; email bcmillar@niph.dnet.co.uk).

MR PETER J.A. MOORE is a fifth form Grammar school pupil at Ballymena Academy, Ballymena, Co. Antrim, with an interest in contemporary digital artforms.

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Enhancing immunity to malaria

Despite all efforts, malaria is still one of the world's most important infectious diseases, causing around 655,000 deaths each year, particularly in young children. Widespread vaccination would make a big change, but despite decades of effort, of 20 possible vaccines that are still undergoing clinical evaluation, only one shows enough protection to have moved into a field trial.

New ideas are needed. One route to immunity now attracting attention is that people who survive repeated natural infections eventually become immune. Ways to achieve this result, but without the risk and suffering from repeated illness, are now under serious study. Else Bijker and Robert Sauerwein from The Netherlands have recently re-examined epidemiological studies of the effects of different antimalaria interventions.

The best strategy to develop full immunity would probably allow people to acquire the infection naturally, via mosquito bites, while using drugs to limit symptoms. Travellers visiting malaria-endemic areas are routinely recommended to take antimalaria drugs to prevent infection. The reasons why this has not been adopted by local populations include lack of sustainability and acceptance by the community, and the risk of drug-resistant forms of the parasite developing.

However, there have been some trials over the decades with administration of a prolonged supply of antimalaria drugs into the general population, or specific vulnerable groups such as young children and pregnant women. Despite different methods of assessment, most studies demonstrated reduced illness and death in children and adults while taking the drugs and no increase after provision of the drugs stopped. Very clear support for development of immunity also comes from experiments with animals and human volunteers who were deliberately infected with the malaria parasite while taking various antimalaria drugs.

Bijker, E.M. & Sauerwein, R.W. (2012). Enhancement of naturally acquired immunity against malaria by drug use. *J Med Microbiol* 61, 904–910 (doi:10.1099/jmm.0.041277-0).

Vaccines and adjuvants – JMM special issue

The July issue of JMM is a special issue of the journal containing seven review articles on vaccines and adjuvants that were offered at a symposium on vaccines held at the SGM Spring Conference in Harrogate in April 2011. These articles highlight the current major challenges in vaccine development, as well as the latest advances in vaccines, novel adjuvants and vaccine-delivery technologies.

The issue also includes an editorial giving an overview of the symposium and the reviews. All the articles are open access.

Go to:

<http://jmm.sgmjournals.org/content/current>

These field and experimental studies counter the long-held medical opinion that providing long-term antimalaria drug therapy substantially impairs development of natural immunity to malaria. Even more positively, this is a new way of looking at an old problem and deserves support to see whether it can be translated into an effective strategy for life-long immunity for people living in countries where malaria is endemic.



Acute oak decline

The oak tree is an iconic symbol in the UK, in addition to its importance for timber and the landscape. These trees can live for over 1,000 years if they escape the hazards of animals, humans and disease. A new disease, acute oak decline (AOD), is causing considerable concern. Symptoms first appeared in the UK in the 1980s, but now it seems to be more common and infections have a high mortality. It can cause death within 5 years of oaks that have lived for several human generations. Memories of Dutch elm disease, which killed virtually all mature elm trees in the UK in the 1980s, have fuelled efforts to prevent a similar fate for oak trees.

Trees suffering from AOD ooze dark sticky liquid from cracks in the bark and leaf buds. These cankers on the trunk give ready access to vital tissues within the tree, and death results from the combined activities of bacteria, insects, fungi and other environmental factors. However, the initial event seems to be a bacterial infection, and researchers are working to characterize the bacteria involved. This would make it easier to

understand the source of the disease and monitor its spread with the aim of controlling it.

A collaborative effort between researchers in the UK, Spain, Belgium and South Africa has compared the bacteria associated with bark cankers and AOD from Spain and the UK. They used a battery of tests to analyse DNA sequences, test for specific cell chemicals and measure physiological parameters in the isolated bacteria, providing a clear picture of the relationship between the bacterial species present within oaks. There was evidence that the bacteria implicated in AOD belonged to a novel genus. This genus, *Lonsdalea*, was defined for the bacteria implicated in causing disease in oaks. The name is in honour of David Lonsdale, who made a significant contribution to British forestry pathology.

Brady, C.L., Cleenwerck, I., Denman, S., Venter, S.N., Rodríguez-Palenzuela, P., Coutinho, T.A. & De Vos, P. (2012). Proposal to reclassify *Brenneria quercina* ... *Int J Syst Evol Microbiol* 62, 1592–1602 (doi:10.1099/ijs.0.035055-0).

Plague immune system evasion

The human immune system can combat pathogens, relying on perceiving general features of pathogenic organisms, rather than more precise detection of a specific species. The Toll/interleukin-1-like receptor proteins (TLRs) that make the first interaction with patterns on the pathogen start a signalling cascade that ultimately activates the innate immune system. Bacteria also have this type of protein (called Tdp), but they are thought to use it to subvert their mammalian host's signalling systems.

Researchers have been studying a Tdp in *Yersinia pestis*, the pathogen responsible for plague. This bacterium is already known to interfere with TLR signalling to its own advantage. The researchers therefore decided to study the differences in ability to evade the immune system in bacteria with and without the *Y. pestis* Tdp (YpTdp). The YpTdp gene sits next to a region of DNA that was acquired from a virus and is important for both transmission of the bacterium by its flea vector and pathogenic success. The YpTdp gene itself looks like it might also be from a virus.

Spear, A.M., Rana, R.R., Jenner, D.C., Flick-Smith, H.C., Oyston, P.C.F., Simpson, P., Matthews, S.J., Byrne, B. & Atkins, H.S. (2012). A Toll/interleukin (IL)-1 receptor domain protein from *Yersinia pestis* interacts with mammalian IL-1/Toll-like receptor pathways but does not play a central role in the virulence of *Y. pestis* in a mouse model of bubonic plague. *Microbiology* 158, 1593–1606 (doi:10.1099/mic.0.055012-0).

The study showed that the intact YpTdp protein reduced activity in the immune signalling pathway. However, when *Y. pestis* was tested with or without YpTdp for its ability to infect mice, there was surprisingly little difference. This study therefore proposed that YpTdp either has a very subtle role in virulence or is important for a particular infection route or host. Looking for insight, the researchers assessed how the bacterial cells responded to saline solutions and measured how well the cells stuck to surfaces or clumped together. It became clear that cells lacking YpTdp clumped together much more and survived less well in saline conditions. These results suggest very clearly that the *Y. pestis* Tdp protein has roles in addition to immune evasion, but further work will be needed to describe the complete function of this protein.

Bodewes, R., Nieuwkoop, N.J., Verburgh, R.J., Fouchier, R.A.M., Osterhaus, A.D.M.E. & Rimmelzwaan, G.F. (2012). Use of influenza A viruses expressing reporter genes to assess the frequency of double infections *in vitro*. *J Gen Virol* 93, 1645–1648.

Double trouble

The emergence of very lethal varieties of bird flu has concentrated the attention of researchers worldwide. Since 2003, almost 600 laboratory-confirmed cases of this flu (influenza A type H5N1) have been reported worldwide, and 59% resulted in the death of the patient. Fortunately, this variety cannot so far transfer regularly between people. However, many other, less lethal, varieties of flu can, so researchers think that in time the H5N1 virus will acquire this ability from them. Understanding how this happens may give opportunities to delay or prevent the transfer.

There are several barriers. Both viruses have to infect at the same time. Humans and pigs can be infected by flu viruses adapted to both birds and mammals, giving the viruses the opportunity to meet and exchange genetic material. The viruses have to meet within the same cell, not just the same individual. Until now researchers had little idea of how often co-infections happened, or if specific conditions are necessary, but a team at the Erasmus Medical Centre in the Netherlands have devised a method to detect co-infections.

They have trialled their methods in cultured cells using several strains of influenza A virus. The key was to add a gene for a coloured protein to the viral genetic material. During an infection, the host cell was forced to make a red- or green-coloured protein along with all other viral proteins. Cells with co-infections were yellowish due to a mixture of the red and green proteins. The researchers tested two methods for detecting the colours, one using an automated

cell counter, the other relying on high-powered microscopy and computer analysis. Both methods gave similar results, giving the researchers confidence in their estimates of the number of viral particles needed for co-infections and the effects of different flu strains. They showed that cells readily become infected with two types of flu virus, but also provide a way to study the factors required.

Green, red and yellowish cells that were infected with one or more viruses that contain genetic material encoding different fluorescent proteins.

Population Genetics of Bacteria

Editors S.T.Walk & P.C.H. Feng
Publisher American Society for Microbiology (2011)
Details US\$149.95 | pp. 360
 ISBN 978-1-55581-535-6
Reviewer Charles Penn,
 University of Birmingham

This is an excellent book, celebrating Thomas Whittam who died in his prime as a key contributor to understanding of the biology of our most important model bacterium. However, only 4 of 18 chapters really reflect the title. There is very little digression towards the broader landscape of bacterial diversity in the context of population genetics and evolution. It is largely a wide-ranging compendium of authoritative reviews of the biology of *Escherichia coli*, with a slant towards evolutionary and population biology with Whittam's contributions to the field in mind, but with much else besides. There is a focus on *E. coli* as a pathogen, but its wider existence in the environment and as a commensal organism in the digestive tract – the 'niche' – is also reviewed. I recommend the book unreservedly to anyone interested in the broader biology of *E. coli* and it should be available in any institution where microbiology is taught.

Reviews on the web

Reviews of the following books are available on the website at www.sgm.ac.uk/pubs/micro_today/reviews.cfm. To join our panel of reviewers, email y.taylor@sgm.ac.uk

Yeast Research: A Historical Overview

Authors J.A. Barnett & L. Barnett
Publisher American Society for Microbiology (2011)
Details US\$159.95 | pp. 392 | ISBN 978-1-55581-516-5
Reviewer Alan Wheals, University of Bath

This unique book has been developed from a number of articles originally published in *Yeast*. Written by a scientist for scientists, it covers research from the late 18th century up to 2000. There are many useful figures, interesting original quotations (including from those who got things completely wrong) and photographs of some of the key protagonists. It is a book to dip into, and I always found myself hooked and read more than I planned to. Yeasts are now at the forefront of genetics research, but this book reminds us of their seminal importance in the development of biochemistry and microbiology amongst other sciences. Putting research into a historical context, it should be in the library of all institutions where these sciences are studied. Students should be encouraged to read parts of it if only to show them that there was science before genomics!

Bacteria: the benign, the bad, and the beautiful

Author T.M. Wassenaar
Publisher John Wiley & Sons Limited (2011)
Details £26.95 | pp. 232 | ISBN 978-1-11810-766-9
Reviewer John Heritage, University of Leeds

I'm Sorry I Haven't a Clue is the antidote to panel games. In her preface, Trudy Wassenaar describes this book as 'an antidote to neutralize some of the bad press that bacteria frequently receive'. Nevertheless, a fair proportion of the book is devoted to damage. To its benefit, it also considers prions, viruses, fungi, protozoa and larger parasites alongside bacteria. The rest of the text encompasses an impressive array of topics. The text is lively and engaging, although her Editor has not always helped: the promise not to use labels for the nutritional types of bacteria in an early chapter is broken in later chapters. On occasion, the text is too simplistic (cell envelopes are more than membranes) and it is occasionally wrong (penicillins DO kill bacteria). But these are minor criticisms. I learned from the book and, like *I'm Sorry I Haven't a Clue*, I found Trudy Wassenaar's book witty, fun and educational.

Nitrification
Editors B.B. Ward, D.J. Arp & M.G. Klotz
Publisher American Society for Microbiology (2011)
Details US\$159.95 | pp. 460 | ISBN 978-1-55581-481-6
Targeted Drug Strategies for Cancer and Inflammation
Editors A.L. Jackman & C.P. Leamon
Publisher Springer-Verlag GmbH & Co. KG (2011)
Details £126.00 | pp. 265 | ISBN 978-1-44198-416-6

Small DNA Tumour Viruses

Editor K. Gaston
Publisher Caister Academic Press (2012)
Details £159.00 | pp. 324 | ISBN 978-1-90445-599-8
Reviewer Sally Roberts, University of Birmingham

Small double-stranded DNA tumour viruses have long been appreciated for their provision of insight into fundamental biological processes. In this sense, this book brings our knowledge of the molecular biology of this group of viruses up to date and shows that the power of these viruses to probe biological processes is not on the wane. The book is composed of 14 chapters written by leading researchers; all are of high quality and up to date (2011 references). Nine of the 14 are given over to aspects of papillomavirus functions. The bias to this particular virus is difficult to avoid considering the current nature of research and the scientific interest this virus holds. Nevertheless, polyomaviruses and adenoviruses have been, and are still, important contributors to the field; perhaps to appreciate this, a little more coverage of these viruses would have been desirable. The chapters on mechanisms of viral plasmid maintenance and on virus interactions with cellular DNA damage response pathways do compare the different mechanisms used by the various viruses. The chapter on adenoviruses and the immune system gives an in-depth account of how the immune system sees this virus and how this can be used to design effective adenovirus for vaccine delivery and clinically effective oncolytic adenoviruses. Papillomaviruses are dealt

with on several levels, including the function of individual proteins, mechanisms of viral genome replication and how the virus induces host genome instability. The inclusion of a chapter on the isolation of virions from different sources for the study of papillomavirus infection is very timely and identifies how important it is to understand the nature of virion isolates for data interpretation.

This is a very useful book, and a valuable reference for those entering the field, as well as those already ensconced.

Hungry Planet: Stories of Planet Diseases
Author G.L. Schumann & C.J. D'Arcy
Publisher American Phytopathological Society Press (2012)
Details US\$65.00 | pp. 304 | ISBN 978-0-89054-399-3
The Spread of Pathogens Through International Trade
Editor S.C. MacDiarmid
Publisher Office International des Epizooties (OIE) (2011)
Details €60.00 | pp. 351 | ISBN 978-9-29044-837-2

IN APRIL 2012, the organization 'Take the Flour Back' (TTFB) threatened to 'decontaminate' field trials of genetically modified (GM) wheat which produced a pest-repellent aroma. The research team at Rothamsted Research publicly requested that the TTFB did not destroy the field trial, but let it continue so that we might learn more about the effectiveness of such plants in the natural environment. The Rothamsted team noted that the trial was approved by the Advisory Committee on Releases to the Environment and that biological and physical security measures had been implemented. Sense about Science initiated a campaign *Don't Destroy Research*, which attracted over 6,000 signatures and statements from a number of organizations, including those who had reservations about the value of GM crops but thought that the scientific evidence was needed.

In response to this campaign, the SGM made the following statement:

'The Society for General Microbiology (SGM) sees significant potential in the use of biotechnology research to mitigate food insecurity and the use of genetically modified organisms (GMOs) as just one of the many tools in the researcher's toolbox that, with rigorous legislative and ethical review, may yield products or processes to improve food security. SGM will continue to inform the debate about the use of such technology.'

This was taken directly from the *SGM Position Statement on Food Security and Safety* (www.sgm.ac.uk/PA_forms/FoodPS_Web.pdf).

In fact, the demonstration and counter-demonstration on 27 May 2012 passed peacefully, albeit with a heavy police presence, and the field trial was not destroyed. However, the open discussion between TTFB and Rothamsted Research had not taken place several weeks later.

This event once again emphasizes the need for researchers and learned societies to engage in open discussion with the public, with politicians and Government officials, with non-governmental organizations (NGOs) and with special interest groups – providing, of course, that these groups are prepared to engage.

Whatever an individual SGM member's view is on the value and desirability of GM crops in the food chain, or of GM micro-organisms in food preparation (of some vegetarian cheeses, for example), most microbiologists know the value of genetic modification in the laboratory. Without this, many of today's rapid advances in the understanding of fundamental microbiology, infectious disease, and environmental processes would not have been possible.

The SGM is developing a further statement on genetic

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The recent demonstration against GM wheat at Rothamsted Research has highlighted the importance of communication between researchers and the public, opinion-formers and policy-makers.

NIGEL L. BROWN

COMMENT

Don't destroy research

modification, which will cover the research use of genetic modification in plants, animals and micro-organisms, and give some examples of how these genetic modification techniques have been used in a research context, as well as giving information on the regulatory systems in place. We wish to consult the membership on this. Although it is unlikely that we will get full agreement of all members on every aspect of the statement, it is important that the SGM expresses a view that can be used in support of members' work.

The consultation on the *SGM Statement on Genetic Modification* can be found at:

www.sgm.ac.uk/news/gmconsultation.cfm

A proper and full understanding of the scientific evidence is as important in the development of evidence-based policy for special interest groups and NGOs, as it is for politicians and for Governments. At a personal level, I find it entertaining to speak with members of the Soil Association, which has a policy of opposition to GM, on why members are permitted to spray a close relative of the anthrax bacillus and a food-poisoning organism onto organic crops [see Helgason *et al.* (2000) *Bacillus anthracis*, *Bacillus cereus* and *Bacillus thuringiensis* – one species on the basis of genetic evidence. *Appl Environ Microbiol* 66, 2627–2630].

It is important that we all understand and communicate the science, its benefits and its risks.

NIGEL L. BROWN FRSE FRSC FSB, SGM President-elect and Professor of Molecular Microbiology, University of Edinburgh (tel. 0131 650 6443; email nigel.brown@ed.ac.uk)

Please note that views expressed in Comment do not necessarily reflect official policy of the SGM Council.

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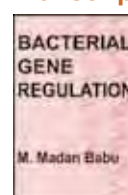
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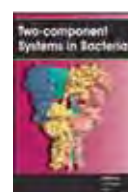
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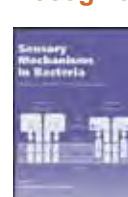
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