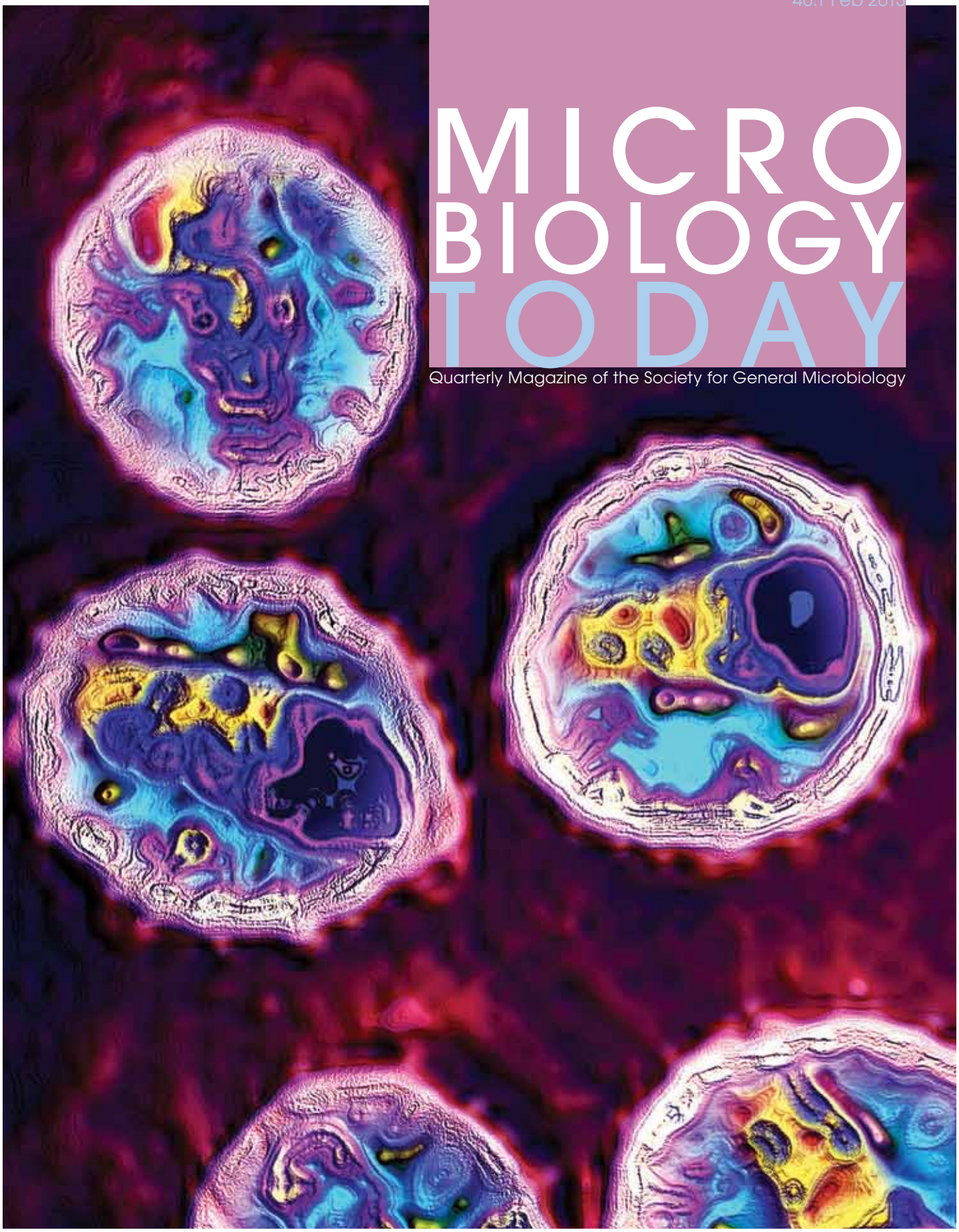
40:1 Feb 2013

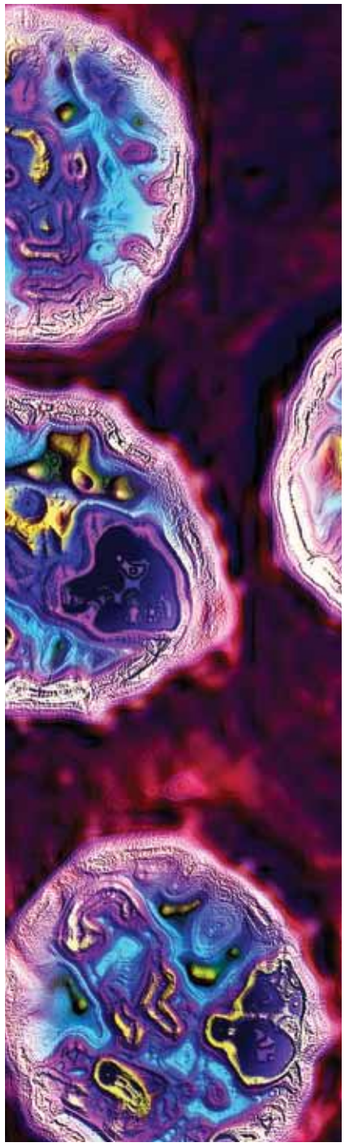
MICRO BIOLOGY TODAY

Quarterly Magazine of the Society for General Microbiology



Viruses and cancer • HIV and immune suppression • Human papillomaviruses • Viral hepatitis and HCC • Vaccines for Epstein–Barr virus

EDITORIAL



Welcome to the first issue of *Microbiology Today* of 2013, which will be a year of great change for SGM.

I will be finishing my tenure as Editor of *Microbiology Today* in September. The excellent Laura Bowater, a senior lecturer in the Medical School from the University of East Anglia will succeed me in the post. I hope Laura will find the post as enjoyable, stimulating and fun as I have – good luck!

This issue of *Microbiology Today* is a 'virology special'; this is in part to recognise the contribution of this year's SGM Prize Medal winner, Harald zur Hausen, and his ground-breaking contributions to understanding the link between viruses and cancer. The issue owes a huge debt to David Blackbourn, whose knowledge and expertise in this area was invaluable in identifying and inviting authors – in fact David did most of the author identification and arm-twisting! We have relied heavily on the Viral Oncology group at the University of Birmingham, who have done a great job. It has been a fascinating issue to edit and I have learned a huge amount in this area.

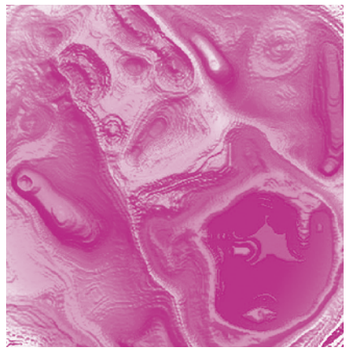
We begin with an overview of viruses and cancer by Laura Hindle & David Blackbourn, followed by several articles covering more specific areas of interest. These cover a range of viruses and diseases such as viral hepatitis and hepatocarcinoma by Jane McKeating & Colin Howard, Epstein–Barr virus by James Turner & Graham Taylor and human papillomaviruses by Jo Parish & Sally Roberts. Robert Newton also provides us with an excellent overview of the epidemiological burden of virus-associated cancers.

We have also included an interview with Professor zur Hausen, where he gives us a great insight into his work and career in virology. In all, it really is a tour de force of the area.

The Comment in this issue is provided by Leighton Chipperfield, Head of Publications at SGM, where he outlines the challenges and opportunities that lay ahead for SGM in the changing landscape that is academic publishing.

I hope you enjoy this issue of *Microbiology Today*.

PAUL A. HOSKISSON, Editor
Email paul.hoskisson@strath.ac.uk



SGM Council 12/13

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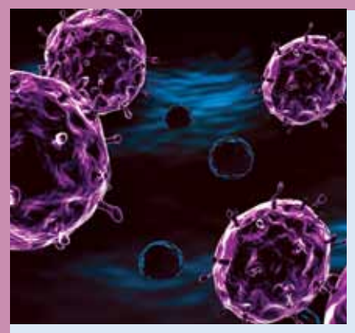

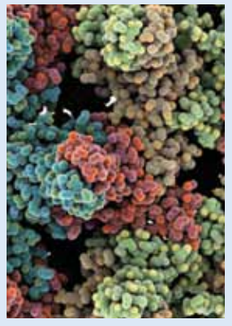

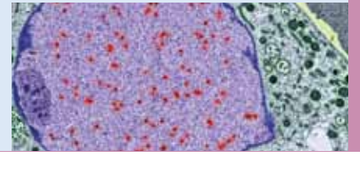

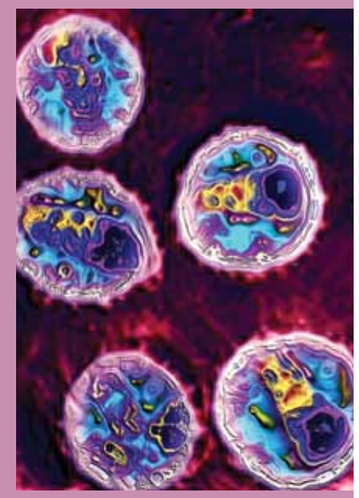

Cover **Coloured transmission electron micrograph of human immunodeficiency virus, one of the seven viruses defined as carcinogens by the International Agency for Research on Cancer.** *James Cavallini / Science Photo Library*

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society for general Microbiology

International Yakult Symposium 2013

The 7th International Yakult Symposium

The Intestinal Microbiota and Probiotics: Exploiting Their Influence on Health

www.yakultsymposium.com

April 22nd-23rd, 2013

The Queen Elizabeth II Conference Centre, London, UK

The gut microbiota is the focus of this event, with international experts presenting the latest findings about its genomics and physiology, as well as the dynamic, metabolic and immunological aspects of its interaction with the host in the context of health and disease. Related to this, the potential influence of probiotics on the composition and function of the microbiota will also be discussed. As always, this symposium will provide a platform for young investigators and established scientists to present their latest basic and clinical findings on the gut microbiota and probiotics. This will be a unique opportunity to engage in an international and high level scientific debate on this exciting field of research, and to exchange opinions on the current knowledge on gut microbiota and probiotics.

Registration Fee	Until 1st March 2013	From 2nd March 2013
Delegates	€100.00	€150.00
Students (Including PhD students)	€50.00	€75.00

Approved by the Society of Biology for purposes of CPD (18 credits), and by the Institute of Biomedical Science (10 credits).

Considering submitting a poster? Registration fee will be waived for one author of posters selected for presentation

science *for health*

FROM THE PRESIDENT

2013 is a year that will bring great change to the Society. For the last 2 years, Council and senior Marlborough House staff have been working hard to meet the challenges that the SGM will face.

We are restructuring our publications activity and Leighton Chipperfield, the Head of Publishing, describes some of the changes in publishing in this issue (p. 52). Open Access (OA) publishing has been widely discussed following the Finch report, but the importance of publication income to learned societies in supporting training and conference activities may not be fully understood by many proponents of OA. The SGM Policy Committee recently contributed to the Society of Biology submission to the House of Lords inquiry into OA publishing.

The new Council Committees have begun to meet and to implement the Strategic Plan 2012–17. This is available on the SGM website at **www.sgm.ac.uk/about/SGM_Strategic_Plan.pdf**. We are beginning to look at many of the activities that the Society undertakes. There is opportunity for all Ordinary Members of the Society to involve themselves more directly in the work of the SGM through standing for election as members of Council or of Divisional Committees. Details are available on pages 9 and 10.

The major structural change for the Society will be relocation of its offices to London. We have found that our current location reduces our opportunities to engage with opinion-formers and with other learned societies. Council has agreed to move over the course of 2013 to Charles Darwin House (**www.charlesdarwinhouse.co.uk**), where we will share facilities with the Society of Biology, the Biochemical Society, the Society for Experimental Biology and the British Ecological Society. The restructured publications department will be the first to move, beginning in February, with other staff following over the course of the year. The argument for the Society to be located outside London to reduce costs is no longer valid, and London provides a bigger pool of the specialist staff that a modern learned society needs.

I encourage all members to promote microbiology, not only in the scientific community, but with politicians and other opinion-formers. 18 November 2012 was European Antibiotic Awareness Day and one letter to a local MP, pointing out the issues around the small number of usable antibiotics and the relative lack of investment in discovering new antimicrobials, led to action. The MP tabled a question with the Department of Health on steps being taken to minimise further resistance and asked the Business, Innovation and Skills Department about investment in new antimicrobials.

With the help of members, the SGM can respond rapidly to issues of microbiological concern. The recent concerns over ash dieback led to us quickly producing a briefing note (**www.sgm.ac.uk/news/hot_topics/Ashdiebackbriefing.pdf**) with the help of Dr Robin Sen of Manchester Metropolitan University. Such briefing notes are valued by politicians, civil servants and others who have to respond quickly to concerns. All members of the Houses of Commons and Lords and elected members of the devolved administrations receive copies of all briefing notes and are invited to receive *Microbiology Today*.

This issue of *Microbiology Today* celebrates the award of the SGM Prize Medal to Professor Harald zur Hausen. It is a mine of useful information about the relationship between viruses and cancer, and will be circulated to health professionals, as well as to SGM members and politicians. The SGM Prize Medal is the premier award of the Society and I am pleased to congratulate Professor zur Hausen and our other prize winners, details of whom can be found on pages 8 and 9.

NIGEL L. BROWN, President
Email president@sgm.ac.uk

NEWS

NEWS OF MEMBERS

Congratulations to **PROFESSOR JAMES PROSSER**, University of Aberdeen, on the award of an OBE in the New Year Honours List for services to environmental science.

The Society notes with regret the passing of **DR CHRISTOPHER K. BOSMAN** (member since 2000).

VOUCHERS FOR MOBILES

An article in the August 2012 issue of *Microbiology Today* (vol. 39, part 3, 143) announced the introduction of mobile-optimised sites for SGM's four journals, *Microbiology* (**m.mic.sgmjournals.org/**), JGV (**m.vir.sgmjournals.org/**), IJSEM (**m.ijs.sgmjournals.org/**) and JMM (**m.jmm.sgmjournals.org/**).

A voucher service for each mobile site is now in place. This enables users belonging to a subscribing institution to link their mobile device to the journals, allowing access to embargoed content when not on the institution's network. To obtain a code, users should connect to their institution's network, select 'Authorize this Device' on the mobile site and follow the instructions. The code needs to be applied to the device within 48 hours. Each mobile device must be vouched for individually.

PUBLICATION IN *MICROBIOLOGY* IS NOW FREE!

SGM's original journal, *Microbiology*, is offering another benefit to authors – completely free publication! All papers accepted since December 2012 will be published completely free of charge. Editor-in-Chief, Agnès Fouet, says, '*I am really pleased that we have made publication in* Microbiology *free. Authors can convey their full report in a well-respected journal that maintains high-quality production standards.*'

Microbiology has a far-reaching readership – all papers are freely available online 12 months after publication – and is well cited, with an impact factor of 3.061. Papers receive fast and high-quality review; a first decision from expert international editors is reached within 4.2 weeks, on average. The journal's research is relevant to and cited by the microbiology community, and could be the ideal place for your next research paper, whether you are a new or returning author.

You can hear more about the benefits of publishing in Microbiology *by watching the Editor-in-Chief's video (**www.youtube.com/embed/t6QRCAu2f7E**). You can also find out more about the journal, including how to prepare and submit a manuscript for publication, by visiting the journal website (**http://mic.sgmjournals.org**).*

IJSEM NEWS

A project is underway at SGM Publishing to reduce the time from acceptance to print publication for papers in the *International Journal of Systematic and Evolutionary Microbiology* (IJSEM). Although authors' accepted manuscripts are available online as 'Papers in Press' within a week, final print publication (as required for valid publication of bacterial names) has been slow. Starting with the January 2013 issue, larger issues will be printed to reduce the waiting time for authors. Papers describing eukaryotic taxa that are not covered by the Bacteriological Code have been fast-tracked during 2012 and are now published quickly.

We would like to thank IJSEM authors for their patience and look forward to delivering much faster publication by mid-2013.

NEW COUNCIL MEMBERS

Sara Burton

After attending a local comprehensive school in Oxfordshire, Sara completed her BSc(Hons) in Applied Biology at Bradford University (1984) which incorporated a very inspirational year at the National Collection of Industrial and Marine Bacteria Ltd in Aberdeen. After working for 4 years in a University of Cardiff spin-out company (Biotal Ltd), Sara undertook a PhD at Exeter in plant molecular biology. After a career break, during which time she taught for the Open University and had two sons, Sara returned to Exeter University where she worked in the Environmental Microbiology Research group. Recently, she has moved to Education and Scholarship and now enjoys her role as Senior Lecturer and Senior Tutor in Biosciences.

Charles Penn

Charles trained in Biochemistry at the University of Liverpool in the late 60s, did his PhD work in bacterial veterinary vaccine development at the Wellcome Foundation labs in Beckenham, Kent, and went on to join Harry Smith in Microbiology, now subsumed into Biosciences, at the University of Birmingham where he has remained. Charles's research career has focussed on bacteria as pathogens with a molecular perspective. Organisms he has engaged with include *Neisseria*, spirochaetes, *Helicobacter*, *Campylobacter* and *E. coli*. He has extensive experience in journal editing, as an Editor of *FEMS Letters*, *Microbiology* and, latterly, the *Journal of Medical Microbiology* as Editor-in-Chief.

Andrew Davison

Andrew Davison has worked in Glasgow since 1976, except for a couple of years off (for good behaviour) that were spent in Bernie Moss' lab at the NIH in the mid-1980s. In 1991, he became a Programme Leader at the MRC Virology Unit, which was recently absorbed into the MRC–University of Glasgow Centre for Virus Research. His expertise is in viral genomics, with a focus on herpesviruses and, more specifically, human cytomegalovirus. He has played an active part in the SGM for many years, having been on the Virus Group Committee in the 1990s and more recently on the Virology Division. He was an Editor of the *Journal of General Virology* from 1999 to 2005. Now that his four children have at last (almost) left home, he has taken up his boyhood hobby of breeding exotic moths.

Maggie Smith

Maggie did her BSc at the University of Leeds in Biochemistry and Microbiology and a PhD in Bristol under the supervision of Professor Ian Chopra. She then went back to Leeds to do a 5-year postdoc with the late Professor Simon Baumberg and this was followed by a 3-year, semi-independent postdoc position with Professor Iain Hunter at the University of Glasgow. Maggie gained her first lectureship at the University of Stirling, but then moved to Nottingham University where she stayed for 10 years and was awarded a personal chair in January 2003 before moving to the University of Aberdeen. This year, Maggie moved again to the Biology Department at the University of York; here she holds a Chair in Microbiology.

SPRING CONFERENCE PRIZE LECTURERS

SGM PRIZE MEDAL

HARALD ZUR HAUSEN

Tuesday 26 March 12:10–12:50

Infections causing human cancers: why do some ubiquitous infections mainly cause regional cancers?

Harald studied Medicine at the Universities of Bonn, Hamburg and Düsseldorf and received his MD in 1960. After his internship, he worked as postdoc at the Institute of Microbiology in Düsseldorf, and subsequently in the Virus Laboratories of the Children's Hospital in Philadelphia where he was later appointed Assistant Professor. After a period of 3 years as a senior scientist at the Institute of Virology of the University of Würzburg, he was appointed in 1972 as Chairman and Professor of Virology at the University of Erlangen-Nürnberg. In 1977, he moved to a similar position at the University of Freiburg. From 1983 to 2003, he was appointed as Scientific Director of the Deutsches Krebsforschungszentrum (German Cancer Research Centre) in Heidelberg. He retired from this position in 2003.

He has received numerous prestigious national and international awards, including the Nobel Prize for Medicine 2008, the Life Science Achievement Award of the American Association for Cancer Research, the German Special Order of Merit with Star and 24 honorary MD and PhD doctorates. He is an elected member of various academies and research organisations, and has become an Honorary Member of a number of biomedical scientific societies. A large number of Special Lectures and Visiting Professorships, Memberships of Editorial Boards and active involvements in the organisation of international meetings complement his CV.

From 2000 to 2009, he was Editor-in-Chief of the *International Journal of Cancer*, and from 2006 to 2010 he was member of the Board of Directors of the International Union against Cancer. From 2003 to 2010, he was Vice-president of the German National Academy for Natural Sciences and Medicine. In 2010, he was appointed Chairman of the Scientific Council of the National Science Transfer and Development Agency in Bangkok, Thailand.

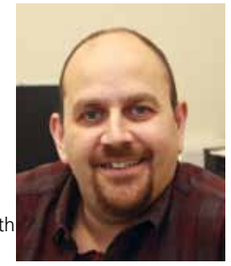
PETER WILDY PRIZE FOR MICROBIOLOGY EDUCATION

DAVID BHELLA

Monday 25 March 17:20–18:05

Beautiful and a little bit scary … viruses and science communication

David is a programme-leader in the MRC Centre for Virus Research (Glasgow). His research focuses on the structural biology of viruses and virus–host interactions. He has a long-standing interest in public engagement and working with school audiences to enthuse students about careers in the sciences, particularly microbiology. Over the past decade, he has built a thriving programme of outreach activities in partnership with Glasgow Science Centre.



HOT TOPIC

PAUL W. O'TOOLE

Tuesday 26 March 17:35–18:05

The human microbiome: overdue recognition for our fellow travellers

Paul obtained PhD at Trinity College Dublin. Following research in Sweden, Canada, New Zealand and the USA, Paul is now Professor of Microbial Genomics at University College Cork, Ireland. His main research theme is the genomics and metagenomics of gastrointestinal bacteria with emphasis on human-associated species and host interaction, particularly commensal lactobacilli. His latest research examines the composition and function of the gut microbiota, its dependence on diet, and its relationship to health, ageing and well-being in humans and animals.

FLEMING PRIZE

ROBERT RYAN

Wednesday 27 March 12:10–12:50

Cyclic di-GMP signaling and the regulation of bacterial virulence

Robert gained his PhD in Molecular Microbiology with David Dowling, followed by a postdoc position with Max Dow in Cork. Thanks to a number of fellowships he has been lucky enough to work in the laboratories of Ute Romling (Karolinska Institute), Chuck Farah (São Paulo), George O'Toole (Dartmouth, USA) and Judy Armitage (Oxford). In 2009, he started his own group in Cork after receiving a Science Foundation Ireland Starting Investigator award. Recently, he was awarded a Wellcome Trust Senior Research Fellowship to relocate his group to Dundee. His work centres around understanding the role that interspecies signalling plays in influencing both bacterial virulence and response to therapy in polymicrobial infections.

COLWORTH PRIZE

JEFFREY W. ALMOND

Monday 25 March 12:10–12:50

Vaccines R&D: challenges for the 21st century

Jeffrey is the Head of Discovery Research and External R&D at Sanofi Pasteur, the largest manufacturer of human vaccines. He is responsible for Sanofi Pasteur's portfolio of exploratory projects aimed at providing pre-clinical proof-of-concept for a range of human vaccine targets. He also identifies and assesses opportunities for external collaboration on vaccine targets and relevant technologies. Before joining Sanofi Pasteur in 1999, Jeffrey was Professor of Microbiology at Reading, and served in various offices, including Chairman of the Virology Division of the IUMS, SGM International Secretary and member of the UK governmental Spongiform Encephalopathies Advisory Committee. He is currently a member of the Medical Research Council and an elected fellow of the UK Academy of Medical Sciences. He has published numerous articles in the field of microbiology, especially on influenza and picornaviruses, HIV and vaccines.

HELP SHAPE THE FUTURE OF SGM

If you are an Ordinary Member, please consider putting yourself forward to join Council and have a bigger say in how your Society develops.

There is one vacancy for an Elected Member to serve on Council from Sept 2013 until Sept 2017. Council has formal meetings four times a year. In addition, Elected Members have an important role to play in several of the Committees that influence different aspects of SGM business, such as publications, finance, policy, conferences, communications and professional development. Committee meetings often take place in addition to formal Council meetings. Council Members are encouraged to participate in SGM conferences where the cost of attendance is supported by the Society.

SGM, under Council's guidance, is undergoing a period of significant change in line with the new strategy (**www.sgm.ac.uk/about/objectives.cfm**) and we would like to recruit a new Council Member willing to commit the time and with the skills and experience to make a positive contribution to the strategy through one or more of the Committees.

If you would like to contribute, we would very much like to hear from you. Alternatively, you may want to encourage a colleague to get involved. Nominations should come from individuals who have been an Ordinary Member for at least 2 years and must be supported by two other Ordinary Members. Please use the nomination form at **www.sgm.ac.uk/about/objectives.cfm** and include information about the skills you can offer and how you would like to contribute to Council. Please send your nominations to **appointments@sgm.ac.uk**

The closing date is **30 April 2013**. Informal enquiries about the role of elected Council Members can be made to Simon Festing (**s.festing@sgm.ac.uk**). If the number of nominations exceeds the number of vacancies, an election will be held in early summer.

SGM CONFERENCES – YOUR CHANCE TO GET INVOLVED

SGM Divisional Committees are looking for enthusiastic volunteers who would like to participate in planning and delivery of scientific conference programmes. Members of the Divisional Committees have an interest in an aspect of one of four cross-cutting themes: Microbial diversity & evolution; Fundamental microbiology; Translational microbiology; and Infectious disease.

Divisions meet twice each year and work independently to plan some conference symposia whilst others are developed with a cross-cutting theme in mind. Each member serves on the committee for 3–4 years and is expected to contribute actively to Divisional Committee business. An individual will usually participate in the planning of several symposia over their term of office and would be likely to take the lead in organising the programme for at least one event.

If you would like to make a contribution to SGM conferences we would very much like to hear from you. Alternatively, you may want to encourage a colleague to get involved and support their nomination.

DIVISIONAL COMMITTEE ELECTIONS 2013

For the 2013 elections, we are inviting nominations to fill 9 vacancies (see below).

Theme	Virology	Prokaryotic Microbiology	Eukaryotic Microbiology	Irish Division
Microbial diversity & evolution	2 vacancies	1 vacancy	No vacancy	1 vacancy
Fundamental microbiology	No vacancy	1 vacancy	No vacancy	
Translational microbiology	No vacancy	1 vacancy	1 vacancy	
Infectious disease	1 vacancy	No vacancy	1 vacancy	

Nominations for the Virology, Prokaryotic and Eukaryotic Microbiology Divisions must fall into the cross-cutting themes as advertised. The Irish Division does not have cross-cutting themes so nominations are open to individuals with any scientific interest.

Nominations should be made using the form available on the SGM website: **www.sgm.ac.uk/meetings/divisions.cfm**. All nominees must be SGM Members and the nomination must be supported by two Ordinary Members. If the number of nominations exceeds the number of vacancies, elections will be held in late spring.

Please send your nominations to **appointments@sgm.ac.uk**. The closing date is **30 April 2013**.

More information about the Divisional Committees and their current members is available at **www.sgm.ac.uk/meetings/divsions.cfm**

COME AND HELP US GIVE BACTERIA THE BRUSH OFF!

As Big Bang returns to London's Excel Centre, SGM will be there!

School members, and anyone with interested children, are invited to come along and take part in our 'hands-on' investigation into the importance of oral hygiene on our stand *Plaque attack: giving bacteria the brush off*.

We are very grateful to Nicola Stanley-Wall for her help in developing this activity.

HEATLEY-PAYNE AND HAYES-BURNET AWARD RECIPIENTS ANNOUNCED

The Heatley-Payne and Hayes-Burnet Awards are offered jointly with the American Society for Microbiology (ASM) and Australian Society for Microbiology. The awards provide funds to support the reciprocal exchange of one early-career Society member to present their research at the other Society's main annual conference and to visit an institution in that country, enabling the recipient to raise their profile among the microbiology community and to initiate and strengthen collaborations.

The recipient of the 2013 SGM Heatley-Payne Award is **Dr Siobhan Watkins** (left) of University of Portsmouth, who will attend the ASM General Meeting in Denver and visit the University of Maryland to further her research on freshwater cyanophages from the south of England. **Dr Barry Johnson** (right) of National Institutes of Health is to receive the reciprocal American Society for Microbiology award. Barry will visit Peter Cherepanov of Cancer Research UK London Research Institute and present his work on modelling and inhibition of HIV-1 integrase at the SGM Spring 2013 Conference.

The SGM Hayes-Burnet Award for 2013 has been awarded to **Dr Rebecca Sumner** (left) of University of Cambridge. Rebecca will visit Associate Professor David Tscharke at the Australian National University and then attend the Annual Scientific Meeting in Adelaide. At the University, she will deliver a seminar on her research and receive training in analysing adaptive and memory immune responses of vaccinia virus in a murine model. The Australian recipient is **Dr Johanna Kenyon** (right), University of Sydney. Johanna will join us at the SGM Autumn 2013 Conference and visit Professor Gordon Dougan of the Wellcome Trust Sanger Institute as part of an ongoing collaboration on the capsule locus in *Acinetobacter baumannii* genomes.

CONFERENCES

SGM Spring Conference 25–28 March 2013

SGM Autumn Conference 2–4 Sept 2013

Manchester Central Convention Complex – www.sgmmanchester2013.org.uk

With just under a month until the Spring Conference 2013 there is still time to register and be part of this international event. For the latest programme details and to book online, visit **www.sgmmanchester2013.org.uk** – *see you there!*

CONFERENCE SNAPSHOT

Viruses and human cancer: causes to cures (25–26 March)

Viruses are associated with the development of about 11% of all human cancers, with the incidence of the majority of these occurring in developing regions of the world. The International Agency for Research on Cancer has defined seven viruses as carcinogens; the herpes viruses Epstein–Barr virus (EBV) and Kaposi's sarcoma herpes virus (KSHV), high-risk human papillomaviruses (HPV), human T cell lymphotrophic virus (HTLV-1), hepatitis B and C viruses (HBV and HCV) and human immunodeficiency virus type 1 (HIV-1). New associations between viruses and cancers are emerging, for example Merkel cell polyomavirus (MCPV) and the role this virus plays in the development of Merkel cell carcinoma.

Some types of adenovirus and polyomavirus have been found to induce tumours in rodents; these have provided invaluable model systems to study mammalian tumorigenesis. Oncolytic viruses have also been exploited as novel therapies for the treatment of cancers.

Why attend

The aim of this symposium is to realise the impact of virus infection on the incidence of human cancers worldwide, to gain an understanding of the mechanisms underlying virus-associated cancers and to appreciate the issues surrounding treating and preventing them. It will focus on the epidemiology and the pathogenesis of cancer-causing viruses, host–virus interactions, the therapeutic exploitation of viruses to treat cancers, and the current state of play in the development of vaccines and other novel antiviral therapies.

The symposium will be perfectly complemented by this year's SGM Prize Medal lecture (26 March at 12:10) from Nobel Laureate **Professor Harald zur Hausen**, who received his Nobel Prize in 2008 for his work establishing the role of papillomaviruses in the development of cancer of the cervix.

For details of other exciting symposia and workshops, visit the conference website **www.sgmmanchester2013.org.uk**

Networking workshop and supper for early-career delegates (24 March)

The workshop brings together early-career delegates before the start of the conference. Delegates who attend get to know some friendly faces and pick up tips and advice on making the most of networking opportunities in the coming days. The session costs £13, includes supper and can be booked when registering to attend the conference.

PRIZE LECTURES

For biographies of the speakers, see pp. 8–9.

GRANTS

Grants are available to eligible

- Associate Postgraduate Student Members
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Apply online at **www.sgm.ac.uk/grants/**

Manchester town hall.
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Brighton beach and pier.
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The Autumn Conference will take place at the University of Sussex, located near the seaside town of Brighton, famed for its cafes, the historic Lanes, and the world famous Royal Pavillion.

This exciting conference will appeal to both bacteriologists and eukaryotic microbiologists from a variety of different backgrounds, especially those interested in infectious disease. Symposia over the three days will cover many different areas of microbiology research.

Impact of bacteriophage in the environment will cover the increasing awareness and impact of bacteriophage on the ecology of the biosphere, while ***Microbial modulation of cellular responses*** will highlight the way different bacterial toxins and effectors subvert, inhibit or activate host-cell pathways to the benefit of pathogens. ***Pathogen genomics – current clinical applications*** will show how clinical practice is changing based on the data generated by next-generation sequencing technology, and ***Regulatory phosphate-based molecules*** will outline progress in understanding the actions of phosphate-based regulatory molecules.

SGM and the British Society for Medical Mycology are hosting a joint symposium on ***Fungal diseases, diagnosis and drug discovery***. The programme spans contributions from world-leading scientists on the major human fungal pathogens, such as *Aspergillus*, *Candida*, *Cryptococcus*, dermatophytes and plant pathogens, as well the latest diagnostic techniques and advances in drug discovery. ***Microbial survival in the host*** will showcase the diverse strategies mounted by fungal and parasitic pathogens to survive within the human host.

Registration and abstract submissions will open shortly. Keep an eye on the SGM website and e-newsletter for the latest details.

Brighton Royal Pavillion.
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SAVE THE DATES

SGM Spring Conference 2014
Arena and Convention Centre, Liverpool
14–17 April 2014

Other SGM-sponsored meetings

British Yeast Group Meeting 2013
20–22 March 2013
Britannia Hotel, Nottingham
www.britishyeastgroup.org

3rd Oxford Bone Infection Conference
28 March–1 April 2013
Oxford Town Hall, Oxford
www.hartleytaylor-registration.co.uk/docs/OBI0flyer.pdf

Merkel Cell Carcinoma: New Insights & Emerging Therapies
7 May 2013
Edinburgh International Conference Centre
www.iid2013.org/satellite-meetings

EMBO Workshop on Integrating Omic Approaches to Host–Pathogen Interactions
25–27 June 2013
Radisson Blu Hotel, Liverpool
www.embo.org/events/calendar.html

14th International Conference on *Pseudomonas* 2013
7–11 September 2013
Lausanne, Switzerland
www3.unil.ch/wpmu/pseudomonas2013

MICRO SHORTS

Viruses and cancer

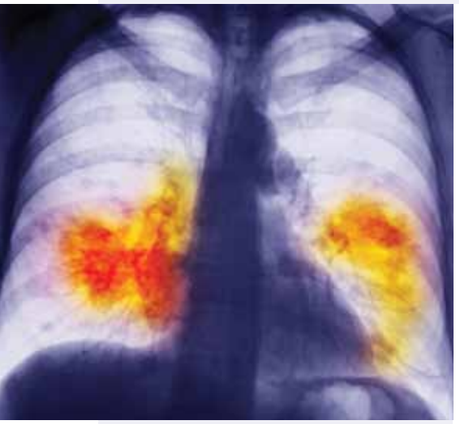
The development of cancer is a multistage process and it is clear that infectious agents either directly cause or are strongly associated with up to 17% of malignancies in the developed world. Viruses play a significant role by directly causing aberrant cell growth through the action of transforming genes, the establishment of chronic inflammatory processes or virus-induced immunosuppression that predisposes to oncogenesis, or the provision of a critical first 'hit' in the multistage oncogenic process.

Vaccination against certain viruses has proven beyond any question that certain cancers are preventable, as exemplified by the success of vaccination against hepatitis B, preventing hepatocellular carcinoma, and human papillomavirus in the case of cervical carcinoma. In the veterinary arena, vaccination of chickens against Marek's disease virus (an oncogenic herpesvirus) has proven efficacy in preventing lymphomas. Nonetheless, there is much to be done.

In many cases where there is a strong association of a particular virus with a tumour, the function and significance of virus-encoded gene products expressed in transformed cells is poorly understood. In addition, little is known of the environmental co-factors or host genetics that may predispose to virus-associated cancers, and the existence of a 'hit-and-run' mechanism of virus-induced oncogenesis has few proponents and is deserving of further scrutiny.

From a different perspective, in recent years considerable effort has been placed in the development of viruses as potential treatments against human cancers, based on either the delivery of 'suicide' genes, the development of genetically manipulated viruses that selectively replicate in transformed cells or the development of viruses with selective tropism for tumour cells. The development of oncolytic viruses shows considerable promise as evidenced by the increasing number of clinical trials currently in progress.

Stacey Efstathiou *Editor-in-Chief, JGV*



Chest X-ray showing lung cancer. *Photodisc / Thinkstock*

JGV

Fighting lung cancer with viruses

Viruses could help control certain fast-growing lung cancer cells, according to researchers at Johns Hopkins University. In recent years, Seneca Valley virus – which selectively targets cancerous cells but not normal somatic cells – has shown promise as a potential anti-cancer treatment. However, some types of aggressive 'small cell lung cancer' have previously been thought to be resistant to infection. By manipulating the viral genome to produce a green fluorescent 'reporter' protein, the researchers found that a small sub-population of these cancer cells is in fact highly susceptible to the virus. The researchers also confirmed that only cancerous cells were targeted: when they infected tumour-bearing mice with the virus, it did not replicate in normal tissues. The ability to infect only a subset of tumour cells could prove useful in anti-cancer treatments. For example, viruses could be used to deliver toxins to specific cancer-affected regions of the body.

J Gen Virol *doi:10.1099/vir.0.046011-0*
Adam Kucharski *Imperial College, London*

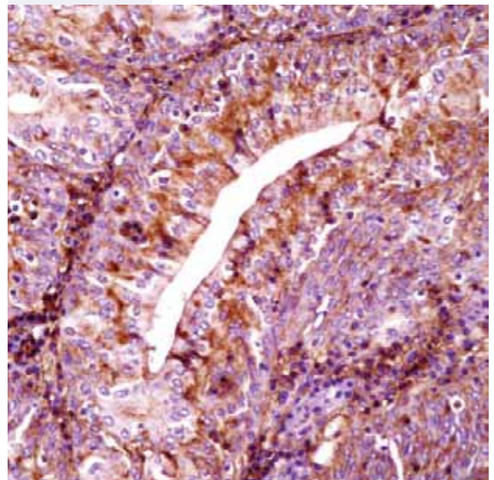
Water buffalo. *Stockbyte / Thinkstock*

JGV

Papillomavirus infection-linked cancer in fern-grazing buffalo

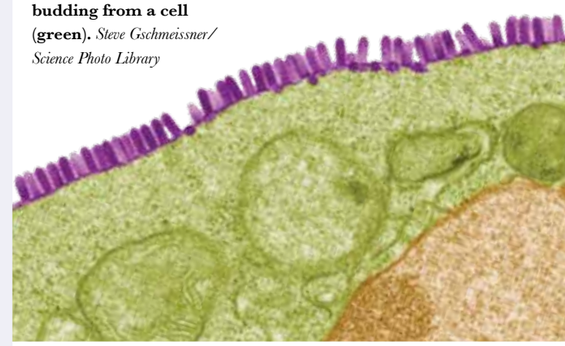
Bovine papillomavirus may infect over 90% of buffaloes grazing on ferns in Turkey. Ingesting ferns is thought to trigger papillomavirus BPV-2 activation, leading to cancerous growth, perhaps through suppression of the buffalo immune response. In addition, BPV-2 has been clinically detected in cancerous bladder tissue specimens from buffaloes. BPV-2 infection promotes induction of the E5 oncoprotein, promoting cancerous cell growth. Fluorescently imaging these proteins on tumour samples by microscopy showed the platelet-derived growth factor (PDGF-β) receptor interacting with E5 and BPV-2, again providing evidence of BPV-2 involvement in virus-induced cancers. The association between fern ingestion and papillomavirus infection has also been seen in humans who have developed throat cancer in Brazil. It is economically important in farming to understand the strategies that BPV-2 papillomavirus uses to cause cancer in cattle and buffalo. Discovering more about the 189 types of papillomavirus and their ability to infect other animal species could lead to potential preventative strategies and treatments.

J Gen Virol *doi:10.1099/vir.0.047662-0*
Rebecca Way *University of Aberdeen*



Cancerous cells from the bladder of a water buffalo. *Dr Sante Roperto, Università di Napoli Federico II, Italy*

VSV particles (purple) budding from a cell (green). *Steve Gschmeissner/ Science Photo Library*



JGV

Battling cancer with viruses

The use of viruses specifically to kill cancer cells is an increasingly emerging area of research due to the impaired ability of many cancer cells to clear virus infection. Research outcomes have been so successful that one virus has already been approved for clinical use in China. Researchers at the University of North Carolina discuss the potential of a widely studied virus, Vesicular stomatitis virus (VSV), to be used as an anti-cancer agent in a recent review. VSV causes infections in animals, including horses, but is generally asymptomatic in humans. So far, VSV has been genetically modified to reduce toxicity and increase selectivity of killing cancer cells. One such VSV strain has been developed to encode interferon, which enhances the immune system to improve oncoselectivity. It has shown so much promise that a phase 1 clinical trial is now underway. With some fine tuning of oncolytic properties, VSV may soon be used alone or as an adjunct to current therapies to fight cancer.

J Gen Virol *doi:10.1099/vir.0.046672-0*
Naomi Osborne *Thermo Fisher Scientific*

Introducing viruses and cancer

LAURA N. HINDLE &
DAVID J. BLACKBOURN

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Almost 1 in 5 cancers are caused by infectious agents, the majority of which are viruses. In this article, the authors present an overview of cancer and tumour virology to complement the accompanying articles in this issue.

AT THE SPRING 2013 SGM CONFERENCE, viruses and cancer will be emphasised with a symposium entitled '*Viruses and cancer: causes to cures*'. This symposium will be complemented by the pre-eminent SGM Prize Medal Lecture, to be given by Harald zur Hausen (pp. 8 & 48). Professor zur Hausen was awarded the 2008 Nobel Prize in Physiology or Medicine '*for his discovery of human papillomaviruses causing cervical cancer*'. In turn, his work led to the development of human papillomavirus (HPV) vaccines that are expected to reduce the global burden of cancer of the cervix.

Over one in three people in the UK will develop cancer during their lifetime. Yet far fewer of us are aware of the association of viruses with cancer development. Globally, the latest figures indicate that of the 12.7 million cases of cancer occurring annually, 16% are attributable to infectious agents. In developing countries, this frequency rises to almost 1 in 4. The majority of these cancer-inducing (oncogenic) infectious agents are viruses, the subject of the present article. Rob Newton provides more insight into the incidence of virus-associated cancers in the following article (p. 22).

In considering the global burden of human cancer, these figures are significant for two reasons. First, these cancers are potentially preventable either by vaccinating people against the oncogenic agents, preventing their infection, or by treating the infections before cancer develops. Second, the study of oncogenic viruses can and has provided a route to understanding the biology of cancer cells.

DISCOVERING CANCER

Although cancer was less common before the 20th century, it is certainly not a new disease. The paleoanthropologist Louis Leakey discovered the first known case of homonid cancer in an archaeological jawbone, which was suggestive of Burkitt's lymphoma occurring at least 300,000 years ago (see timeline on p. 19).

The first contemporary documentation of cancer can be traced back thousands of years to the ancient Egyptians in 3000–1500 BC. In several Egyptian medical manuscripts, such as the Edwin Smith papyrus, a description of cancer can be found.

The concept of behavioural and environmental risk factors influencing cancer development dates back hundreds of years. In 1714, Bernardino Ramazzini noted that nuns developed less cervical cancer (but more breast cancer) compared to the general population. The importance of this observation is reflected in the fact that cervical cancer is now recognised as a sexually transmitted disease, being caused by HPV, a sexually transmitted virus. Ramazzini's work is one of the first great epidemiologic studies and demonstrates the value of epidemiology in helping to identify risk factors in cancer. Subsequently, Percival Pott described in 1755 an occupational cancer of the scrotum in chimney sweeps, caused by their chronic exposure to soot.

In 1838, German pathologist Johannes Muller demonstrated that cancer is made up of cells, while his student, Rudolph Virchow (1821–1902), concluded that all cells, including cancer cells, are derived from other cells. These ideas founded the modern cellular theory of cancer.

DISCOVERING TUMOUR VIRUSES

The origins of virology date back to the end of the 19th century, with Beijerinck studying tobacco mosaic disease in plants and Loeffler and Frosch working on the aetiology of foot-and-mouth disease. Around a decade later, the theory that viruses might cause certain cancers began to emerge, but it took many years for this idea to become widely accepted. Ellerman and Bang published observations on the viral transmission of leukaemia in chickens in 1908 and, in 1911, Peyton Rous reported on sarcoma in chickens being caused by what later became known as Rous sarcoma virus (RSV). He found that he could transfer the sarcoma to other chickens by their inoculation with a cell-free filtrate of the tumour. His work was widely discredited at that time, but in the decades that followed more tumour

viruses were discovered (see timeline). This accumulating evidence began to change opinions and, in 1966, Rous was awarded the Nobel Prize in Physiology or Medicine '*for his discovery of tumour-inducing viruses*', pioneering work he began over 50 years earlier.

The discovery of RSV led to the identification by Harold Varmus and Michael Bishop of the *src* gene that is responsible for RSV-induced tumours. They showed that *src* was a derivative of a normal cellular gene. This discovery of a cellular gene with cancer-inducing potential (or proto-oncogene) was noteworthy because it indicated that some tumours can develop by the aberrant expression of cellular genes responsible for controlling the mechanisms by which cells either divide or die. Expression of the oncogene (a mutant of a proto-oncogene) then permits cell division to proceed unchecked. For this discovery, Varmus and Bishop were awarded the 1989 Nobel Prize in Physiology or Medicine '*for their discovery of the cellular origin of retroviral oncogenes*'. RSV is a retrovirus, which means that it encodes an enzyme activity to reverse transcribe its RNA genome into a 'proviral' DNA copy that integrates in to the host chromosomal DNA. It was complicit in the award of yet another Nobel Prize in Physiology or Medicine to Howard Temin and David Baltimore (with Renato Dulbecco) in 1975 for their discovery of this enzyme activity: reverse transcriptase.

HUMAN TUMOUR VIRUSES

Several types of viruses are now known to be associated with the cause of human cancers. Indeed, according to Harald zur Hausen, viruses confer a risk of developing cancer second only to smoking tobacco. The mechanisms by which they do so are beyond the scope of this article, but some of the accompanying articles address this topic. The known oncogenic human viruses are listed in Table 1 and described briefly below.

EBV

The first human tumour virus was discovered in 1964 when Tony Epstein and Yvonne Barr visualised herpesvirus-like particles in cells from endemic (i.e. occurring in individuals of African origin) Burkitt's lymphoma – the same tumour recognised by Louis Leakey in 1932. This virus was later found to be a novel herpesvirus and was named Epstein–Barr Virus (EBV). The link between EBV and Burkitt's lymphoma was met with scepticism initially, as EBV is insufficient to cause lymphomas: approximately 90% of the population is infected with EBV. However, overwhelming evidence now supports the causal association of EBV with endemic Burkitt's lymphoma, and EBV is now also associated with Hodgkin lymphoma and nasopharyngeal carcinoma (NPC), amongst others. Indeed, Harald zur Hausen's work contributed to the recognition of the role of EBV in Burkitt's lymphoma and NPC. Graham Taylor and James Turner discuss EBV in more detail in the accompanying article (p. 34).

Since the discovery of EBV, strong evidence for five other viruses being associated with the development of human cancers has accumulated, and a sixth virus, Merkel cell polyomavirus (MCPyV), is likely to be added to the list (see Table 1), equating to seven oncogenic human viruses.

TABLE 1. The seven human oncogenic viruses and the major malignancies with which they are associated.

Virus	Malignant disease
Epstein–Barr virus	Burkitt's lymphoma; Nasopharyngeal carcinoma; Hodgkin lymphoma
Hepatitis B virus	Liver cancer
Human papillomavirus	Cervical cancer
Human T-cell leukaemia virus type 1	Adult T-cell leukaemia
Hepatitis C virus	Liver cancer
Kaposi's sarcoma-associated herpesvirus	Kaposi's sarcoma; Primary effusion lymphoma
Merkel cell polyomavirus*	Merkel cell carcinoma

**A causal association between Merkel cell polyomavirus and Merkel cell carcinoma has yet to be formally established.*

HBV & HCV

Hepatitis B virus (HBV) was discovered in 1968 and linked to the development of hepatocellular carcinoma (HCC) in 1975. Subsequently, an HBV vaccine was developed to protect against HBV infection and was implemented in 1980. It is still in use today and was the first vaccine to prevent the development of a specific human cancer. The early studies correlating reduced HBV infection and decreased HCC incidence in Taiwan provided the essential epidemiological link between the virus and the tumour.

In 1989, Michael Houghton and his team discovered hepatitis C virus (HCV) during their studies of non-A, non-B hepatitis. The World Heath Organization estimates that there are more than 170 million people chronically infected with HCV who are at risk of developing liver cirrhosis and HCC. Jane McKeating and Colin Howard discuss HBV and HCV in their accompanying article (p. 30).

HPV

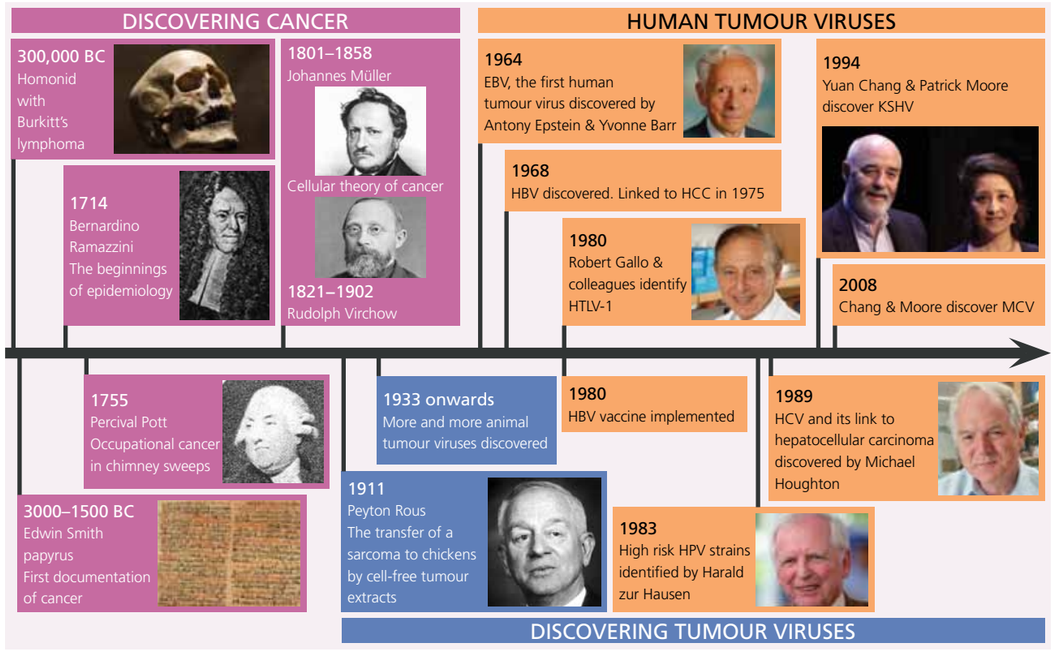
In the early 1980s, Harald zur Hausen identified novel strains of HPV DNA in cervical cancer biopsies. Thus, in 1983 his lab isolated HPV type 16 (HPV-16) in ~50% of the biopsies and in 1984 he reported HPV-18 in ~20%. The importance of these viruses in the cause of cervical cancer was demonstrated by the frequent clonal integration of their genomes in the tumour cells, suggesting the viruses were driving the proliferation of the malignant cells. Moreover, two HPV genes, E6 and E7, were always expressed in the tumours and in pre-malignant lesions, suggesting that these viral proteins were responsible for the malignancy. In 2008, the year of Professor zur Hausen's Nobel Prize, anti-HPV vaccines were introduced into the UK for school-age girls with the aim of preventing their infection with the so-called high-risk strains of the virus, thereby reducing the incidence of cancer of the cervix. Sally Roberts and Jo Parish provide further information on HPV in their accompanying article (p. 26).

HTLV-1

Since RSV, the first oncogenic virus discovered, is a retrovirus, the potential of retroviruses to cause cancer in humans has been of great interest and under intense investigation. The identification of human T-cell leukaemia virus type 1 (HTLV-1) in cutaneous T-cell lymphoma in 1980 by Robert Gallo and colleagues provided one opportunity to analyse the role of this retrovirus in human disease development. It is now recognised as the aetiological agent of adult T-cell leukaemia (ATL). This virus is endemic in certain geographic regions, such as southern Japan and central Africa. However, as with infection with so many oncogenic viruses, only a proportion (1–4%) of infected individuals will develop ATL and the onset of disease can take decades. HTLV-1 can also cause a non-malignant, progressive neurological disease called HTLV-1-associated myelopathy (HAM) or tropical spastic paraparesis (TSP). HTLV-1 transforms cells into a malignant state through the action of the Tax protein. Tax has a multitude of activities, including being able to transform human T-cells by transactivating various cellular promoters, such as those of cytokines and cytokine receptors, leading to signalling cascade activation.

KSHV

Kaposi's sarcoma (KS) was first described in elderly Mediterranean men in 1872 by Moritz Kaposi. The lesions are unusually angioproliferative and inflammatory



Viruses and cancer timeline. *Images: skull, Digital Vision/Thinkstock; Ramazzini, Pott, Smith papyrus & Gallo, public domain; Müller & Virchow, US National Library of Medicine; Rous, NYPL/Science Source/ Science Photo Library; Epstein, Prof. Sir Anthony Epstein CBE FRS, Wolfson College, Oxford; zur Hausen, Armin Kübelbeck; Chang & Moore, I. Atherton, SGM; Houghton, © University of Alberta*

> ” Are there other human viruses yet to be discovered that can therefore be targeted to provide hope in the treatment and prevention of their respective tumours? ”

in nature. It was originally a quite rare cancer, also seen in certain individuals living in Africa and in organ transplant recipients. However, its appearance in young gay men during the 1980s coincided with the beginning of the AIDS pandemic and it is now an AIDS-defining illness. The epidemiology of KS in HIV-infected people, studied largely by Valerie Beral, led many to search for a causal agent that was hypothesised to be a virus. In 1994, the husband and wife team of Yuan Chang and Patrick Moore used a new technique (representational difference analysis) to identify new DNA fragments in KS tissue compared to healthy tissue of the same patient. These fragments belonged to a new virus that Yuan and Patrick called Kaposi's sarcoma-associated herpesvirus (KSHV). Fifteen years after its discovery, KSHV was formally acknowledged as the causal agent of KS and a rare lymphoma called primary effusion lymphoma. Of the 84 genes encoded by KSHV, a subset [e.g. latency-associated nuclear antigen (LANA) and viral cyclin, as well as virus-encoded microRNAs] are expressed during latency drive cell proliferation and inhibit apoptosis. KSHV lytic proteins (e.g. a viral cytokine and viral chemokines) also contribute to the unique pathogenesis of KS.

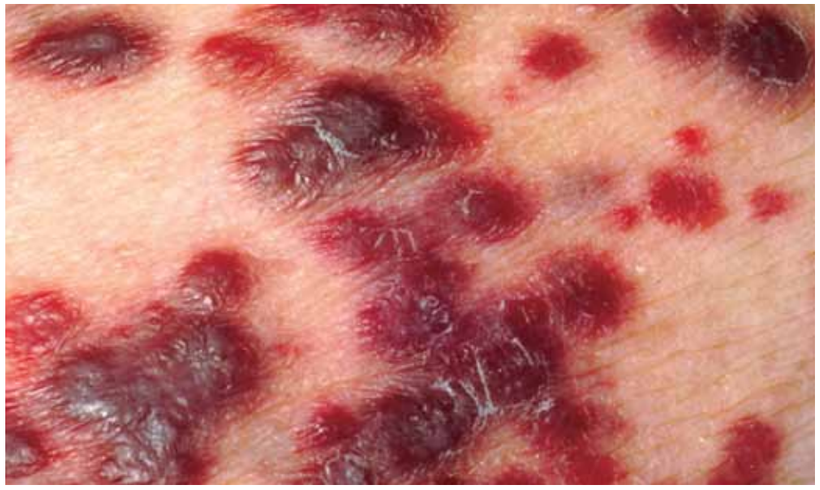
MCPyV

Undeterred by their considerable success in discovering KSHV, Yuan and Patrick went on to discover yet another virus, Merkel cell polyomavirus (MCPyV), this time by a technique they devised called digital transcriptome subtraction (DTS). This virus is very likely to be the cause of Merkel cell carcinoma, an aggressive cutaneous malignancy that arises from neuroendocrine mechanoreceptors (Merkel cells) in the basal layer of the epidermis. As indicated by its name, MCPyV belongs to the *Polyomaviridae* family, members of which have a strong track record in causing tumours, though not necessarily in humans.

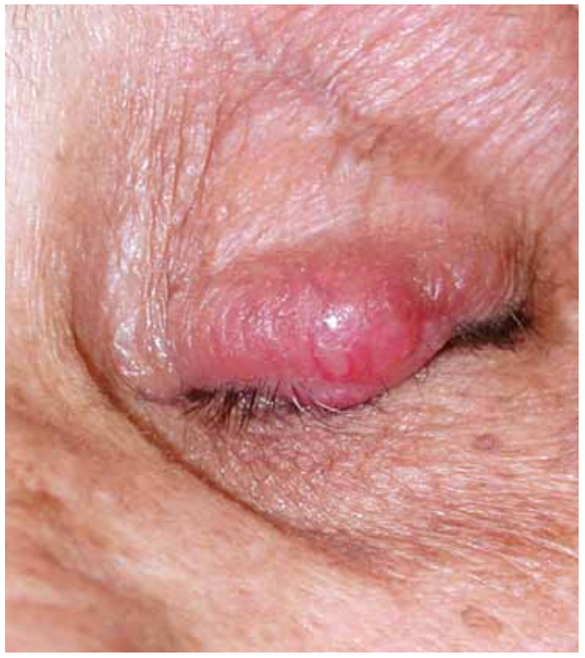
In recognition of their considerable contributions to tumour virology, by their discovery of two novel viruses and their contributions to understanding the biology of them, Yuan and Patrick were awarded the SGM Marjorie Stephenson Prize in 2012, for which their lecture at the Spring conference in Dublin was entitled '*Old themes and new variations in human tumour virology*' (a video of this lecture is available on the SGM *YouTube* channel at **http://bit.ly/14dcTsv**).

TUMOUR VIRUSES DO NOT ALWAYS CAUSE CANCER

A common theme of human tumour viruses is that they are not rare, yet they confer a significant risk for cancer development. This begs the question: why doesn't everyone infected with such viruses develop cancer? First, there are checkpoints built into the mechanism controlling cell division, and overcoming these checkpoints to turn a healthy cell into a malignant transformed cancer cell is not a one-step event. Alfred Knudsen hypothesised in 1971 that one cancer in particular, childhood retinoblastoma, could evolve in as few as two steps. In general it is recognised that multiple (perhaps 4–6) steps need to be overcome in order to generate a transformed cell. Various factors (host genetics, diet, lifestyle, etc.) contribute to each step. Second, the immune system plays an important role in preventing virus-mediated tumorigenesis. Since our immune system is highly adapted to distinguish self from non-self, and viruses represent non-self, the immune system can in many cases recognise viral proteins expressed in transformed cells and eliminate those cells. When the immune system is compromised, surveillance is reduced and the risk of cancer is increased. Thus, cancer development is multistep and multifactorial. Tumour viruses can contribute one of the steps in the pathway.



Kaposi's sarcoma skin plaques on the skin of an AIDS patient. *National Cancer Institute*



Merkel cell carcinoma on the eyelid of an 80-year-old patient. *Paul Nghiem MD PhD; www.merkelcell.org*

THE FUTURE

Understanding virus-associated cancer has made an important impact on improving human health. The implementation of an HBV vaccine dramatically reduced infection with this virus, and concomitantly HBV-associated HCC.

Another success is likely to be the efficacy of HPV vaccines in reducing the human burden of cancer of the cervix. New generation therapeutics inhibiting HCV replication and undergoing clinical trials may likewise reduce the burden of HCC associated with this virus. Hopefully these success stories will continue.

But what's next? Are there other human viruses yet to be discovered that can therefore be targeted to provide hope in the treatment and prevention of their respective tumours? With current and rapidly developing molecular tools, we may not need to wait too long to find out.

LAURA N. HINDLE & DAVID J. BLACKBOURN

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FURTHER READING

www.nobelprize.org/nobel_prizes/medicine/

www.who.int/csr/disease/hepatitis/en/index.html

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Collectively, infections are the most important established cause of cancer after tobacco. What are the prospects for prevention of infection-associated cancers, and what challenges does the research community face?

Cancers attributable to infection – the global burden

ROBERT NEWTON

USING GLOBAL DATA on cancer incidence and mortality from 2008, it was estimated that there were 12.7 million new cancer cases that year and 7.6 million deaths; about two-thirds of cancer deaths occurred in less-developed countries. Of those cancer cases, about 16% (approximately 2 million cases) were estimated to be attributable to infections (viruses, macro-parasites and a bacterium). About 1.9 million cases were caused by human papillomaviruses (HPVs), hepatitis B and C viruses (HBV and HCV) and the gastric bacterium *Helicobacter pylori*. The proportion of cancers caused by infection tends to be higher in less-developed than in developed regions (approximately 23 versus 7%), reflecting the background prevalence of the underlying causal infections; indeed in parts of sub-Saharan Africa, the proportion is more than a third of all cancer cases. Among women, carcinoma of the uterine cervix is by far the most common infection-associated cancer (about 50% of the total) and, in men, liver and gastric cancers account for about 80% of the total. Those cancers that are attributable, at least in part, to underlying infections are shown in Table 1.

Estimating the burden and geographical distribution of cancer and specifically of infection-associated cancer is far from straightforward. Cancer incidence is defined as the frequency of new cases of cancer in a defined population over a specific time period and accurate data are important, not just for identifying levels of disease, prioritising health service activity and monitoring success of cancer control initiatives, but also because understanding patterns of disease occurrence underpins epidemiology and can provide insights into aetiology. For example, Denis Burkitt's careful mapping of the distribution of the tumour that now bears his name led him to postulate an underlying infectious cause, ultimately leading to the discovery of the first human oncogenic virus – the Epstein–Barr Virus (EBV).

The series *Cancer Incidence in Five Continents* (CI5), first published in 1962 and soon to emerge in its 10th volume, compiles and presents incidence data from the best (as defined by highly specific criteria for data quality and completeness) population-based cancer registries in the world. However, there is significant geographic variation in the availability of such data – whilst the most recent volume of CI5 covers about 83% of the population of North America, 6, 4 and 1% of the populations of South America, Asia and Africa, respectively, are covered by such registries. Taking Africa as an example, out of 53 countries, only five have cancer registries of sufficient quality to be included in the latest volume of CI5 – Algeria, Egypt, Tunisia, Uganda and Zimbabwe (http://globocan.iarc.fr). In addition, there are around 50 local registries (which do not meet the stringent inclusion criteria for CI5) covering a further 7% of the African population, although these predominantly encompass urban rather than rural areas. In such countries, cancer registration is bedevilled by three related problems: (i) inadequate characterisation of disease – histological verification of diagnosis is typically only available for a proportion of cases; (ii) incomplete ascertainment of cases, particularly at older ages; and (iii) inadequate ascertainment of population denominator data (from a census). Therefore, any assessment of the burden of cancer – and within that, the burden just of those cancers caused by infections – is complex and potentially inaccurate.

In addition to the problems of measuring the burden of specific cancers highlighted above, there are other concerns associated with estimating the proportion of each cancer type caused by specific infections (the Population Attributable Fraction). It requires the best available evidence on the causal effect of each infection together with an accurate estimate of the prevalence of

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> "Understanding the role of infections as a cause of cancer is important, since many infection-associated tumours are avoidable."

TABLE 1. Cancers caused – at least in part – by infectious agents

Infectious agent(s)	Cancers
Epstein–Barr virus	Nasopharyngeal carcinoma, Burkitt's lymphoma, post-transplant lymphoproliferative disease, extra-nodal NK/T-cell lymphoma, Hodgkin lymphoma, gastric carcinoma, lympho-epithelioma-like carcinoma
Hepatitis B virus	Hepatocellular carcinoma, cholangiocarcinoma, non-Hodgkin lymphoma
Hepatitis C virus	Hepatocellular carcinoma, cholangiocarcinoma, non-Hodgkin lymphoma
Kaposi's sarcoma-associated herpesvirus	Kaposi's sarcoma, primary effusion lymphoma, multicentric Castleman's disease
Human immunodeficiency virus type 1	Kaposi's sarcoma, non-Hodgkin lymphoma, Hodgkin lymphoma, carcinomas of the cervix, anus and conjunctiva (possibly also the vulva, vagina, penis and liver) [note: HIV-2 has been associated with Kaposi's sarcoma and non-Hodgkin lymphoma]
Human papillomavirus type 16	Carcinomas of the cervix, vulva, vagina, penis, anus, oral cavity, oropharynx, larynx and tonsils [note: HPVs 18, 31, 33, 35, 45, 52, 58 and to a lesser extent, 39, 51, 56, 59, have also been associated with cancer of the cervix in particular]
Human T-cell leukaemia virus type 1	Adult T cell leukaemia/lymphoma
Merkel cell polyomavirus	Merkel cell carcinoma
Helicobacter pylori	Non-cardia gastric carcinoma, gastric B-cell lymphoma of mucosa-associated lymphoid tissue
Clonorchis sinensis	Cholangiocarcinoma
Opisthorchis viverrini	Cholangiocarcinoma
Schistosoma haematobium	Urinary bladder cancer [note: *Schistosoma japonicum* has also been linked with colorectal and liver cancers]
Malaria	Burkitt's lymphoma

For most of the associations shown, the evidence has been considered robust enough that the International Agency for Research on Cancer (IARC) have classified the infections as being Group 1 carcinogens (definitely carcinogenic to humans). For Merkel cell polyomavirus and malaria, the classification is Group 2A (probably carcinogenic to humans).

infection among cases (which may vary by geographic region). Inevitably, the estimates rely both on the quality of source data and, where data are few, on the statistical methods used to overcome these problems. For example, human papillomavirus (HPV) is considered to be a necessary cause of cancer of the cervix and Kaposi's sarcoma-associated herpesvirus (KSHV) of Kaposi's sarcoma, but EBV or human T-cell leukaemia virus type 1 (HTLV-1) cause only a proportion of lymphomas and leukaemias. Nor do these estimates take into account the impact of multiple infections on cancer risk, such as the combined effects of EBV and malaria on the risk of Burkitt's lymphoma.

One further problem, of course, is that there may be other cancer sites or types, not listed in Table 1, that have an underlying infectious aetiology yet to be discovered. For example, the substantial excess risk of cutaneous squamous cell carcinoma among immune-suppressed individuals has led many to suspect an underlying infectious aetiology – certain cutaneous HPV types have been investigated, but evidence remains scant. Historically, such epidemiological clues have provided the evidence required to prompt a search for an underlying infectious cause of cancer. The extraordinary geographic variation in the incidence of Burkitt's lymphoma and its association with the distribution of holo-endemic malaria is a classic example. Take too, the association of cancer of the cervix with sexual behaviour, highlighted in a seminal paper by Beral in 1974 (and followed by others), which led to the identification of the sexually transmitted infection HPV-16 by zur Hausen and colleagues in 1983. Similarly, the distinctive epidemiological features of Kaposi's sarcoma – again highlighted by Beral and others – prompted a search for the underlying infectious cause, subsequently identified by Chang & Moore in 1994. More recently, the association between human immunodeficiency virus (HIV)-related immune suppression and Merkel cell carcinoma prompted the discovery of Merkel cell polyomavirus (MCV), again by Chang & Moore. Indeed, throughout the history of infections and cancer, it is the multi-disciplinary combination of epidemiology and virology that has proved highly successful in uncovering the causes of a range of malignancies.

Understanding the role of infections as a cause of cancer is important, since many infection-associated tumours are avoidable. For example, malignancies caused by HPV and HBV are preventable by vaccination. Most notably, in Taiwan, the incidence of hepatocellular carcinoma has fallen markedly since the introduction of vaccination against HBV, coupled with the provision of immunoglobulin at birth to prevent vertical transmission. Similarly, vaccines against HPV have shown nearly 100% efficacy in preventing HPV-16 and -18-induced precancerous lesions of the cervix. No vaccine is yet commercially available for any other cancer-causing infection, but for HCV, iatrogenic transmission can be avoided with safer injection and transfusion practices. This is true for some HIV infections, which can also be avoided via behaviour change and, more recently, by widespread use of anti-retroviral drugs, which reduce transmission of infection at a population level. Perinatal transmission of HTLV-1 has been greatly reduced in Japan by avoidance of prolonged breast-feeding, although this is not an option for many developing countries, where alternatives may not be available and where the risk of death from diarrhoeal disease rises markedly if breast-feeding is curtailed. *H. pylori* is a treatable infection and indeed prevalence of infection – and incidence of stomach cancer – has been falling in many populations for years. The value of large-scale eradication trials, however, remains uncertain.

So, the prospects for prevention of infection-associated cancers are good, although it may be decades before the impact of prevention programmes are manifest in the general population. It also seems likely that further discoveries will be made, linking known or novel infections to additional cancer sites or types. Finally, the growing importance of co-infection as a risk factor for certain cancers is becoming better recognised and presents fresh challenges to the research community.

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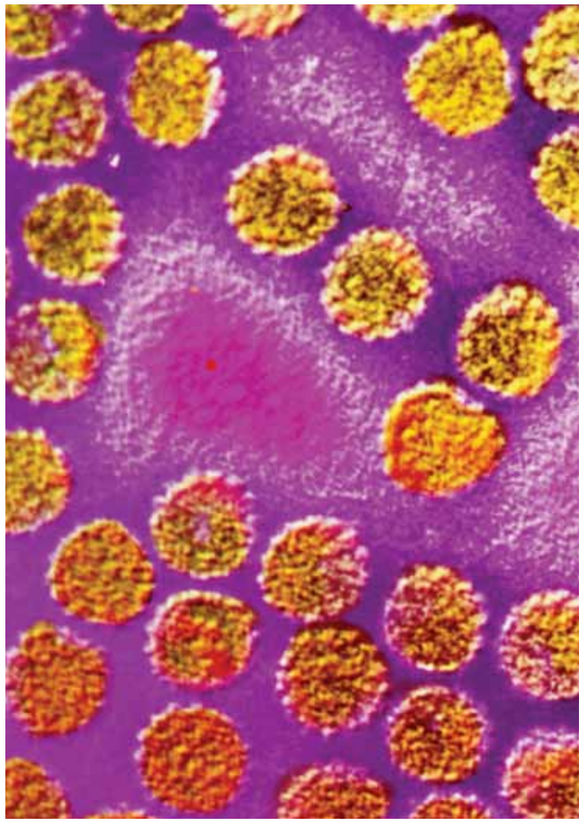
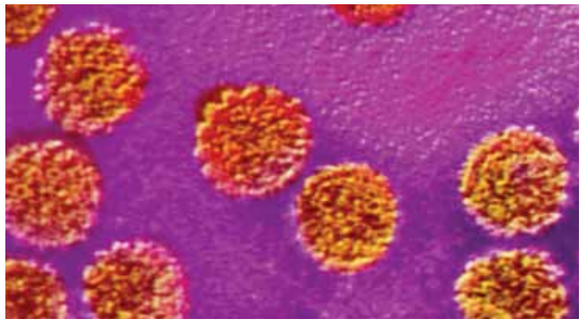


Human papillomaviruses

JO PARISH &
SALLY ROBERTS

Warts on the skin caused by human papillomavirus (HPV) may be relatively harmless, but a few of the nearly 120 strains of HPV identified to date have far more serious consequences. What mechanism do they use to induce cancer and what can be done about it?



HUMAN PAPILLOMAVIRUSES (HPV) are small, double-stranded DNA viruses that infect epithelial tissue, such as skin and the 'wet' mucosal epithelial linings of the anogenital tract and oropharynx, generally inducing warts and papillomas. To date, nearly 120 distinct genotypes of HPV have been identified and whilst infections caused by the majority of these types are not a clinical burden, a small number have been shown to induce disease of significant clinical relevance. Some types are linked to the development of non-melanoma skin cancers, and some, such as HPV-6 and HPV-11, are the primary cause of genital warts. A subset of 13 HPV types is associated with the development of cancers of the anogenital tract (cervix, vulva, vagina, penis and anus) and of the head and neck (tonsil, base of tongue and oropharynx). Even within this group of 'high-risk' viruses, some types are more prevalent than others; HPV-16 is most commonly associated with squamous cell carcinoma of the cervix and head and neck carcinomas, whilst HPV-18 is the most frequent type found in cervical adenocarcinomas.

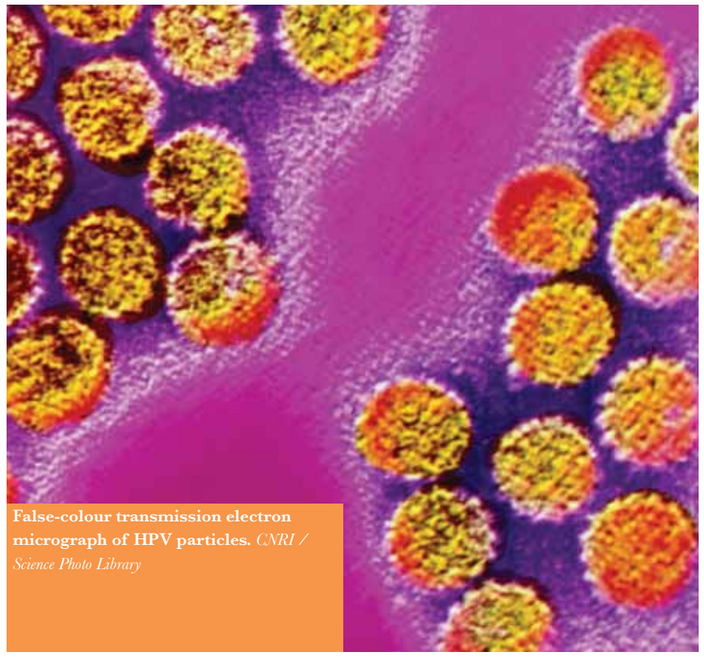
HPV-INDUCED CARCINOGENESIS

What is it about the high-risk viruses that differentiates their pathogenesis from that of the vast majority of HPVs? This was largely answered when the functions of the viral proteins E6 and E7 of high-risk viruses were compared with those of the non-cancer-causing viruses. These two HPV proteins act in a cooperative fashion to promote cell proliferation so the virus can utilise the host's DNA replication machinery, and to ensure cell survival such that the virus replicates before the cell dies. The E6 and E7 proteins of high-risk viruses have evolved different strategies to accomplish these functions.

Thus, through deregulation of two major tumour suppressor pathways (Rb and p53), the viral oncoproteins create an environment that is beneficial for virus replication in the differentiating cell of the infected epithelium. However, since the p53 pathway has a critical role in sensing genomic damage and instigating its repair, the high-risk viruses, through deregulation of p53 signalling have created an environment that promotes genetic instability of cellular DNA that subsequently goes unchecked. Persistent high-risk infections therefore have an increased risk of the emergence of immortal cells, which have a better growth advantage than surrounding cells, and an increased risk of acquiring oncogenic mutations leading to malignancy.

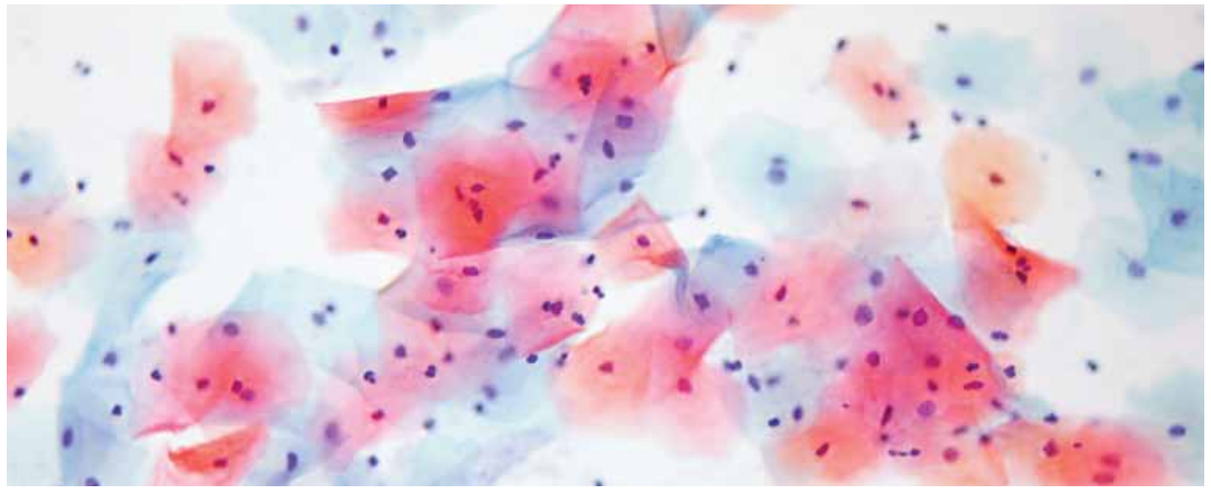
Another characteristic of high-risk HPV types relevant to their oncogenic nature is the tendency of their genomes to integrate into the host DNA. The site of breakage within the viral genome is preferentially restricted to a region encoding the viral transcriptional

The key role of the high-risk E7 oncoprotein is to induce hyperproliferation of host cells by targeting multiple processes controlling cell-cycle regulation. This includes the retinoblastoma (Rb) family of tumour suppressors that regulate entry into S phase, where DNA synthesis occurs. By binding to Rb and inducing its degradation, E7 induces the release of the E2F family of transcription factors that activate the expression of genes necessary for S phase entry. The host response to unscheduled activation of the cell's replication machinery is the induction of apoptosis. This is counteracted by the E6 oncoprotein that has evolved several strategies to block this cell signal, including the targeted degradation of the main executioner of this response, the tumour suppressor protein p53.

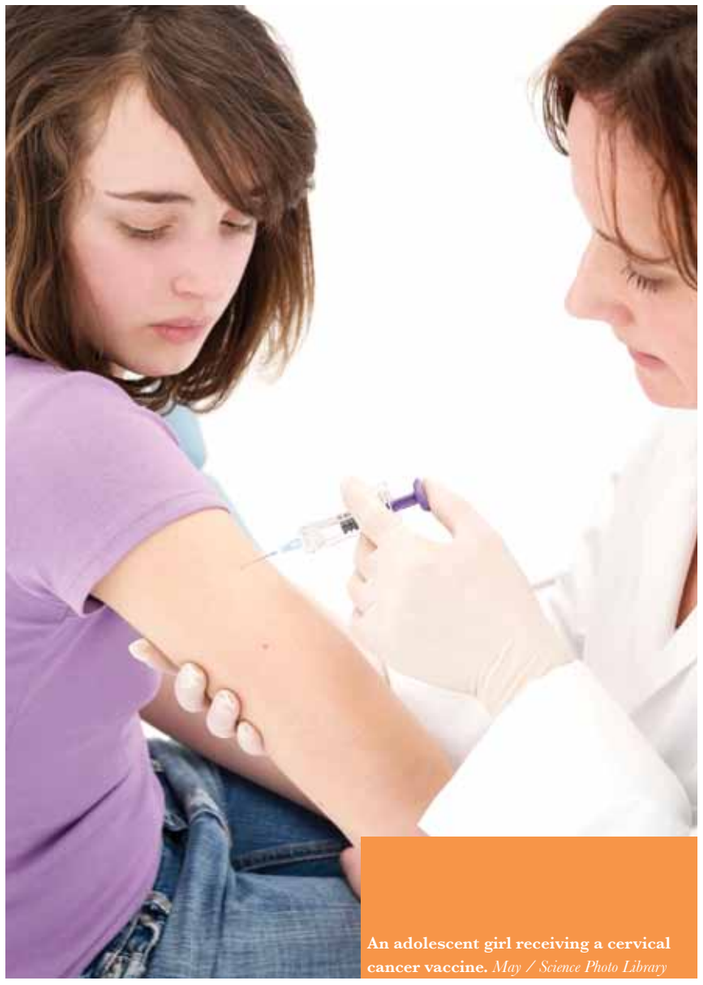


False-colour transmission electron micrograph of HPV particles. *CNRI / Science Photo Library*

> "The development of HPV-associated cancer is a late and rare complication of persistent infection by high-risk HPV types and is the end game of a chain of events that unfold over many years."



Light micrograph of HPV-infected cells from a cervical smear showing typical clear cytoplasm and enlarged nuclei (purple). *Biomedical Imaging Unit, Southampton General Hospital / Science Photo Library*



An adolescent girl receiving a cervical cancer vaccine. *May / Science Photo Library*

regulator, E2. The consequence of integration is therefore the severance of the negative feedback signal mediated by E2 upon the expression of E6 and E7, resulting in unchecked expression of these two oncoproteins.

The development of HPV-associated cancer is a late and rare complication of persistent infection by high-risk HPV types and is the end game of a chain of events that unfold over many years. However, infection by these viruses is necessary for the initiation and maintenance of the cancer phenotype and the virus is therefore an important target for antiviral intervention and therapeutic treatments.

COMBATING HPV-INDUCED DISEASE

To combat HPV-induced disease, clinicians and researchers have developed an arsenal of prophylactic and therapeutic strategies. Nonetheless, HPV-associated disease is still significant, particularly in the developing regions of the world, where high-risk HPV infections and the consequent cancers are rarely diagnosed or treated; cervical cancer remains the most common cancer in women worldwide, especially in sub-Saharan Africa. Moreover, in these parts of the world the recently developed prophylactic vaccines are not widely available for financial and logistical reasons.

The introduction of cervical screening in 1964 in the UK has been followed by substantial reductions in mortality caused by cervical cancer. When it was realised that HPV was a necessary and sufficient cause of cervical cancer, it was hoped that the detection of HPV DNA sequences in cervical smears could be used to improve the effectiveness and efficiency of cervical screening. Towards this end, the NHS is trialling a new protocol for cervical screening in which women found to have borderline or mild dyskaryosis are routinely tested for HPV sequences. Those women that are positive for high-risk HPV will be sent directly for microscopic examination of the cervix (colposcopy), instead of cytological surveillance every 6 months. Women who are negative, however, will be returned for routine surveillance every 3–5 years. This new screening protocol will reduce the rate of repeat smears, but increase the number of women referred for colposcopy.

Notwithstanding the extraordinary progress that has been made towards the diagnosis and treatment of cervical and other anogenital malignancies in more developed countries, HPV-associated cancers continue to be an important source of morbidity and mortality. In 2010, there were over 6,500 new cases of HPV-associated cancers diagnosed and over 2,000 deaths from these cancers in England alone.

In the UK, since 2008 there has been a national programme for the vaccination of girls aged 12 to 13 using a bivalent vaccine called Cervarix, which targets HPV-16 and HPV-18 that together cause 70% of cervical carcinomas. In 2012, the NHS announced a change in the HPV vaccine used. Gardasil, a quadrivalent vaccine which confers resistance to HPV-16, -18, -6 and -11 is now in use. Trials with both of these vaccines have shown significant protection against HPV-16- and HPV-18-related carcinomas and, in addition, Gardasil has an efficacy of almost 90% against genital warts.

The antigens in both vaccines are virus-like particles (VLPs) composed of the L1 major capsid protein. Due to conformational changes that are required at the surface of HPV virions during virus entry into the host cell, virus entry takes several hours. The presence of VLP-induced antibodies prevents attachment of the virus to the basement membrane underlying the epithelia and entry into host cells. This means that while Gardasil and Cervarix are extremely effective for prophylactic use, individuals that already have a persistent HPV infection cannot benefit from vaccination. It is for this reason that the vaccine is specifically targeted to young girls before they have reached their sexual debut. The prevention and treatment of HPV-associated disease in unvaccinated individuals therefore remains a priority. At present, therapies for anogenital HPV infections are limited. Surgical ablation, which is effective in the short-term but associated with high recurrence rates, and cytotoxic agents, such as trichloracetic acid and podophyllotoxin, are common in the treatment of genital warts, but have issues with patient tolerance. Immune modulators, such as Imiquimod, applied topically to genital warts have high efficacy and reduced recurrence rates, but acute and severe local inflammation can be problematic.

Maintenance of the malignant phenotype absolutely requires the expression of E6 and E7 oncoproteins. Targeting these proteins to treat HPV-induced disease is therefore an appropriate strategy. Trials of therapeutic HPV vaccines composed of E6 and E7 peptides in various forms have shown efficacy in the clinical regression of benign and pre-cancerous lesions, but a successful outcome is not so obvious in patients with high-grade cancer.

In addition to the development of therapeutics useful in treating HPV-associated disease, work is on-going to develop antiviral compounds. The inhibition of HPV DNA replication by chemical inhibition of the viral E1 helicase is one such strategy and, while potent molecules have been developed *in vitro*, these compounds are not effective *in vivo*. Similarly, the potential to block DNA binding of E1 or the viral replication/transcriptional regulator protein E2 has been explored, with only a handful of compounds showing activity *in vivo*.

Undoubtedly, the development of prophylactic vaccines has been an important step in our effort to control HPV infection. However, it is clear that the incidence of some HPV-associated cancers is increasing and, along with high levels of HPV-associated cancers in the developing regions of the world, the race to prevent and treat HPV infection is far from over.

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JANE A. McKEATING & COLIN R. HOWARD

Viral hepatitis and hepatocellular carcinoma

What strategies can we use to tackle virus-induced liver cancer, a serious and increasing public health problem?

PRIMARY LIVER CANCER, or hepatocellular carcinoma (HCC), is the most common liver malignancy with an estimated 750,000 new cases and 695,000 deaths per year, rating third in incidence and mortality in the world. Whilst the majority of cases occur in the Far East and Sub-Saharan Africa, HCC diagnosis is increasing in Europe. Recent Cancer Research UK figures project a 40% increase in HCC in the UK between 2010 and 2030. Whilst incidence and mortality for other common cancers are declining, this cancer represents an increasing public health problem. HCC is a complex and heterogeneous tumour with limited treatment options and poor prognosis due to recurrence and metastases. Hence, there is a real need to increase our understanding of the mechanisms underlying HCC pathogenesis to provide new targets for therapeutic intervention and vaccination.

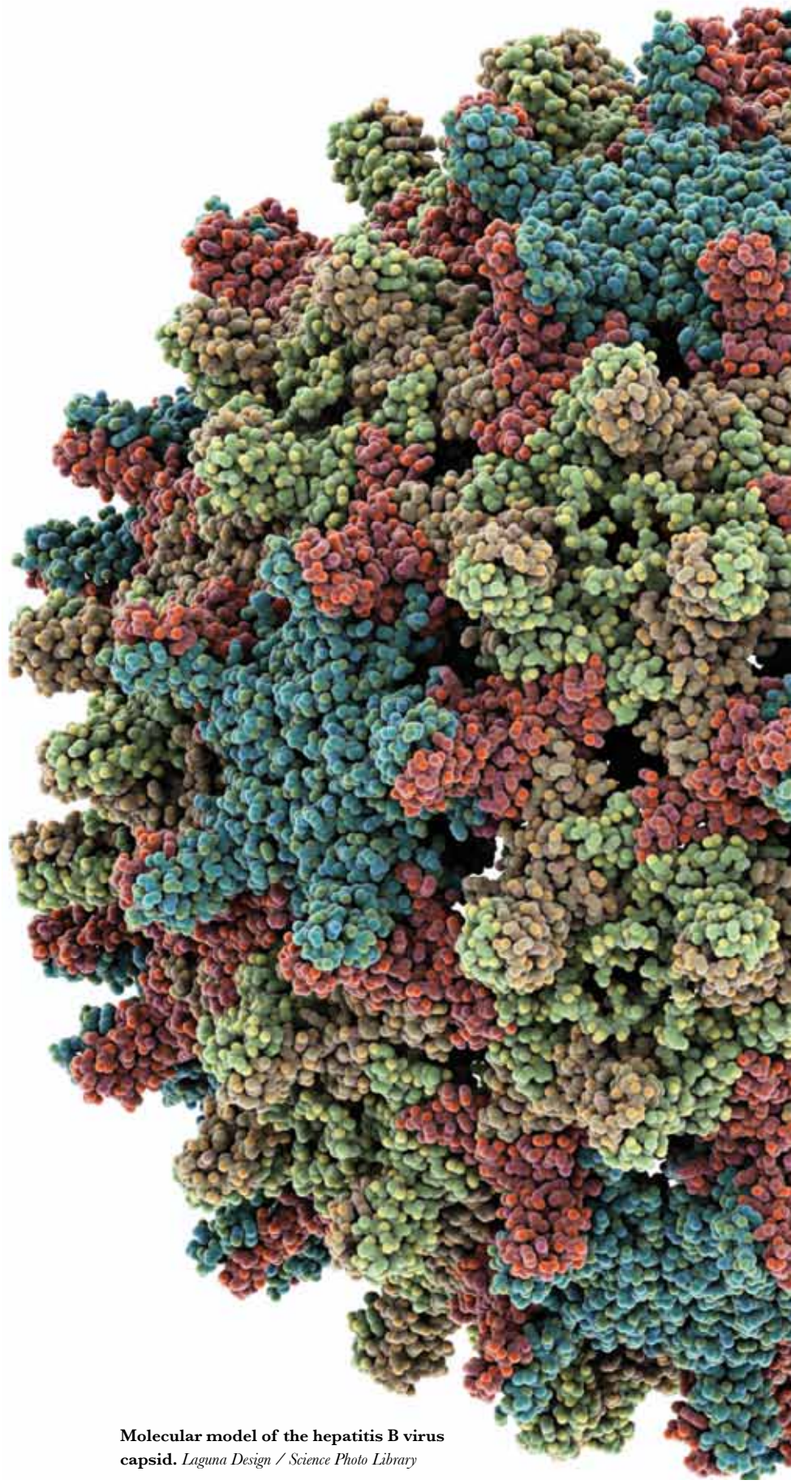
Hepatitis B virus (HBV), a DNA virus in the family *Hepadnaviridae*, has been implicated in the development of HCC. Depending on the geographic area, more than 50% of HCC cases are attributed to HBV and infected subjects have an approximate 100-fold increase in the relative risk of developing HCC compared to uninfected patients. By comparison, smoking increases the risk of cancer tenfold. In contrast, where HBV prevalence is low, such as the USA, Europe and Japan, chronic hepatitis B is associated with fewer than 20% of HCC cases. These countries have witnessed a marked increase in the incidence of hepatitis C virus (HCV)-associated HCC, an RNA virus closely related to the flaviviruses.

The liver undergoes rapid regeneration following destruction of hepatocytes, maximising the opportunities for the development of chromosomal abnormalities leading to HCC. The observation that HBV and HCV, two viruses with such widely differing replication strategies, are the major agents predisposing the human liver to cirrhosis and hepatoma suggests an indirect role for infection in the carcinogenic process. Abnormalities arising from prolonged infection with either virus are most likely exacerbated by environmental factors, such as aflatoxin, alcohol abuse or the release of superoxides and free radicals associated with chronic inflammation.

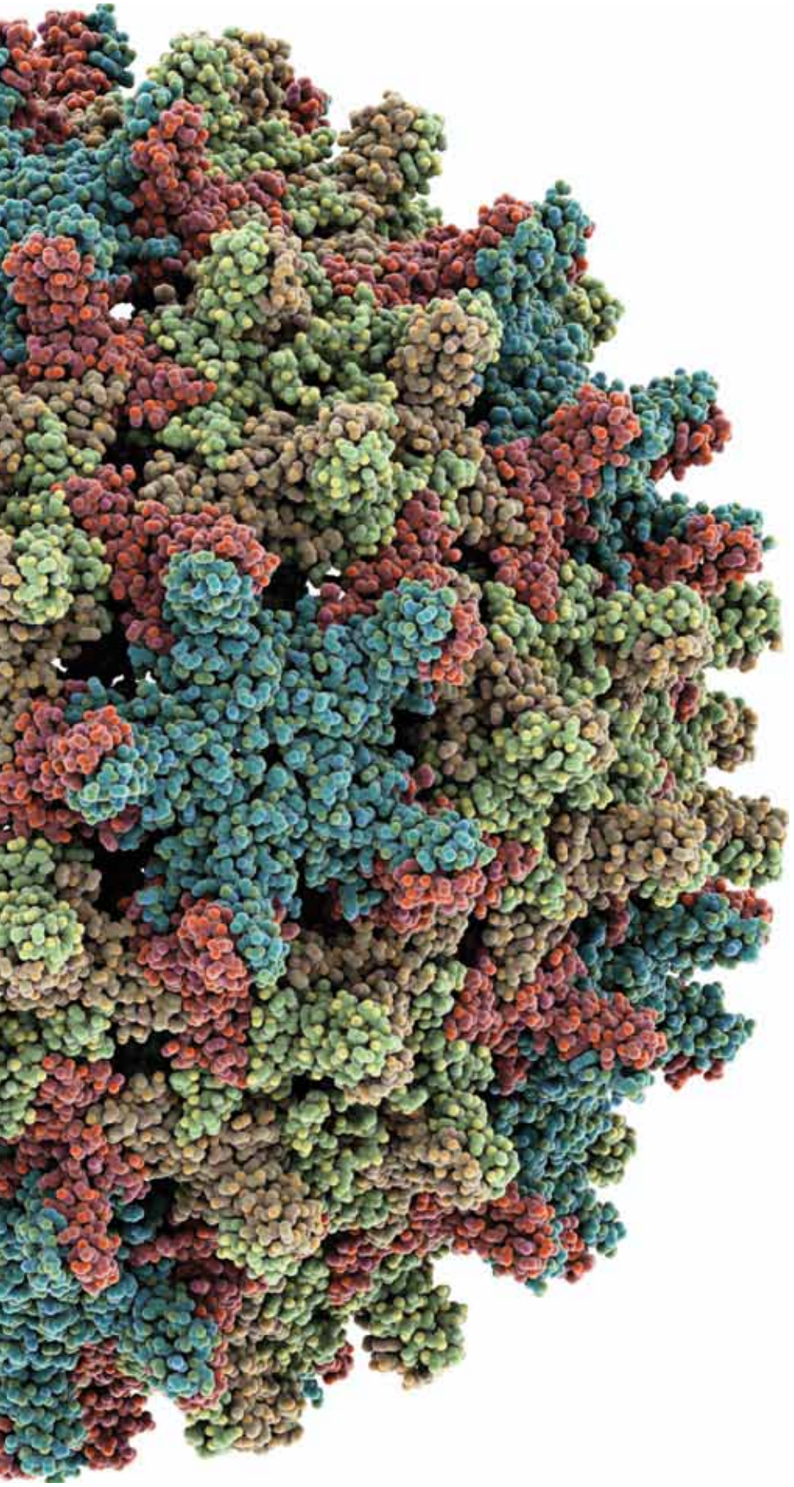
HBV

The evidence for a causal relationship between HBV infection and HCC is overwhelming. Active HBV infection and HCC share a common geographic distribution and most HCC cases arise in HBV carriers. A landmark prospective study of 22,000 individuals in Taiwan showed that men positive for HBV had over 200 times the rate of HCC, compared to a similar, uninfected cohort. HBV infection may lead indirectly to hepatoma development following chronic liver injury, due to immune attack on virus-infected hepatocytes. Chronic liver regeneration predisposes to tumour development. This concept is supported by the fact that alcoholic cirrhosis predisposes to HCC.

Woodchucks (*Marmota monax*) infected with the woodchuck hepatitis B virus



Molecular model of the hepatitis B virus capsid. *Laguna Design / Science Photo Library*

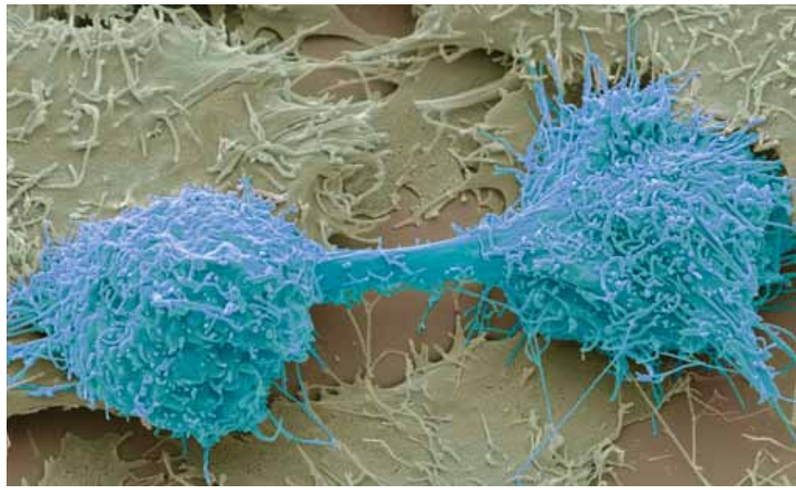


> "The introduction of HBV vaccines into childhood immunisation programmes over the next two decades will lead to a marked reduction in HCC in countries where the virus is endemic."

(WHBV) have provided a valuable model to study the role of HBV in HCC pathogenesis, with the majority of animals infected as neonates developing liver cancer by 3 to 4 years of age. Activation of the *N-myc* oncogene has been associated with the integration of WHBV DNA in over 90% of tumours; however, this insertional activation of a common oncogene has not been found in human HCC.

Tumours are usually clonal with respect to the integrated viral sequences, suggesting that integration occurs prior to the expansion of tumour cells, many years prior to the development of cancer. The hepadnavirus genome does not contain a known oncogene: cellular enzymes such as topoisomerase I are thought to be responsible for recombination, which is not restricted to any specific region of the host chromosome. HBV integration promotes genetic instability by undergoing repeated mutations, deletions and inversions. The mammalian hepadnaviruses contain a gene, X, which encodes a *trans*-activating protein that is absent in the genome of non-oncogenic avian hepadnaviruses; however, conclusive evidence that the X gene is a mediator of hepatocyte oncogenesis is lacking. It has been noted that X may be required for the early stages of oncogenesis, but not for later stages, since HBV gene expression is close to zero in HCC tumours. Unregulated X expression is associated with hepatocyte carcinogenesis in transgenic mice. The surface glycoproteins, or truncated products, may also participate in carcinogenesis but none of the seven HBV polypeptides appear to act as dominant oncogenes.

Coloured scanning electron micrograph of an HCC cell undergoing mitosis. *Steve Gschmeissner / Science Photo Library*



HCV

Over 75% of individuals parenterally exposed to HCV develop a persistent infection and, among this cohort, up to 5% develop HCC later in life. Although this percentage is small, globally this represents around 9 to 10 million cases at any one time. HCV causes chronic liver injury that can progress to severe fibrosis and cirrhosis. HCV is a positive-stranded RNA flavivirus that replicates in the cytoplasm and does not integrate into the host genome, supporting the hypothesis that hepatocellular carcinogenesis occurs via indirect effect(s) of infection on chronic inflammation and hepatocyte injury. However, inflammation alone is not sufficient to cause HCC since conditions such as autoimmune hepatitis rarely develop HCC. Several HCV-encoded proteins have been reported to play a role in the development of HCC in experimental and transgenic animal systems. However, many of these reports have studied HCV proteins expressed in isolation, raising questions on the physiological relevance of the model systems. Recent advances allowing the assembly of infectious HCV particles *in vitro* will enable studies to investigate the effect(s) of virus replication on host cellular pathways involved in oncogenesis.

MicroRNAs (miRNAs) are increasingly a focus of interest in the role of HBV or HCV in hepatocarcinogenesis. HCV replication is dependent upon miR-122, a liver-specific miRNA that plays a key role in tumour suppression, and HBV has been shown to alter the expression profiles of this and other miRNAs. But how these altered profiles predispose hepatocytes to cellular transformation remains to be elucidated.

CONCLUSION

Most HBV chronic infections are acquired in the first few months of life and such long-term carriers are at high risk of developing HCC in adulthood. For this reason, it is recommended that infants in regions of high HBV prevalence are vaccinated at or shortly after birth. Vaccination against HBV has proven effective, not only in reducing the prevalence of HBV carriage, but in lowering the incidence of HCC later in life, thus making HBV vaccines the first widely available vaccine against a human cancer.

Antivirals are increasingly effective for the treatment of chronic HBV and HCV infection and, although their use may retard the development of cirrhosis and HCC, there is no definitive evidence that their application can prevent the development of HCC unless administered early after infection and virus infection is resolved. In both cases, surveillance is key in order to identify those individuals at risk of developing HCC: the introduction of HBV vaccines into childhood immunisation programmes over the next two decades will lead to a marked reduction in HCC in countries where the virus is endemic. It is to be hoped that a similar strategy could prove equally as effective to reduce the burden of HCV infection and thus effectively eliminate virus-induced liver cancer in years to come.

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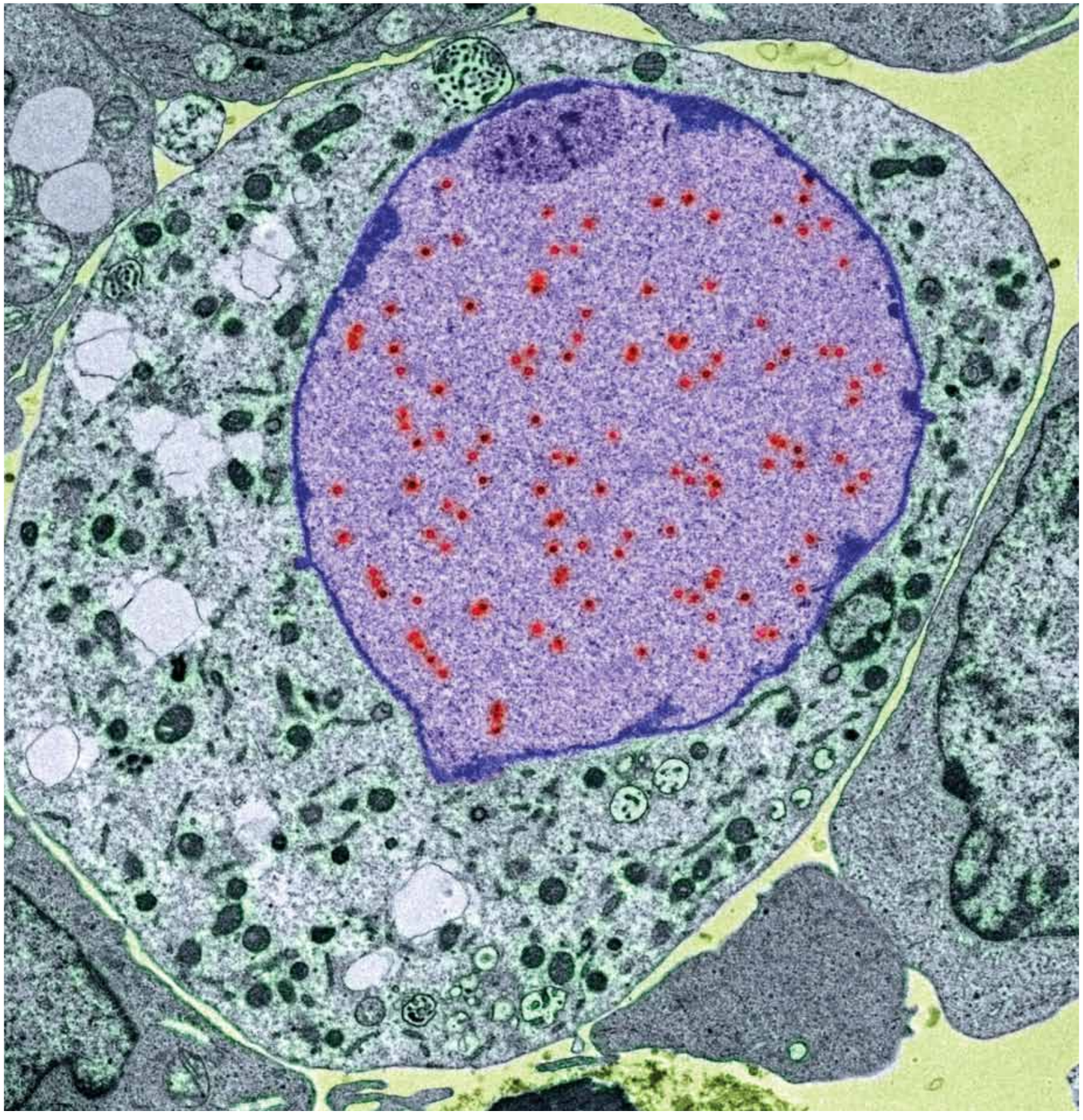
Epstein–Barr virus: opportunities for prophylactic and therapeutic vaccines

JAMES E. TURNER & GRAHAM S. TAYLOR

Epstein–Barr virus is now known to be associated with several forms of cancer, in addition to its potential to cause glandular fever. Are vaccines the answer to conquer this ubiquitous virus?



Coloured transmission electron micrograph of EBV particles (red) in the nucleus of a malignant white blood cell. *Steve Gschmeissner / Science Photo Library*

THE BURDEN OF EBV-ASSOCIATED DISEASES

Given that it infects over 90% of people worldwide, Epstein–Barr Virus (EBV) is a highly successful pathogen. We have co-evolved with this virus over millions of years, achieving a state of détente. EBV infection during childhood, which until recently was the normal state of affairs, usually passes unnoticed. Improvements in living standards mean that, increasingly, infection is delayed until adolescence or later, whereupon EBV infection can cause infectious mononucleosis (glandular fever) with symptoms of fever, sore throat, swollen lymph nodes and a debilitating fatigue that can persist for months. While most people mount a strong immune response able to control their EBV infection, the virus nevertheless establishes a lifelong infection of B cells hidden from the immune system. Periodically, the virus reactivates in some of these cells to complete its life cycle, producing new viruses that are spread to other people via saliva.

However, since its discovery in 1964 in Burkitt's lymphoma cells, several other cancers have been linked to EBV. In terms of morbidity and mortality two cancers stand out. Nasopharyngeal carcinoma (NPC) is rare in most Western countries but prevalent throughout South East Asia. Some 75,000 cases occur each year, of which almost all are positive for EBV. More recently, EBV has been found in almost 10% of gastric carcinoma

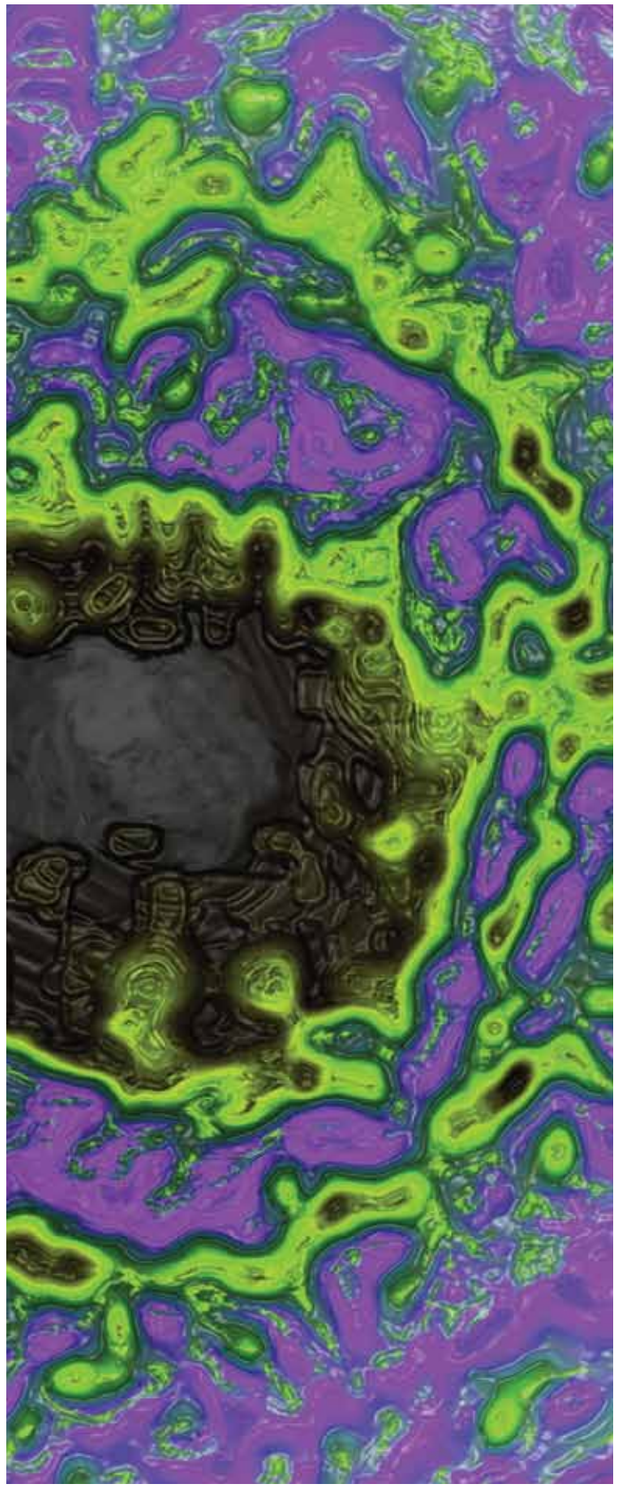
"Even if the perfect prophylactic EBV vaccine became available tomorrow, millions of people already infected with the virus will go on to develop virus-associated cancers."

tumours. Although the proportion of virus-positive gastric carcinomas is much lower than NPC, there are far more cases of this disease worldwide (an estimated 1 million cases per year). This means that the number of virus-positive cases of these two cancers is actually very similar. EBV is also associated with several different lymphomas, the most common being Hodgkin lymphoma. In total, almost 200,000 cases of EBV-associated cancer occur each year worldwide.

PROPHYLACTIC VACCINES TO PREVENT EBV INFECTION

Prophylactic or preventative vaccines have been successfully developed for several viruses including two human tumour viruses (hepatitis B virus and human papillomavirus). Given the burden of EBV-related disease in terms of cancer, but also the debilitating effects of infectious mononucleosis, a similar vaccine to prevent EBV infection would have a substantial health and economic impact. Most vaccine efforts to date have focused on a single EBV protein, called gp350, because antibodies to this protein brought about by natural virus infection are also able to inhibit virus infection of cells in the laboratory. A clinical trial performed in EBV-uninfected young adults showed that a vaccine consisting of purified gp350 protein reduced the incidence of infectious mononucleosis, but was unable to protect against virus infection. While such a vaccine could offer some benefit, for example by reducing the incidence or severity of infectious mononucleosis in uninfected adolescents, the need for an effective prophylactic vaccine remains.

Since the gp350 vaccine alone could not protect against EBV infection, a truly preventative vaccine is likely to need additional antibodies targeting other virus proteins, as well as perhaps also enlisting the T cell arm of the immune system. Ideally, this would be achieved using a live but attenuated vaccine strain of EBV. However, the fact that EBV is associated with cancer development raises enormous, probably insurmountable, regulatory issues for such a vaccine. One possible alternative therefore could be to use a vaccine comprised of EBV virus-like particles. Since these particles lack virus genetic material, the risk of the vaccine causing cancer is removed while the presence of multiple viral proteins, displayed in a particulate form, broadens and enhances the antiviral immune response. However, the key question of whether a strong immune response against EBV can protect against infection remains unanswered. Our research group is addressing this fundamental question in collaboration with Professor Paul Kellam's research group at the Wellcome Trust Sanger Institute in Cambridge. Since different EBV strains circulate in the population, and each strain can be identified by its own genetic signature, we are using deep sequencing to see if people are protected against acquiring additional EBV strains following their initial infection. Evidence of such natural protection following EBV infection would be a strong stimulus for developing second-generation prophylactic EBV vaccines.



Coloured transmission electron micrograph of an EBV particle. *James Cavallini / Science Photo Library*

THERAPEUTIC VACCINES TO TREAT EBV-ASSOCIATED CANCERS

Even if the perfect prophylactic EBV vaccine became available tomorrow, millions of people already infected with the virus will go on to develop virus-associated cancers. Irrespective of progress towards a prophylactic vaccine, the desperate need for better treatments for EBV-positive NPC, gastric carcinoma and lymphoma remains. One way this could be achieved is by making use of the fact that all EBV-associated cancers express one or more EBV proteins. It should therefore be possible to eliminate these cancers by harnessing relevant antiviral immune responses. This has clearly proved to be the case for post transplant lymphoma, an EBV-associated cancer that can occur in patients who are immunosuppressed following organ or stem cell transplantation. These tumours result from the loss of the normal anti-EBV immune responses that usually prevent virus-infected cells from growing out of control. Consequently, restoring these immune responses by infusing EBV-specific immune cells grown in the laboratory often results in the elimination of the cancer.

Post-transplant lymphoma does, however, represent a somewhat idealised situation for such immunotherapy because the cancer cells contain at least eight EBV proteins and some of these are good immune targets. In contrast, all other EBV-associated cancers contain fewer viral proteins that are poorer targets for the immune system. This is presumably because these other cancers have developed in individuals with relatively 'normal' immunity. Nevertheless, several clinical trials have shown that infusing EBV-specific immune cells into patients with EBV-positive Hodgkin lymphoma or NPC can result in clinical benefit. These trials serve as very important proofs of principle, but producing the immune cells requires highly specialised facilities and staff; consequently, the cost per patient is high. The challenge now is therefore to develop ways to focus the immune response against the smaller number of viral proteins present in these cancers in a way that can be applied to large numbers of patients worldwide. To achieve this goal, our research group has developed a genetically engineered vaccine based on Modified Vaccinia Ankara (MVA), a safe attenuated strain of poxvirus. Into MVA we introduced the genes for the two EBV proteins that are present in almost all EBV-positive cancers. This vaccine has recently completed testing in two early-phase clinical trials performed in collaboration with Cancer Research UK and colleagues in Hong Kong, London, Manchester and Birmingham. The results of these trials show that the vaccine can boost immune responses to one or both of the EBV proteins when administered to NPC patients and, equally importantly, is well-tolerated with relatively minor side effects. The vaccine is now being tested in two new much larger clinical trials that will measure the ability of the vaccine to shrink, or even eliminate, EBV-associated tumours.

"The challenge now is therefore to develop ways to focus the immune response against the smaller number of viral proteins present in these cancers in a way that can be applied to large numbers of patients worldwide."

CONCLUSION

EBV is a fascinating virus and its study has revealed novel aspects of the interaction between viruses, the immune system and cancer. The results of many years of basic research have already been translated into the clinic and efforts by several research groups worldwide continue to develop and refine exciting new therapies that will benefit human health.

JAMES E. TURNER & GRAHAM S. TAYLOR
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Bacteriophage practical

Aspects of virology feature in many A-level specifications but practical virology is virtually absent in school because of difficulties in handling the micro-organisms (both perceived and real). Bacteriophages (viruses that only infect bacteria) are relatively easy to handle and can be used to illustrate many concepts of virology, such as counting infectious virus particles.

A PLAQUE ASSAY is a technique for detecting viruses. The underlying principle offered here is a serial dilution (gradually diluting a suspension of bacterial viruses and testing for infectivity). The outcome should be an agar plate covered with 'plaques' (holes in a field of constant bacterial growth), where the virus has infected and killed the host bacterium.

The school-friendly method detailed here offers a step-by-step guide to carrying out a plaque assay using T4 bacteriophage and its host, *Escherichia coli*.

T4 bacteriophages infecting an *E. coli* cell. *Juergen Berger / Science Photo Library*

AIM

To calculate the number of viable phage in a suspension.

METHOD

Note: Aseptic technique should be used throughout this experiment

Stage 1 – Preparing your dilution series of T4 bacteriophage

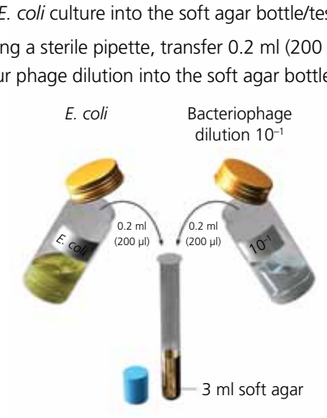
Each group of students requires 10 nutrient agar plates, 10 bottles each containing 9 ml sterile distilled water and 10 sterile pipettes.

1. Label one agar plate '10^{-1}' and the next one '10^{-2}' and so on until '10^{-10}'.
2. Label the sterile water bottles '10^{-1}', '10^{-2}' and so on until '10^{-10}'.
3. Transfer 1 ml of bacteriophage suspension into the sterile water bottle labelled '10^{-1}' and mix well.
4. Using a sterile pipette (not the one used previously), transfer 1 ml out of the '10^{-1}' bottle and place it into the '10^{-2}' bottle. Replace the lid and mix well.
5. Continue this process (transferring 1 ml from one dilution to the next using a new sterile pipette each time) until you have made the '10^{-10}' dilution.

Stage 2 – Inoculating cultures of bacteria with T4 bacteriophage dilutions

The following steps (1–6) must be completed for each dilution

1. Collect your '10^{-1}' agar plate and the bacteriophage dilution bottle labelled '10^{-1}'.
2. Collect 3 ml of molten soft agar from a water bath (set at 50°C). When opening the soft agar, ensure you are working aseptically (near a Bunsen burner).
3. Using a sterile pipette, transfer 0.2 ml (200 µl) of *E. coli* culture into the soft agar bottle/test tube.
4. Using a sterile pipette, transfer 0.2 ml (200 µl) of your phage dilution into the soft agar bottle/test tube.



5. Place lid on bottle/test tube. Carefully rotate/roll the bottle between two fingers in an upright position, to mix the solution (do not shake).
6. Carefully pour the inoculated soft agar onto your '10^{-1}' agar plate. Replace the lid of the agar plate and carefully rotate the plate in a circular motion so the soft agar is evenly spread over the underlying agar. Leave the plate for approximately 10 minutes for the soft agar to set (at room temperature).

Once all agar plates have been inoculated with soft agar and the agar has set, invert the plates and incubate them at 30°C for 24 hours. Empty bottles/test tubes should be sterilised and cleaned before reuse.'

RESULTS

The bacteria grow as a lawn (a field of confluent growth) across the agar. Small circular gaps in the lawn of bacteria are known as plaques. Here, bacteria have been killed by the bacteriophage so are unable to grow.

Count the number of plaques at a dilution where there are between 20 and 200 plaques present. This will allow calculation of number of plaque-forming units (PFUs) per ml of original suspension using the formula:

$$\text{PFU/ml} = \frac{\text{(number of PFUs)}}{\text{(dilution x 0.2)}}$$

1. Enter the number of PFUs into the top line of the equation.
2. Enter the dilution you chose for your average PFU where the equation says 'dilution'. For example, if you chose 10^{-3}, enter 0.001, or if you chose 10^{-7}, enter 0.0000001.

NOTES

- Soft agar is half-strength nutrient agar. It must be sterilised and be molten (kept at 50°C) for students to use.
- The bacteriophage must be able to infect the bacterium you use. They are highly specific.
- Advice on bacteriophage and obtaining a culture can be sought from culture suppliers/collections

JAMES REDFERN, Manchester Metropolitan University

Good bugs, bad bugs

Fun Kids is the UK's only children's radio station. With a core audience of between 4 and 9 years old, it's not the SGM's usual audience, but when we were invited by Fun Kids to develop a series about microbiology, we jumped at the chance.

In the series, called *Good bugs, bad bugs*, microbiology is introduced through the characters Benny (the good bug) and Mal (the bad bug) in a fun and engaging way, covering areas of microbiology from microbial transmission to sewage treatment, and food production to algal blooms! We asked Chair of the Communications Committee Joanna Verran (JV) and *Microbiology Today* Editor Paul Hoskisson (PH) if they would help with the planning and development of the series. Here they let us know how they got on.

Why did you get involved with this project?

JV Seemed like a fun idea! It's great to think about how to get microbiology out to as many different audiences as possible – and why not start them young!

How did you get on with the work involved?

JV Not too badly – once I got focused into the programme's language it was enjoyable to think about how best to get important points across in a simple, but accurate and of course entertaining, way.

PH The work wasn't really difficult or time-consuming, it was a nice respite from the usual things that academics do…

What did you think of the final episodes, were they what you expected?

PH They were much better than I thought they would be. Reading the scripts makes you imagine how the characters would sound, but the *Fun Kids* team have really brought them to life.

Did this project make you think differently about how you communicate?

PH It's interesting how doing something like this makes you consider all of the ambiguity in any sentence, especially when trying to simplify microbiology for a young audience.

What was the most challenging part of this project?

JV Making sure that we were consistent with our messages and language across episodes. It was also nice working with Paul and the team at SGM via 'track changes'!

PH It was interesting that as a scientist you try not to think about micro-organisms in an anthropomorphic way, yet in this project, that is exactly what we were trying to do in order to get the message across – I found this a particular challenge.

Which was your favourite episode?

JV I love them all!

PH Not sure I can choose … Episode 1, probably as it gives a nice overview of the breadth of microbiology.

Benny or Mal?

JV Benny the beneficent!

PH Benny, obviously – I work on *Streptomyces*!

Given the chance would you like to take part in 'Good bugs, bad bugs – another look down the microscope'?

JV Definitely!

PH Yes! The diversity and importance of microbiology to virtually every aspect of life on the planet is a great thing to get across to kids and this was a great way to go about it!

What advice would you give to anyone interested in getting involved with any aspect of microbiology outreach?

JV If you like talking about microbiology (or indeed any area of science!), then it is always good to think about how you are going to explain things in a way that is clear and accurate – but it has to also be interesting or people simply won't listen. It is about engaging, not pontificating. Outreach and engagement activities demand a lot of energy and concentration for extended periods, but they are also stimulating, rewarding and exciting, and often enlightening as well. Always listen to your audiences if you want them to listen to you!

So, if you like the sound of it then I would definitely encourage you to get involved! You get a lot of experience on the job and it makes you love your subject even more than before.

Good bugs, bad bugs is available to listen or download on the Fun Kids website **www.funkidslive.com**. If you are interested in microbiology outreach, or becoming an SGM Expert, get in touch with our Education and Outreach Officer (v.symington@sgm.ac.uk).

Since the show went on air in mid-December, Good bugs, Bad Bugs has reached 200,000 listeners, been downloaded 2,165 times, has 156 subscribers on iTunes, had 600 entrants to a competition in its name and the webpages dedicated to it have had over 1,500 page views!

Standing up for Science

Erica Kintz

Young scientists often forget how uniquely qualified they are to comment and offer their opinions on poorly performed research and suspicious scientific claims. The Standing up for Science workshop for early career researchers, held on November 16th at the University of Glasgow, sought to remedy that situation.

Organised by Sense about Science (**www.senseaboutscience.org**), a charity dedicated to helping the public better understand science and equipping them to inquire about research, the workshop was not intended as a training course on media relations but instead allowed participants to engage in a discussion about the process of how science is portrayed in the media.

This was accomplished by running several sessions that offered perspectives from each side of science reporting. In the first session, researchers gave examples of their experiences interacting with the media and offered advice on how to make sure your research is not misrepresented. This included being prepared when speaking with journalists and being sure you can explain how your research relates to the bigger picture so that audiences can relate to it. Professor Sergio Della Sala of the University of Edinburgh went so far as to say that if science was being misreported, it was often the fault of the scientist for not taking the necessary care in releasing the information!

This was followed by an enlightening session with journalists offering their perspective on why occasionally science reporting goes awry. They listed hectic days covering multiple stories, limited time frames and their loss of control over a story after giving it to their editors as the major reasons that errors are made. They made the argument that fewer mistakes would be made if more scientists were willing to take the time to converse with them over the facts in their articles.

The day was interspersed with group work sessions that allowed the participants to come together and reflect on their responsibilities as researchers when engaging with the public and media, and also explore reasons why we feel uncomfortable doing so. Common answers given were a lack of experience and a fear that no one would take our opinions seriously. These feelings were addressed in the final session of the day, which provided participants with options on how they could get involved with helping correct inaccuracies in science reporting and establish themselves as someone the public can trust for scientific facts. One piece of advice included starting small; we were encouraged to contact local media over their science articles. Another was establishing an online presence with science-related blogs and social media accounts. Finally, we learned more about the Voice of Young Science network, also run by Sense about Science. This programme helps early-career researchers connect and address issues important to them; it is easier and less intimidating to combat problems with a group of like-minded individuals than to think you have to face it on your own.

The day allowed participants to learn more about the process of science reporting, from preparing press releases with the University to how science stories are chosen and researched by journalists. It also provided an opportunity for participants to address their concerns over what may go wrong if and when their science becomes a topic of media attention and offered advice and encouragement on how to become more involved with science in the media. Hopefully, the 50 participants have been inspired to overcome their reluctance and act as champions of good science for the benefit of the general public.

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SGM supports Standing up for Science workshops. Society members can apply for a priority place as well as assistance with travel and subsistence by contacting ***pa@sgm.ac.uk***

SGM JOURNALS

See what the microbiology community has been reading…

MOST READ ARTICLES – *MICROBIOLOGY*

Hartmann, N., Schulz, S., Lorenz, C., Fraas, S., Hause, G. & Büttner, D. (2012). Characterization of HrpB2 from *Xanthomonas campestris* pv. *vesicatoria* identifies protein regions that are essential for type III secretion pilus formation. *Microbiology* **158**, 1334–1349; *doi:10.1099/mic.0.057604-0*

Figueira, R. & Holden, D.W. (2012). Functions of the *Salmonella* pathogenicity island 2 (SPI-2) type III secretion system effectors. *Microbiology* **158**, 1147–1161; *doi:10.1099/mic.0.058115-0*

Hermosa, R., Viterbo, A., Chet, I. & Monte, E. (2012). Plant-beneficial effects of *Trichoderma* and of its genes. *Microbiology* **158**, 17–25; *doi:10.1099/mic.0.052274-0*

MOST READ ARTICLES – IJSEM

Kaur, I., Kaur, C., Khan, F. & Mayilraj, S. (2012). *Flavobacterium rakeshii* sp. nov., isolated from marine sediment, and emended description of *Flavobacterium beibuense* Fu *et al.* 2011. *Int J Syst Evol Microbiol* **62**, 2897–2902; *doi:10.1099/ijs.0.035691-0*

Wieme, A., Cleenwerck, I., Van Landschoot, A. & Vandamme, P. (2012). *Pediococcus lolii* DSM 19927^T and JCM 15055^T are strains of *Pediococcus acidilactici*. *Int J Syst Evol Microbiol* **62**, 3105–3108; *doi:10.1099/ijs.0.046201-0*

Hedberg, M.E., Moore, E.R.B., Svensson-Stadler, L., Hörstedt, P., Baranov, V., Hernell, O., Wai, S.N., Hammarström, S. & Hammarström, M.-L. (2012). *Lachnoanaerobaculum* gen. nov., a new genus in the *Lachnospiraceae*: characterization of *Lachnoanaerobaculum umeaense* gen. nov., sp. nov., isolated from the human small intestine, and *Lachnoanaerobaculum orale* sp. nov., isolated from saliva, and reclassification of *Eubacterium saburreum* (Prévot 1966) Holdeman and Moore 1970 as *Lachnoanaerobaculum saburreum* comb. nov. *Int J Syst Evol Microbiol* **62**, 2685–2690; *doi:10.1099/ijs.0.033613-0*

Data accessed 22 Jan 2013

MOST READ ARTICLES – JGV

Steckbeck, J.D., Kuhlmann, A.-S. & Montelaro, R.C. (2012). C-terminal tail of human immunodeficiency virus gp41: functionally rich and structurally enigmatic. *J Gen Virol* **94**, 1–19; *doi:10.1099/vir.0.046508-0*

Martínez-Guinó, L., Ballester, M., Segalés, J. & Kekarainen, T. (2011). Expression profile and subcellular localization of Torque teno sus virus proteins. *J Gen Virol* **92**, 2446–2457; *doi:10.1099/vir.0.033134-0*

Radford, A.D., Chapman, D., Dixon, L., Chantrey, J., Darby, A.C. & Hall, N. (2012). Application of next-generation sequencing technologies in virology. *J Gen Virol* **93**, 1853–1868; *doi:10.1099/vir.0.043182-0*

MOST READ ARTICLES – JMM

Sardi, J.C.O., Scorzoni, L., Bernardi, T., Fusco-Almeida, A.M. & Mendes Giannini, M.J.S. (2013). *Candida* species: current epidemiology, pathogenicity, biofilm formation, natural antifungal products and new therapeutic options. *J Med Microbiol* **62**,10–24; *doi:10.1099/jmm.0.045054-0*

Jarmuda, S., O'Reilly, N., Żaba, R., Jakubowicz, O., Szkaradkiewicz, A. & Kavanagh, K. (2012). Potential role of *Demodex* mites and bacteria in the induction of rosacea. *J Med Microbiol* **61**, 1504–1510; *doi:10.1099/jmm.0.048090-0*

Watkins, R.R., David, M.Z. & Salata, R.A. (2012). Current concepts on the virulence mechanisms of meticillin-resistant *Staphylococcus aureus*. *J Med Microbiol* **61**, 1179–1193; *doi:10.1099/jmm.0.043513-0*

Professional development for early-career researchers: how to organise a conference

" Advanced planning is key to success. Last minute changes are inevitable, but if you are well organised these are far easier to manage. "

Susan Wong
SGM Head of Scientific Conferences

This article is aimed at early-career researchers who are thinking about organising a scientific conference. Some general tips and information are given, including the top tips of the SGM Head of Scientific Conferences, Susan Wong. Two early-career researchers who have '*been there, done that*' describe their experiences.

Photo: David Martin

Scientific conferences help drive the process of science (and scientists' careers) by giving researchers an opportunity to disseminate their research, get feedback and learn about new research tools and ideas. While the internet has improved the ways researchers can keep up to date with the latest findings and discuss these with fellow researchers, there is still great value in attending meetings because of the formal, and particularly informal, opportunities to interact face-to-face with other scientists. This is particularly true for the increasing numbers of conferences that are run by early-career researchers for early-career researchers. Such meetings allow scientists at the start of their careers to interact with others in similar positions, take heart from learning that they are having the same problems, and meet their peers and collaborators of the future. Taking on a role in the organisation of such an event affords the early-career researcher even greater networking opportunities with both speakers and delegates and allows them to develop their skills in areas such as leadership and communication and to learn the professionalism of managing events.

10 RULES FOR ORGANISING A SCIENTIFIC CONFERENCE FOR EARLY-CAREER RESEARCHERS*

- **Rule 1** Opportunity for discussion is the most important thing (but the science helps attract attendees)
- **Rule 2** Allow for plenty of planning time
- **Rule 3** Study all potential financial issues affecting your event
- **Rule 4** Create a balanced agenda (that supports the achievement of Rule 1 in different ways)
- **Rule 5** Carefully select your keynote speakers (not just for their interesting and topical research, but who are approachable and will interact positively with the conference delegates)
- **Rule 6** Make sure the members of the organising committee have delegated roles and communicate regularly
- **Rule 7** Identify your target audience and advertise
- **Rule 8** Exploit social media
- **Rule 9** Prepare for emergencies
- **Rule 10** Make the impact of your conference last

**Adapted from 10 rules for organising a scientific conference (http://bit.ly/UUgSFq)*

TOP TIPS FROM THE SGM HEAD OF SCIENTIFIC CONFERENCES

Planning and attention to detail is extremely important when organising a conference. There are many elements to consider; for example, the theme of the conference, the target audience and a suitable venue. Susan Wong reflects on two aspects: budgeting and sponsorship.

BUDGETING

I find preparing the budget is one of the hardest aspects of conference planning because there are numerous variables which can be difficult to estimate. There are the obvious costs that are easy to identify, such as speaker travel, venue hire and food. However, to help me identify many of the hidden costs I do a walk through of the event from the delegate's point of view. For example, the delegate will arrive at the registration desk to register (expense = signage, name badge, delegate pack). Then they will make their way to the first session (expense = more signage) to listen to talks (expense = AV support, water for speakers and chair) and so on.

ATTRACTING SPONSORSHIP AND GRANTS

Once I have established my outgoing costs, I can then offset against any sponsorship secured. The remaining balance will give me some idea of how much delegates might need to pay.

Attracting funding can be tricky. I recommend asking senior researchers for information on their contacts (e.g. who do they buy their laboratory consumables from?). With their permission, you can then contact the companies with '*I was given your details by …*'. This is more likely to receive a response than a '*to whom it may concern*' request. I suggest thinking broadly about the sponsorship opportunities you offer. Don't just think about sponsors being provided with an exhibition stand on the day or having their logo featured on the webpage and opening slide for the speaker whose travel costs they contributed to. Could you offer the opportunity to include marketing materials in the delegate pack, or provide delegates with a branded pen or notebook (that's one less cost for your budget)? If you are having an exhibition area, it is extremely important that the sessions keep to time as you want to make sure that delegates arrive in the exhibition area when you said they would so your (paying!) exhibitors have ample opportunity to talk to them.

Also check out organisations such as SGM who offer grants to support conferences.

SOME THINGS (BUT NOT EVERYTHING) YOU WILL NEED TO THINK ABOUT

- Who will book the speakers' travel and accommodation? Specify in advance what expenses will be covered.
- Even if there is no registration fee, have a pre-registration system to give an idea of the number of delegates so you have enough seats, food and drinks (but not too much).
- Will you allow people who haven't pre-registered to turn up on the day? How will the registration desk handle that?
- Will all abstracts submitted be accepted or will there be a review process? Give reviewers deadlines.
- Will you supply session chairs with a clock to ensure good timekeeping?
- Set clear deadlines for the programme book and print it as late as possible.
- How will you evaluate the event (on-the-day form, online survey)?

2 weeks before the event

- Send venue details to exhibitors with information on deliveries, parking permits, set-up and shut-down times and what's included.
- Send information to speakers with venue directions, phone number and a reminder of the time and location of their presentation + facilities available.

1 week before the event

- Meet with 'on the day' helpers so everyone knows what to do and when.

On the day

- Have a plan.
- Do a health and safety check of the venue.
- Greet speakers and session chairs.
- Include time for cleaning up.

After the event

- Thank-you letters for exhibitors, speakers and session chairs.

SGM has example documents from its own events which we are happy to share with members organising their own event. Contact ***conferences@sgm.ac.uk***


Photo: David Martin

MY EXPERIENCE

Eleni Karinou – Organising Committee Member, 3rd Annual PiCLS Symposium, University of Dundee

The PhD Student's Association in the College of Life Sciences (PiCLS) is a proactive team of students facilitating networking between PhD students in different subject areas. PiCLS organises an annual symposium where eminent researchers in biological sciences are invited to speak and network with students. I attended the symposium in 2011 and was intrigued by the idea of a symposium organised solely by students and decided to get involved.

The organising committee of the 2012 Symposium consisted of 9 people, all PhD students within the college and, like me, most of them were organising a conference for the first time. I was responsible for finding sponsors for the speakers' travel expenses.

The 3rd Annual PiCLS Symposium was a 1-day event held on 6 July 2012. There was a morning and afternoon session of talks, and a poster session over lunch. The event was attended by around 150 PhD students, postdocs and group leaders, mostly from the College of Life Sciences. The invited speakers were proposed by students and staff from the College. Delegates were able to submit abstracts for oral presentation or posters, with presenters selected by principal investigators of the College. On the day of the symposium, the invited speakers helped us choose prize winners from the presenters. The event received sponsorship from various scientific societies, journals and supplier companies who were offered trade stands or advertisements.

As an organiser, what I enjoyed most was the stimulating discussions with the rest of the committee during the preparation of the symposium and the team work. Our biggest challenges were raising money and finding a day suitable for all our busy speakers. The experience was at times stressful and tiring, but it was a lot of fun. It required good organisation and communication skills (making sure there was lots of communication between members of the organising team was really important for the success for the event) and I feel it has helped me to be more efficient and conciliatory. My tip for others who get involved in organising a conference would be: don't be afraid to ask other people for their opinion.

http://picls.lifesci.dundee.ac.uk/symposium2012/index.html

*SGM supported this event by offering funds from the Student Society Sponsored Lectures scheme (**www.sgm.ac.uk/grants/sssl.cfm**) towards the travel and accommodation costs of Professor Pascale Cossart, Institut Pasteur, and offering a prize for the best poster on a microbiological topic presented by a registered PhD student.*


Photo: David Martin

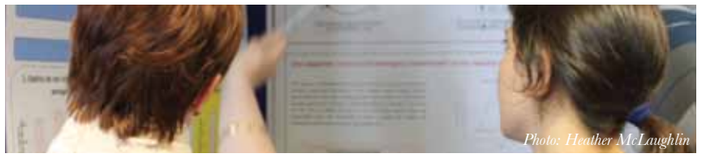


Photo: Heather McLaughlin

MY EXPERIENCE

Robert Ryan – Co-chair, Young Microbiologists Symposium on Microbe Signalling, Organisation and Pathogenesis 2012, University College Cork


Photo: Heather McLaughlin

In 2008, I was invited to speak at the John Innes Centre Young Microbiologist Symposium. It was a great event, but was only for researchers at Norwich Research Park. It made me think that an open event for young microbiologists was missing in the microbiology landscape. For this reason I instigated the Young Microbiologists Symposium (YMS) at University College Cork. The YMS was intended to bring together young microbiologists and to provide an opportunity for these scientists to present their work and receive constructive feedback, to network with other students, postdocs, young PIs and senior scientists in the field, and facilitate future collaborations.

I organised the inaugural event in 2009 and co-chaired the second event in 2012 (thanks to Dr Delphine Caly my co-chair and to members of the research group who helped with the preparation and on the day). The experiences of 2009 did prepare me for the level of work expected in running a good event. However, the various issues and problems that arose in running the event the second time round were very different and highlighted that, in organising a conference, you can never predict the problems you will encounter, so you have to be prepared to adapt as need arises. Organising these events has improved my ability to delegate and my fund-raising skills, and has taught me the importance of patience, trust and planning in conference organisation. I feel the experience of organising these events has helped both with my own research and in progressing my career.

The YMS on *Microbe Signalling, Organisation and Pathogenesis* 2012 attracted over 120 participants from more than 15 countries, ranging from first-year PhD students to starting principal investigators. The 2-day programme included three keynote talks, five plenary sessions (four on predefined topics, one featuring nine 'hot-spot' poster talks), and two lunchtime poster sessions. Each delegate had to present a poster. Thanks to the support of our sponsors, we were able to set the registration fee at only €25 and to offer a number of prizes for best poster and best short talk.

From the event, I really enjoyed watching junior scientists 'put it up' to the gathered eminent scientists and seeing those eminent scientists dispensing sage advice during the event. I really think that having a platform for junior scientists to present their work to a broad audience is key for them to develop as scientists. For institutions, these types of events showcase the work going on in the department to a wide audience and can be an excellent recruitment tool to attract postdocs and students.

www.ucc.ie/yms2012/index.html

SGM sponsored the lectures of Professor Cynthia Sharma, University of Würzburg, and Dr Trevor Lawley, Wellcome Trust Sanger Institute, from the Regional Meetings Grants scheme (www.sgm.ac.uk/grants/regional.cfm).

If you have any other topics that you would like to see featured in Microbiology Today *as a 'How to' article, please email* **k.mcgregor@sgm.ac.uk**

INTERVIEW

Professor Harald zur Hausen

Nobel Prize winner and distinguished virologist Professor Harald zur Hausen has been awarded the 2013 SGM Prize Medal (see p. 8). In this interview with Professor David Blackbourn, he reflects on his career and offers his opinions on some issues currently facing virologists.

Q *What inspired you to pursue a career in microbiology?*

A Since my days as a schoolboy I was interested in questions related to microbiology and cancer. This was probably triggered by reading some of the biographies of well known scientists like Louis Pasteur and Robert Koch.

Q *What challenges did you face during the development of your career?*

A Every scientist experiences some ups and downs during the lifespan of such activities. Clearly, there was some scepticism initially when we started to work on the question on viruses causing human cancers, but during the past decades this has gradually faded away.

Q *How do the challenges differ for those developing their careers today?*

A I do not believe that the challenges differ very much today from those which I experienced during my career.

Q *What advice would you give to scientists in the early stages of their career wishing to follow in your footsteps in microbiology?*

A To select an original aspect of research, to work persistently and not to trust too much in prevailing dogmas.

Q *Given the increasing emphasis on funding translational research, what is the best way to ensure 'basic' science research continues?*

A Clearly, we need basic research in order to successfully translate research for clinical application. If we do not support basic research, we will have very little to translate.

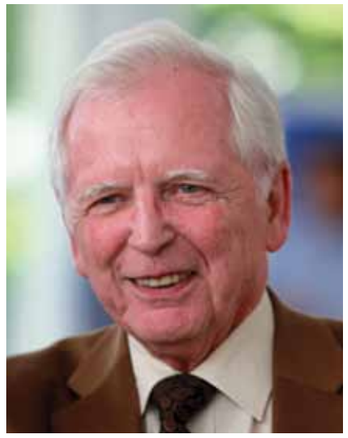
Q *There's been a vaccine for the 'high-risk' types of human papillomavirus that cause cancer of the cervix for several years and a hepatitis B virus vaccine for many years. Why do you think vaccines against other oncogenic human viruses have yet to be implemented, when the presumptive health care benefits would be so significant?*

A The problem with some of the other oncogenic human viruses is that they mutate quite rapidly and quickly (e.g. hepatitis C virus), or even in some cases, like human immunodeficiency virus 1 and 2, they act indirectly, and these infections are also very difficult to prevent because, again, there is a high mutation rate in those viruses.

In other cases, such as Epstein–Barr virus and human herpes virus type 8, vaccines could be developed. The present non-availability of such vaccines is probably due to the lack of interest by the pharmaceutical industry.

Q *Are there more oncogenic human viruses yet to be discovered, or more links between known viruses and cancer yet to emerge?*

A In my opinion it is worthwhile to search intensively and carefully for viruses linked to cancer, particularly whenever the epidemiology may hint to relationships between infectious events and cancer development.



H. zur Hausen. *Armin Kübelbeck*

REVIEWS

Horizontal Gene Transfer in Microorganisms

Edited by M. Pilar Francino

Published by Caister Academic Press (2012)

£159.00 pp. 202

ISBN 978-1-90823-010-2

As an expert on bacterial plasmids I can be guilty of thinking about Horizontal Gene Transfer (HGT) in terms of the elements and processes that make it happen rather than its consequences for the transferred genes or their recipient genomes as this book does. It is a refreshing stimulus that considers HGT from many perspectives and is the perfect resource to justify teaching bacterial genetics, not as a means for mapping genomes, but to understand the processes that are driving their evolution. This book is a valuable source of ideas, facts and references with which to develop such new teaching resources.
I will be recommending that our library buys copies to be accessed by students ranging from enthusiastic first-year undergraduates taking my Genetics course to PhD students researching topics for a dissertation. Although not rich in figures, the text is clear with good subheadings and is easy to dip into.

CHRIS THOMAS,
University of Birmingham

Two-component Systems in Bacteria

Edited by R. Gross & D. Beier

Published by Caister Academic Press (2012)

£180.00 pp. 426 ISBN 978-1-90823-008-9

Two-component signal transduction systems (TCSs) are common amongst bacteria. Over the past 15 years or so, sequence data have revealed the widespread occurrence and importance of these systems, and notably the variation and atypical features displayed by many systems. This explosion of information has led to a re-evaluation of how they should be classified and organised, to considerations of the atypical and more complex multi-component systems and to a realisation of the profound roles of these systems in bacterial cell physiology. This volume draws on some selected examples of TCSs to illustrate current advances in knowledge. The editors bring together a series of well-written reviews by highly regarded researchers, starting with how TCSs are classified and organised, and current understanding of structural knowledge, and moving on to novel aspects of signal transduction mechanisms, TCS function and gene regulation. Roles for phosphatase activities, orphan and atypical response regulators, antikinases, 'connectors' that link systems and multi-component systems are all described, together with important examples of systems in pathogenic and multicellular species. This book is an excellent choice for graduate-level education and researchers in the field and would be a useful addition to any research group, department or university library in a research-active institution or pharmaceutical company.

MARY PHILLIPS-JONES, University of Central Lancashire

Microbes: Concepts and Applications

By P.S. Bisen, M. Debnath & G.B.K.S. Prasad

Published by John Wiley & Sons Limited (2012)

£133.00 pp. 724 ISBN 978-0-47090-594-4

This new book, written by three authors who collectively possess a wealth of experience in the field, is a comprehensive text covering subjects as diverse as medical microbiology, microbes in agriculture and the use of micro-organisms as tools for industry and research. In this respect, at less than 700 pages, this text must be considered to be a concise overview and this is reflected in the somewhat basic nature of the text and diagrams. On a positive note, however, the breadth of the text provides the reader with a solid basic introduction to the world of microbes.

This traditional text is directly aimed at undergraduate students. Unlike many new texts of this type, however, there is no supplementary information-technology-based material. Coupled with a price tag of over £130, access is likely to be limited to copies located in institutional libraries and these two factors may result in the text missing its target audience. Given the price, it is perhaps also disappointing that the text and figures are entirely in black and white, which are unlikely to engage students new to the field.

SUE LANG, Glasgow Caledonian University

Rhabdoviruses: Molecular Taxonomy, Evolution, Genomics, Ecology, Host–Vector Interactions, Cytopathology and Control

Edited by R.G. Dietzgen & I.V. Kuzmin

Published by Caister Academic Press (2012)

£159.00 pp. 276 ISBN 978-1-90823-011-9

As with many virus families, the number of newly identified species that are classified into one of the genera within the *Rhabdoviridae* is ever-increasing, as is the public health threat posed by this family – only last month the isolation of a novel Rhabdovirus (Bas-Congo virus) linked to an outbreak of acute haemorrhagic fever in the Democratic Republic of Congo was reported. Whilst this is too recent to be included here, this book nevertheless provides an up-to-date, if rather dry, account of this family of viruses covering all six genera and six isolates awaiting official classification. For each virus there is a keen focus on evolution, phylogenetics, epidemiology and methods for limiting morbidity and mortality. The level of detail and factual style adopted throughout means it is not a book you would pick up to read on a whim but rather use for reference. It will be of particular interest to those individuals who are intimately involved with these viruses and those who are joining the field, for whom it would make an excellent resource.

EDWARD WRIGHT, University of Westminster

Career Planning for Research Bioscientists

By Sarah Blackford

Published by Wiley-Blackwell (2012)

£199.99 pp. 192 ISBN 978-1-4051-9670-3

Sarah Blackford draws on her years of experience coaching bioscience researchers on careers and career planning to produce this guide. The book explains career planning approaches, gives practical ways to increase your self-awareness, and ideas for how to be proactive in enhancing your employability – and all written with reference to the experiences and opportunities available to bioscience doctoral students and postdocs. It is this feature which distinguishes this book from others in the marketplace that discuss these issues for a generic audience. Consideration is given not just to jobs in academic research, but a whole range of possibilities, both inside and outside science, supported by detailed career profiles of 20 PhD-qualified bioscientists. Whether you already have ideas about what type of job you want, or have no idea what your options are, you will find something in this book to make you think about taking the plunge towards your next job in a proactive and productive way.

KAREN McGREGOR, SGM

Polar Microbiology: Life in a Deep Freeze

Edited by R.V. Miller & L.G. Whyte

Published by American Society for Microbiology (2012)

US$159.95 pp. 312 ISBN 978-1-55581-604-9

This book is derived from the 4th Polar and Alpine Microbiology conference in Banff (2008), one of a series of meetings that began in 2004 in Finland and have grown steadily in popularity. As a result of broad representation of the community, this is a well balanced and up-to-date presentation of current thinking in the field. Of particular interest are sections on genome and expression analysis, Antarctic metagenomic studies, subglacial environments and cold-active biomolecules in biotechnology. The layout follows a logical progression from taxonomic diversity, through molecular adaptations to ecology and then future challenges. It is a good reference source and contains many useful and informative tables, such as summaries of primers used, reports of sub-zero metabolic activity, relevant genomes sequenced, molecular adaptations and biodiversity studies. The reference lists cite work from most, if not all, of those present at the meeting and could be said to present an introduction to an exciting era in polar microbiology.

DAVID PEARCE, British Antarctic Survey

COMMENT

New frontiers in scientific publishing

LEIGHTON CHIPPERFIELD

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Around the world, the ways in which scientific research is published and accessed has begun to attract significant attention. I joined SGM in August 2012 with an exciting remit: to modernise our publishing business and prepare SGM for the challenges and opportunities that lie ahead. So what is happening and how is SGM responding?

1. PLANNING FOR A SUSTAINABLE FUTURE

Like many learned societies, SGM is actively involved in the dialogue on Open Access (OA). Across science, the proportion of OA articles is increasing, although most research is still published in subscription-based journals. With governments, funding bodies and even institutions all developing their own OA policies, the global picture remains complex, and it seems likely that different geographies and disciplines will move at their own pace.

For societies like SGM, OA presents both challenges and opportunities. Under the 'Gold' OA model supported by the UK Finch Report, revenue to a journal would shift from traditional subscriptions to author fees underwritten by funding bodies. For SGM, the main opportunities of OA lie in increasing usage of our existing journals, and providing an alternative model for launching new titles in future.

Whatever model proves sustainable for an individual publication, the only certainty is that authors will continue to be its lifeblood. Now more than ever, societies like SGM need to ensure their publications are relevant and compelling, offering a high level of service to our valued authors and doing more to ensure they return again and again.

2. DIGITAL IS HERE

When I entered scientific publishing in 1999, print was still king. Speak to a librarian now and the message has changed dramatically. The functionality, speed, searchability and measurement of the online journal had already begun to make print redundant before the dawn of mobile. Latest data supports the change in reading habits, showing that researchers are accessing more articles online, but spending less time reading each one. Yet, infrastructure limitations in some developing countries mean any type of e-access remains problematic. And a hardcore of personal customers still like to receive their print journal.

Whilst providing this choice of 'delivery channel' is desirable, it comes at additional cost to the publisher – and ultimately the reader. It is clear that most if not all scientific publication will ultimately move to a fully digital environment. The speed with which print dies is up for debate!

3. GLOBAL AUTHORSHIP

The transition of journal usage from print to digital over the past 10 years has coincided with the widespread adoption of online submission and peer-review systems. These developments have opened up a global market of authors and readers for previously 'local' journals.

The last decade has also seen the growth of certain countries' output of research papers, primarily driven by R&D investment. Notably, China has consistently increased its article share over the past 15 years, now accounting for 1 in 10 published papers – surpassing traditional big players such as the UK, Japan and Germany. Along with Brazil and India, papers from China form the highest area of submissions growth for SGM's titles. At SGM we will be engaging more proactively with microbiology authors worldwide, ensuring that we bring readers the best microbiology research from wherever it may emanate.

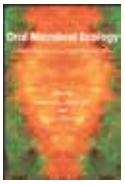
And that's just the tip of the iceberg. We're also considering how developments such as the 'semantic web', text and data mining, and social media can make our content ever more rich and discoverable.

There has never been a more exciting time to be involved in publishing great science – and we'd like you to get involved. After all, these are your publications.

Look out for more information on the new SGM website. In the meantime, why not follow us on Twitter at **@PublishingSGM** to hear first about some exciting announcements!

LEIGHTON CHIPPERFIELD, Head of Publishing at SGM
(*Email* l.chipperfield@sgm.ac.uk; *Twitter* @leightonc)

New Books



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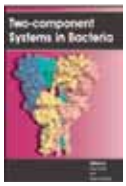

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