Microbiology TODAY

43:1 February 2016

Fungal Diseases

Mycotoxins, food security and climate change
A plague on our ashes
Candida – living with a killer fungus
From peaches to patients: the many faces of cryptococci
The hidden viruses of the fungal kingdom

MICROBIOLOGY SOCIETY

CHLORAMPHENICOL

CAPSULES

Widely distributed throughout the body, including CSF[1]

Oral levels comparable to i.v. levels[2]

Rarely implicated with *C.difficile*[3,4]

Effective against serious infections including:

- *H. influenzae*[1,5]
- Typhoid[1,5]
- MRSA[2]
- VRSA[6]
- Neisseria[1,5]
- Legionella[1,5]
- Rickettsia[1,5]
- *C.difficile*[7-10]
- *E. coli*[1]

Abbreviated Prescribing Information
Chloramphenicol Capsules BP 250mg

Presentation: Hard Gelatin Capsules.
Indications: Typhoid fever and life-threatening infections, particularly those caused by *Haemophilus Influenzae*, where other antibiotics will not suffice.
Posology: For oral administration.
Adults and elderly: 50 mg/kg body weight daily in 4 divided doses. For severe infections (meningitis, septicaemia), this dose may be doubled initially, but must be reduced as soon as clinically possible. Children: Not recommended.
Contra-indications: Known hypersensitivity or toxic reaction to chloramphenicol or to any of the excipients. Should not be used for the prophylaxis or treatment of minor infections; during active immunisation; in porphyria patients; in patients taking drugs liable to depress bone marrow function; during pregnancy, labour or by breast-feeding mothers.
Special warnings and precautions for use: Use only if other treatments are ineffective. Use should be carefully monitored. Reduce dose and monitor plasma levels in hepatic or renal impairment; in the elderly; and in patients concurrently treated with interacting drugs.
Interactions: Chloramphenicol prolongs the elimination, increasing the blood levels of drugs including warfarin, phenytoin, sulphonylureas, tolbutamide. Doses of anticonvulsants and anticoagulants may need to be adjusted if given concurrently. Complex effects (increased/decreased plasma levels) requiring monitoring of chloramphenicol plasma levels have been reported with co-administration of penicillins and rifampicin. Paracetamol prolongs chloramphenicol half-life. Chloramphenicol may increase the plasma levels of calcineurin inhibitors e.g. ciclosporin and tacrolimus. Barbiturates such as phenobarbitone increase the metabolism of chloramphenicol, resulting in reduced plasma chloramphenicol concentrations. In addition, there may be a decrease in the metabolism of phenobarbitone with concomitant chloramphenicol use. There is a small risk that chloramphenicol may reduce the contraceptive effect of oestrogens. Chloramphenicol reduces the response to hydroxocobalamin. Chloramphenicol is contra-indicated in patients taking drugs liable to suppress bone marrow function e.g. carbamazepine, sulphonamides, phenylbutazone, penicillamine, cytotoxic agents, some antipsychotics including clozapine and particularly depot antipsychotics, procainamide, nucleoside reverse transcriptase inhibitors, propylthiouracil.
Pregnancy and Lactation: The use of chloramphenicol is contra-indicated as the drug crosses the placenta and is excreted in breast milk.
Effects on ability to drive and use machines: No significant effect on driving ability.
Undesirable Effects: Reversible dose related bone marrow depression, irreversible aplastic anaemia, increased bleeding time, hypersensitivity reactions including allergic skin reactions, optic neuritis leading to blindness, ototoxicity, acidotic cardiovascular collapse, nausea, vomiting, glossitis, stomatitis, diarrhoea, enterocolitis, Gray Baby Syndrome particularly in the newborn, which consists of abdominal distension, pallid cyanosis, vomiting, progressing to vasomotor collapse, irregular respiration and death within a few hours of the onset of symptoms.
Overdose: Stop chloramphenicol immediately if signs of adverse events develop. Treatment is mainly supportive. If an allergy develops, oral antihistamines may be used. In severe overdosage e.g. Gray Baby Syndrome, reduce plasma levels of chloramphenicol rapidly. Resin haemoperfusion (XAD-4) has been reported to substantially increase chloramphenicol clearance.
Pack size and Price: 60 capsules £377.00
Legal Category: POM.
Market Authorisation Number: PL17736/0075.
Market Authorisation Holder: Chemidex Pharma Limited, 7 Egham Business Village, Crabtree Road, Egham, Surrey TW20 8RB, UK.
Date of preparation: October 2014.
See Chloramphenicol Capsules Summary of Product Characteristics for full prescribing information.

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

References:
1. Martindale: The Complete Drug Reference. Chloramphenicol. [Online]. Available from: http://www.medicinescomplete.com [Accessed 17th September 2015]. **2.** Fluit, A.C., Wielders, C.L.C., Verhoef, J., and Schmitz, F.J. Epidemiology and susceptibility of 3,051 Staphylococcus aureus isolates from 25 university hospitals participating in the European SENTRY Study. Journal of Clinical Microbiology. 2001; 39(10): 3727-3732. **3.** Kelly, C., LaMont, T. Patient information: Antibiotic-associated diarrhea (Clostridium difficile). www.uptodate.com. 2011. **4.** Bartlett J.G. *et al.* Antimicrobial agents implicated in Clostridium difficile toxin-associated diarrhea of colitis. Johns Hopkins Med J. 1981; 149(1): 6-9. **5.** Feder. H, Chloramphenicol: What we have learned in the last decade. Southern Medical Journal. 1986; (79)9: 1129-34. **6.** Weigel LM *et al.* High-level vancomycin-resistant Staphylococcus aureus (VRSA) associated with a polymicrobial biofilm. Antimicrobial Agents and Chemotherapy. Published online ahead of print on 30th October 2006. http://aac.asm.org/cgi/reprint/AAC.00576-06v1.pdf. (Accessed on 17th September 2015). **7.** Ensminger, P., Counter, F., Thomas, L., Lebbehuse, P. Susceptibility, resistance development, and synergy of antimicrobial combinations against Clostridium difficile. Current Microbiology. 1982; 7: 59-62. **8.** Poilane, I., Bert, F., Cruaud, P., Nicolas-Chanoine, MH., Collignon, A. Interest of the disk diffusion method for screening Clostridium difficile isolates with decreased susceptibility to antibiotics. Pathologie Biologie (Paris). 2007; 55(8-9): 429-33. **9.** Cattoir, V., Ould-Hocine, ZF., Legrand, P. Antimicrobial susceptibility of Clostridium difficile clinical isolates collected from 2001 to 2007 in a French university hospital. Pathologie Biologie (Paris). 2008; 56(7-8): 407-11. **10.** Brazier, JS., Levett, PN., Stannard, AJ., Phillips, KD., Willis, AT. Antibiotic susceptibility of clinical isolates of clostridia. Journal of Antimicrobial Chemotherapy. 1985; 15(2): 181-5.

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Editorial

Fungi are widespread in nature and perhaps it is unsurprising that they are often viewed as the benign eukaryotic members of the microbe world. They are responsible for some of the staples of modern living as well as artisan foods, such as leavened bread, blue cheese, craft beer and vintage wines. However, fungi are also responsible for diseases that threaten our food crops and lead to significant economic losses.

Naresh Magan and Angel Medina explain how fungi produce mycotoxins that include some of the most toxic naturally-produced compounds found in food. The authors outline how recent predictions suggest that pests and fungal pathogens are moving at the rate of 5–6 km per year from the equator to the poles with the Earth's changing climate. These new conditions increase the risks of contamination in certain regions that are considered to be 'bread baskets' for food production, which may lead to increased contamination levels by existing mycotoxins, or emigration of other mycotoxins to new regions.

It is not just our food crops that are being impacted by fungi but some of our best-loved woodland trees. Anne Edwards and Allan Downie describe how it became evident that ash dieback disease had established in native woodlands in the east of the UK. They highlight how an open access and crowdsourcing approach led to the establishment of a website (**http://oadb.tsl.ac.uk/**) used to record new observations about the disease's spread. It also provided access to scientific data, generated by scientists who were establishing a foundation of knowledge (using genome analysis) about this pathogen and the tolerance (resistance) map of our native ash trees to this disease.

Fungi are also responsible for revolutionising modern medicine and health; the first clinically important antibiotic was produced by a famous fungus, *Penicillium notatum*. However, there is a dark side to fungi when it comes to human health. The Centers for Disease Control and Prevention states that "fungal infections that are resistant to treatment are an emerging public health problem". Although fungal infections contribute significantly to human morbidity and mortality, their impact on our health is not widely recognised. We have addressed this concern in this issue. Firstly, Neil Gow, Ingrida Raziunaite, Fiona Rudkin, Katja Schaefer and Bhawna Yadav have written an article that highlights how *Candida* thrive as harmless commensal organisms in our oral cavities, gastrointestinal or urogenital tracts and more rarely on the skin. Around 50% of us are colonised at any one time without any noticeable symptoms, but these organisms are opportunistic pathogens that cause infections when our immune system is compromised, or our protective bacterial microflora is depleted.

Candida is not the only fungus causing recent global concern. Since the 1980s, cryptococcal infections have emerged as another major threat to human health as a result of the HIV/AIDS pandemic and a more widespread use of immunosuppressive therapies. Paula Seoane, Rafael Schneider and Robin C. May describe how *Cryptococcus neoformans* and *Cryptococcus gattii* spores are inhaled, leading to problems ranging from skin irritation to blindness; these infections account for almost one million infections per year and around 650,000 deaths.

Finally, Paul Rowley's article turns the tables on fungal infections, examining how there are mycoviruses that infect many important fungi, but often do not cause obvious disease within their host. Instead it appears that many mycoviruses are beneficial to fungi. This may explain the widespread distribution of mycoviruses throughout all fungal taxonomic groups.

Sowmiya Moorthie and Leila Luheshi from the PHG Foundation, an independent thinktank with a special focus on genomics and other emerging health technologies, provide this edition's Comment. They discuss how low-cost whole genome sequencing technology is beginning to transform the way clinical and public health microbiologists and epidemiologists manage the threat of infectious diseases.

As advances in technology impact upon our health and our climate, it is clear that fungi will continue to demand our respect as they pose significant threats to both our environment and our wellbeing. However, as this edition highlights, effective investment in research and developments in technology may also provide at least some of the answers and solutions to this growing problem.

Laura Bowater
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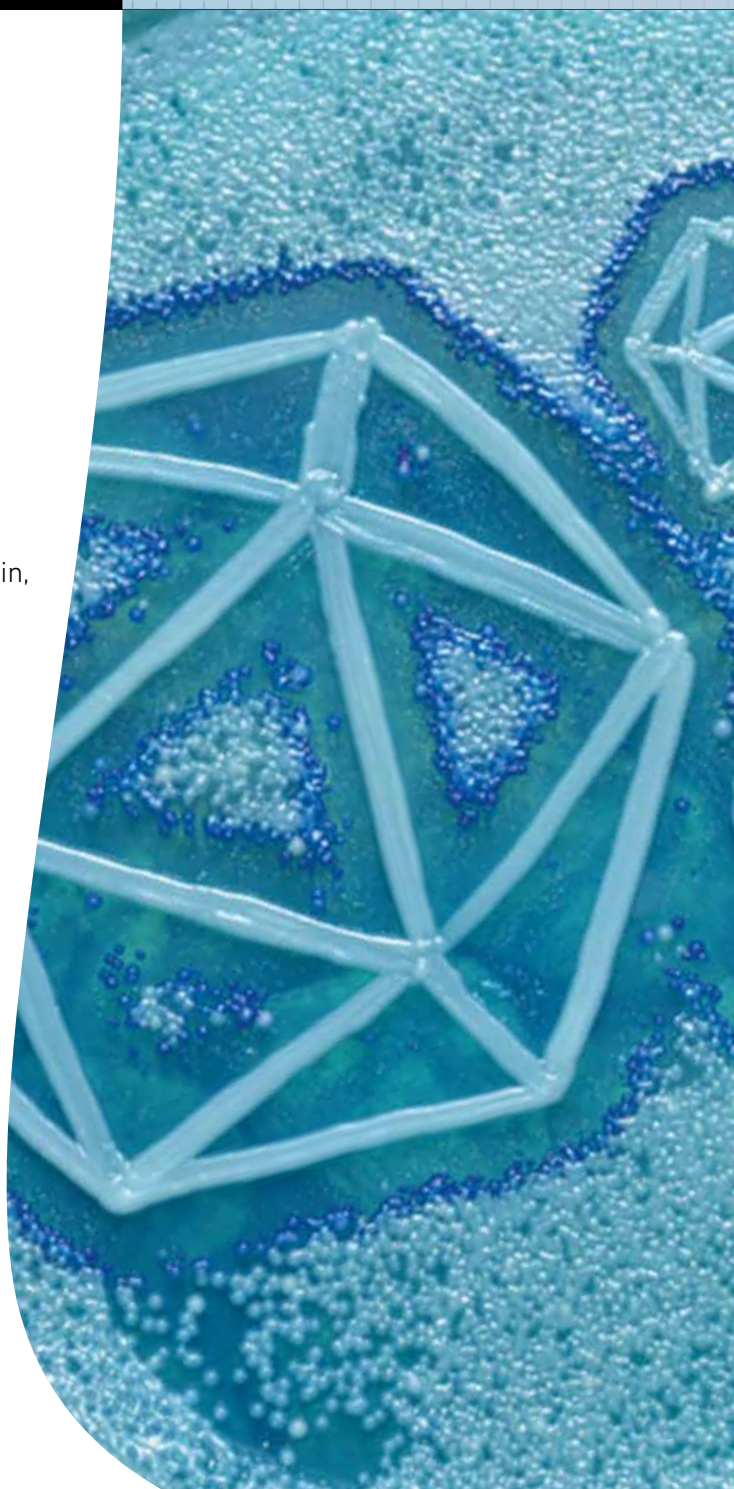

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Features

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Coloured scanning electron micrograph of conidiophores of the fungus *Aspergillus* sp. Microfield Scientific Ltd/Science Photo Library

MICROBIOLOGY SOCIETY

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From the President

A Happy New Year to all of you. This is my first 'From the President' message. The format of this column is short so I am going to have to reign in much of my natural inclinations to tell you how excited I am to have the honour of acting as your spokesperson for the next three years. Some, but not all, of you know that I am a eukaryotic microbiologist, but I do have very broad tastes in microbiology. I hope to convince people by my actions that my approach will be team-based – and as far as I am concerned we, as Society members, are all parts of the same microbiology team.

Good teamwork is based on good communication and a sense of belonging to something that is greater than the individual. So my open plea is to ask you to contribute to the discussion and the future of our Society.

There are a number of Society initiatives I am particularly enthusiastic about. In a previous role at another society I put my shoulder behind establishing a powerful new forum for members at the early stages of their career. We were rewarded for this in many ways – increased membership, better, more appropriate decision-making, engagement with members at an earlier stage, and investment in the society's future and sustainability. It is therefore gratifying to take up office at a time when the Microbiology Society has already started to create the Early Career Microbiologists' (ECM) Forum.

This Forum will be involved in activities to ensure that matters of importance to early career microbiologists are fully embedded and addressed across the Society, from our journals through to the conferences programme. From January 2016 everyone from a qualifying membership constituency will be invited to join – if you have not received an invite but feel you qualify, please let us know. Be clear about this – the Forum will entrust considerable power and influence in our early career members in framing the future of our Society. To find out more about the initiative, please read Peter Cotgreave's comments in the 'From the Chief Executive' article.

The Society has redrafted its strategic vision to ensure it is fit for purpose and is relevant, succinct and clear. This vision remains faithful to the original remit for the Society, set out by Alexander Fleming to promote microbiology and the interactions between microbiologists, but like the microbes we study, it is also constantly evolving. We have refined four strategic pillars: International, Membership, Engagement and Knowledge Transfer, and Sustainability. Within that frame our strategic priorities remain largely unchanged and we will use our collective expertise to ensure that our resources stimulate research, public awareness and policy-making as effectively as possible.

In this context the theme of this issue is 'Fungal Diseases'. To coincide, the Society will be publishing a briefing on serious Human Fungal Diseases that will be distributed to parliamentarians and policy-makers.

My personal congratulations to the winners of the Annual Conference 2016 prizes, all of whom will be giving their Prize Lectures at our Annual Conference, which takes place in Liverpool from 21 to 24 March – more details about the winners can be found in the News section and on the Society's website. The Conference will also host other outstandingly interesting microbiological presentations and there is still ample opportunity to contribute to the meeting via an offered paper or poster presentation. Delegates can register online and read the Conferences pages in this issue to find out more about what's planned for the Annual Conference and the Society's 2016 Focused Meetings.

The Society runs elections each year for positions on its Council, Committees and Divisions (and the new ECM Forum). Being part of these governing bodies gives members the opportunity to influence the decisions and direction of the Society, and to contribute to the fantastic projects and activities the Society produces in support of the microbiology community. Please go to our website for a list of openings, and help our determination to get full engagement from our members by nominating those who would like to make a contribution to the running of the Society.

Neil Gow
President
president@microbiologysociety.org

From the Chief Executive

One of my favourite parts of working for the Microbiology Society is meeting the wide range of members in universities, charities, industry and public service, studying every type of microbe in a myriad of different situations. It is obvious that many of you at the early stages of your careers could play a bigger role in shaping the future of the Society if we had the structures in place to facilitate it. So we have established the Early Career Microbiologists' Forum, to give you not just a voice but real influence and decision-making power.

The Early Career Microbiologists' Forum will be a vehicle for those members who are embarking on their careers to do several things. You will be able to meet, share experiences and learn from one another. You can get involved with activities across the organisation, including conferences, professional development, policy work and publishing. Most importantly, your enthusiasm, ideas and innovation will help shape the Society's programmes. We will have better meetings, more impactful events and more widely read publications because we will be drawing much more heavily than we do at present on the ideas of undergraduates, postgraduate students, postdocs and other early career microbiologists.

Everybody knows that in any university research laboratory, the students and postdocs are major engines of progress. Their professors are all too busy sitting on committees. The same kind of picture is often true in industry, the health service and charities. The Microbiology Society wants to draw on this pattern, and ensure that we too can harness the passion that early career members display for microbiology in all its variety.

At the beginning of the year, every member who is an undergraduate, a postgraduate, a postdoc or is in a similar career stage will be invited to join the Forum. At the Annual Conference in March, the Society's new President, Professor Neil Gow, will officially launch the Forum, and then early career members will elect their own Executive Committee over the spring. The Chair of the Executive Committee will be a full member of the Society's Council, and the other members of the Executive Committee will sit on the relevant major committees. Only by making the Forum a fully integrated part of the Society's governance structure can we guarantee that we really strengthen the organisation for the future. So this is a real chance to get involved in the governance of the Society, to make sure our activities cater to the needs of early career microbiologists. As the Forum evolves, it will become central to helping us to plan conferences, improve our professional development programmes, and grow our outreach and communications activities.

More established members need not worry; we will not be neglecting you. We are already examining ways to enhance our communications and interactions with Full Members and Honorary Members.

Although they do not always realise it, people in the early stages of a scientific career are learning, practising and perfecting a very wide range of skills that are transferrable to other situations. Here are just a few: report writing, giving presentations and other communication skills; networking; group and team working; ethics, regulation and governance; project management; critical thinking; risk assessment; fundraising and financial management; teaching and training others; succession planning; not to mention workplace politics. We want to give you a chance to use these skills in ways that develop your own careers at the same time as strengthening the Society's activities on behalf of our members.

The Early Career Microbiologists' Forum is new, and it will no doubt develop, evolve and improve. To help it do so, we need to know what members want and how we can support your careers. If you have any thoughts or ideas, please let me know, or invite me to come to your lab to meet the students, postdocs or other early career researchers, to hear directly from you how the Microbiology Society can help to connect and empower your communities.

Peter Cotgreave
Chief Executive
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News

2016 events

The following Society events are taking place this year:

- **Annual Conference 2016**, 21–24 March 2016, ACC, Liverpool
- **Focused Meeting: Molecular Biology of Archaea 5**, 1–3 August 2016, London School of Hygiene and Tropical Medicine, UK
- **Focused Meeting: Molecular Biology and Pathogenesis of Avian Viruses**, 27–29 September 2016, Charles Darwin House, London, UK

See pages 30–33 for more details.

Antifungal resistance parliamentary briefing

The Society will be raising the important issue of antifungal resistance with policy-makers later this month, with the publication of our latest parliamentary briefing. The briefing will provide an overview of the challenges posed by antifungal resistance and highlight research being undertaken by microbiologists to tackle this problem.

The Society distributes a series of policy briefings to UK and Irish parliamentarians throughout the year to provide expert information on current issues and to raise the profile of microbiology. Recent briefings include *Microbiology and Climate Change* and *Food Security from the Soil Microbiome*. The briefings are also a great resource for teachers and students. Briefings can be downloaded here: **www.microbiologysociety.org/briefings**

New for 2016: Forum for early career members

The Society is establishing a forum for student and early career members of the Society, as part of a full programme of activities and resources to support the professional development of its members. If you're an undergraduate or postgraduate student member you will be invited to join, as will postdoctoral researchers and other early career members of the Society.

To steer the Forum, we'll be putting together an Executive Committee with roles that bring an early career viewpoint to all of our different streams of work, from conference content to policy work:

- **Chair:** will work with Council and the Professional Development Committee.
- **Chair-Elect:** will work with the Professional Development Committee, which oversees Professional Development at the Society.
- **Treasurer:** will look after the financial responsibilities of the Forum.
- **Conferences Representative:** will work with the Scientific Conferences Committee, which considers the scientific content of Society meetings.
- **Programmes Representative:** will work with the Policy and Publishing Committees, which look after the Society's impact in the policy arena and oversee journal publications, respectively.
- **Communications Representative:** will work with the Communications Committee, which looks after *Microbiology Today*, Education and Outreach, and the Society's other communications outlets.
- **International Representative:** will work with the International Working Group, which ensures the Society is considering its international endeavours.

To find out more about the Forum and each role, make sure you attend our information session at the Annual Conference at 1.30pm on Monday 21 March 2016.

Positions on the Executive Committee will be open to election by members of the Early Career Microbiologists' Forum in Spring 2016, so if you're interested in having an impact on the work of the Microbiology Society, put yourself forward!

Deaths

We are sad to announce the deaths of the following members.

Professor David Greenwood, who joined the Society in 1970.

Professor John Michael Thresh, who joined the Society in 1969.

Please contact **mtoday@microbiologysociety.org** if you wish to notify the Society of the death of a member whose details can be included in this section.

Small World Initiative applications open!

After the Society's successful Small World Initiative undergraduate and school partnership programmes in 2015, we would like to invite members to apply for the 2016 programmes. Applications are now open to run either an undergraduate programme or a school partnership programme, or you can apply for both! There is huge scope to use the programme in whichever way fits into your teaching and course structure, from standalone modules, embedding into the curriculum, or as an extra activity for students. Teachers and technicians at the Association of Science Education conference in January were also given a practical taster session of what the Small World Initiative entails. Both programmes involve students looking for antibacterial compounds in soil samples, and emphasise a more realistic research experience. Details of both programmes are available at **www.microbiologysociety.org/smallworld**

The Society has also been out and about collecting soil samples from well-known sites. You may have seen our news story about Professor Nigel Brown and four-year-old Rory Spence collecting at 10 Downing Street in the summer. Professor Melanie Welham, Executive Director of Science at BBSRC, and Dr Simon Kerley, Head of Terrestrial Sciences at NERC, collected a soil sample from Polaris House, home of the Research Councils, later on in the year. We will be continuing to collect samples from sites of interest throughout 2016, and the results can be seen on our Facebook page: **www.facebook.com/smallworldscience**

Microbial Genomics – call for papers

The Society's newest journal, *Microbial Genomics* (MGen) invites submissions that use genomic approaches to further our understanding of microbiology, from clinically important pathogens to microbial life in diverse ecosystems. The scope covers all of microbiology, including microbial evolution, population genomics and phylogeography, outbreaks and epidemiological investigations, impact of climate or changing niche, metagenomic and whole transcriptome studies, and bioinformatic analysis. The international Editorial Board is led by Co-Editors-in-Chief, Professors Stephen Bentley and Nicholas Thomson, from the Wellcome Trust Sanger Institute, UK. MGen is fully open access and article processing charges are currently being waived during the launch period. Browse the latest articles and find out how to submit at **mgen.microbiologyresearch.org**

Upcoming grant deadlines

Date	Grant	Notes
1 March 2016	Travel Grants	For conferences and courses from 1 April onwards*. Also for members not eligible for Society Conference Grants to apply for support to present at the Annual Conference
15 March 2016	Microbiology in Schools Fund	For School Members looking for funding for microbiology teaching initiatives taking place on or after 1 May 2016
1 April 2016	Research Visit Grants International Development Fund Education and Outreach Grants	For visits and events from 1 June 2016 onwards

Rolling application

Local Microbiology Event Sponsorship – all members can apply for funds to support microbiology-related events, e.g. sponsored talks.

**Please note, you do not need to have received confirmation of abstract acceptance to apply for these grants as conditional offers will be made. In this case, evidence of acceptance is required to claim your grant.*

2016 Prize winners

The Society is delighted to announce our 2016 Prize winners, recognising significant contributions to the field of microbiology. All of our winners will deliver their Prize Lectures between 21 and 24 March at the Society's Annual Conference 2016. This year's winners are:

Prize Medal

Professor Philippe Sansonetti from the Pasteur Institute and the Collège de France

Marjory Stephenson Prize

Professor Steve Oliver from the University of Cambridge

Colworth Prize

Professor Gurdyal 'Del' Besra from the University of Birmingham

Peter Wildy Prize

Professor Wendy Barclay from Imperial College London

Fleming Prize

Dr David Grainger from the University of Birmingham

Keep an eye on the Society's website over the forthcoming weeks for interviews with the winners about their research.

The Society joined with British Society for Antimicrobial Chemotherapy for schools event at FIS 2015

As part of the hugely successful FIS conference in Glasgow in November 2015, the Microbiology Society and the British Society for Antimicrobial Chemotherapy (BSAC) organised a joint primary school event at the Glasgow Science Centre with 95 Primary 7 students attending from two local schools. They all had the opportunity to do a DNA extraction from *Escherichia coli* while discussing how to look for genes relevant to antibiotic production and resistance, thanks to John Schollar from the National Centre for Biotechnology Education. They also looked at antibiotic-producing *Streptomyces* on agar plates, provided by Dr Paul Hoskisson and assisted by Society member Sarah Brozio, as well as taking part in a series of activities from the E-Bug project run by Public Health England. After a welcoming and fun introduction by Professor Nigel Brown, who chaired the session in the auditorium, the students then listened to two inspiring talks by Dr William Malcolm from Health Protection Scotland and Dr Paul Hoskisson from the University of Strathclyde, followed by a Q&A session.

Help shape the future of your Society

In March, nominations to Society Council, Committee and Divisions will open, including positions on the new Early Career Microbiologists' Forum! Participation in the Society's activities offers an exceptional opportunity to develop professional and personal skills, gain new experiences and contribute to the voice and direction of the Society.

If you are interested in making a difference and committed to shaping your Society, check the governance pages on our website for full details on vacancies and information on how to apply.

The Society welcomes contributions and feedback from members. Please contact **mtoday@microbiologysociety.org** with ideas.

Benjamin Thompson
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Mycotoxins, food security and climate change: do we know enough?

Naresh Magan and Angel Medina

Importance of moulds

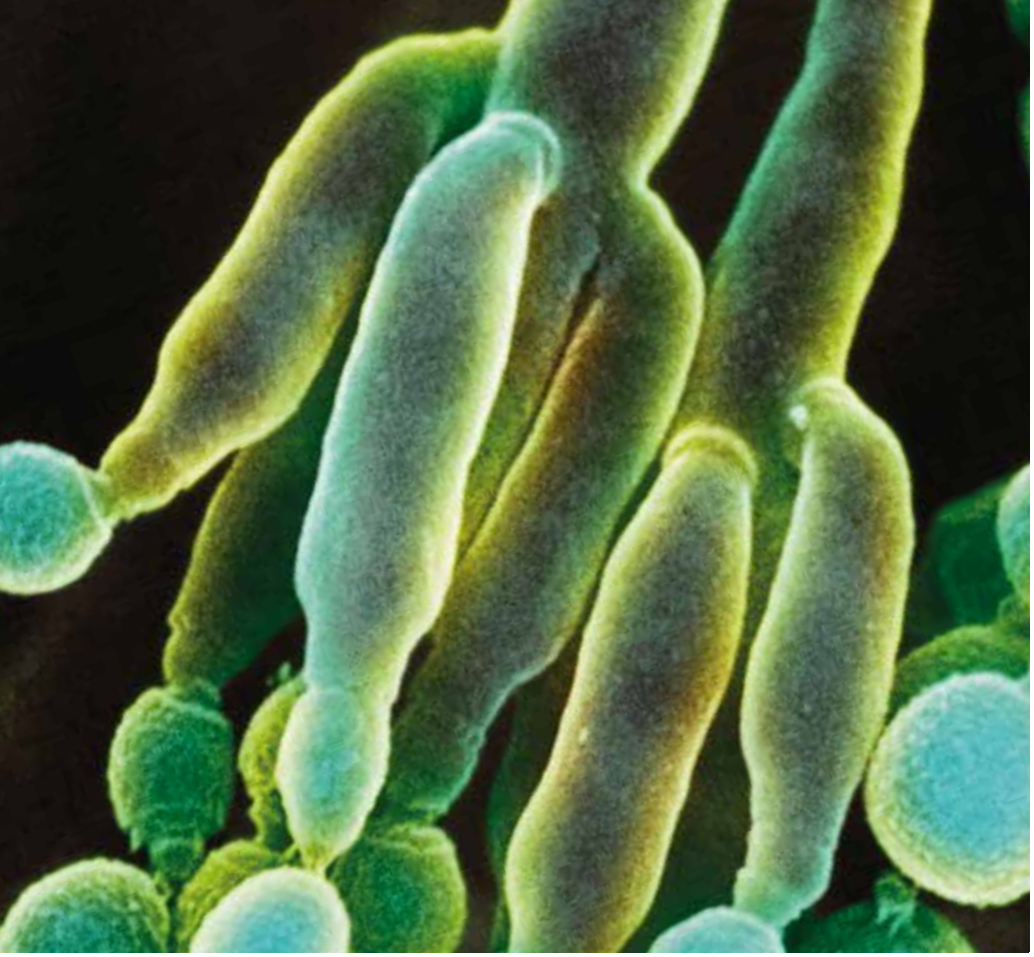
Filamentous fungi are ubiquitous in the environment. They produce millions of spores that allow them to colonise almost all natural habitats. Indeed, they are essential components of the cycling of nutrients in the environment. They can produce a battery of enzymes that allow them to colonise surfaces including humans, animals, food and building fabric. They have both positive and negative impacts on our daily lives. On the one hand, they have been utilised successfully for the production of antibiotics, pharmaceutical metabolites, industrially and medically useful enzymes and, of course, as food. Mushroom production is probably the most successful and economically important exploitation of filamentous fungi. On the other hand, both yeasts and filamentous fungi are responsible for significant economic losses because they cause human and animal diseases. Their spores are responsible for human allergies, cause plant diseases and attack man-made materials, especially building materials under damp conditions. Who has not heard of athlete's foot, thrush, dry rot, or observed the rapid fungal decay of woody materials?

One man's pharmaceutical metabolite is another man's mycotoxin

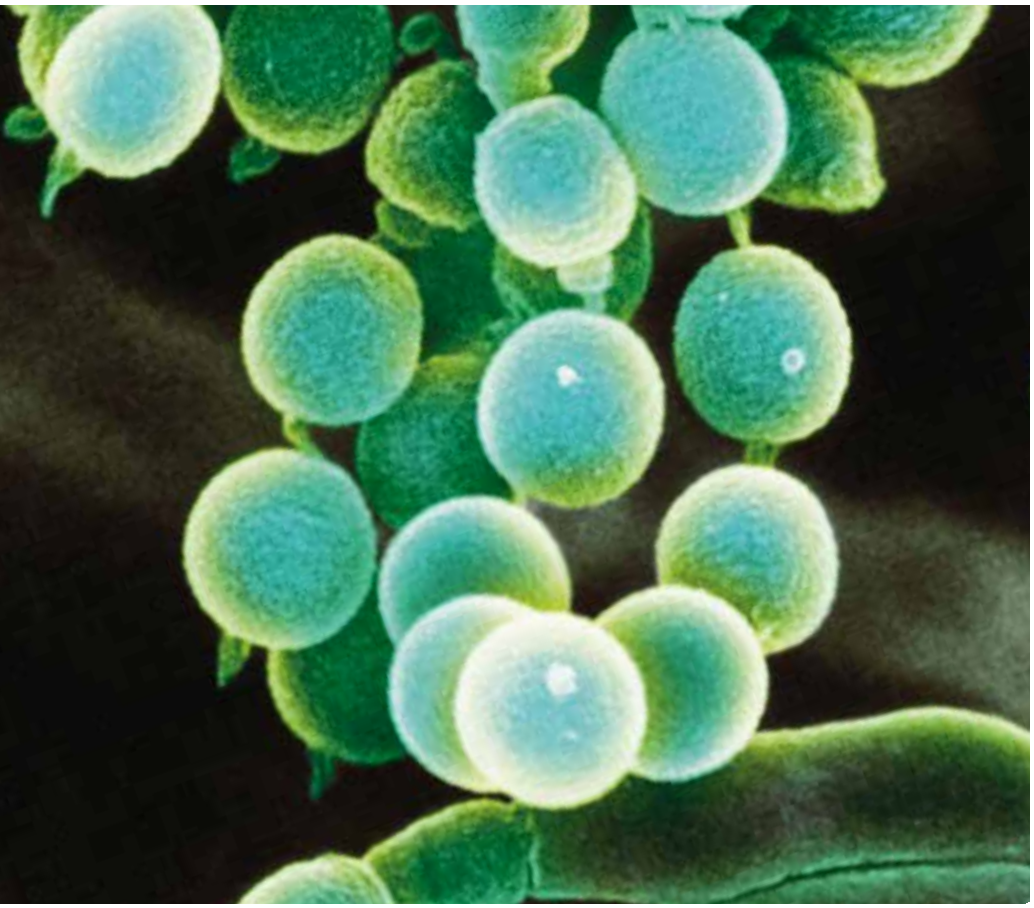
Discovery of mycotoxins and their importance

In the early 1960s, the death of hundreds of thousands of turkey chicks prior to Christmas resulted in an investigation of the probable causes. The turkey feed was identified as the culprit and, after chemical analysis, it was shown that certain secondary metabolites produced by a contaminant filamentous fungus were toxic, and aflatoxin was identified. The fungus responsible was found to be *Aspergillus flavus*. This stimulated scientific research into this area, with the term mycotoxins coined for any toxic secondary metabolite, naturally produced by fungi. Subsequently, aflatoxins were shown to be the most toxic naturally-produced compound in food and were classified as a class 1A carcinogen by the International Agency for Research on Cancer. Thus, the turkey chicks had probably died from liver failure. This resulted in a surge of interest to discover whether other mycotoxins naturally produced by moulds might be present in different food commodities.

Over the last five decades, it has been shown that cereals, nuts, spices, dried fruits, coffee, cocoa, fruit juices, grapes and red wine may all contain mycotoxins produced by filamentous moulds under warm and humid conditions. The mycotoxins of



Coloured scanning electron micrograph of *Penicillium chrysogenum* showing conidia being extruded from a conidiophore. Dr Jeremy Burgess/Science Photo Library



importance from a food safety perspective include aflatoxins (B_1, B_2, G_1, G_2 and M_1), ochratoxin A, patulin, fumonisins (B_1, B_2, B_3), type A (T-2 and HT-2 toxin) and type B trichothecenes (deoxynivalenol and its derivatives, nivalenol) and zearalenone. They are very heat stable and survive processing, and thus are very difficult to destroy. These mycotoxins are produced by *Aspergillus*, *Penicillium* and *Fusarium* species.

They have attracted attention because of their adverse health effects on humans and animals. Aflatoxins, especially aflatoxin B_1, is genotoxic, i.e. can damage DNA, and causes liver cancer in humans and animals. The most recent serious outbreak reported is of school children in rural Kenya who had consumed mouldy maize. This resulted in about 150 fatalities and up to 500 children being hospitalised because of acute exposure to aflatoxins. Other mycotoxins have a range of health effects including kidney damage, gastrointestinal impacts, reproductive disorders or suppression of the immune system. The WHO/JECFA committee has used available data to establish a tolerable daily intake (TDI) level. This is an estimate of the quantity of mycotoxin that someone can be exposed to daily over a lifetime without it having a significant risk to health. The intake of raw or processed food commodities will vary in different regions of the world. For example, maize is a staple food in parts of Africa, while in Europe it may be used predominantly as a small part of the daily diet. Thus, in terms of consumer safety, this complicates the exposure assessments. The European Union has the strictest legislative limits worldwide for mycotoxins (see Table 1). This affects food production within the EU and imports from other countries.

Indeed, it has been shown that in 2014, at the EU borders, from the overall rejections of food/feed commodities for human and animal use, 35% were due to mycotoxin contamination levels above the legislative limits (Rapid Alert System for Food and Feed, RASFF).

Minimising strategies

The development of minimisation or prevention strategies has focused research on mycotoxins for many decades. These have to be considered in the context of the production of many food/feed commodities in tropical and sub-tropical climatic regions. The temperatures and relative humidities are conducive to the growth of mycotoxigenic moulds and toxin contamination during pre-harvest growth of crops and post-harvest, where drying and storage are relatively difficult to manage. While prevention is better than cure, this is often very difficult in such environments.

It is important to understand the optimum and marginal boundary conditions of temperature and relative humidity for growth and mycotoxin production, especially by the key species (*Aspergillus*, *Penicillum* and *Fusarium*), as it can provide the platform for minimisation strategies. This type of data has been used to dry and store food/feed commodities under conditions which do not allow colonisation and mycotoxin contamination by these moulds, especially during storage and subsequent downstream processing, e.g. flour, pasta, fruit juice, dried fruit, nut products, coffee and cocoa processing.

Minimisation strategies have included the use of relatively resistant cultivars (where available), effective pre-harvest Good Agricultural Practices, timing of application of chemical or biological control treatments for pests/fungal infection, and prevailing weather conditions. Hygiene issues, in relation to both pests and mould contamination, are critical during medium and long-term storage and during transport of food/feed commodities. In a global market, these are transported over long distances through different climatic conditions. Many food products are hygroscopic and can easily absorb water and allow mycotoxigenic moulds to grow, and perhaps increase contamination and compromise quality. It has also been shown that storage under marginal conditions, which allow these toxic moulds to grow, will cause quality and nutritional losses, as well as result in rejection for food use. Often, only a small change in dry matter (<0.5%) can result in contamination with mycotoxins above the legislative limits.

The problem of mycotoxins varies with season and is very unpredictable in temperate regions of the world. Thus integrated approaches to combine different types of environmental and crop data, pre-harvest and post-harvest, have now been taken to try and provide an early warning of the relative risk of specific mycotoxins, to try and minimise contamination in food and feed chains.

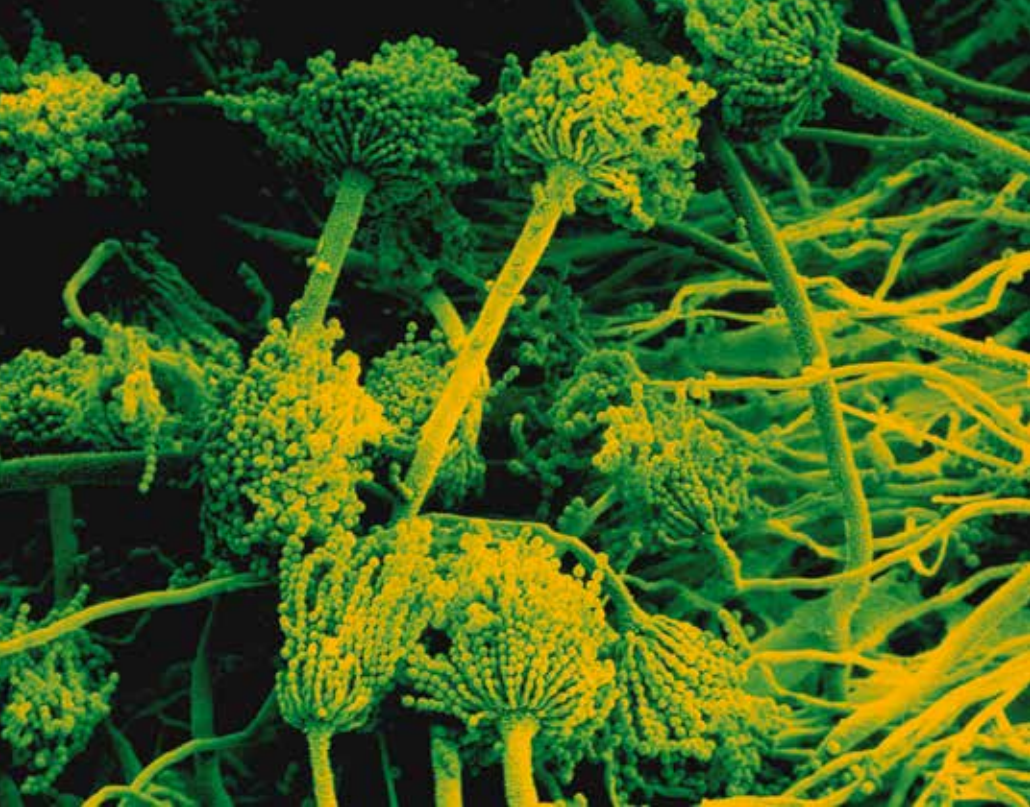
Table 1. Important commodities for which EU legislative limits exist

	Aflatoxin	Ochratoxin A (OTA)	Patulin	*Fusarium* toxins
Groundnuts	+	+		
Nuts	+	+		
Dried fruit		+	+	
Cereals	+	+		+
Maize	+	+		+
Spices	+	+		
Baby foods	+	+	+	+
Coffee		+		
Cocoa		+		
Grape juice		+		
Fruit	+	+	+ (apple)	
Milk, egg	+			
Wine		+		

Climate change, food security and mycotoxins

There are many reports which have shown that predicted changes in weather patterns in different regions of the world will impact on agricultural sustainability. For example, in Europe, southern Europe is considered to be a hot spot for climate change (CC), where combined changes of elevated CO_2 (x2 existing levels), increases in temperature (+2–4°C) and rainfall/drought extremes will have negative effects on food production. Similar impacts are expected in parts of North and South America, e.g. Brazil, and Africa and Asia. This could compromise food security and availability.

A report by the European Food Safety Authority (2012) showed that cereal crops will ripen much earlier in the season in the future than at present and this could result in the potential for additional impacts of pests and diseases, which could increase the prevalence of mycotoxin contamination and affect yields and cereal quality.



Coloured scanning electron micrograph of the common soil-dwelling fungus *Aspergillus flavus*.
Manfred Kage/Science Photo Library

Indeed, in southern Europe and the Balkans, extremely hot summers have already resulted in changes in the maize cultivation ecosystems, resulting in a switch from contamination with *Fusarium* species and fumonisin mycotoxins to *A. flavus* and aflatoxin contamination, which exhibits a much higher toxicity. This has impacted on feed quality and the risk of entry of aflatoxin M_1 (a conversion product of aflatoxin B_1 from feed) into milk and thus the dairy production chains. Recent studies at Cranfield University suggest that under CC conditions, *A. flavus* will grow in a similar way on maize-based substrates or maize grain but that aflatoxin B_1 production will be stimulated. This could have profound implications of mycotoxin contamination of cereals.

Recent global predictions suggest that pests and fungal pathogens are moving at the rate of 5–6 km per year from the equator to the poles. In addition, the diversity of pests and diseases will increase, impacting on sustainable food production. Under these new conditions, there are risks of mycotoxin contamination increasing in certain regions which are considered to be 'bread baskets' for food production. This will be linked to increased mycotoxin contamination due to increased pest damage. Increased contamination levels may occur of existing mycotoxins, or emigration of other mycotoxins may occur to new regions where they were not previously prevalent. Potential also exists for new mycotoxins occurring for the first time because of extreme stress of CC. This could have profound impacts on food sustainability in many regions of the world, with developing countries taking the brunt of the impacts, possibly resulting in negative social consequences.

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A plague on our ashes

Anne Edwards and J. Allan Downie

In late autumn 2012, it became evident that ash dieback disease had become established in native woodlands in the eastern regions of the UK. This was the leading edge of an epidemic that had already swept east to west across mainland Europe over a period of about 20 years.

We were aware of the disease because of our involvement in helping manage Ashwellthorpe Lower Wood, an ancient coppiced woodland in South Norfolk. This woodland, owned by the Norfolk Wildlife Trust, is a Site of Special Scientific Interest (SSSI) and its name, Ashwellthorpe, comes from the Vikings, for whom the ash (*Fraxinus excelsior)* was sacred. It was devastating to see young coppiced regrowth showing early signs of what looked like ash dieback. Since this occurred just a few miles from where we work at the John Innes Centre (which specialises in plant and microbial research), we asked ourselves and our colleagues what we could do to help an iconic native tree.

As a first step, we extracted and tested DNA from infected branches and our fears were confirmed: the trees were infected with the fungus *Chalara fraxinea*, the causal agent of ash dieback. Symptoms of the disease include the wilting (dieback) of young leaves in spring, dying of leaves in late summer while they are still attached to the tree, lesions and cankers on stems and branches, and dieback of the crown. Young saplings and coppice regrowth can succumb quite rapidly, some within one growing season. Older trees can survive an initial attack but many stop growing and may become prone to secondary infections. In other parts of Europe, over 90% of the ash trees were killed or severely affected by the disease, so there was an outcry in the UK as the general public and media realised that this iconic tree may disappear from our landscape.

A new pathogen in Europe

What was already known about the disease-causing fungus? Scientists from across Europe had established that *Chalara fraxinea* is the vegetative (anamorphic) form of the fungus, which kills trees by invading stems and trunks and blocking the vasculature. The fungus also has a sexual form, which was originally named *Hymenoscyphus pseudoalbidus*, because it looked similar to, and has the same host as, *Hymenoscyphus albidus*, which grows widely (but non-pathogenically) on ash trees across Europe. Due to its distinctive characteristics, the pathogen was renamed *Hymenoscyphus fraxineus*, and we now know that where the disease is present, *H. fraxineus* is completely displacing *H. albidus*. Both species live in ash leaf litter and spread by releasing sexual (haploid) spores into the air and infecting surrounding trees. Spores fired upwards from fruiting bodies land on ash leaves, germinate and penetrate as the vegetative form into the petiole and main leaf stem (rachis). When the rachis falls, it takes the fungi with it and sometime during the winter and following spring, the fungi enter the sexual phase of the lifecycle. Pre-fruiting structures start to appear, some of which develop into tiny white cup-shaped mushrooms (ascocarps) less than 0.5 cm wide. There can be 20 of these mushrooms on a single petiole and when they mature in summer, they release highly infective ascospores (around 1,500 per hour every morning in summer months) and the whole cycle starts again.

Normally, trees rid themselves of the saprophyte *H. albidus* in autumn with leaf fall. However, *H. fraxineus* grows faster and more aggressively on ash trees and so, rather than being contained within the leaves and leaf stems, *H. fraxineus* can grow into the woody parts of the tree. There it continues to grow slowly over winter and then in spring probably grows rapidly as the tree starts to initiate new leaf growth. This rapid fungal growth in the phloem and xylem of branches can then strangle the growth of the distal young leaves, causing the characteristic 'dieback' symptoms.

Had the harmless native saprophyte turned into a killer or was the destructive *H. fraxineus* itself a saprophyte which had found itself in a foreign environment without its natural host? The latter theory gained popularity when it was found that Asian ash species such as *Fraxinus mandschurica* were unaffected by ash dieback. Genome sequencing has revealed that *H. fraxineus* has a considerably larger genome (60 megabases) than the saprophyte *H. albidus* (40 megabases) and so these are two related but rather different species. It is probable that *H. fraxineus* was introduced into Eastern Europe, possibly due to movement of trees or leaves from somewhere in East Asia, where *F. mandschurica* is adapted to growth with *H. fraxineus*.

Scanning electron micrograph of the wood of an ash tree (*Fraxinus excelsior*) showing xylem tracheids. Power and Syred/Science Photo Library

Genetic tolerance in ash trees

F. excelsior can respond in different ways when challenged by *H. fraxineus*. Many trees appear to be exceptionally sensitive, dying within a few years of infection; a few others (about 5% in Denmark) seem to be much more tolerant to the disease. In between these two extremes, there is a range of responses. Danish scientists had grown several clones of grafted trees in many different environments and fortuitously a couple of these showed some tolerance (one high and one intermediate) to the disease. Since this tolerance was consistently observed in various locations and in different environments, it could be concluded that the tolerance was genetically determined.

Genomics of host and pathogen

With funding from the BBSRC and Defra, a research consortium called Nornex (**http://nornex.org/**) was set up including groups from the John Innes Centre, The Sainsbury Laboratory and The Genome Analysis Centre (all in Norwich), the Universities of Exeter, Edinburgh and York, FERA, Forest Research, the University of Copenhagen, and the Norwegian Forest and Landscape Institute. The aims were to (a) use genomics-based tools to establish a foundation of knowledge on the pathogen, (b) establish laboratory-based tests of pathogenicity and assays of growth and survival of the pathogen, and (c) use genomics and transcriptome-based approaches in ash trees to try to map tolerance (resistance) to the disease.

These aims were underpinned by a desire to try to take a different approach and use an open access and crowdsourcing approach. As part of that,

Coloured scanning electron micrograph of a fruiting body of the fungus *Chalara fraxinea* (*Hymenoscyphus pseudoalbidus*), the causal agent of ash dieback. Crown © Courtesy of FERA/Science Photo Library

We have preliminary data from the sequencing of tree leaf RNA, identifying potential genetic markers that could be associated with inheritance of tolerance to the disease.

a website called openashdieback (**http://oadb.tsl.ac.uk/**) was established to host new observations and provide access to data generated by the consortium. In view of the intense public interest, we also developed and released Fraxinus, a Facebook-based citizen science genomics-based game (**https://apps.facebook.com/fraxinusgame/**). This enabled non-specialists to contribute to the genomic studies of the pathogen by helping to improve genetic variant predictions from DNA sequence alignments. Many computer programs have been devised to optimise alignments. However, none can improve on the pattern recognition skills of the human eye. Once an alignment process is complete, genetic variations such as single nucleotide polymorphisms (SNPs) or insertion-deletion polymorphisms (INDELs) can be identified and further studied in relation to alterations in, for example, pathogenicity.

The research

Three years on and what has been achieved? We have a good genome sequence of *H. fraxineus*, revealing that it does not contain the great diversity of genes for wood degradation like those used by wood-rotting fungi, but it does possess cell wall-degrading enzymes such as cellulases and pectate lyases used for cellular penetration. It also synthesises toxins, effectors and predicted protein inhibitors to help it evade plant defences. Genome sequencing of different isolates has revealed that there is less genetic diversity in European isolates than in Asian isolates and it seems highly likely that the original *H. fraxineus* came from Asia. We have preliminary data from the sequencing of tree leaf RNA, identifying potential genetic markers that could be associated with inheritance of tolerance to the disease. We believe that we have established a framework that will enable us to predict which trees will be tolerant to the disease, to understand the nature and diversity of the pathogen, and to carry out laboratory-based tests of pathogenicity in tree seedlings. All of these can be used to rebuild a genetically diverse population of trees tolerant to this disease that, over time, will probably kill or severely damage 80–90% of the UK ash tree population.

Fraxinus, a Facebook-based citizen science genomics-based game. Anne Edwards and Allan Downie

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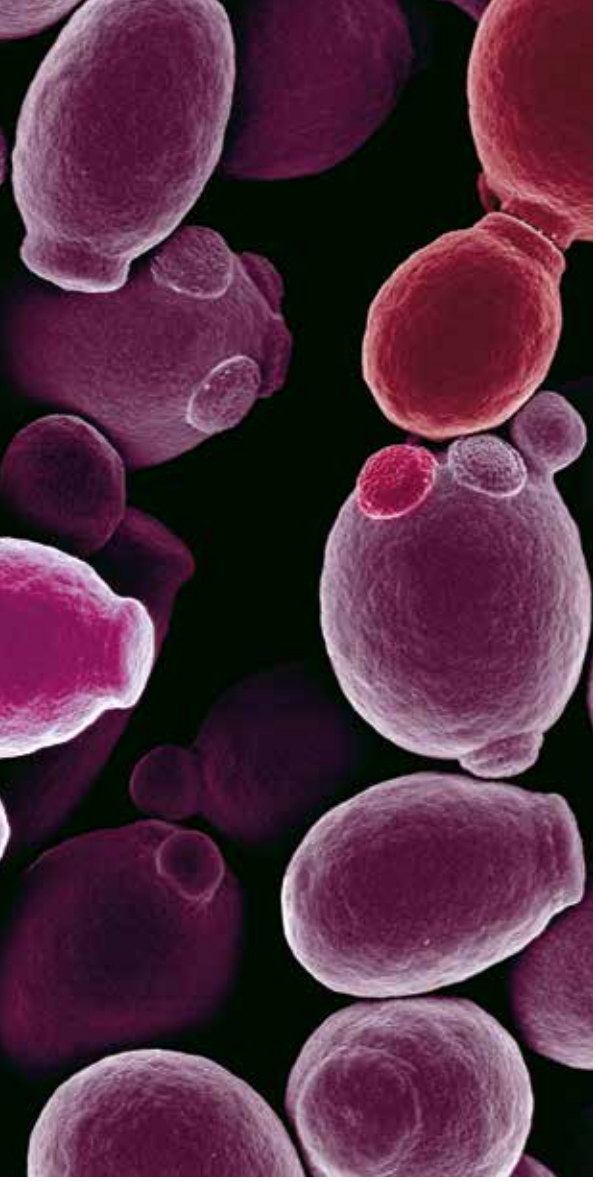
Candida: living with a killer fungus

Neil A. R. Gow, Ingrida Raziunaite, Fiona M. Rudkin, Katja Schaefer & Bhawna Yadav

If you are sneezing your way through winter and wondering whether your immune system is functioning well, then realise that it is at least holding at bay a fungus that colonises most of us, and kills more than 50,000 immunologically vulnerable people every year.

Recent medical advances in the treatment of cancer, trauma, organ failure, HIV and other conditions save many people who years ago would not have survived. These are the new group of patients who are vulnerable to attack by killer fungi, including about a half-dozen species of *Candida*, that profit from any weakness in immunity and health. These species collectively account for the fourth highest burden of human bloodstream infections (around 250,000 each year), of which as many as 40% may not survive. Unfortunately, these organisms do not have a large community of microbiologists backing up our need to know more about them. But we are gradually learning how to hit harder



Coloured scanning electron micrograph of *Candida albicans*. Nature's Geometry/Science Photo Library

with better drugs, to diagnose earlier and to understand the underpinning immunology of fungal infections.

The *Candida* conundrum

Candida species are yeast-like fungi, which normally thrive as harmless commensal organisms in microbiota of the mucous membranes of the oral cavity, gastrointestinal tract or urogenital tracts and more rarely on the skin (Fig. 1). Typically, around 50% of us are colonised at any one time without any noticeable clinical symptoms. However, these organisms are also extremely serious opportunistic pathogens that cause infections when the immune system is compromised, immune barriers are breached or the protective bacterial microflora is depleted. In otherwise healthy individuals, *Candida* species can establish superficial mucosal infections called 'thrush' or 'yeast infections'. However, patients with severely weakened immune systems due to injury, surgical trauma, organ transplantation, long-term antibiotic or chemotherapy treatment, or those with inherited genetic mutations in protective immune signalling pathways, have increased risk of developing more severe forms of disease that can include life-threatening invasive bloodstream or systemic infections. The use of medical implants and central intravenous catheters can also lead to formation of elaborate *Candida* biofilms, which seed bloodstream infections that are difficult to dislodge and are more resistant to antifungal drugs. Another risk category is those fighting other immunosuppressive diseases, such as HIV/AIDS, which has created a vulnerable worldwide population of millions of people who are susceptible to infections from *Candida* and other fungi, like *Cryptococcus*.

Superficial infections of mucosal surfaces are extremely common, occurring in ~25% (~1.7 billion) of the healthy population globally. Around 50–75% of women in their childbearing years suffer at least one incidence of vulvovaginitis and 5–8% (~100 million) women have at least four thrush episodes annually. A further 10 million cases of oral thrush and 2 million cases of oesophageal are added to the annual

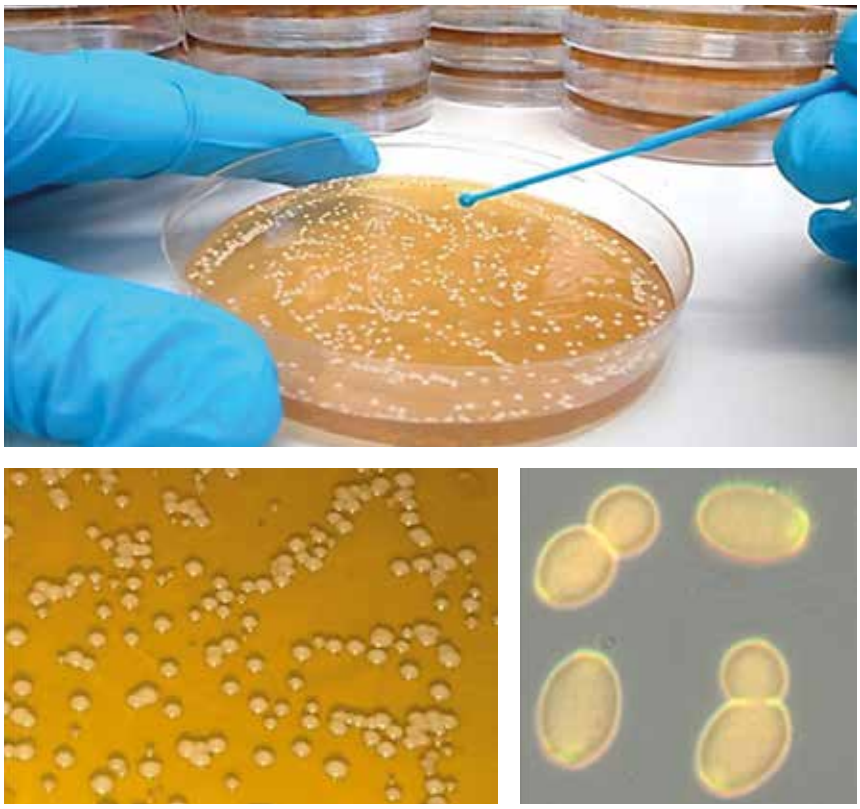


Fig. 1. **Cultivation of yeast cells of *Candida albicans* in the laboratory.** Neil Gow

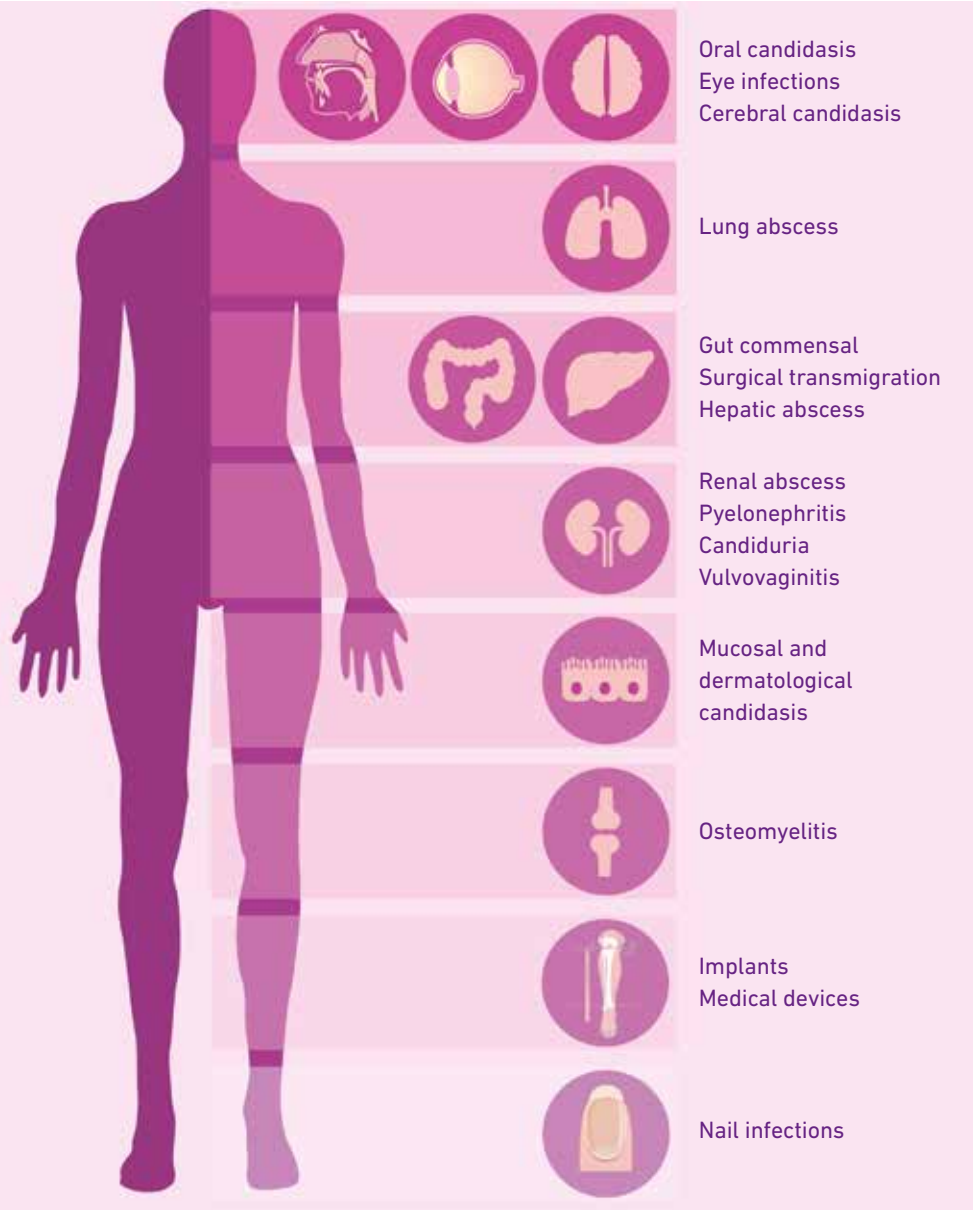


Fig. 2. **Clinical manifestations of *Candida* disease at different body sites.** With thanks to Prashant Sood

disease burden by HIV/AIDS and other mitigating factors. Although less frequent than superficial infections, invasive fungal infections have high mortality rates, often worse than those of bacterial and viral diseases. During these systemic infections, *Candida* has the potential of colonising almost all organs of the human body, leading to life-threatening invasive organ failure and pathological immuno-inflammation (Fig. 2). Annually, candidaemia causes more than 50,000 deaths and is the fourth most common cause of bloodstream infections. More than 250,000 people worldwide are affected by invasive candidiasis, and mortality (up to 37–44%) remains high despite the availability of antifungal drugs.

Hot topics in research

At the time of writing, more than 1,300 papers were published on *Candida* in 2015 alone. This high research activity in the field is yielding fascinating new insights into these pathogens. Human genomics has revealed mutations in human genes such as dectin-1, CARD9, AIRE, IL-12R, STAT1, STAT3, which contribute to susceptibility to *Candida* infections. These observations help us understand the signalling pathways that govern antifungal immunity. A major recent discovery has been the first example of a membrane pore-forming toxin of *Candida* called Ece1 that helps explain why the hyphae of *Candida albicans* cause tissue damage. We are beginning to learn how *Candida* in the gut contributes to the immunomodulatory influence of the gut microbiome and how the fungus adapts during human infection and sidesteps immune surveillance. It was shown recently, for example, that *Candida albicans* generates a specialised GUT form that is adapted for commensal carriage in the intestine. We are also beginning to understand why our immune systems struggle to keep up with *Candida* infections because its cell wall constantly changes its surface properties and is therefore a moving target for our phagocytic white blood cells. Next generation genome sequencing, and a constantly improving set of genetic tools including CRISPR Cas9, are making our knowledge of the connections between the *Candida* genotype and (pathogenic) phenotype ever more accessible.

> **The development of diagnostic tests which are cheap and portable to low-income countries in field hospital conditions is urgently required.**

Future prospects – making a difference

Diagnosing invasive *Candida* infection is challenging because symptoms are often non-specific. Current methods rely primarily on blood culture, which is slow and of limited sensitivity. PCR, serological and proteomic-based methods have been a valuable addition to diagnostics in reducing sample turnaround time and increasing sensitivity. However, these methods do not always discriminate *Candida* colonisation and invasion. Because late diagnosis equates to a poor prognosis, the focus on improving diagnostics is a clinical need as important as generating new antifungal drugs. In addition, the development of diagnostic tests which are cheap and portable to low-income countries in field hospital conditions is urgently required.

Disappointingly, the recent introduction of new antifungal therapies has only had a relatively minor impact on the mortality rates associated with invasive candidiasis. This is in part a knock-on effect of suboptimal diagnostic testing together with drug-associated limitations such as emergence of resistance, toxicity, drug–drug interactions and problems in the route of drug administration. At present, the pipeline of new antifungals is being developed by predominately smaller biotechnology companies rather than Big Pharma, and the focus of their work has been mainly, but not exclusively, on improving the efficacy and half-life of already approved classes of antifungal drugs. In 2015, two new antifungals have emerged – an echinocandin (CD101 IV [Biafungin] – under development for *Candida*) and new triazole (isavuconazole – now licenced by the FDA and in Europe for *Aspergillus* and *Mucor*), both with improved clinical characteristics in various patient settings. Of course, it would be extremely valuable to be able to prevent infection through vaccination of vulnerable patients. However, research into fungal vaccines has lagged behind that of other pathogens and there are currently no antifungal vaccines approved for clinical use. A new generation of experimental vaccines based on *Candida*-specific and pan-fungal cell wall components are beginning clinical trials. Two of these target recurrent vaginal *Candida* infections (NDV-3 [Novadigm] and PEV-7 [Pevion]), and several others have shown efficacy in pre-clinical animal models of infection. In addition, novel immunotherapies which boost antifungal immune competence may be part of future options in antifungal treatment. As we move forward, addressing these research areas is likely to be of upmost importance if we are to reduce the global burden of fungal infections and make inroads to the rather grim statistics relating to candidiasis and medical mycology in general.

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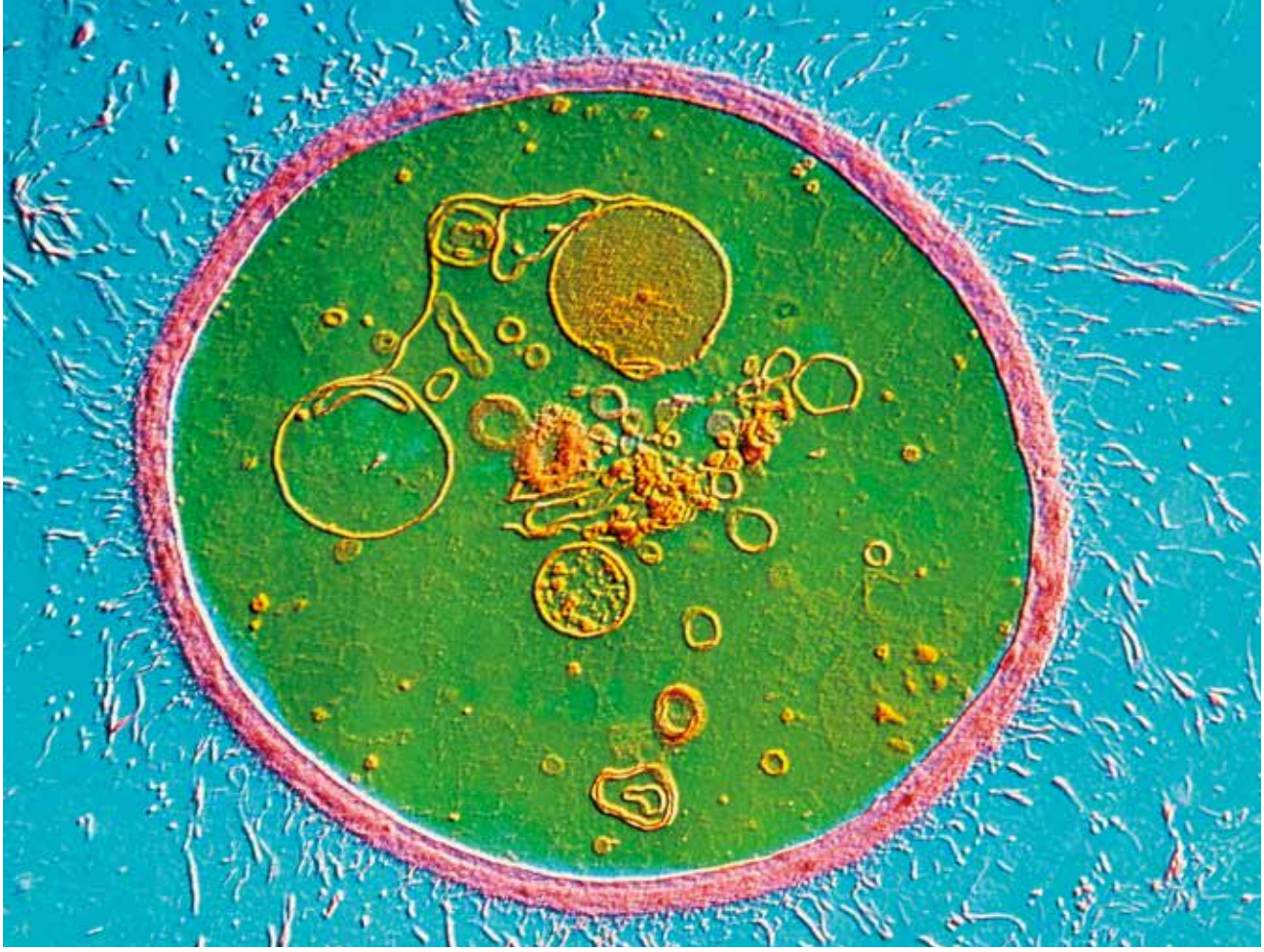


Coloured transmission electron micrograph of *Cryptococcus neoformans*, the cause of cryptococcosis, showing a single, circular encapsulated yeast. CNRI/Science Photo Library

From peaches to patients: the many faces of cryptococci

Paula I. Seoane, Rafael Schneider and Robin C. May

Human diseases caused by fungal pathogens have long been neglected as a medical problem, but the dramatic increase in immunocompromised individuals over the last 50 years, resulting both from the HIV/AIDS pandemic and more widespread use of immunosuppressive therapies, has led to an annual toll of over 2 million deaths due to fungal infections. Additionally, over 300 million people are chronically infected by fungi, leading to problems ranging from skin irritation to blindness.

Cryptococcus species

Amongst the life-threatening fungal pathogens, *Cryptococcus neoformans* and its close relative *Cryptococcus gattii* account for almost 1 million infections per year and around 650,000 deaths. Cryptococcal infections were recognised as a major threat only in the 1980s with the emergence of AIDS, but, in fact, the organism had been first isolated in 1894 by an Italian researcher, Sanfelice, from fermented peach juice and, in the same year, from a patient with a chronic granuloma.

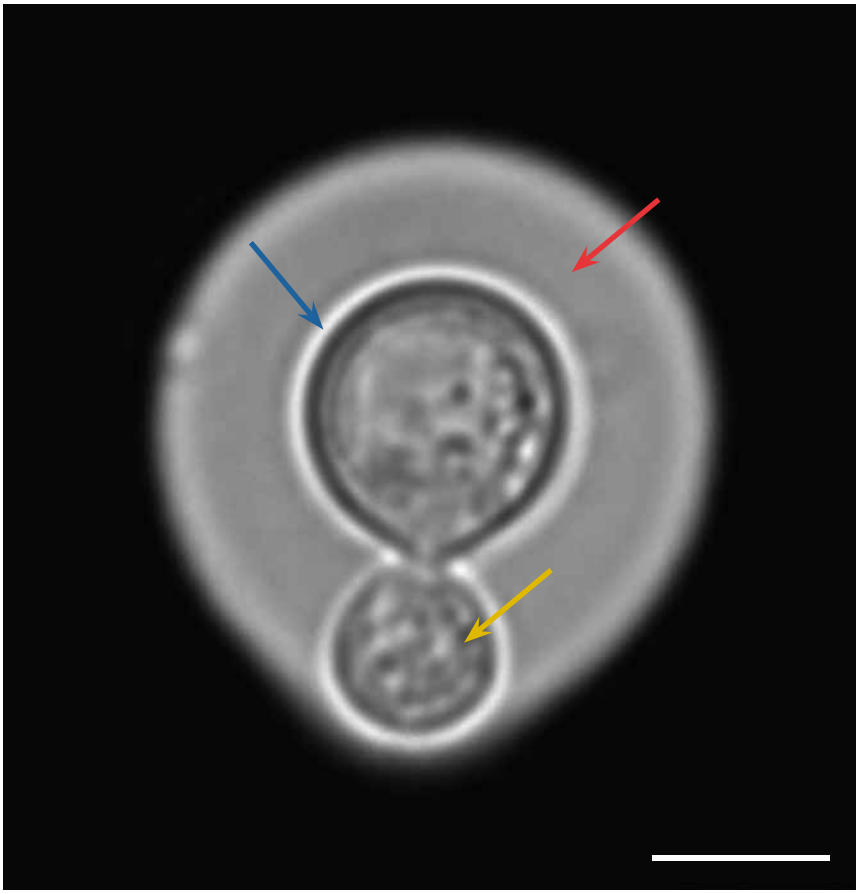
Both pathogenic *Cryptococcus* species are found in a diverse range of niches in the environment, particularly in decaying vegetation of several tree species. *C. neoformans* is also found in bird faeces, which partly explains the high incidence of this species in urban locations.

Cryptococcosis

Cryptococcosis results from inhalation of fungal cells or spores from the environment, causing subsequent lung infection. The first step to disease development is the arrival of fungal cells deep in the alveoli of the lung. Consequently, desiccated yeast cells or spores are considered the most important infectious propagule due to their small size (~3 μm) in comparison to active yeast cells (4–10 μm), since only small cells can penetrate so far into the lung. In most individuals this initial pulmonary infection is rapidly contained, but in people lacking an appropriate immune response, the infection can spread to the blood and central nervous system, causing meningoencephalitis, which is rapidly fatal without treatment.

The ability of these environmental fungi to cause human infections is underpinned by a number of classical virulence factors, most notably the production of a polysaccharide capsule (Fig. 1) which protects *Cryptococcus* from phagocytosis, and the production of melanin pigment, which protects the fungal cell from oxidative damage. Perhaps most remarkable, however, is the ability that cryptococci have to evade immune activation.

Fig. 1. ***Cryptococcus gattii*** **cell stained with India ink, showing capsule (red), fungal cell wall (blue) and the budding yeast (yellow). Bar, 5 μm.** Paula Seoane, Rafael Schneider and Robin C. May



How does *Cryptococcus* evade the immune system?

Normally, exposure to fungal cells triggers a potent inflammatory response. However, *Cryptococcus* yeast cells are remarkably immunologically inert. Not only do they fail to elicit pro-inflammatory cytokines from dendritic cells (as opposed to other fungi such as *Candida albicans*), they actively promote the production of anti-inflammatory cytokines such as IL-10 or IL-4. This cytokine profile enables *Cryptococcus* to repolarise the immune response, reducing the so-called Th1 response (a potent inflammatory and antimicrobial response, which is particularly effective in eradicating intracellular pathogens) and instead shifting towards a Th2 profile, an inflammatory state that is targeted towards large pathogens such as parasitic worms and is ineffective at removing single-celled pathogens such as cryptococci. In parallel, a

proportion of the infecting yeast cells expand dramatically in size to form giant or 'titan' cells. These cells are thought to arise from replication without concomitant mitosis, since they are polyploid and uninucleate, and block phagocytosis both of themselves and, interestingly, of normally-sized neighbouring cryptococci via a mechanism that is not yet characterised.

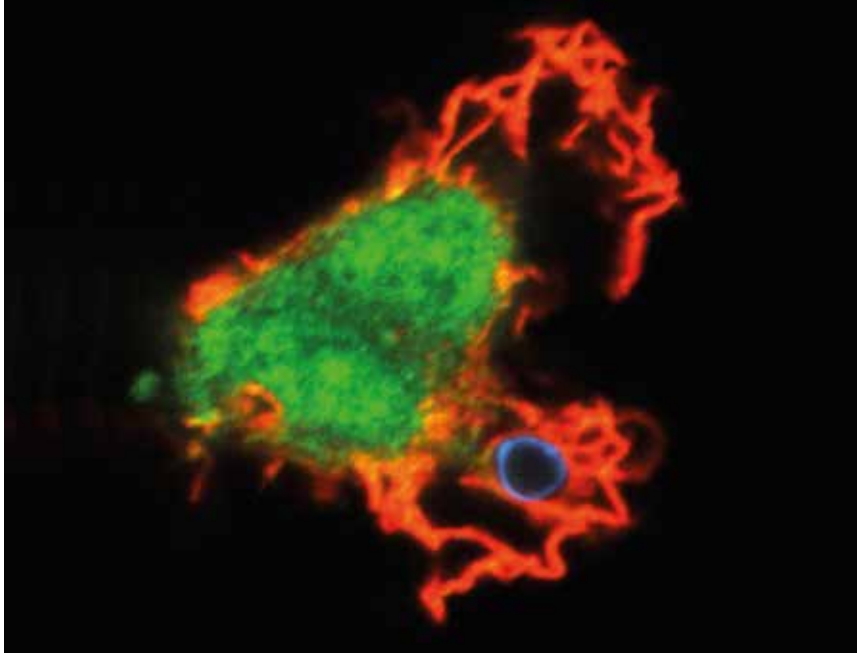


Fig. 2. ***Cryptococcus neoformans*** **cell (blue) being engulfed by a human macrophage (red and green).** Paula Seoane, Rafael Schneider and Robin C. May

Cryptococcus and phagocytes

If these strategies all fail and the invading fungus is engulfed by host phagocytes, cryptococci are able to engage an extra line of defence and persist as facultative intracellular pathogens (Fig. 2). Once inside the host cell, *Cryptococcus* cells have developed numerous mechanisms to both reduce the antimicrobial properties of the phagosome and to neutralise the low pH and reactive oxygen species that are abundant in this organelle.

Once established within the phagocyte, cryptococci are able to replicate rapidly but can also escape the macrophage via an intriguing non-lytic exocytosis, also known as vomocytosis (Fig. 3). Following vomocytosis, both the expelled cryptococci and the macrophage are undamaged. Thus this escape mechanism ensures minimal proinflammatory signaling, and is therefore thought to pose an advantage over lytic escape.

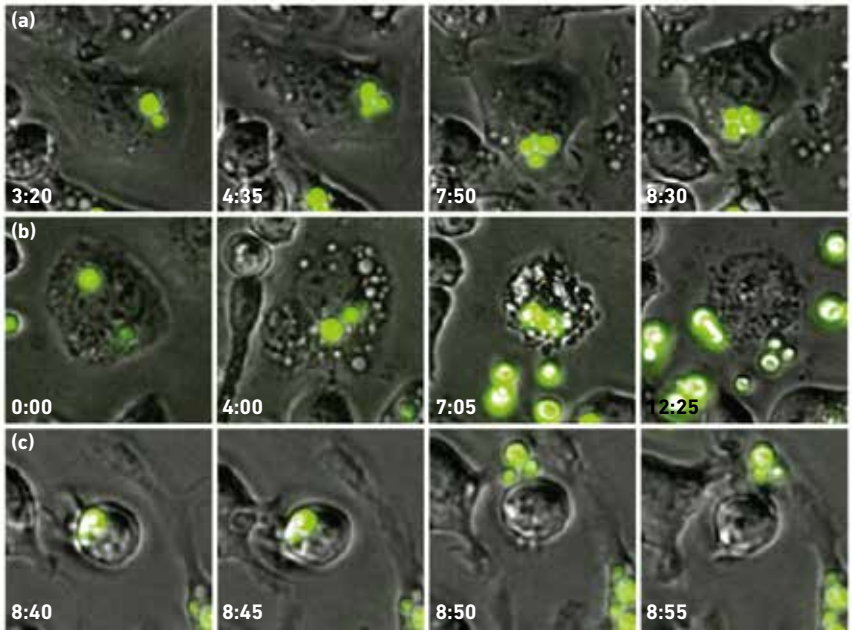


Fig. 3. **Time-lapse images of J774 macrophages infected with GFP-tagged** ***Cryptococcus neoformans*** **exemplifying intracellular replication (a), lytic escape (b) and vomocytosis (c). The time post-infection is shown in each panel.** Paula Seoane, Rafael Schneider and Robin C. May

How does *Cryptococcus* reach the brain tissue?

The most dangerous consequence of cryptococcal infection is meningoencephalitis, resulting from dissemination of the fungus to the central nervous system. To infect this immune privileged site, cryptococci must exit the lungs, enter peripheral blood circulation and bypass the blood–brain barrier (BBB). It now appears that cryptococci accomplish this feat in three ways (Fig. 4). Firstly, yeast cells can make their way through tight junctions of the endothelial cells using proteases such as Mpr1, in a process called paracytosis. Secondly, yeast cells can infiltrate the BBB by transcytosis, a process that is mediated by the interaction between hyaluronic acid in the cryptococcal surface and CD44 present in the luminal endothelium, resulting in direct uptake of the fungus by endothelial cells and migration through the cell's cytoplasm to reach the brain tissue opposite. Finally, a third possibility involves cryptococci crossing the BBB whilst concealed within phagocytes, a so-called 'Trojan Horse' route. Evidence supporting this

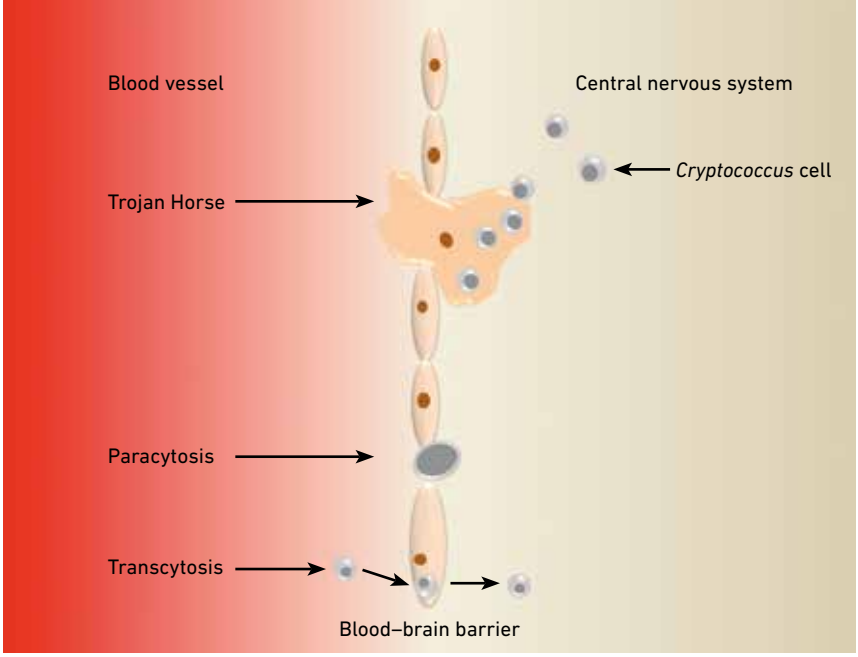


Fig. 4. **Cryptococci can infect the central nervous system by three routes: Trojan Horse, paracytosis or transcytosis.** Paula Seoane, Rafael Schneider and Robin C. May

It now appears that the high pathogenicity of this lineage results from a novel "division of labour" virulence mechanism in which cryptococcal cells collaborate to drive extremely rapid intracellular proliferation and thus overwhelm the host.

mechanism comes from studies in mice where depletion of alveolar macrophages significantly reduced cryptococci burden in the brain tissue and direct infection with *Cryptococcus* results in lower dissemination to the brain than adoptive transfer of infected monocytes.

Cryptococcus: one genus, several pathogens

One of the most remarkable findings of recent years has been the use of comparative genomic/phenotypic studies to reveal subtle differences in the biology of different cryptococcal lineages. Typically, infections with *Cryptococcus gattii,* although much rarer than *Cryptococcus neoformans* infections, cause more aggressive disease symptoms and respond more slowly to antifungal drugs. However, within each species certain lineages appear to be more pathogenic than others. For instance, the VNB lineage of *Cryptococcus neoformans* is associated with poorer patient outcomes than other strains. Most dramatic, however, is the involvement of the VGIIa lineage of *Cryptococcus gattii* in a large cryptococcosis outbreak that started in 1999 on Vancouver Island, Canada. During the following decade, 236 human cases with 19 deaths were reported, almost none of which were in people with classical immune-compromising conditions. Now known as the Pacific Northwest Outbreak, this disease cluster now represents the most serious outbreak of invasive fungal disease in the healthy population to date. It now appears that the high pathogenicity of this lineage results from a novel 'division of labour' virulence mechanism in which cryptococcal cells collaborate to drive extremely rapid intracellular proliferation and thus overwhelm the host, even in the presence of a fully functional immune response.

Summary

Since its recognition as a major threat to human health in the 1980s, research on *Cryptococcus* has highlighted the extraordinary range of virulence factors used by this organism to drive disease. In particular, its ability to modulate host immunity and to enter the central nervous system by hiding inside macrophages has revealed unique aspects of host–pathogen biology. Intensive ongoing genetic, cell, biological and clinical investigations offer the prospect of us soon learning much more about this enigmatic human pathogen.

Acknowledgements

The authors would like to thank Dr Ewa Bielska for providing the image for Figure 1 and Dr Jenson Lim for Figure 2. The authors are supported by funding from the Darwin Trust of Edinburgh (P.S.), the Science Without Borders Program – CNPq (R.S.) and the European Research Council (R.C.M.).

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Further reading

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The hidden viruses of the fungal kingdom

Paul A. Rowley

Mycoviruses growing on medium. Paul Rowley

There are countless examples of plant, animal and bacterial viruses that cause severe symptoms of disease, sometimes with considerable socio-economic consequences. Viruses of fungi, otherwise known as 'mycoviruses', infect many medically and commercially important fungi, but often do not cause obvious signs of disease.

Mycoviruses may have evolved to minimise their burden upon fungi because their entire life cycle occurs exclusively *within* their host cell. Specifically, mycoviruses replicate within fungi but are never released from infected cells to the environment. Mycoviruses are transmitted to a new host by cell division or cell-to-cell fusion. Consequently, if a mycovirus were to cause severe disease, this would profoundly limit their own replication and spread, as their survival is inescapably linked to the success of their host. The apparent benign nature of mycoviruses may potentially explain their widespread distribution throughout fungi. However, fungi have not 'rolled out the welcome mat', as they mount many potent antiviral defences to limit mycovirus replication and spread. Similarly, mycoviruses can subvert fungal antiviral defences through a variety of fascinating mechanisms. The study of mycoviruses offers many unique scientific and commercial opportunities, including the use of mycoviruses and their toxins to control pathogenic fungi, and as a model system to study the fundamental principles of virus–host interactions.

Mycoviruses: nice guys finish last

In contrast to viruses of plants, animals and bacteria that were first described around the beginning of the 19th century, mycoviruses eluded detection by scientists until the 1960s. This was mainly because most fungi infected with mycoviruses do not exhibit any hallmarks of a 'typical' virus infection, such as cell lysis or extracellular disease transmission. Mycoviruses of microscopic fungi were first discovered within antibiotic-producing strains of the *Penicillium* genus. These mycoviruses were only identified because their double-stranded RNA genomes elicited an immune reaction in animals experimentally injected with extracts from infected *Penicillium* species. Similarly, 'killer fungi', that produce antifungal toxins, were described well before the characterisation of the mycoviruses that are responsible for toxin production.

Intracellular biological warfare

Persistent virus infection requires that a virus replicates efficiently and spreads within a host population. Fungi encode a variety of antiviral mechanisms that target mycoviruses to disrupt these processes, while mycoviruses have evolved countermeasures to subvert them.

One example of a potent antiviral mechanism within fungi is RNA interference (RNAi), which recognises and processes mycovirus double-stranded RNAs, leading to the inhibition of mycovirus replication. Disruption of RNAi within fungi can lead to excessive mycovirus replication, resulting in the dilapidation of fungal colonies. Several mycoviruses are known to interfere with fungal RNAi to prevent the inhibition of their replication. In the absence of an active RNAi system, fungi have been shown to leverage alternative pathways to limit mycovirus infection. For example, within *Saccharomyces cerevisiae* the *SKI* genes target mycovirus RNAs for degradation. Mycoviruses counter *SKI* genes by protecting their RNAs with folded RNA structures, RNA modification or by stealing protective 'caps' from host RNAs. 'Vegetative incompatibility' is another striking example of how fungi protect themselves from mycoviruses by preventing cell-to-cell fusion between unrelated fungal species. This often creates a line of demarcation between two incompatible fungi, usually due to cell death, blocking mycovirus transmission.

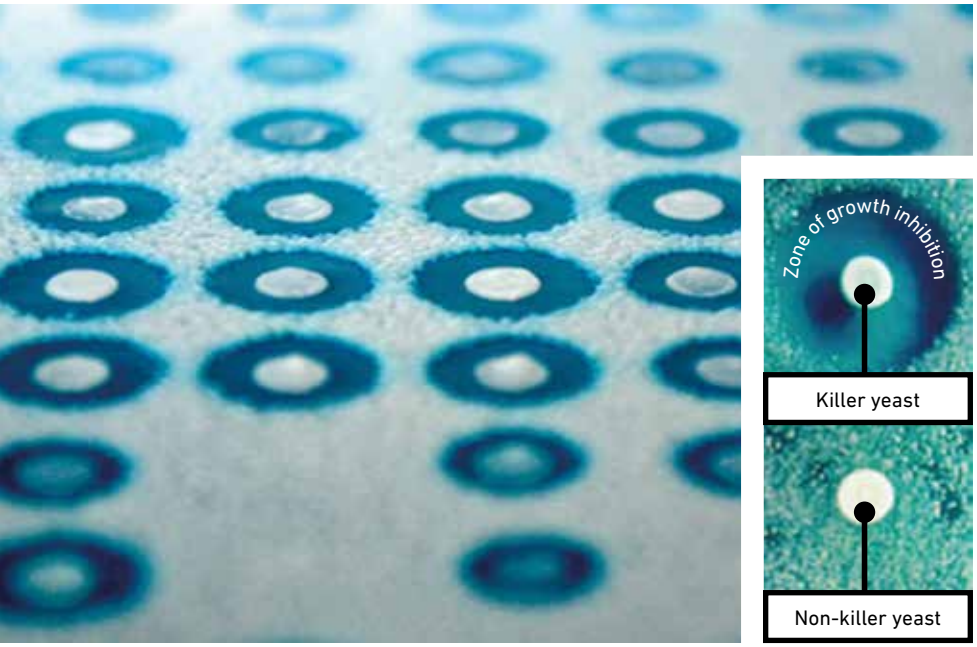
From an evolutionary standpoint, competing virus–host interactions are known to select for the accumulation of mutations that benefit either the host or the virus. For example, if a mycovirus were to steal a fungal protein to aid in its replication, evolution would select for mutations within the fungal protein that would prevent its acquisition by the mycovirus. Faced with an altered fungal protein, compensatory mutations may arise within the mycovirus that again allows the hijack of the fungal

protein. This back-and-forth antagonistic evolutionary cycle can be thought of as a biological arms race, which leads to signatures of evolution that can be detected by statistical methods. There is some evidence of arms race dynamics occurring within fungi; however, their relevance to mycovirus infection remains to be investigated.

Killer satellites

The budding yeast *S. cerevisiae* is an important producer of fermented foodstuffs and is chronically infected with several different types of mycoviruses. As a result of infection by mycoviruses, 'killer' *Saccharomyces* yeasts secrete protein toxins that kill competing fungi. In the laboratory, killer strains cultured on solid growth media produce dramatic clear zones free of other yeasts. These antifungal toxins are produced by satellite double-stranded RNAs that are dependent on the *Totiviridae* family of mycoviruses for their stable maintenance. Satellite RNAs 'steal' proteins that are produced by totiviruses and use them for their own replication. Alone, totiviruses have a minimal impact upon *S. cerevisiae*, but the additional presence of satellite RNAs provides an important example of a beneficial virus system.

Viral killer toxins have been described within many fungi, but there are also examples of killer toxins produced from double-stranded DNA linear plasmids and the genomes of some fungi. Killer toxins can have a very broad host range and kill important human and plant pathogens, but the commercial use of these toxins is often limited due to low environmental stability, narrow host range and potential toxic side effects. However, there has been some success in the production of novel antifungal antibodies and peptides derived from killer toxins and the use of killer fungi as biocontrol agents in agriculture.

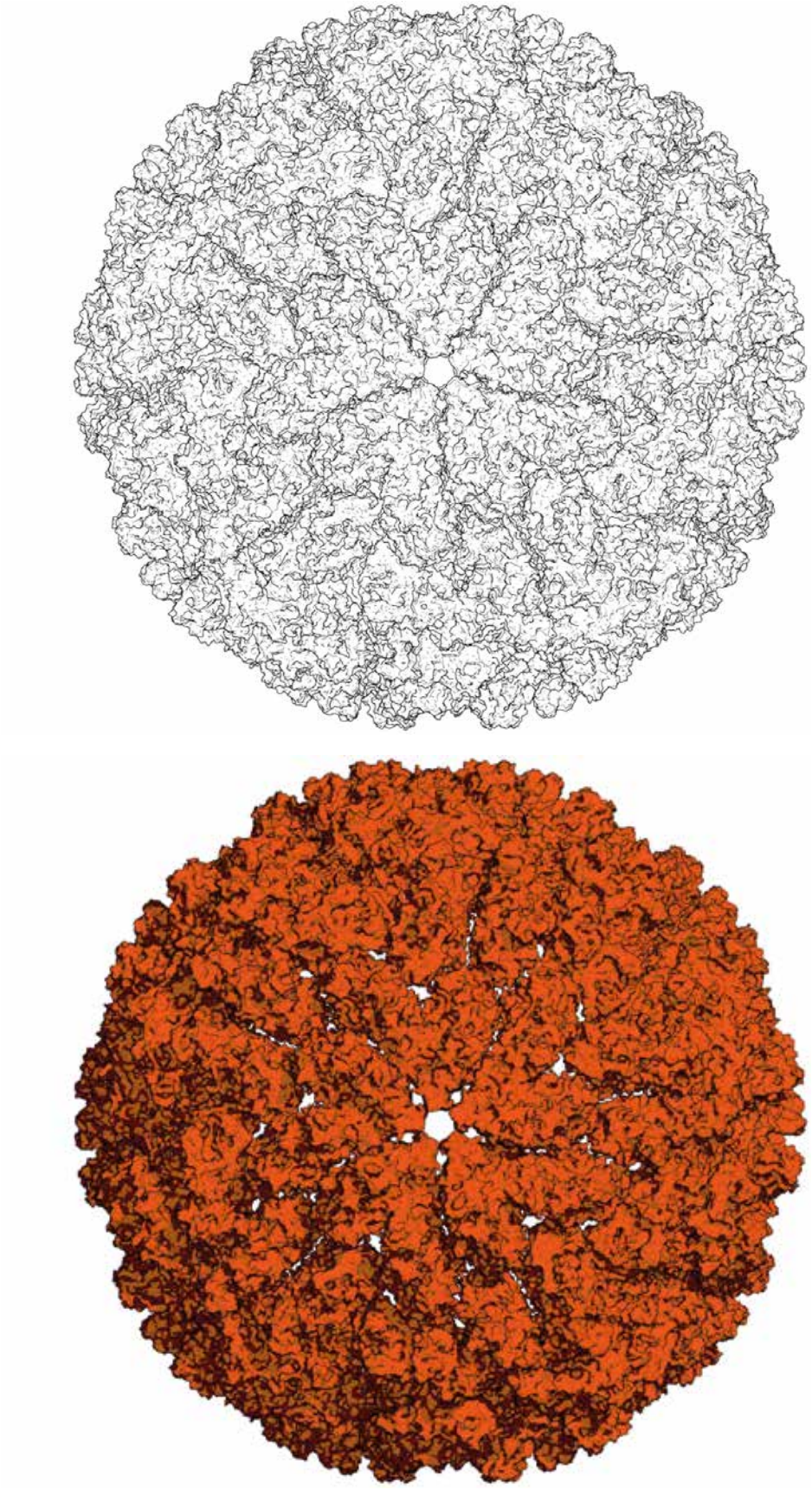


Circular colonies of killer *S. cerevisiae* producing a viral killer toxin that prevents the growth of a competing yeast strain. Paul Rowley

The broader application of mycovirus-based management of pathogenic fungi is worthy of further research, as there are many examples of mycovirus-dependent hypovirulence in pathogenic fungi of commercial fruits, tubers and cereals.

Mycoviruses as an antifungal biocontrol

There are a considerable number of agricultural diseases that are caused by fungal invasion of economically important plants. For example, chestnut blight is a canker-producing disease of *Castanea* species of chestnut, caused by the fungus *Cryphonectria parasitica*. The fungus was introduced into the USA from Asia in the 19th century, ultimately leading to the loss of an estimated half a billion chestnut trees, forever changing the woodland landscapes of North America. Microbiological analysis of recovering American chestnut trees identified strains of *Cryphonectria parasitica* that were hypovirulent (less able to cause disease). Hypovirulence was found to correlate with the presence of a mycovirus of the family *Hypoviridae*. Efforts to control chestnut blight have used hypovirulent *Cryphonectria parasitica* to transmit mycovirus to pathogenic *Cryphonectria parasitica*. There has been mixed success of this approach, as therapeutic outcomes appear to be dependent on factors such as the method of treatment application and the vegetative incompatibility of hypovirulent *Cryphonectria parasitica*. The



The structure of the L-A totivirus capsid from *S. cerevisiae*, which contains the viral double stranded RNA genome. Paul Rowley

development of transgenic hypovirulent *Cryphonectria parasitica* to improve mycovirus transmission is an area of active research.

The broader application of mycovirus-based management of pathogenic fungi is worthy of further research, as there are many examples of mycovirus-dependent hypovirulence in pathogenic fungi of commercial fruits, tubers and cereals. However, mycovirus infection can result in fungal hypervirulence (more able to cause disease), and so a comprehensive understanding of host–virus interactions would avoid potential undesirable outcomes of therapeutic mycovirus infection and increase the utility of current therapies.

There are about 100,000 known fungal species (with an estimated 0.8–5.1 million species in total), but only about 250 mycoviruses have been so far discovered. With the current renewed focus on the development of novel antimicrobial compounds, the untapped diversity of mycoviruses could potentially improve our understanding of the evolution, mechanism and utility of mycovirus-based strategies focused against pathogenic fungi.

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Further reading

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Xie, J. & Jiang, D. (2014). New insights into mycoviruses and exploration for the biological control of crop fungal diseases. *Annu Rev Phytopathol* **52**, 45–68.

Annual Conference 2016

21–24 March, ACC Liverpool

#microbio16

The programme for this year's Annual Conference will be even bigger than before. With the conference attracting more speakers, exhibitors and delegates, it is an event not to be missed!

In addition to the full scientific programme, there will also be the following activities.

Pre-Conference Networking Workshop

Sunday, 18:00–20:00, Hall 2N

On Sunday evening we will be holding our popular pre-Conference workshop. This is aimed at undergraduates, postgraduates and postdocs who are new to conferences or who want some tips on making new connections. The workshop includes activities to hone your networking skills and enhance your conference experience, as well as providing a chance to meet fellow delegates in advance of the Conference.

The event requires pre-booking during conference registration – the ticket price is £12.00 per person and includes dinner. We hope to see you there!

Live at Lunch sessions

Early Career Forum Launch Event

Monday lunchtime, Hall 2F

The Society is establishing a Forum for student and early career members of the Society. Early career members will be invited to join the Forum, which will be steered by an Executive Committee elected from within the group. Join the President and Chair of the Professional Development Committee in a lunchtime session to find out more about the roles that will be up for election during 2016.

An Audience With...

Tuesday lunchtime, Hall 2F

Join Benjamin Thompson, Head of Communications, for an informal Q and A with our Prize Medal winner Professor Philippe Sansonetti. This will be an opportunity to find more about how Philippe discovered microbiology, a bit about his background, his first hand hints and tips on how he developed his career, his breakthrough research, and some of his highlights and challenges thus far.

Big Data or Bust

Tuesday lunchtime, Hall 2N

This one-hour lunchtime session is intended to stimulate discussion and raise awareness around this timely subject of data sharing and integration in the context of pathogen genomics. During the hour there will be an interactive panel and audience discussion chaired by the PHG Foundation. It will help inform the value of effective and responsible data sharing, and the challenges to data sharing and integration.

International Committee on Taxonomy of Viruses

Wednesday lunchtime, Hall 2F

Join the International Committee on Taxonomy of Viruses as they host a live debate on virus speciation and phylogeny. The debate will be chaired by Ursula Gompels, who will ask the panel challenging questions and there will be a live vote. It will be followed by a networking session.

Liverpool waterfront. ACC

Follow the Society on Twitter to keep up-to-date: **@MicrobioSoc**

Prize Lecture Winners

Main Plenary Hall 1A

Peter Wildy Prize Lecture

Professor Wendy Barclay

Monday, 18:10

Microbiology Society Prize Medal Lecture

Professor Philippe Sansonetti

Tuesday, 09:00

Fleming Prize Lecture Award

Dr David Grainger

Tuesday, 18:10

Marjory Stephenson Prize Lecture

Professor Steve Oliver

Wednesday, 09:00

Unilever Colworth Prize

Professor Gurdyal Besra

Wednesday, 18:10

Small World Initiative (SWI) Project Monday all day, Hall 2F

The Small World Initiative is being supported in the UK and Ireland by the Microbiology Society and will give the general public, students and educators in the UK and Ireland the opportunity to work with scientists as part of a global initiative to discover new antibiotics from soil bacteria. It has initially run in undergraduate courses at six universities and in eight school partnerships. A series of 'pop-up' events is giving the public the opportunity to submit their soil samples and track the analysis process. If you would like to run the Initiative in your university, form a partnership with a school or if you are interested in the Citizen Science project, come to this session. You can also visit the Society's stand at the Conference for information.

Meet the Speaker Monday–Wednesday, 19:30–20:30, Lower Gallery

Each evening we will be providing delegates and guests the opportunity to meet and greet some of the key speakers appearing at this year's event. Located in the Lower Gallery with nibbles and comfy seating this event will provide you the perfect opportunity to ask those pressing questions. Check our programme at the Conference for who will be making a guest appearance.

Live Debate Tuesday, 19:15, Hall 2N

Why not join Jake Dunning and Stuart Nichol, who will be our hosts this year for our lively debate? The debate will focus on the human face of Ebola and Ebola trials. Following this, we will provide some time and reflection to our members who have worked on the front line, looking at pictures and commending their contribution to this research.

Social Programme

MicroRoc Monday evening, Poster and Exhibition Space

Society members will be airing their musical talents on stage. Council members Nicola Stonehouse (Leeds – vocals) and Steve Diggle (Nottingham – bass) will be joined by ex-Council members Matt Hutchings (UEA – drums) and Mark Harris (Leeds – guitar), together with Ville Friman (York – guitar), and some special guests.

Science Showoff Wednesday evening, Poster and Exhibition Space

You will have the chance to see a special gig from the highly recommended Science Showoff on Wednesday night. This is a chaotic science comedy cabaret featuring Steve Cross, and the gig will have a microbiology theme to showcase new ways to talk about and share the science of living things. Expect some guest stars from the Conference, taking the stage in a completely new way.

Food can be purchased on site and a cash bar will be open until 22:00. We hope you can join us.

CPD credits

Our Annual Conference has now been accredited by the Royal Society of Biology (114 credits), Institute of Biomedical Science (38 credits) and the Royal College of Pathologists (30 credits). Please ask the Professional Development team at the Conference for information or contact **grants@microbiologysociety.org**

Online registration

Online registration is open until Monday 14 March. View the full programme and register today: **www.microbiologysociety.org/conferences**

Focused Meetings

Focused Meeting 2016: #Archaea5

Molecular Biology of Archaea 5

1–3 August 2016

London School of Hygiene and Tropical Medicine, London, UK

Scientific Organisers Thorsten Allers (University of Nottingham, UK)
Malcolm White (University of St Andrews, UK)

Archaea were identified as a separate group of organisms in the 1970s and are the third domain of life, alongside eukarya and bacteria. Archaea are single-celled organisms that contain no nucleus or organelles and have some similarities with bacteria but are evolutionarily distinct. They survive in some of the most extreme habitats on Earth, including volcanic springs, hypersaline lakes and deep sea vents.

This Focused Meeting is jointly hosted by the Microbiology Society and the Genetics Society, with generous support from the BBSRC. The meeting supports the microbiology community and its understanding of this domain of life, highlighting how modern techniques, including CRISPR, are aiding scientific understanding of this group of organisms.

It is the fifth in the international conference series, Molecular Biology of Archaea. The conference will run over three days. On the first day of the meeting there will be a BBSRC-sponsored workshop on Genetic Manipulation of Archaea.

A wide range of prestigious, international speakers will be talking at this meeting, including Tom Williams (Bristol University, UK), Julie Maupin-

Focused Meeting 2016: #Avian16

Molecular Biology and Pathogenesis of Avian Viruses

27–29 September 2016, Charles Darwin House, London, UK

Scientific Organisers Mike Skinner (Imperial College London, UK)
Venugopal Nair (The Pirbright Institute, UK)

Avian viruses have contributed immensely to our understanding of not only virology but important aspects of biology including cancer, immunology and cell biology. In recent years, the role of birds as sources of zoonotic viruses (avian influenza, West Nile, Japanese encephalitis, the equine encephalitis viruses) has become apparent. With a plethora of viruses, and with frequent occurrence of emergence of novel pathogens and continuing diversity, the vaccination strategies widely used by the industry are being challenged. This timely meeting focusing on avian viruses will

Monticelllo / iStock / Thinkstock

Furlow (University of Florida , USA), and Iain Duggin (University of Technology Sydney, Australia).

Key topics will include:

- DNA, chromosomes and cell cycle
- RNA, CRISPR and viruses
- Molecular assemblies and protein modification
- Genomes and evolution

bring together the international scientific community to assess the extent of the problem and help find solutions.

Topics will include:

- Molecular biology and genetics of avian virus replication
- Tropism and host range restriction
- Pathogenesis of avian viruses
- Host antiviral responses and virus immunomodulation
- New and improved approaches to the control of avian viruses

Registration and abstract submission is open for both meetings. Visit: **www.microbiologysociety.org/focusedmeetings**

Get involved

The Society welcomes Focused Meeting proposals throughout the year on any aspect of microbiology.

The Scientific Conferences Committee meets twice a year to review the proposals. If you have an idea please complete the form online and return to the Conference and Events Office by the next deadline, **17 June 2016**.

Focused Meetings offer benefits to both delegates and organisers in many ways, from networking to learning. We asked our 2015 session organisers to provide us feedback on their experience.

Submit your Focused Meeting proposal. Visit: **www.microbiologysociety.org/proposals**

Previous organisers

Alain Kohl

University of Glasgow, UK

International Meeting on Arboviruses and their Vectors

"The International Meeting on Arboviruses and their Vectors (IMAV) 2015 was my first experience of running a Focused Meeting. It turned out to be a great occasion that really fulfilled the aims of bringing the community together and showcasing great science. The experience and support of the Society team was hugely important in the smooth organisation and running of the event – I and everyone else on the Organising Committee are very grateful for all their work and help along the way."

Nick Read

University of Manchester, UK

International Meeting on The Invasive Fungus

"Organising a Focused Meeting jointly between the Microbiology Society and the British Mycological Society on the topic of 'The Invasive Fungus' proved to be a joy! The exceptional administrative support and interpersonal skills of the Society team at every step along the way made the meeting an outstanding experience and success for the organisers, speakers and delegates."

JMM Case Reports annual round up

This year has seen an exciting development for *JMM Case Reports*, the Microbiology Society's first open access journal. We have seen the journal move from strength to strength and take on some pivotal changes, including publishing accepted papers within three days and Editorial Board restructures. The journal also held its first board meeting at the Society Annual Conference in Birmingham last year.

Dr Robert Hall has joined *JMM Case Reports* as a Co-Editor-in-Chief alongside Dr Johannes Kusters, who has been influential in the creation of the Editorial Board and progress of the journal. In 2016, we will see both Editors-in-Chief working to pilot translated abstracts for *JMM Case Reports*. Of the journal, Dr Hall has said: "With high-quality reviews and expedited publication, the Case Report can enjoy a revival, and return to its rightful place as the source for the most up-to-date clinical isolates and research data on microbial pathogenesis, evolution, epidemiology, diagnostics, and of course case management. It is particularly gratifying to be working with our professional society on a project for the benefit of our international microbiology community."

The Editorial Board has also expanded, taking on four new Executive Editors and six Editors, increasing the international and diverse scope of the journal. The new additions to the Editorial Board will be influential to the advancement of the journal and the great efforts of existing Editors, who we thank dearly for their hard work.

Elizabethkingia meningoseptica: an unusual cause for septicaemia, a Case Report in the 'blood/heart and lymphatics' subject category, has been one of the most well-received papers of the year. The paper was published last February and has gathered momentum since 2015 (**http://microb.io/1MlxeeS**).

Thank you to everyone who has had a hand in the growth of *JMM Case Reports* and we, the Society, hope that the journal continues to develop and encourage the progress of medical microbiology.

Further reading

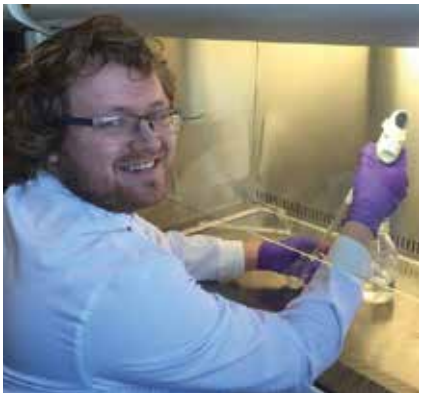
Swain, B., Rout, S., Otta, S. & Rakshit, A. (2015). *Elizabethkingia meningoseptica*: an unusual cause for septicaemia. *JMM Case Rep* doi:10.1099/jmmcr.0.000005

Colin Ratledge Center for Microbial Lipids

A new research centre for lipid research has been opened at Shandong University of Technology in Zibo City, Shandong Province, China. The centre has been named in honour of Society member Professor Colin Ratledge, Emeritus Professor of Biochemistry in the School of Biological, Biomedical and Environmental Sciences at the University of Hull, UK. Professor Ratledge is one of the foremost researchers in the field of microbial oils that are produced commercially as sources of various polyunsaturated fatty acids. The Center for Microbial Lipids was opened by Professor Ratledge on 16 October 2015. It will develop new ideas as to how to improve lipid production in a variety of micro-organisms.

C. Ratledge

Grants



L. Sherry

Where could a Microbiology Society grant take you?

Dr Lee Sherry is a postdoctoral researcher at ENS de Lyon, France. Lee previously undertook his PhD studying influenza viruses, with Dr David Jackson at the University of St Andrews.

During 2015, Lee received three different Society grants: a Research Visit Grant, to support a trip to the Institute of Medical Virology, University of Zurich, to work with Dr Jovan Pavlovic; a Society Conference Grant to present at our Annual Conference 2015 in Birmingham; and a Travel Grant to present at the American Society for Virology (ASV) 34th Annual Meeting in Ontario, Canada. We asked Lee how the grants have helped his professional development.

What did you do during your research visit?

We wanted to characterise the impact of specific mutations in our protein of interest, MxA, using biochemical analysis of purified protein. The Pavlovic group were welcoming, making it very easy to settle in. To learn protein purification, I shadowed one of Jovan's students, Patricia, who is an expert in MxA purification, having purified many mutants throughout her PhD.

I arrived in Zurich with my plasmids, ready to express the mutants. However, we didn't get great expression. As a result we changed the plan and I was only able to express and purify the protein – this was still a valuable technique that I was able to take back to the lab. I presented some of my work to the department in Zurich and received useful feedback that helped shape the rest of my PhD project.

How was your experience of presenting your research?

I gave oral presentations at both the Microbiology Society and ASV conferences. It was a little nerve-wracking to begin with but I quickly eased into the talks; by the end I was almost enjoying myself! The talks were well received, and I was asked some interesting questions, which were followed up during the breaks. The talks were great for networking and getting other perspectives on our work.

How did your experience of travelling, collaborating and presenting help your career?

The conferences were both helpful for learning how to succinctly disseminate my ideas in a short oral presentation; I can explain my work much more clearly now. The research visit had a big impact on my PhD project as the feedback received led to a completely new chapter in my thesis. My visit also broadened my search for potential jobs: I had previously only considered working in English-speaking countries, but after the trip I realised that I enjoyed working in a different culture even if I didn't speak the language. Now, here I am: working in Lyon, learning French as I go.

Any advice for PhD students looking to enhance their career prospects?

My main advice is to take advantage of any grants that are on offer. If there is an experiment that you would like to do but is not possible at your institute, check your eligibility for a Research Visit Grant. It is a great opportunity to learn a new technique, start a collaboration and even embrace a different culture.

To find out more about our grants, see **www.microbiologysociety.org/grants**

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Schoolzone

Fungi in schools: a neglected potential

Ten years ago, Moore *et al.* (2005) concluded that the most likely answer to the question "how much are your children taught about fungi in schools?" was "very little or nothing at all". They remarked that the word 'fungus' did not appear in the then current National Curriculum for England Programme of Study for Science, and although fungi tended to be treated reasonably in the specifications for the GCSE Biology examinations, the references were largely along with bacteria as decomposers without reference to the basic distinction between the two groups.

The situation is a little better today but a feeling of missed opportunities to learn about a group that is of fundamental importance to so much of everyday life remains among the sadly dwindling numbers of professional mycologists as well as by concerned observers.

Much effort has been made by the British Mycological Society (BMS) in attempts to remedy the situation by lobbying educational advisers to examination boards and producing a range of classroom resources and materials, e.g. Fungi 4 Schools (see **http://microb.io/10y1bg8**). In addition, BMS is a sponsor of the Microbiology in Schools Advisory Committee (MiSAC) whose activities show that whatever the position of formal mycology education, there is an untapped interest and enthusiasm for the subject in schools. The evidence lies in the high level and quality of responses to the MiSAC Annual Competition when a fungal topic is featured.

The MiSAC Annual Competition

The annual competition is one of the main activities of MiSAC, an organisation founded in 1969 following a joint initiative by the Society for General Microbiology (now the Microbiology Society) and the Society for Applied Bacteriology (now the Society for Applied Microbiology, SfAM). The other main activities are developing information resources and practical activities, giving talks and workshops, providing advice through a helpline, and serving as a recognised authority on health and safety (see **www.misac.org.uk/about.html**). MiSAC is a voluntary organisation funded by annual sponsorship from BMS, CLEAPSS, Microbiology Society, National Centre for Biotechnology Education, Quekett Microscopical Society, SfAM and Scottish Schools Education Research Centre.

The competition receives additional special sponsorship for prize money and administrative costs, usually from one of the annual sponsors. There are two entry groups, Key Stage 3 and Key Stage 4 (equivalent to ages 11–14 and 14–16, respectively), which attract entries from throughout the UK and often some from Ireland and British schools in Europe. Each year's topic is linked to the National Curriculum but the requirements are framed to encourage students to explore beyond its boundaries. The topics range widely over areas such as environmental issues, health care, food production and food safety. Other topics have involved producing a social media profile for a microbe and a requirement to use a microscope. The requirements specify a particular format, e.g. information leaflet,

Above: *from left to right* KS3 winners (1st, 2nd, 3rd) and KS4 winners (1st, 2nd, 3rd).

Right: Thai schools competition winners (*from left to right* 1st, 2nd, 3rd).

poster or news article, and target group, e.g. classmates or the general public (see **www.misac.org.uk/competition.html**). The requirement for 2016, the 28th competition and funded by SfAM, is to produce a news story for an internet news media site on 'How microbes work for us'.

Fungal topics in the UK

BMS has funded the following MiSAC competition topics: 'Fungi: friends and foes'; 'I've got you under my skin: Fungal infections of the human body'; 'Fungi in your shopping trolley'; 'Medicines from fungi'; 'Helpful and harmful fungi'; and 'Fearsome fungi'. It is encouraging to report that the number and quality of the entries is always on a par with those on other aspects of microbiology.

In view of the theme of this issue of *Microbiology Today*, it is appropriate to provide a flavour of the student experience by reference to 'Fearsome fungi', the topic in 2014. The objective was to produce a poster to inform classmates about one fungus of choice in a specific event of historical importance or more recently newsworthy. As usual, a list of possibilities was provided for guidance. Those who chose an historical event referred mainly to the Irish potato famine (expressly allowed for purposes of the competition), the Witches of Salem and the First World War. Those who focused on a more recent or present day problem referred mostly to poisonous and psychedelic mushrooms, diseases of the skin and lungs, and losses affecting bees, frogs, crops and trees.

Fungal topics in Southeast Asia

While visiting Southeast Asia over several years to conduct mycology research, one of us (M.W.) has taken the opportunity to discuss the teaching of microbiology in schools in Thailand, Malaysia, South Korea, Taiwan and China. This involved meetings with government officials, presenting UK teaching materials including those produced by MiSAC and BMS to teachers and for teacher training, and co-producing a range of microbiology educational resources in some of those countries in collaboration with educational institutes.

One particularly successful approach was to introduce the concept of competitions for students by using the well-established MiSAC model. This work bore fruit first of all in Thailand in the form of competitions on fungal topics for students aged 14–16 in 2014 and 16+ in 2015. They were jointly sponsored by the Institute for the Promotion of Science and Technology Teaching (IPST, part of the Thai Ministry of Education), BMS and MiSAC, of which the latter two provided financial support and organisational expertise, respectively.

The purpose of the competitions was to produce public information posters on 'Helpful and harmful fungi' (2014) and 'Fungi and healthy living' (2015). The latter topic was particularly interesting to us in the UK in that most entries focused on the Asian tradition of using fungi such as shiitake or *Ganoderma lucidum* for enhancing health whereas responses to a similar theme in the UK gave most attention to mycoprotein, the normal gut flora and probiotics, although oriental foods were not entirely neglected.

The competitions were arranged to coincide with international mycology conferences held in Bangkok (10th International Mycological Congress in 2014) and in Khon Kaen (Mycology in Southeast Asia in 2015), and attracted entries from all over Thailand. Successful posters were displayed on, and winners participated in, the final day of the conferences where they explained, in English, their choice of approach for the poster and were presented with money awards and certificates by the President of BMS.

The success of the two competitions has been such that IPST intends to make it an annual event for Thai schools. Furthermore, a similar competition, supported by BMS and MiSAC, is currently being organised in China in 2016 to coincide with the International Mycology Meeting in Changchun, Manchuria.

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Further reading

Moore D. & others (2005). *Mycologist* **19**, 152–158.

Outreach

Microbiology comes to Harvey Nichols

Professor Jo Verran launched a series of food microbiology events as part of Manchester Science Festival.

All event photos Natasha Hall-McKenna

'Menus Made By Microbes' was the first in a series of events designed to give micro-organisms a more positive image by raising awareness of their value in food production, food preservation and nutrition. The event was inspired partly by previous events hosted by the Microbiology Society and the Society for Applied Microbiology at the Cheltenham Science Festival – the former hosting a sit-down menu, the latter focusing on cheese and wine.

Over the next 12 months, microbiologists at Manchester Metropolitan University will be hosting events that encourage different audiences to enjoy some wonderful and diverse foods whose origins or processing we owe to micro-organisms. What better way to learn than through eating!

The first of these events took place during Manchester Science Festival, in the Harvey Nichols restaurant in the Manchester store, and was directed at an adult, 'gastronaut' audience. Preliminary planning involved microbiologist Professor Joanna Verran working with nutritionist colleague Haleh Moravej, who founded the hugely successful MetMUnch (**www.metmunch.com** /**@MetMUnch**), student-led social enterprise at Manchester Metropolitan University, and chef Richard Fox (**www.richardfoxcooks.co.uk**), award-winning writer, cook book author and chef presenter, also known as the 'beer chef'. The team designed a wonderful high-class menu that presented a fantastic range of food. Richard worked with the chef at Harvey Nichols on the design and delivery of the different courses. The resultant five-course menu utilised a range of foods that owed their nature, flavour, smell, nutritional value and/or texture to micro-organisms. Wines were donated by Alliance des Crus Bourgeois du Medoc, and were served at table along with the food by the waiting staff.

Each table of 10–12 was hosted by a microbiologist, a nutritionist, or the chef. Almost 50 members of the public attended the evening, including members of the development team for the City of Science programme. The evening began with a drinks reception and vertical

The Menu

Drinks Reception – 7pm
Libby Riley's **ginger beer** on arrival*
Sparkling **lemonade** as non-alcoholic alternative

Canapés
Welsh rarebit, **sourdough crostini tapenade**, **sour cream** polenta

Bar
Including a special microbe-inspired **cocktail** from Harvey Nichols:
Black truffle magic: a wondrous mix of **whisky**, **coffee**, **chocolate** and **truffle** perfume
(non-alcoholic version also available)

Call for dinner – 7.45pm
Introduction and demonstration

Dinner – 8.30
Complimentary **wines** at table
(one glass per person)
Kindly provided by Alliance des Crus Bourgeois du Médoc

Appetiser
Prosciutto platter, apple and sultana **sauerkraut**

Starters
Warm salad of deep-fried **Roquefort** and smoked **tofu**,
Sauternes poached pears

Mains
Truffled mushroom risotto, rosemary and **beer flatbread**

Dessert
Chocolate tart, framboise **beer** sauce
Served with **Kriek beer**
Tea/**coffee** and **chocolate** petit fours

**Recipe from Microbes on the Menu, published by the Microbiology Society*

canapés before guests went to their tables. Jo and Richard turned out to be an excellent comedy duo, providing an entertaining discussion/demonstration addressing many aspects of the microbiology that had contributed to the menu and accidentally highlighting some of the misconceptions around different types of micro-organisms. Subsequently, additional courses and wine were served at table, and diners were free to discuss the menu, the microbiology – or whatever they wished – with one another, and with their hosts. All diners were invited to keep their menu cards, provide feedback, and take with them a gifted 'Mind your Microbes' fridge magnet.

Feedback was plentiful and positive. The quality of the food and the service was complimented, as was the expert but informal and entertaining 'double act' of microbiologist and chef. The nature and content of discussion at table varied, but always included some microbiology.

Our next event will take place in March, during British Science Week, and will focus on a 'Ploughman's lunch' – bread, pickles and cheese alongside some beer. In July, during the celebrations for Manchester European City of Science, we will host a World Family Picnic, encouraging picnickers to bring as many diverse fermented foods as possible to the party. Our final event, in September, will be a street food event, focusing particularly on Asian-style, stir-fry type foods.

Acknowledgements

We would like to thank the Microbiology Society and the Society for Applied Microbiology for sponsorship of the event.

Joanna Verran

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Please visit our website for more information:
www.menusmadebymicrobes.com

Membership Q&A

In this issue, we're pleased to introduce **Dorina Timofte.**

D. Timofte

Where are you currently based?

Since 2009 I have been an academic at the Liverpool School of Veterinary Science and I am based at the Leahurst campus, a green and leafy part of the Wirral peninsula.

What is your area of specialism?

Veterinary clinical microbiology. I lead the Microbiology Diagnostic Laboratory in the Liverpool School of Veterinary Science, which is a very busy, but vibrant environment. The clinical material received frequently leads to research projects and is also used for teaching veterinary students about the all-important relationship between clinics and the laboratory findings. Our activities are very similar to those of a human clinical microbiology laboratory, where, every day, there are clinicians waiting for quick, quality results and a patient that needs the best possible health care.

And more specifically?

The quality of our diagnostic product and our training is key for current and future therapeutic management of animal patients with clinical infections. Furthermore, the rise of antimicrobial resistance, which we find in farm and companion animals, led me to develop an interest in understanding the role that particularly companion animals may play as a reservoir of resistance genes, as well as the bilateral interspecies transfer that can occur between humans and animals. From this point of view, the diagnostic lab is very well placed for surveillance of the trends in antimicrobial resistance. We play a key role in understanding the cloudy picture of antibiotic resistance development, both as a receiver and deliverer of information. As such, we need to capture the waves and trends in resistance seen in clinical isolates, but also we need to make sure that the information that is sent out to clinicians is accurate, tailored to each case and does not encourage further development of resistance. As a microbiologist and a parent, I do worry about the prospect of a world in which penicillin would not be effective anymore for treating a child's streptococcal infection.

I feel that it is also important that our experience is shared internationally and I found the International Development Fund (IDF) scheme of the Microbiology Society an excellent vehicle to share my experiences and to contribute to the training of other microbiologists in the area. I was awarded an IDF grant in 2012, which supported the organisation of a workshop in Romania, aimed at transferring knowledge and technology to local diagnostic laboratories on laboratory detection of extended spectrum beta-lactamases (ESBL), meticillin-resistant *Staphylococcus aureus* (MRSA) and other resistance phenotypes. Both human and veterinary diagnostic microbiologists attended and it was the first time in Romania when human and veterinary microbiologists had met to discuss the problem of antimicrobial resistance. Given the success of this first workshop, I re-applied to the IDF scheme in 2014, this time proposing work with human microbiologists in Romania to tackle the emerging problem of carbapenemase-producing Gram-negative organisms. In this project, the IDF funds have supported a pilot project for the implementation of detection of carbapenemase-producing *Enterobacteriaceae* and non-fermentative bacteria in two Romanian hospitals. The project is ongoing and through its findings, we hope to raise awareness of the danger posed by the spread of carbapenemase-producing organisms in the absence of coordinated surveillance at hospital and national level in Romania.

Tell us about your education to date

I completed my formal school and university education in Romania. I gained a Doctor of Veterinary Medicine from the Faculty of Veterinary Science at Iași Agricultural University in 1991. The anti-communist revolution happened while I was in my final years at university and this coincided with universities opening their doors to younger staff; therefore, I did not hesitate when a position of teaching assistant was available in the microbiology department of the faculty where I graduated. In 1992 I embarked on a six-year PhD programme, which was available on a part-time basis allowing me to continue my academic career at the same time.

Where did your interest in microbiology come from?

I always enjoyed biology in general but decided to take a degree in the more complex subject of veterinary science. Microbiology was the subject that I most enjoyed studying and I was fortunate to be offered the position of teaching assistant in microbiology at Iași.

What are the professional challenges that present themselves and how do you try to overcome them?

In my day-to-day job, the biggest challenge is getting the right balance between teaching veterinary students, pursuing my research interests, developing new diagnostic assays and getting involved in all the clinical cases

that pass through our laboratory. I am also a strong believer that family should always come first, and there are already too many things to balance and I am not sure if I do meet that particular challenge.

What is the best part about 'doing science'?

There are a lot of things, I enjoy the ever-changing scenes and that two days are never the same. I guess a research project can be a little bit like a piece of art, where it is all in your mind, you just have to give it shape and make it relevant and interesting for other people as well.

Who is your role model?

In life, Audrey Hepburn, especially for the charity work that she did as a UNICEF ambassador. In science, probably my husband, Professor Stuart Carter, whose Yorkshire philosophy to 'always get things done', is now embedded in my work ethic. Stuart and I met via an EU teaching exchange programme, and got married soon after that; therefore, we nominate ourselves as the ideal example of a successful European collaboration.

What do you do to relax?

Whenever I get the chance I try to follow my passion for gardening. Working in the garden has the power to take away all my work thoughts and worries. Being between my flowers is therapeutic and de-stressing, but I can't explain how it works.

What one record and luxury item would you take to a desert island?

The record would be Romanian choral music by the Madrigal Ensemble and the luxury item – my espresso coffee pot; it helps me function in the morning.

Tell us one thing that your work colleagues won't know about you!

I could say I used to be a painter as I also graduated from arts school, but unfortunately I have not touched any brushes since being in my current job.

If you weren't a scientist, what would you be?

Either a painter or a landscape gardener. It would be difficult to decide which one of the two.

If you would like to be featured in this section or know someone who may, contact Paul Easton, Head of Membership Services, at **p.easton@microbiologysociety.org**

We are the Champions

The Champions scheme was launched at our Annual Conference in 2014, and our Champions have been busy since then, spreading the microbiological word far and wide. Their efforts have been diverse, reflecting their own wide range of interests and expertise.

In the past 18 months, around 20 events have been held in the UK, Ireland and other countries, including Turkey. We estimate more than 1,000 people have been involved in a Champions-related event and have been introduced to the Society as a result. Here's just a small taste of what they've been up to.

Our Champion based in Turkey, Agah Ince, helped coordinate the first symposium of *Blastocystis* at the Gazi University Faculty of Medicine, Ankara, in May 2015. A total of 70 delegates attended including representatives from Australia, Japan, Russia, China, Taiwan, India, Pakistan, Qatar, Iran, Iraq, Turkey, Spain, France, Denmark, UK, USA and Mexico. Agah's efforts on behalf of our Society and the other partners involved produced a symposium of world-class standing. "Symposia like this are a very good chance for our regional postgraduate students to come together to hear the most up-to-date information and research methods on microbial genomics" said Agah.

In terms of wider more mainstream engagement, it's hard to go past food and drink as the vehicles through which to gain an audience's attention. This was proven on two separate occasions during the year. Our Champion in Dundee, Marilia Costa, hosted a pub quiz with a microbiology-themed suite of questions and succeeded in delivering a very successful night to colleagues and friends. "People love pub quizzes," said Marilia, "and I thought, why not a microbiology one? I organised

Blastocystis conference Ankara Turkey. Agah Ince

JAM talk Birmingham. Amanda Rossiter

Arikana Massiah (left) and Ben Johns (right) at FIS. Microbiology Society

Brewing event Dublin. UCD Science

the event to be open to everyone but mainly undergraduate and PhD students attended. It was exciting to see them thinking, talking and discussing the questions. It was a fun night and I am sure people learned something new about the micro world."

On a similar theme, Tadhg O'Croinin, our Dublin-based Champion, hosted a two-day event introducing the wider public to the mysteries of brewing. "This workshop was extremely successful in that it helped students not only to understand the science behind the brewing process but also the critical role that microbiology plays in this important industry and the broader biotechnology sector." Both events struck a chord with audiences relatively new to microbiology and, judging by the feedback, both will have a very definite place in future programmes.

We were delighted to see a new initiative coming from a Birmingham-based Champion, Amanda Rossiter. Amanda and some of her colleagues are running a series of 'JAM Talks' (Junior Award in Microbiology Talks). This is a series of talks by PhD students, which will be 'judged' by visiting peers from other universities, with a prize awarded to the best presentation at the end of the series. It's a brilliant idea. Students get involvement in an awards scheme and can use this to enhance their CV; visiting judges can take the idea back to implement in their own universities; it grows an informal network of students and colleagues across universities who can meet up at Conference; and it raises the awareness of the Society too.

Over the past months, we have looked closely at Champions to see how we can make the initiative even more relevant and attractive for members. As a result we are changing the focus of it somewhat.

Champions will in future be offered more opportunities to become involved in Society-led initiatives as well as those of their own. For example, we intend to offer Champions more roles at our own events, which may be developmental or call more on their existing skills and expertise at different levels. This way Champions can use their Society experiences to build their own CVs and networks to develop their careers, while at the same time helping build the Society. The first practical example of this saw two Champions, Arikana Massiah and Ben Johns, attend the 2015 Federation of Infection Societies (FIS) Conference in Glasgow as Society representatives. As Arikana said, "I got to meet scientists from different backgrounds and specialities who are at different stages in their career, which was great for networking. I would most certainly do this again."

Ben thoroughly enjoyed his experience too. "There were some fantastic lectures given on a wide variety of topical subjects, a good selection of stalls from different exhibitors and some useful networking opportunities in the hall during poster sessions. As a Society Champion I found attending this conference invaluable."

Further opportunities will be presented to Champions in the coming months. If the Champions initiative is something that sounds of interest to you, why not get in touch? We are always looking for more members to get more closely involved in our work. If you would like to find out more about the Champions and how to become one, please contact me.

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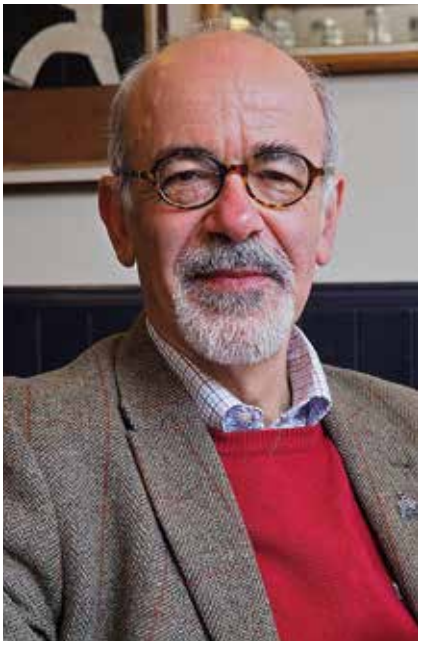
Honorary Archivist

The Microbiology Society has a long-standing history and a role has been created to ensure the knowledge in the Society archives is maintained. The role has been taken up by Gilbert Shama. We asked him about his background and what intriguing items he has found in the archives during the initial stages of his research.



P. Khayat

Where are you currently based?

I am currently working in the Department of Chemical Engineering at Loughborough University.

What is your area of specialism?

I am involved in a number of activities; they mainly are concerned with eradicating micro-organisms from various media and environments. I started quite a few years ago with UV light as a means of sterilising liquids, and then extended my research to include the surfaces of solids including foods. More recently I have been investigating the elicitation of hormetic responses in fresh produce as a means of preventing food wastage through fungal spoilage. I'm also working closely with electrical engineers on the application of atmospheric pressure gas plasmas for similar applications to those described above in relation to UV.

Tell us about your education to date

I attended Kilburn Grammar School in London. My first degree was in Chemical Engineering from UMIST. I then went on to take an MSc in Biological Engineering from Birmingham. My PhD was in Microbial Physiology from Imperial College, London.

Where did your interest in microbiology come from?

I didn't study biology at school, but became introduced to microbiology through biochemical engineering which I studied as part of my first degree and, I suppose one could say, became hooked!

What will your role as Honorary Archivist involve?

The Society will be celebrating the 75th year of its foundation in the year 2020 and the post was created principally with this anniversary in mind. I am looking forward to working with the staff of the Society as they prepare for 2020, and also in meeting with Society members and hearing their views as to how the occasion should be marked.

What made you apply for the role of Honorary Archivist?

The prospects for communicating the history of the Society and the achievements of its members to both the current and future generations of microbiologists as well as to the public at large.

What is the most interesting item you have found in the archive so far?

I was examining a photograph at the Society offices of what I believe is an unpublished photograph taken at the International Congress for Microbiology in 1936. I was scanning the sea of faces of the attendees seated round tables at what must have been the Congress Dinner when the face of Alexander Fleming jumped out at me – it was as though I had encountered an old friend!

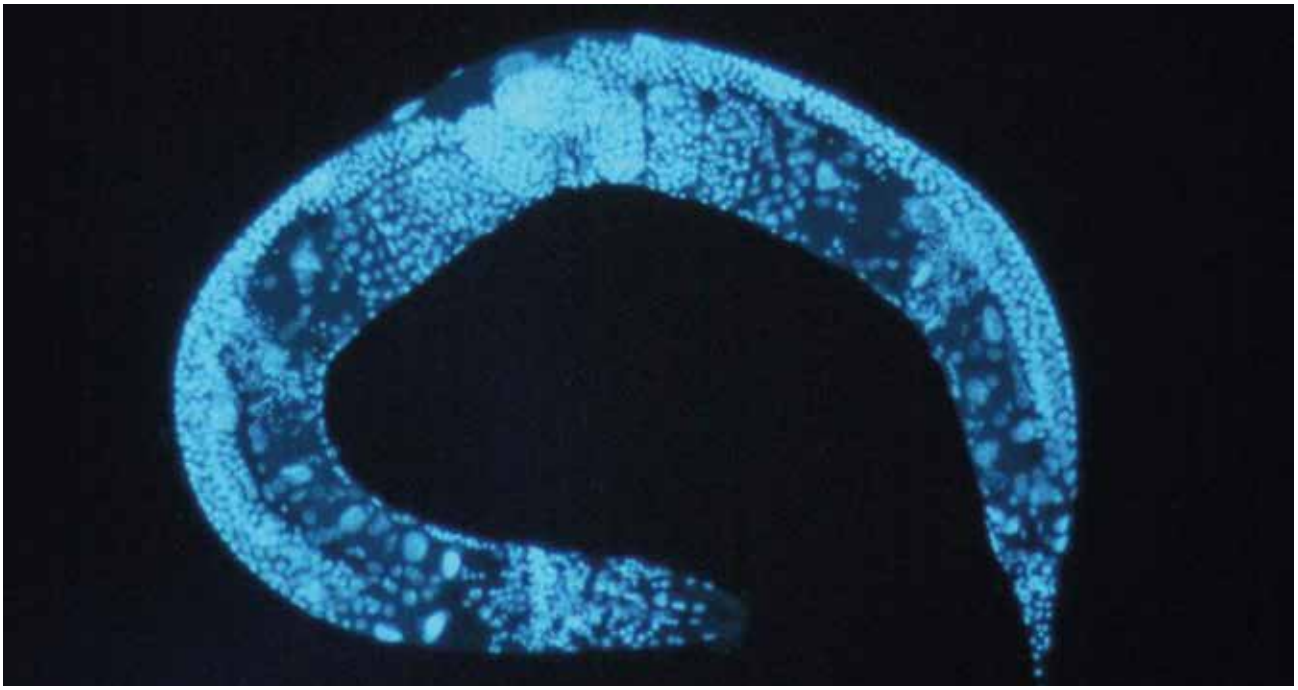
What are you most looking forward to finding in the archives?

What excites me most about going through archives is simply not knowing what one will come across – coming face to face with the unexpected.

What most excites you about the history of science?

I would say uncovering previously unknown facts but also making novel connections between the past and the present.

Caenorhabditis elegans. National Institutes of Health



Best of the blog

As we start to peer blinking into the light of a new spring here in the UK, it's time to have a little look back at some of the content we posted on our blog at the end of 2015.

Last year, Society member Dr Lucy Thorne visited the Uganda Virus Research Institute in Entebbe with support from one of our Research Visit Grants. Lucy kindly videoed her trip when she went to the laboratory of Professor Alison Elliott to find out how common intestinal viruses are in Ugandan children (**http://microb.io/1M6PVWl**).

At the time of writing, the new Star Wars film is yet to be released (hopefully it'll be good); not such a long time ago, we had a post entitled *Deadlier than Darth: Death by worm-star* (**http://microb.io/1Z6lwkb**), which details work by Society member Dr Laura Clark on the discovery of a new species of bacteria that causes *Caenorhabditis elegans* worms to stick together by their tail spikes in lethal star-like formations. This post contains an amazing GIF that's well worth your time.

The last of our 2015 Focused Meetings was about the Industrial Applications of Metal–Microbe Interactions. Two blog posts came from research presented at the meeting: one, written by Anand Jagatia, about how microbes may help in the detection of arsenic in drinking water in Bangladesh (**http://microb.io/1MuKg0Y**), the other about research from the University of Edinburgh (**http://microb.io/1kmMhSG**) that is investigating the possibility of using bacteria to mine asteroids and Martian rock (no, really).

In other Martian news, I spoke to the astrobiologist Dr Lewis Dartnell about the recent discovery of liquid water on the Red Planet, and what this might mean for the field of microbiology. In the same episode, Anand spoke to Dr Kevin Newsham about the impact of climate change on soil fungi (**http://microb.io/1H79P2n**).

Lastly in this roundup, it's worth noting some of the places where new microbes have been discovered. Over the past few months, they've been isolated from such diverse locations as sea urchins in the Sea of Japan (**http://microb.io/1Po3GaO**), the Russian wheat aphid (**http://microb.io/1WhyLk7**) and the faeces of penguins in the Antarctic.

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Reviews

Human Fungal Pathogens

Edited by A. Casadevall, A. P. Mitchell, J. Berman, K. J. Kwon-Chung, J. R. Perfect and J. Heitman
Cold Spring Harbor (2015)
US$135.00 ISBN 978-1621820758

There are some very good texts on different types of infectious agents but there is a definite need for a good textbook devoted to fungal pathogens. The book, as the title indicates, is about the fungi that infect the human host. The focus is very much on the fungus (e.g. classification, evolution and genetics), rather than the human disease, which is fine if your interest is more in fungal biology than the role they play in disease. I believe that the book would have benefitted from an introductory chapter putting fungi in context of other infectious agents in the role that they play in human disease, and the expanding importance of fungi with increasing numbers of susceptible hosts due to HIV infection or immunosuppressive medical procedures. Also, I feel there should have been more about the clinical syndromes associated with fungi. There is a whole section on treatment but relatively little on diagnosis or drug susceptibility testing. In terms of diagnostics, newer molecular techniques are better covered than more conventional methods still widely used in some laboratories. Chapters are not numbered and there are no obvious delineations between groups of chapters into different sections, although the Contents page suggests that there are. This doesn't help with navigating around the book when in search of information. There is a vast amount of interesting and useful information, but in my opinion the content could have been laid out in a more logical fashion, with more clearly delineated sections (e.g. role of fungi in infectious disease, syndromes associated with fungal infection, mechanisms of disease, laboratory diagnosis, antifungal treatment and drug susceptibility testing, new development in the study of fungal disease), making it easier to find the information required.

Christopher Ring
Middlesex University

Bacteria–Plant Interactions: Advanced Research and Future Trends

Edited by J. Murillo, B. A. Vinatzer, R. W. Jackson and D. L. Arnold
Caister Academic Press (2015)
£159.00 ISBN 978-1910190005

A lot has been discovered recently in the area of bacterially made effectors that can modify different aspects of plant signalling. The opening chapter provides a useful integrative overview of evolutionary relatedness and targets of several of these effectors delivered to plants via the Type III secretion systems of various bacterial plant pathogens. One of the best models is *Pseudomonas syringae*, and so inevitably, there is some overlap with the chapter by Lindberg & Collmer, focusing on the transfer, evolution and mechanisms of loss and biological activities of effectors produced by *P. syringae*. The chapters on (a) the fire blight pathogen *Erwinia amylovora,* (b) *Acidovorax* spp., (c) Gram-positive bacterial pathogens and (d) human pathogens on plants, are all good perspectives on these areas, well referenced and would be a good starting point for people wanting an overview. Two chapters are related to biocontrol, and the final chapter is a summary of the biology of phages and how they may influence the populations of bacteria interacting with plants.

As a reference work, this book has two limitations. The first is that the most recent citations are from 2013. The second is that there are not focused chapters on pathogens from the *Xanthomonas*, *Ralstonia*, *Xylella, Agrobacterium* or *Pectobacterium* genera, all of which are among the most economically important plant pathogens. For example, there is no description of the xanthomonad Transcription-Activator-Like Effectors (TALEs) and how their internal repeats of amino-acid sequences define DNA recognition sites. Perhaps the absence of such chapters reflects the intended perspective of this book, but if that is the case, the absence of chapters on the associative or symbiotic nitrogen-fixing bacteria, or the rapidly developing areas of rhizosphere and phytoplane genomics is also a significant omission. If the book is aimed at generalists, then it is rather lacking in schematic models in most chapters. If it is aimed at specialists, then it has the problem of its citations already being a couple of years out of date. Perhaps I am reflecting on the impossibility of simultaneously having such a book be both up-to-date and comprehensive. Balancing the costs of books such as this, against the potential speed of publication and rapid availability of reviews via web-based publications, perhaps my reservations should be seen as more broadly questioning the viability of this genre of publication.

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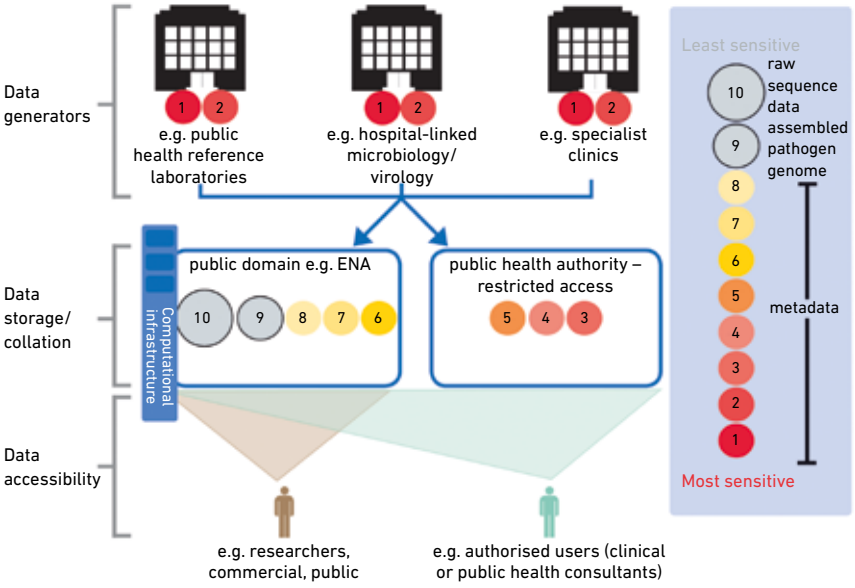
John Innes Centre

Comment

Pathogen genomics into practice: from promising research to real health impact

Sowmiya Moorthie and Leila Luheshi



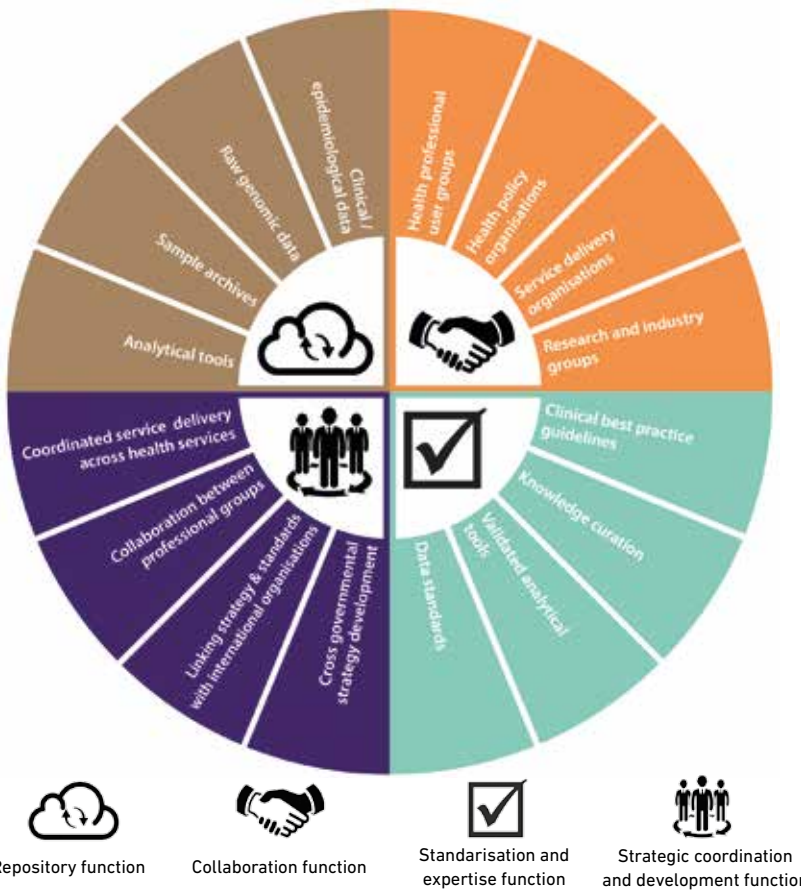
The size of circles (not to scale) are indicative of the relative data storage burden (computational disc space) of the different subsets of data. Raw genomic data will consume the greatest disc space (therefore costing more to store than other data types) and so its longer term storage would be better suited in a consolidated repository for high-volume data storage. PHG Foundation

Low-cost whole genome sequencing technology is catalysing a transformation in the way clinical and public health microbiologists and epidemiologists can manage the threat of infectious diseases. In comparison to existing microbiological methods, genomic methods offer greater sensitivity and specificity, as well as providing a description of a wide range of clinically and epidemiologically relevant characteristics of a pathogen, including identity, virulence determinants, drug resistance and relatedness to other pathogens.

In principle, genomics can be used to improve the management of infectious disease by allowing more precise diagnosis, detection and tracking of antimicrobial resistance and outbreak control. However, in practice evidence demonstrating that genomics improves patient care or population health, and is affordable when implemented in 'real world' pathways within the NHS, remains limited. Problematically, many of the benefits of genomics are expected to accrue only when it is deployed at scale, in an integrated health system-wide manner. As it is more or less impossible to pilot such an approach without significant capital and resource investment, a 'calculated risk' may have to be taken to commit to a genomic future for microbiology well in advance of all the necessary scientific evidence being available.

A nationally coordinated system of service development and delivery will be essential to realising the benefits of genomics for infectious disease management; the most fundamental components of this system being cross-organisational data integration, strategic coordination and strong leadership to manage the radical changes in microbiology service provision that will be required.

Obtaining clinically useful information from pathogen genomes is reliant on our ability to compare them to other genomic data and combine this with relevant epidemiological or clinical information. The success or failure of genomics as a tool to improve infectious disease management will depend



heavily, therefore, on the timely collation, integration and sharing of genomic and clinical/epidemiological metadata across the health system. These actions will also underpin the research and development needed to drive the expansion of the utility of genomics to a wider range of organisms and investigations than are currently feasible.

Achieving this vision of genomics-enabled microbiology services that are continuously innovating and expanding in scope requires the development of infrastructure to provide repositories for data, knowledge and samples, along with quality standards and data privacy safeguards to ensure their responsible use. This is no easy task considering the large number of different groups involved in producing and using this data, from front-line clinical staff, genomics researchers and clinical scientists, through to national agencies involved in food safety or animal health. The task is further complicated by the fact that infectious diseases do not recognise borders, and so international cooperation on these issues will also be essential. Although it may seem a daunting prospect, acting now to develop these mechanisms wherever possible, while many services are in the relatively early stages of development, will lead to future benefits as sequencing becomes more widespread and the need for a coordinated approach becomes ever more pressing.

Effective development of a national data management system to deliver the benefits of pathogen genomics now and in the future will not happen organically. Instead it will require strategic leadership and coordination. The various disciplines and organisations involved must agree on and work towards a common vision of how a future genomics-enhanced infectious disease management system will look. The benefits of such a cooperative approach are that the health system will be able to minimise duplication of effort, and share both resources and risks.

In addition to this 'top down' strategic collaboration, it will be equally important to bolster 'bottom up' cooperation amongst 'front-line' professionals. By sharing and developing knowledge, expertise and best practice around genomics, they can accelerate delivery of the highest quality care to patients and improve the protection of the health of our population. This means providing opportunities and systems to gather input from a wide range of professional groups, ranging from infectious disease physicians, medical microbiologists and infection control nurses, to clinical laboratory scientists and academic researchers, all of whom have a stake in realising the effective development and implementation of pathogen genomics services.

From our extensive analysis of the technology, health service, microbiology systems and extensive stakeholder consultation, we believe that genomics could, and indeed will be used as a front-line tool in the management of some infectious diseases in the near future. However, realising this vision necessitates overcoming current technological limitations and improving our understanding of the clinical and epidemiological significance of genomic variation, with the concomitant adoption of this new knowledge by health services in a timely manner. We are convinced this can be achieved if a prompt, concerted effort is made to share data, knowledge and expertise and if the strategic coordination and leadership needed to deliver a whole system approach are provided by those tasked with protecting the public's health from infectious diseases.

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Further reading

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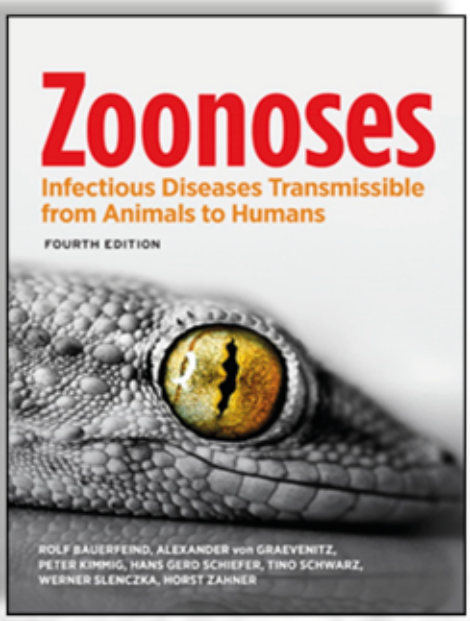

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