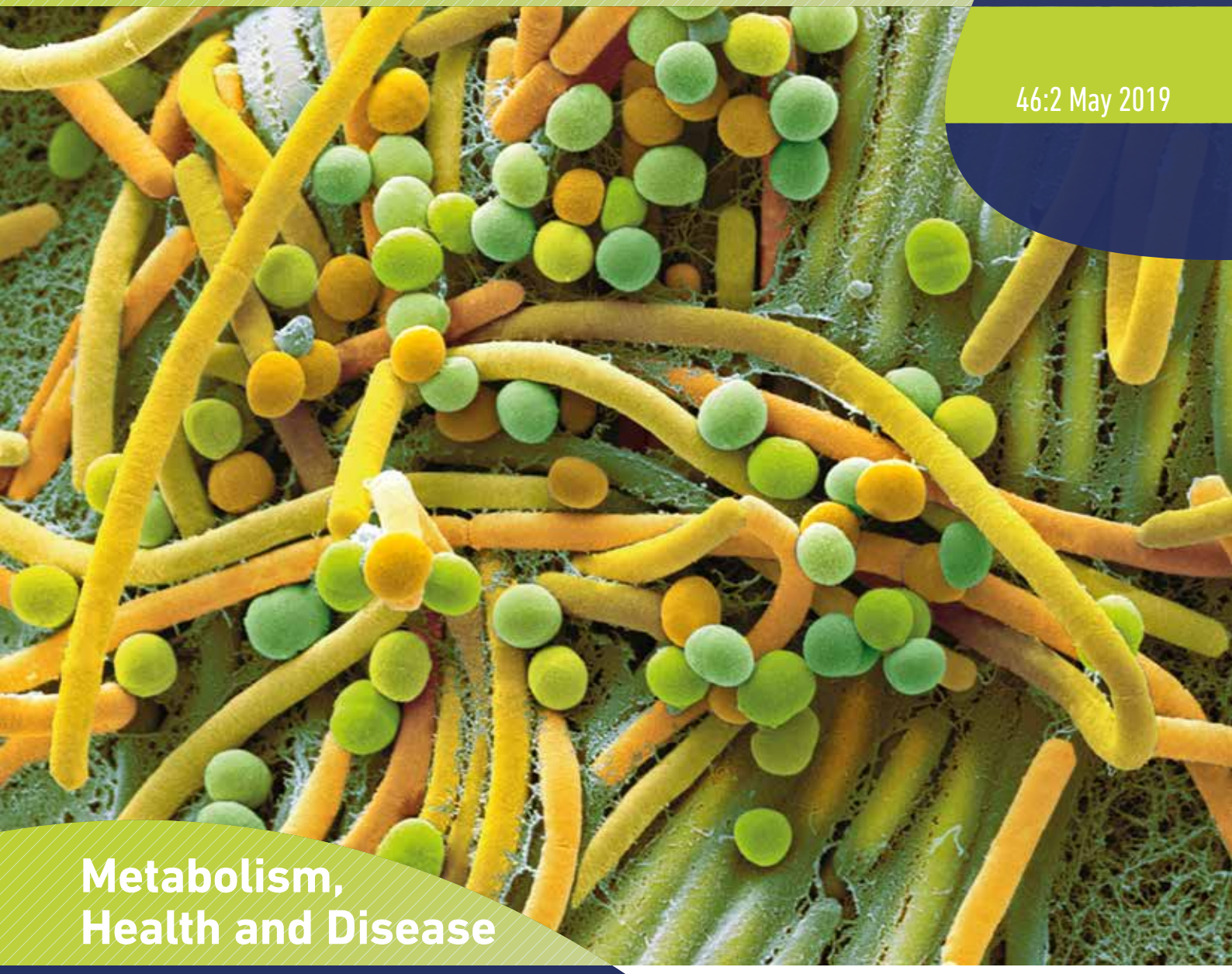
Microbiology TODAY

46:2 May 2019



Metabolism, Health and Disease

Where bacterial metabolism and virulence intersect
How sialic acid impacts on metabolism, health and disease
Modelling virus infections of the skin in 3D
Human noroviruses and gut bacteria: friends, frenemies or both?
The intestinal microbiota in health and disease

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Editorial

Welcome to the May edition of *Microbiology Today*, and up for investigation in this edition are microbial metabolism, health and disease. The ability of microbes to metabolise different substrates enables them to thrive in a vast diversity of niches, including various parts of the human host. The way microbes interact with metabolites influences how they affect the health of their host and can be linked to disease. This month our authors explore the fascinating range of ways in which these microbes and their metabolism can impact health.

Whole Picture

To start us off on this theme, Kim Hardie reflects on how metabolism and the ability to utilise essential nutrients forms the basis of a healthy microbial cell. Revealing some of the many complex interactions linking metabolism and virulence, Kim demonstrates how these two factors are intertwined and can influence bacterial fitness within a population. Kim explains how these complex interactions can influence infection severity and concludes by providing some perspectives on how new technology could help further elucidate the intricate relationships between metabolism and virulence.

Next, Andrew Bell, Emmanuele Severi, Nathalie Juge and Gavin Thomas explore the various functions of sialic acid. Sialic acid is a metabolite of significant importance in bacterial–host interactions. Our authors outline the strategies microbes have devised for utilising sialic acid for different purposes. They reveal the ways in which both commensals and pathogens can use sialic acid, for example as food and for camouflage. They then explain how sialic acid has inspired antiviral design and could be utilised for future anti-infection purposes.

Moving from bacteria to viruses, Sally Roberts and Joanna Parish consider how the development of organotypic raft cultures has improved our ability to study virus infection strategies. Explaining the basics of this technology, they describe how these rafts can be used to form fully differentiated epithelia. They explain how these organotypic rafts have been used to gain insights into the replication of herpesviruses, such as Epstein–Barr virus, and how they could be used in the future to support the testing of antivirals.

Staying with viruses, Matthew Moore discusses the difficulties in controlling norovirus, the outcome of infection (spoiler, it's not good) and the complexities of *in vitro* cultivation of norovirus. Historically difficult to cultivate; it was only in 2014 that successful cultivation and replication of norovirus in human B cells was achieved, using enteric bacteria as a co-factor. Matthew reveals the advances in this field since 2014 and addresses the questions which will need to be answered to take this research forward.

We stay with the intestinal theme as Katharine Seton and Simon Carding walk us through the role of intestinal microbiota in health and disease. Starting with the microbiome in early life and highlighting the factors that impact on the health of our microbiome, they consider the impact of bacterial products on host health. With research increasingly making links between dysbiosis and disease, Katherine and Simon address the complexities of this area of research, the available evidence and the therapeutic potential in this area.

The Comment piece for this edition is written by Courtney Kousser, Farhana Alam and Rebecca Hall, and looks at the importance of fungi, their interactions within the human microbiome and the roles they can play in health. Explaining the range of interactions fungi can have with other microbes, they highlight how fungi can provide a route for bacterial dissemination, as well as impacting on the virulence of polymicrobial biofilms. The rising antimicrobial resistance of fungal pathogens and their ability to modulate the host immune system makes these microbes a fascinating part of the microbial world.

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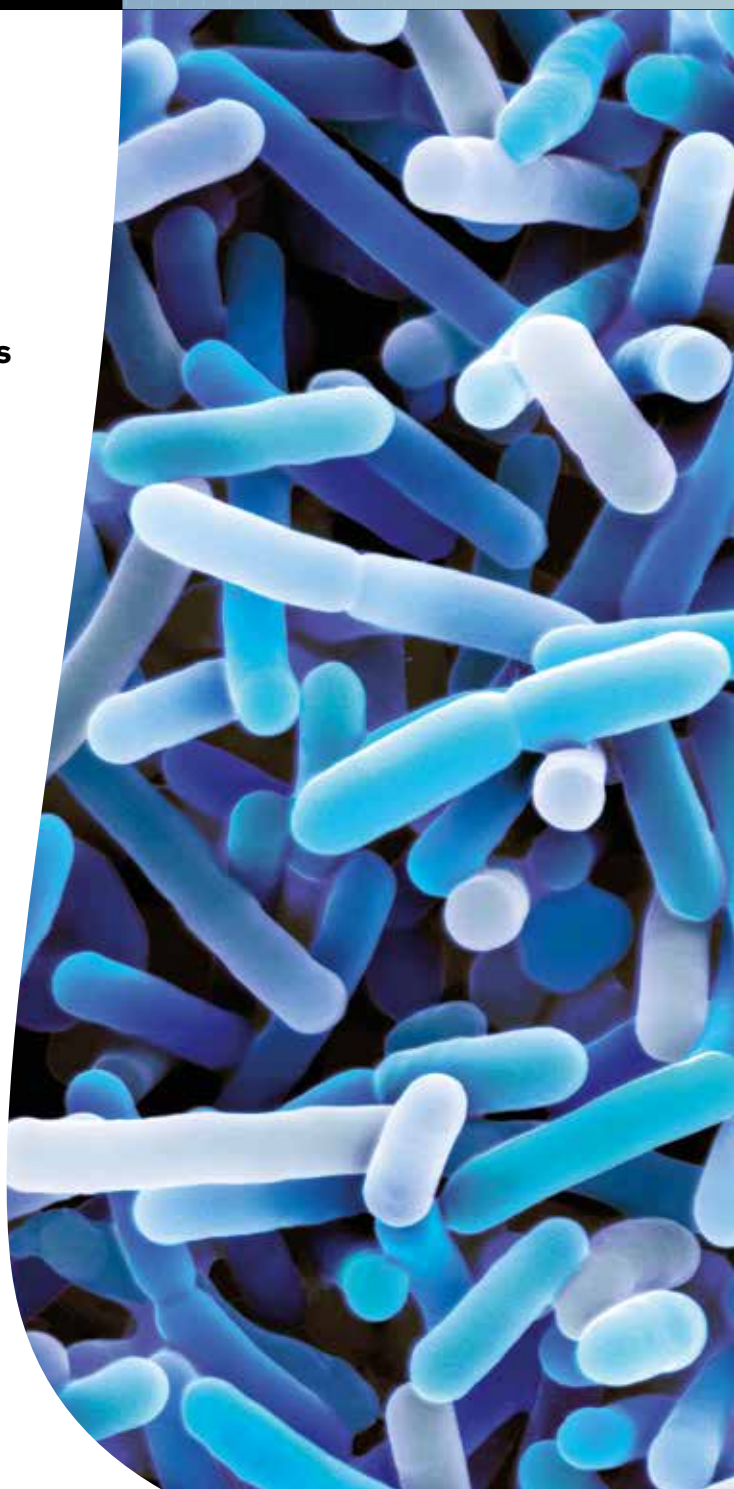
Articles



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Features

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Faecal bacteria. Scanning electron micrograph of bacteria cultured from a sample of human faeces. Magnification: x6000 when printed 10 cm wide. Steve Gschmeissner/ Science Photo Library

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From the President

The Microbiology Society's 75th anniversary activities for 2020 are gaining momentum. You may be aware of the recently launched United Nations Sustainable Development Goals (UN SDGs) project, A Sustainable Future, and our call for evidence. We are seeking your views to find out how microbiology can and does contribute to achieving the UN SDGs. We would welcome your input and response to this ambitious project to showcase the impact of microbiology and how it relates to the 17 goals that will transform our world. The questionnaire can be found on the Microbiology Society website microbiologysociety.org/SDGs.

As part of the 75th anniversary celebrations we will be extending the Annual Conference in 2020 so it runs over five days, with the first day showcasing our Fleming Prize winners. This event will outline a vision for the future impact of microbiology on science and society and will reflect on some of the science that outstanding microbiologists, at all career stages, are involved in to overcome global challenges. More information on the programme will be announced on our website later in the year.

I enjoyed my first Annual Conference as President of the Microbiology Society and attending talks on the range of microbial science the Conference celebrates. I was truly inspired by the work of my fellow microbiologists and am keen to find out more about the work taking place across the UK and Ireland. I hope to meet you at one of the upcoming Roadshow events, taking place in Dublin, Plymouth, Manchester and Liverpool in Autumn. I was really heartened by the warm welcome I received at the Leeds and Newcastle Roadshow events in March. I enjoyed meeting members at these events and finding out more, not only about their research but also their concerns for the future and possible ways in which the Society might help.

The Focused Meeting series for 2019 begins in June with two events, one on anaerobes and the second on yeasts. You can find out more about these events and three further Focused Meetings taking place later in the year on pages 80–81. Another key event in the Society calendar is the Early Career Microbiologists' (ECM) Forum Summer Conference 2019, taking place in Dublin on 21–22 June. The Society is keen to create a supportive environment for those starting out in their career, with peer-led sessions to help enhance the professional development of researchers. If you are an early career researcher, it is a great opportunity to build networks and develop your skillset.

When presenting work, there is also the consideration of publishing your research. The publishing landscape has changed significantly in the last decade and continues to change, with a range of terminology and different ways to publish that we all need to be aware of. To the uninitiated it can be difficult to navigate. Our Journals Team can help your understanding of the process with an article on pages 84–85 on Open Access, outlining how this works.

The Microbiology Society journals provide the microbiology community with a place to publish their findings. This now also includes our new journal, *Access Microbiology*, which will publish replication studies, negative or null results, research proposals, data management plans, additional research methods and interdisciplinary work. Articles published are free to read and currently free to publish, as article processing charges are waived at the current time.

I will soon be stepping away from publishing research articles and running a lab to focus more on my role at the Society and a range of other commitments. On reflection, looking back at my career to date, I see that the key milestones and points where I have forged ahead were built on collaboration, adaption and the willingness to search for answers when I was uncertain of the outcome. As we face changes such as AMR, opportunities in genome research and an increasing understanding of the importance of microbial communities, I continue to be amazed by the microbial world and its key role in our continued existence. I am determined to champion the field and help ensure microbiology is firmly on the agenda, helping support you in finding the answers to some of the significant challenges our community faces.

Judith Armitage
President
president@microbiologysociety.org

From the Chief Executive

In the past few months, two events have very powerfully shown the value of a membership charity like the Microbiology Society in supporting members. Back in March, our new President, Judith Armitage, began her members' Roadshow by visiting Leeds and Newcastle, where we met a large number of members to learn more about how the Society can support your career progression. Then, last month the Annual Conference was a festival of microbiology and friendship where over 1,300 researchers came together to share results, make new connections and renew existing ones.

At the Roadshow events, Judy described her own career path, and the thing that clearly struck a chord with many early career members was that Judy's success has not always been plain sailing. Everyone faces significant challenges in a research career. Judy's advice was clear – find a scientific question that fascinates you and keep working at it even if it's not fashionable, and build a strong support network of collaborators.

Of course, one of the most effective ways of doing this is to attend the Society's Annual Conference, and this year's event in Belfast was a brilliant example. As we do every year, we brought together scientists interested in microbes, their effects and their practical uses, and created as many opportunities as we could to get you talking to one another about your science, the challenges you face and your careers.

If it's possible, next year's Annual Conference is going to be even better. 2020 will be the 75th anniversary of the Microbiology Society, and one of the ways we will celebrate is by adding an extra day to the Conference, organised by former winners of the Fleming Prize Lecture. The programme will include two keynote lectures – one from Bonnie Bassler, famous for her pivotal role in the discovery of quorum sensing in bacteria, and one from Nobel Laureate Paul Nurse, who won the Fleming Prize in 1984. There will be inspiring talks, ranging from 'The expanding virosphere' by Eddie Holmes, one of the world's leading experts on virus evolution, through to Mark Pallen of the Quadram Institute, talking about 'What ancient DNA can tell us about pathogens from the past'.

But as well as established experts, there will be a platform for early career microbiologists, including a number of 'Five-Minute Theses', where PhD students will present their results to the Society's membership. We will learn more about the career paths of some of the Fleming Prize winners, where the winners will outline what went well and what challenges they met along the way. Many of the Fleming Prize winners already have the date of next year's anniversary Annual Conference in their diaries, 30 March to 3 April 2020 in Edinburgh, and I can't wait to see so much microbiological talent in the same room and at the same time.

In the meantime, this year has an exceptional series of Focused Meetings, starting with Anaerobe 2019 in Cardiff in June, organised by Sheila Patrick and colleagues, which will look at changing perceptions of anaerobic bacteria. Later the same month, Janet Quinn and colleagues are organising the British Yeast Group meeting in Newcastle, which will look at the journey from discovery to the impact of research. The International Meeting on Arboviruses and their Vectors, being held in Glasgow in September, is now an established and unmissable meeting that Alain Kohl regularly organises with colleagues.

October will see a special meeting in Dublin organised by Joan Geoghegan and Charles Dorman. The Irish Division will celebrate a century of microbiology at Trinity College Dublin with a meeting on Microbes in Medicine. Charles is Professor of Microbiology at Trinity; he is also a member of Council and he won the Fleming Prize Lecture in 1994, underlying the long-established links between the Society and microbiology in Ireland. The last Focused Meeting of the year will be in Oxford at the end of October, where Freya Harrison and colleagues will focus on antimicrobial drug discovery from traditional and historic medicine. Finally, in November, we are delighted to host the Federation of Infection Societies (FIS) Annual Conference in Edinburgh.

There is something for everyone in the programme and I hope to see you at one of the meetings.

Peter Cotgreave
Chief Executive
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News

Get the latest updates, search for the Microbiology Society on:

@MicrobioSoc

Nominate a deserving microbiologist for a Microbiology Society Prize Lecture

Nominations for the Prize Lectures 2020 and Prize Medal 2021 close on 10 June 2019, and are welcomed from all members. If you know a researcher whose work is deserving of recognition, nominate them on our website (**microbiologysociety.org/prizelectures**). The Society is committed to creating and encouraging a diverse and inclusive culture within our membership and the microbiology community. Please consider the full breadth of the field when making your nomination.

Access Microbiology – first articles online

The Microbiology Society's newest journal, *Access Microbiology*, has published its first articles. *Access Microbiology* introduces a new service to members of our community, allowing the publication of replication studies, negative or null results, research proposals, data management plans, additions to established methods, and interdisciplinary work. To find out more about the journal, or to read the latest articles, visit our website (**acmi.microbiologyresearch.org**).

Society-Supported Conference Grants 2020

Members who are planning to organise a conference can apply for a grant of up to £2,000 towards funding the costs of invited speakers. Awards for 2019 meetings have been allocated, but applications are now welcome for meetings in 2020. Visit **microbiologysociety.org/SSConferencegrants** for details.

FIS 2019

The Microbiology Society is proud to be hosting the Federation of Infection Societies (FIS) Conference 2019 this November at the EICC in Edinburgh, UK. Visit **microbiologysociety.org/FIS19** to see what's in store this year and submit an abstract to be part of this event. Registration opens in early June and abstracts will close on 5 August 2019. Follow us on Twitter **@MicrobioSoc**, using the hashtag **#FIS19**.

Focused Meeting 2020 proposals

Focused Meetings incorporate presentations from leading scientists with opportunities for those new to the field to present their research via offered talks and poster presentations. Applications to organise a Focused Meeting are invited from any field of microbiology and can be based around an established community, a hot topic or an emerging one. Information, including previous events, is on our website (**microbiologysociety.org/focusedmeetingproposals**). Send your proposal by 10 June 2019 for consideration by our Scientific Conferences Committee.

Funding for local events

Did you know that members of the Early Career Microbiologists' (ECM) Forum have access to a special fund for their own events? Apply online for up to £500 to support local events that bring ECMs together.

Membership subscription rates

The Society is looking to align its membership subscription rates to ensure they comply with current legislation. We will no longer be offering reduced rates for members who elect to pay by direct debit. In future, all members will pay the same rates for their grade of membership, irrespective of the way they choose to pay. We will be communicating the new rates soon. If you have any queries, please contact **members@microbiologysociety.org**.

Grant deadlines

Date	Grant
1 June 2019	Travel Grants to support members presenting at conferences or attending training courses from 1 July to 30 September.
Various dates	Society Conference Grants to attend a Focused Meeting this summer.

For more information please visit the website **microbiologysociety.org/grants**.

FIS 2019

11- 14 NOVEMBER, EDINBURGH, UK

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MICROBIOLOGY SOCIETY

ON BEHALF OF THE FEDERATION OF INFECTION SOCIETIES

Registration open: 6 June 2019

Abstract deadline: 5 August 2019

Grant deadline: 1 September 2019

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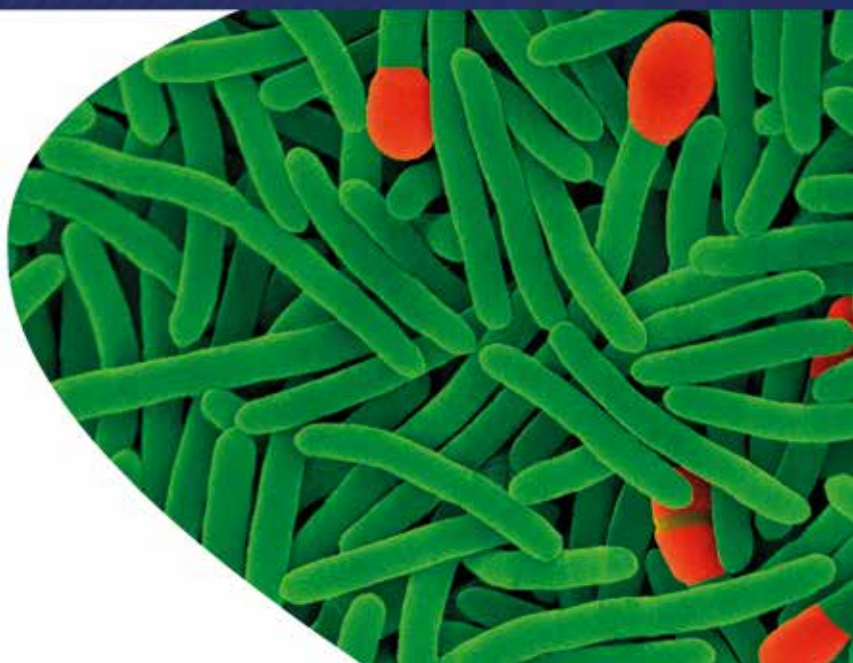
Special Online Collection in 2019

In collaboration with Anaerobe 2019: Changing perceptions of anaerobic bacteria; from pathogen to the normal microbiota and back



Call for papers

Submission deadline:
September 2019

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Elinor P. Thompson

Chair of the Eukaryotic Division

Elinor Thompson

The Society has four Divisions (Eukaryotic, Prokaryotic, Virology and Irish) which consist of Society members who support the organisation and plan sessions and symposia for the Society's events programme. Each Division Chair and Chair-Elect sit on the Scientific Conferences Committee and the Chair reports into the Society's governing body, Council. In this article we introduce Elinor Thompson, Chair of the Eukaryotic Division. She tells us about her background and her role on the Division.

I am a Senior Lecturer at the University of Greenwich and my research is mostly on families of membrane proteases involved in signalling and regulation, in a range of model organisms – my work on the social amoeba and model eukaryote *Dictyostelium* is the reason I became involved with the Eukaryotic Division. My lab has a longstanding interest in organelle function too, and our molecular biology resources mean we are drafted in to help with a whole range of biology or medical projects.

When did you first decide you wanted to do science (and why)?

I thought about this when I was applying to study microbiology at university. The interviewers' questions at University College London made me realise that scientific, or at least technical and medical, thoughts had always been around me. One of my grandmothers was a midwife and health visitor, the other was a pharmacist, and my father is an engineer. I also grew up in the deepest, nowhere countryside with lots of nature around. As with so many scientists, the most important people were probably my secondary- and high-school science teachers, Mr Cross and Mr Smith – the former lent me and my friend the school telescope to take home at weekends, and the latter did a whole course in microbiology as part of our Biology A level. I am on video somewhere demonstrating sub-culturing at the age of 16! I did work as a scientific writer and editor for a while after graduating, though, until I was sure I wanted to do a PhD.

When did you join the Microbiology Society and why did you join?

I worked at the Society on the *Journal of General Virology* when I graduated, to take a break from academic life, so I knew about the Society from that point, and joined as soon as I went to University College London to do an MSc then PhD.

Please describe your role on the Division.

I was a Division member and Chair Elect before taking over as Chair, so I have been involved in organising sessions for the conferences for a few years, trying to think of subjects and speakers who will attract a good audience at the Annual Conference. The admin for this is deciding session order, evaluating offered talks and posters for sessions, and the Chair keeps an eye on all the sessions. The nicest jobs are meeting up as a Division to discuss progress, attending the Conference, of course, and the extras such as judging the Sir Howard Dalton Young Microbiology of the Year Competition (which is always humbling in the quality of the talks).

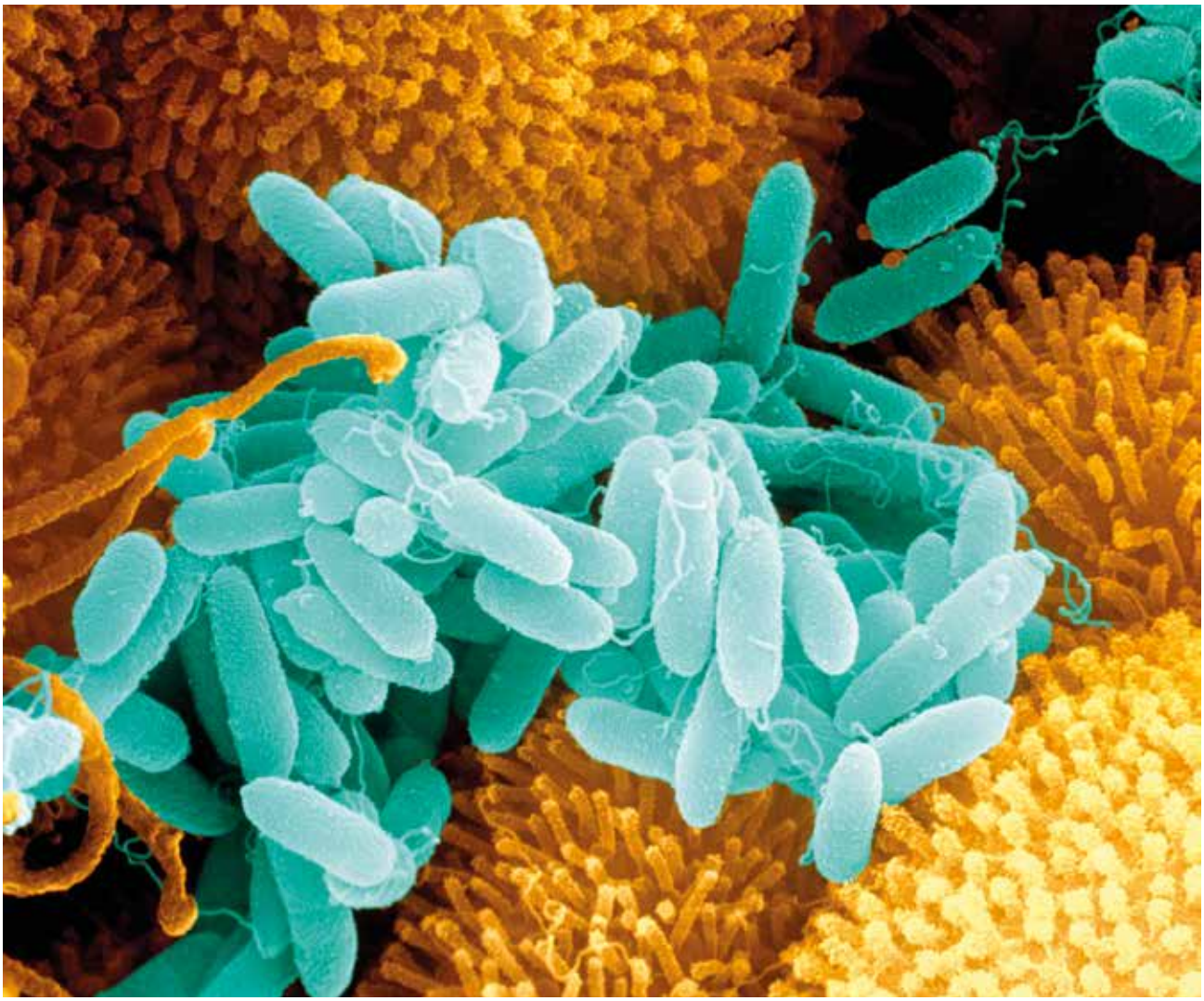
What motivated you to be part of the Division?

I started scientific life as a microbiologist and had been a member of the Society for a long time. My students and I have benefitted from Microbiology Society support and I am honoured to have been able to return the favour.

Are you a member and would you like to join one of the Divisions? Find out more about the Divisions and what they do on our website (**microbiologysociety.org/divisions**). The Council and Committees shadowing scheme is also a fantastic opportunity to gain an insight into the work of the Society and gain first-hand experience of our Council and Committee activities. Find out more on the Society website: **microbiologysociety.org/shadowingscheme**.

Where bacterial metabolism and virulence intersect

Kim R. Hardie



Coloured scanning electron micrograph of *Pseudomonas aeruginosa* bacteria (blue) on ciliated human nasal epithelium. Juergen Berger/Science Photo Library

'We are what we eat', and so are the bacteria that live on us. If bacteria do not have the building blocks or metabolic pathways and capacity to create their healthy cell, they will be disadvantaged when it comes to establishing an infection.

For example, an incomplete peptidoglycan or lipopolysaccharide (in Gram-negative bacteria) would leave them weakened and more susceptible to harsh environments, the immune system or antimicrobials. Metabolism provides these building blocks, thereby contributing to pathogenicity via boosting cell fitness. Metabolism also generates the substrates (amino acids, sugars, etc.) for virulence factors (which are defined as macromolecules that contribute to infection severity).

Scavenging for nutrients to feed metabolism boosts virulence

It has long been known that bacteria produce macromolecules to scavenge for key molecules required for metabolism, such as iron. If acquisition or utilisation of these resources is impaired, so is their pathogenicity. This may be linked to survival in a certain niche, e.g. blood, or to accomplish a key stage in infection: for example, biofilm formation. Similarly, regulators integrated into nutrient acquisition also control virulence factors, such as the sigma factor linked to metabolism of nitrogen, RpoN or Fur (the ferric uptake regulator). Conversely, virulence regulators also exert regulatory control over metabolic pathways, e.g. EfpR in the plant pathogen *Ralstonia solonacearum* or regulators encoded on the *Salmonella* pathogenicity island 13 (SP-13). In these ways, virulence and metabolism are intimately linked, and this feeds into the 'survival of the fittest' theories of evolution.

Metabolic pathways can be co-opted as a virulence strategy

LuxS is a metabolic enzyme, central to the activated methyl cycle that converts *S*-ribosyl homocysteine to homocysteine, releasing 4,5-dihydroxy-2,3-pentadione (DPD). DPD cyclises spontaneously to generate autoinducer 2 (AI-2), that can serve as a temporally-released metabolite. Some bacteria do solely this, and uptake AI-2 in times of need to feed it back into metabolism. When *luxS* is disrupted, there is a reduction in fitness which can affect pathogenicity, for example, by curbing biofilm formation. Other bacteria have been able to exploit the AI-2 to count their population size, and use it to trigger a specific regulatory response when the population density reaches a critical size: i.e. quorum sensing (QS). If the QS regulon encompasses virulence factors, pathogenicity will be affected directly.

Virulence factor production drains metabolic pathways

On the opposite side of the coin, the production of virulence factors draws on metabolism, and this fitness cost can impair pathogenicity. For example, capsule production and glucose metabolism collide in dictating virulence of *Serratia marcescens*. Unlike AI-2, other QS signal molecules (QSSMs) do not feed back into metabolism as directly, but are produced by dedicated synthases, with the goal of interacting with cognate regulators, e.g. *N*-acyl homoserine lactones (AHLs) and alkyl quinolones (AQs). QS dictates that QSSMs accumulate, thus their production is a drain on the metabolic pathways that are specific to the generation of the substrates from which they originate. The feeder metabolic pathways include amino acid and fatty acid synthesis, and when depleted there is a fitness burden that impacts upon virulence. This impact is serious enough for cheating bacteria (QS responders that do not make QSSMs) to exist in populations.

Balancing the cost of virulence and metabolism breeds population diversity which ultimately fuels pathogenicity

Not every bacterium plays fairly, leading to heterogeneity in populations that enables bacteria to progress infections under adverse conditions, e.g. non-producing cheaters benefit from the production of virulence factors made by other bacteria, but have a reserve in their metabolic bank if environmental conditions change. Likewise, relatively metabolically inert cells, such as persisters, are maintained to enable survival when slow growth is an advantage, where nutrients are scarce, for example, such as in the depths of a biofilm, or during the onslaught of antimicrobials.

Bacteria share metabolic resources to establish an infection

Some pathogens have evolved to make the best of heterogeneous metabolisms in a population by cross-feeding. Cross-

feeding is evident within the complex biofilm communities of plaque in the oral cavity where *Streptococcus gondii* depends on the keystone pathogen *Porphyromonas ginivalis* generating 4-aminobenzoate/para-amino benzoic acid (pABA) for folate biosynthesis. Marvin Whiteley's group demonstrated this co-dependence extended beyond nutrient provision to the promotion of respiratory growth of a pathogen by a commensal that enhanced virulence. This is likely to have implications in polymicrobial infections such as those found in wounds.

Virulence factors can generate a new metabolic resource

Some virulence factors can provide nutrients that provide a fitness advantage. For example, the surface-tethered aminopeptidase autotransporter of *Pseudomonas aeruginosa*, AaaA, can generate arginine locally that can be metabolised by the bacteria, and could be a strategy to survive in environments with limited oxygen, such as within a biofilm microcolony.

A metabolic switch can turn a commensal into a pathogen

The nasopharyngeal commensal *Streptococcus pneumoniae* colonises 65% of individuals. Bacteria from this reservoir can invade the lungs to cause pneumonia, the blood to cause bacteremia, the central nervous system to cause meningitis or ascend the eustachian tube to the middle ear and cause otitis media. Virulence factor switches, for capsule serotype for example, contribute to infection progression by enabling pathogens to survive in different niches. Minhas *et al.* reported that altering uptake and utilisation of the trisaccharide raffinose may be the ultimate determinant controlling whether a *S. pneumoniae* infection is established in the blood or the ear, with clinical isolates from the blood utilising raffinose more efficiently. Interestingly, this highlights how differential carbohydrate metabolism not only alters virulence, but can even impact on the disease caused. Whether the underlying mechanism of the raffinose uptake is linked directly to metabolic status of the bacteria is not entirely clear. It is possible that different host niches have altered sugar availability which influences the need to metabolise raffinose and gain a fitness advantage. It is also possible that depleting the raffinose concentration may alter aggregation and biofilm potential as a virulence strategy.

A metabolic pathogenic strategy that disadvantages the microflora

Salmonella Typhimurium uses one pathogenicity island (SPI-1) to encode a type 3 secretion system (T3SS-1) to promote inflammation in the intestinal tract. The inflammation initiates production of tetrathionate and ethanolamine which can be utilised by the *S.* Typhimurium to trigger rapid expansion of the pathogen at the expense of the commensals.

Concluding perspectives

The interplay between virulence and metabolism is complex, and searching the literature for relevant information is plagued by non-specific terms. However, it is apparent that the two are linked, although it is difficult to define the boundaries between the two. Is a metabolic enzyme/regulator that provides a cell with a fitness advantage during an infection a virulence factor? Is a virulence factor that provides a metabolite better defined as a metabolic pathway component? Current technology platforms are developing fast, and ultimately we will be able to analyse the metabolome and virulence factors simultaneously in single cells in a population. This may perhaps be possible in real time using secondary ion mass spectrometry (SIMS) imaging such as ORBI-SIMS and Nano-SIMS, and Raman coupled to confocal microscopy or fluorescence *in situ* hybridisation (FISH) which will help us decipher these conundrums.

Serratia marcescens. Sinhyu/iStock

Further reading

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Kim Hardie studied for a BSc in Biological Sciences, before completing a PhD investigating *Escherichia coli* haemolysin. She has since worked in postdoctoral positions at the University of Victoria, Canada, and the Institut Pasteur, Paris. Her research at the University of Nottingham has focused on autotransporters, quorum sensing, biofilms and AMR complements, and she holds governance roles within the Microbiology Society and Royal Society of Biology.

What does a typical week involve for you?

A typical week is working 8:00–18:00 on a mixture of research supervision meetings, lectures and workshops for students. It also involves pastoral support and mentoring, interactions with external academics and also far too much admin. Most evenings involve an hour or so on the computer and spending time with my two daughters and husband. For a treat, I cook something special, go to the gym, knit or read a novel. Most weeks involve at least one IT annoyance and if I'm lucky there will be a trip somewhere to examine, plan research, hear science or get involved with external governance.

What inspired you to become a microbiologist?

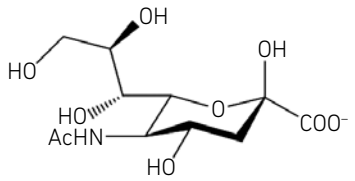
The fascination to understand how bacteria, which are so small and single-celled, can do almost everything a whole organism can do. Microbiology is pure systems biology without even trying, and the ideal component of multidisciplinary science. Most importantly, bacteria do not bleed, so they don't make me squeamish, and they are easier to grow than plants.

A special sugar: how sialic acid impacts on metabolism, health and disease

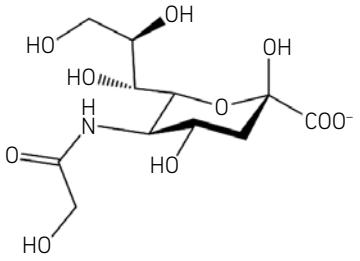
Andrew Bell, Emmanuele Severi, Nathalie Juge and Gavin H. Thomas

We are teeming with microbes that live on surfaces outside and inside our bodies. Our understanding of the gut microbiome in particular is rapidly improving as we start to unpick how complex microbial communities interact with our diet, with other microbes and with our cell surfaces. While many chemicals are important in this milieu, here we focus on sialic acids as a critical set of molecules that underpin many of these interactions and impact on metabolism, health and disease.

Neu5Ac



Neu5Gc



2,7-anhydro-Neu5Ac

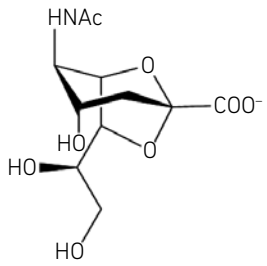


Fig. 1. **Example of sialic acid derivatives. Note that the *N*-glycolyl-neurnaminic acid (Neu5Gc) cannot be made by humans, a biochemical difference that distinguishes us from other great apes, but can be incorporated into our cell surfaces when acquired from the diet.** Andrew Bell

The most common sialic acid, *N*-acetyl-neuraminic acid (Neu5Ac) (Fig. 1) is a relatively simple sugar acid that, apart from its charge, has nothing intrinsically unusual about it. However, when cells contact other cells they often use molecules displayed on the surface, and this is where sialic acids become so important, as they are usually the terminal sugars on the host glycans that pepper proteins and lipids sitting on cell surfaces. Cell-surface or secreted mucin glycoproteins are good examples of sialic acid-coated structures that microbes could encounter at mucosal surfaces, such as the respiratory or gastrointestinal (GI) tract. This unique position as the 'meet and greet' molecule for other human cells, bacterial cells and viruses puts the sialic acids at centre-stage for many important processes.

Sugar-coated pathogens

One of the first microbial functions of sialic acids was connected to the ability of some pathogens to colonise and then

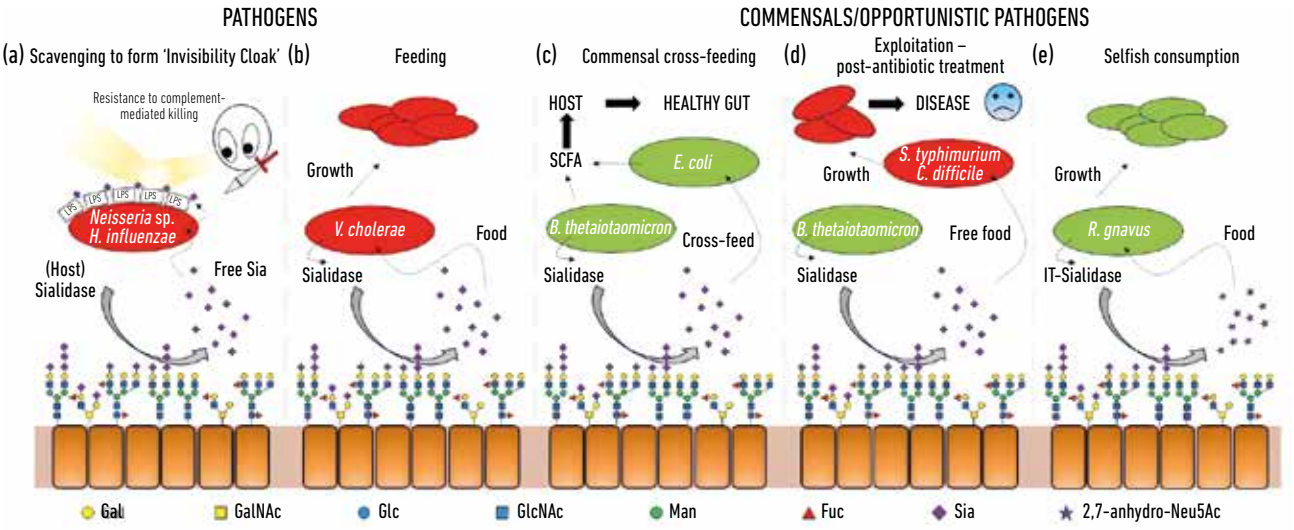


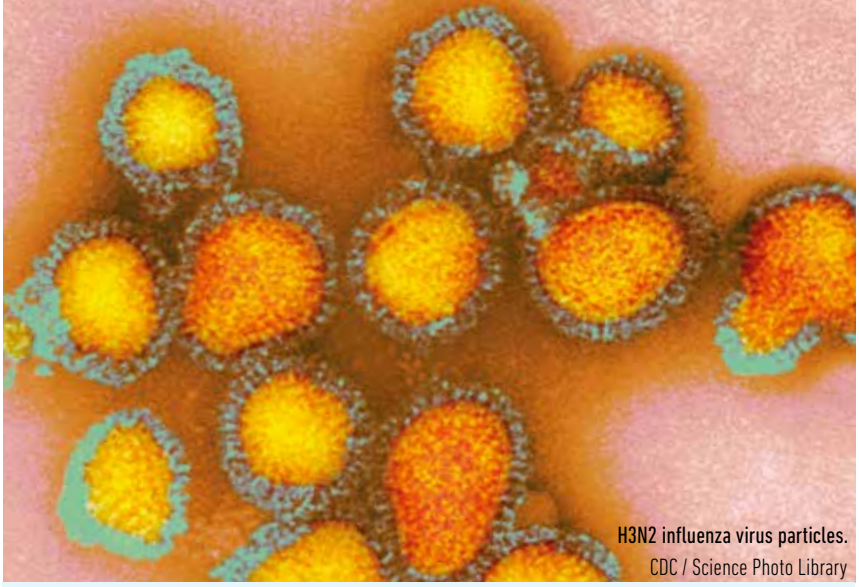
Fig. 2. Cartoon illustration of the various interactions between bacteria and sialic acids present as terminal sugars on a range of host glycans. These are cleaved by sialidases and usually converted to free Neu5Ac with the exception of the IT-sialidase that releases 2,7-anhydro-Neu5Ac. Free sialic acid released by host or pathogenic sialidases can then be used by pathogens as an invisibility cloak (a), or for feeding (b). Cross feeding can occur between members of the gut microbiota or between commensal and pathogenic bacteria sharing the same niche (c, d) while other bacteria have developed selfish mechanisms to reserve sialic acid for their own consumption (e). Emmanuele Severi

cause disease in humans. Indeed, the ex-President of the Microbiology Society, Professor Harry Smith FRS, working at the University of Birmingham, pioneered this work with *Neisseria gonorrhoea*. When scientists in his group isolated the bug directly from the body, it was resistant to killing by human serum (complement-mediated killing), but if the bugs were cultured in the lab for a few generations, this protection was lost and the cells were killed by the serum. His group had discovered that these pathogens steal sialic acid from the host and use it to coat their own cell surface to humanise them. However, as they can only scavenge this sialic acid, its absence in growth media means no further sialic acid is added so they rapidly lose this 'serum protection' and are killed. It turns out that a range of other sneaky bugs use similar strategies to generate their own invisibility cloak using sialic acid, such as *Neisseria meningitidis*, *Campylobacter jejuni* or *Haemophilus influenzae* (Fig. 2a)

Cross-feeding – sharing the sweets around

As well as being used by pathogens as an invisibility cloak, sialic acids are pretty good food for bacteria, as they provide both carbon and nitrogen, and can be used as an energy source. Earlier work showed that pathogens such as *Vibrio cholerae* were happy just to eat sialic acids and that in itself was important for successful host colonisation (Fig. 2b).

In the gut, a major source of sialic acids comes from mucins, which are the main structural components of the mucus layer covering the epithelium surface. The most exposed layer of mucus is the habitat of various commensal bacteria, which have learnt how to feast on mucin proteins, where sugars make 80% of their mass. From a simple topological perspective, the sialic acids, as the terminal sugars, are harvested first, exposing the underlying sugars that can also be subsequently released and eaten. With the advent of next-generation sequencing, we have gained knowledge on the microbes living in this niche, and many have genes for sialic acid uptake and subsequent catabolism. What was exciting was the discovery that some of the commensal anaerobes, like *Bacteroides thetaiotaomicron*, secrete sialidases to release the sialic acid but lack transporters and catabolic genes to actually use it. This seemingly altruistic gesture is required for the bacteria to access underlying sugars and underpins a process of metabolic cross-feeding to other bugs living in the mucus niche, like commensal *Escherichia coli* strains that do not have a sialidase but are good at eating free sialic acid (Fig. 2c). This concept is now recognised as an important aspect of colonisation and niche adaptation. A brilliant exemplification of this was described by the group of Justin Sonnenburg from Stanford University, using a mouse model with a simple defined gut microbiota. Following antibiotic treatment, many of the sialic-acid-eating bacteria were wiped out, resulting in the accumulation of free sialic acid in the gut. When then challenged with pathogens like *Salmonella typhimurium* or *Clostridium difficile*, these pathogens would benefit from the free sialic acid as a nutrient (Fig. 2d). Mutant strains of pathogens lacking the transporters or catabolic genes did not have an advantage, making a direct connection to pathogen outgrowth when the gut microbial community is disrupted.



H3N2 influenza virus particles.
CDC / Science Photo Library

Viruses get in on the act

Viruses also use sialic acids as key molecules during their infection cycle, most famously influenza virus. Initial attachment is the first key step as sialic acids function as the receptors for the virus on respiratory epithelial cells. The type of linkage of the sialic acid to underlying sugars in the glycans often controls the host range of influenza viruses, and pandemic strains often have adhesion protein (hemagglutinin) that recognises the human-like forms of sialic acid attachment and so are particular virulent. Sialic acid is important at the last stage in the viral life cycle as release from the infected cell requires cleavage of sialic acids off the host cell surface. This is catalysed by a viral enzyme called sialidase (or neuraminidase). Inhibition of this enzyme by structural analogues of sialic acid, formulated into Tamiflu® (Oseltamivir phosphate) and Zanamivir, are our front-line treatment for influenza and are a triumph of structure/function inspired drug design.

Mechanisms to reduce the pool of free sialic acid in the gut were therefore proposed as part of a novel anti-infective strategy.

Keeping hold of your own sweets

While much early sialomicrobiology focused on pathogens, more recent work has focused on the commensal bacteria inhabiting the same niche. Today's studies in the field of the gut microbiota are revealing how fierce the competition for Neu5Ac is in our gut and how it can tip the balance between pathogens and commensals. What if a particular bacterium could release sialic acid in a form that only it could access? Work in the Juge Group in Norwich showed that the gut symbiont *Ruminococcus gnavus* has evolved to do so, using a special type of sialidase called an intramolecular *trans*-sialidase (IT-sialidase) which releases 2,7-anhydro-Neu5Ac (see Fig. 1) instead of Neu5Ac. By developing a method to synthesise pure 2,7-anhydro-Neu5Ac, they showed that *R. gnavus* strains were able to grow on 2,7-anhydro-Neu5Ac as the sole carbon source. In addition to the domain catalysing the enzymatic reaction, IT-sialidases comprise a carbohydrate binding domain which helps to mediate the binding of the IT-sialidase to sialic acid rich mucins. *In vivo*, this may favour a mechanism that helps targeting the bacteria towards sialic acid rich regions of the GI tract, therefore promoting bacterial colonisation within the mucus layer. Once located in the right place, the IT-sialidase cleaves off sialic acid from the terminal chains of mucins and releases it in a form, 2,7-anhydro-Neu5Ac, that *R. gnavus* can use as its own source of food, rather than sharing Neu5Ac with other bacteria inhabiting the mucus niche, including pathogens (Fig. 2e). This mechanism provides a competitive advantage over other sialic-acid-eating bacteria inhabiting the mucus niche, by providing a source of nutrient that it can preferentially access. In addition, *R. gnavus* may also help reduce outgrowth of enteric pathogens by reducing the level of Neu5Ac in the mucosal environment, opening ways to a novel therapeutic strategy in an age of increasing antibiotic resistance.

In conclusion, it is clear that sialic acids are critical molecules in many processes where microbial cells and viruses interact with mammalian cell surfaces. In this short article, we have touched on some of these to give an idea of the central functions of these sugars in communication, stealth, colonisation and metabolism in different aspects of heath and disease. Sialic acids have been described as the most important chemicals in the world and will no doubt continue to reveal more about the evolution of humans and their interplay with their microbes.

Further reading

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Andrew Bell is a post graduate student in the Department Gut Microbes and Health at the Quadram Institute studying the impact of a novel mechanism of sialic acid metabolism on gut homeostasis. He obtained his BSc in Biochemistry from the University of East Anglia and spent 2 years working at the John Innes Centre on chlorophyll metabolism in pea (*Pisum sativum*) before joining Nathalie Juge's group at the Quadram Institute in 2015 for his doctoral work.

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Nathalie Juge is a Research Leader at the Quadram Institute Bioscience (QIB) in Norwich, Deputy Leader of the Institute Strategic Programme, the Gut Microbes and Health (GMH), and Honorary Professor at the School of Biological Sciences, University of East Anglia. She leads a Research Group on the glycobiology of host-microbe interactions in the gut with a focus on mucin-derived sialic acid metabolism by the gut microbiota (**https://quadram.ac.uk/nathalie-juge**).

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Emmanuele Severi is a post-doctoral research associate in the Department of Biology at the University of York working in the laboratory of Prof Gavin Thomas. He has worked on sialic acid transport and metabolism at different times in his career, and has been a member of the Society since 2002.

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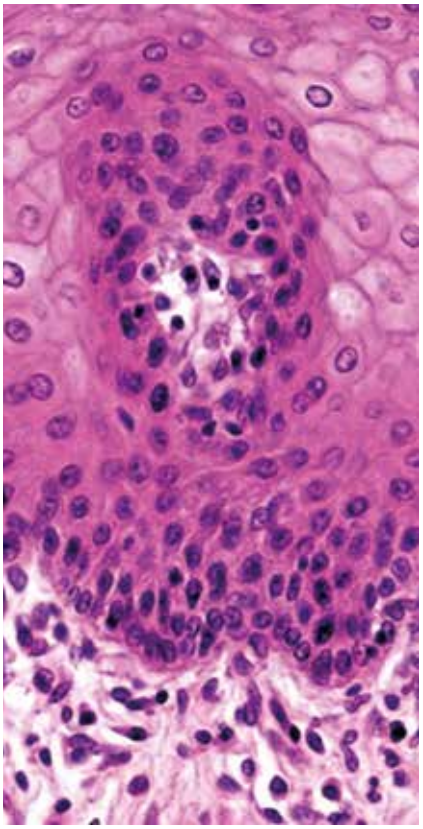
Gavin H. Thomas is a Prof. of Microbiology in the Department of Biology at the University of York and have worked on bacterial sialic acid transport and catabolism for over a decade. He has been a member of the Society since 1995, was Editor of *Microbiology Today* (2003–2006), serving on Council in the same period, served on Communications committee (2012–2015) and the Equality & Diversity committee (2013–2015). He has been an Editor, Senior Editor and is now Deputy Editor-in-Chief of the Society's leading journal *Microbiology* (**http://thomaslabyork.weebly.com**).

Why does microbiology matter?

Gavin: It matters for our health – only now are we really starting to understand the molecular composition and function of our microbiome, which likely impacts on our body in multitudinous ways.

What advice would you give to someone starting out in this field?

Gavin: Read widely and beyond 'your bug' – microbes can do pretty much everything and have usually invented multiple different ways to do it!



Modelling virus infections of the skin in 3D

Sally Roberts and Joanna Parish

Using organotypic raft cultures to study the replication cycle of epithelial tropic viruses has given us revealing insights into the infection strategies and pathogenesis of clinically important viruses.

When we think of skin, we usually have in mind the skin covering the outside of our bodies, but our body cavities (e.g. anogenital tract, oesophagus) and some organs (e.g. tonsil) are also lined by skin or to be more precise – stratified squamous epithelium. Made up of multiple layers and constantly renewed throughout our lives, through a tightly regulated balance between cell proliferation and cell differentiation, our squamous epithelium performs many functions, but one of its major roles is to act as a barrier to micro-organism invasion.

The lower layer of the epithelium is referred to as the 'basal' cell layer and contains proliferating cells, including self-renewing stem cells, whereas the upper or 'suprabasal' layers are made up of differentiating cells (Fig. 1). Keratinocytes are the major constituent cells of squamous epithelium, but other cell types present include local antigen-presenting Langerhans cells and γδ T cells, both involved in immunological surveillance, mechanoreceptor Merkel cells, and melanocytes which give pigmentation and act to block UV irradiation.

The underneath of the epithelium is separated from the dermis, which harbours specialised structures such as hair follicles, sweat and sebaceous glands, and nerve endings by the basal lamina – a highly specialised extracellular matrix structure. Nourishment of the epithelium comes from the basal side by diffusion of nutrients and factors from the underlying dermis. At the onset of differentiation, the basal cells become detached from the basal lamina, stop proliferating and begin differentiation. As they travel upwards they become more differentiated until in skin they

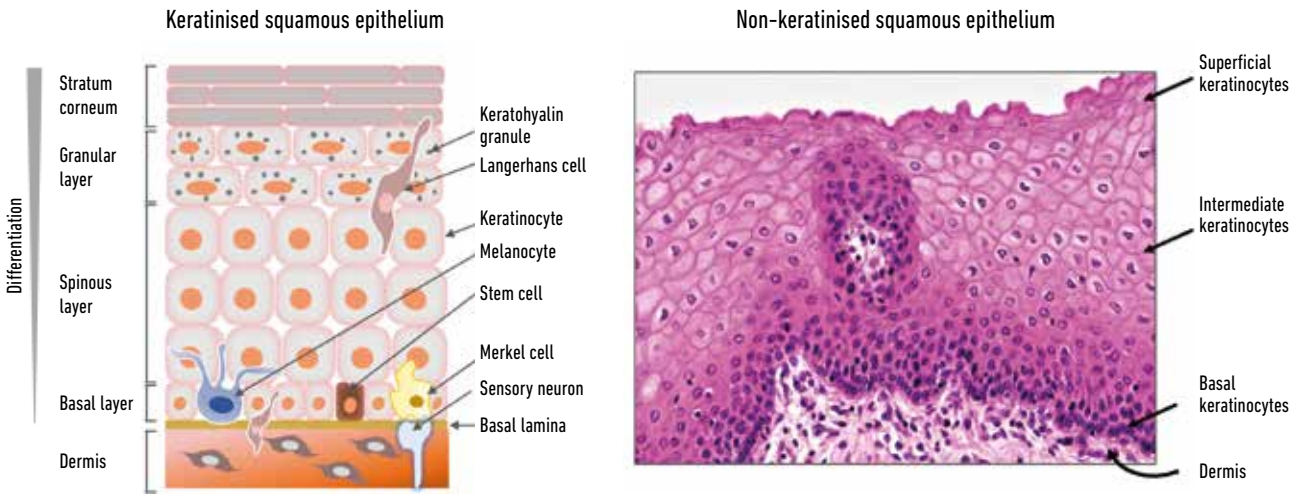


Fig. 1. **Structure of squamous epithelium – keratinising (left) and non-keratinising (right).** S. Roberts, University of Birmingham (left); licensed under Creative Commons CC0 1.0 Universal Public Domain Dedication (right)

form a keratinised, highly differentiated layer that is continually sloughed off, or in 'wet' mucosa (e.g. the uterine cervix), a non-keratinised superficial layer – this process takes about two weeks to complete (Fig. 1).

Growing skin in the laboratory – organotypic raft cultures

Recapitulating the complex process of epithelial differentiation in a laboratory as a way of making 'skin' for treating burns was the 'Holy Grail' in skin research for many decades. One of the most important discoveries was being able to isolate and grow keratinocytes from skin on a feeder layer of mouse fibroblasts for several successive generations – the next big step was to get them to differentiate to form a physiological replica of the epithelium. Since squamous epithelia are surface tissues with their upper regions exposed to the outer/inner environment and nourished from the basal side, the isolated keratinocytes are grown on a plug of collagen (a scaffold) and the structure lifted to the air–medium surface supported by a metal grid or cell culture plastic insert (although originally the collagen plugs were floated on the media surface, probably leading to the 'raft' terminology), so that the underside of the plug is in contact with the tissue culture medium (Fig. 2). The collagen plug is embedded with fibroblasts (isolated from dermis or a mouse fibroblast cell line) and acts as a dermal equivalent mimicking to some degree the mesenchymal–epithelial interactions that occur *in vivo*. After about two weeks in organotypic raft culture the keratinocytes have formed into 3D structures of full thickness and fully differentiated epithelium, and accurately mimic the physiology of squamous epithelium.

Viruses that replicate in the skin

Even though the epithelium is a barrier to infection, a number of clinically important viruses replicate in our epithelia including both alpha- and gammaherpesviruses, human papillomaviruses (HPV), Merkel cell polyomavirus (MCPyV), and poxviruses. Notably, many of these viruses have been designated by the World Health Organization as carcinogens because infections are at risk of developing into cancer. For some viruses the keratinocyte is the target cell for their replication cycle, but skin keratinocytes might also act as the entry portal of various pathogenic arboviruses following a mosquito bite. For others there is some uncertainty surrounding the nature of target cells in the epithelium, and an example is MCPyV which causes aggressive and often lethal Merkel cell carcinoma (MCC), which are located in the basal layer of epithelia. Dermal fibroblasts have been shown to support productive MCPyV replication and are therefore proposed as the target cell, although no viral DNA has been detected in the dermis adjacent to virus-positive MCC – the debate is ongoing.

Herpesvirus replication in 3D

The alphaherpesviruses varicella zoster virus (VSV), which causes chicken pox, and the herpes simplex viruses (HSV) 1 and 2 associated with oral and genital herpes, enter the host via infection of the differentiating squamous epithelial cells and subsequently establish lifelong latency in the dorsal root ganglions. Reactivation of these viruses (VSV – shingles, HSV – recurrent genital herpes) can be problematic for the host and a high burden on healthcare facilities. Primary skin keratinocytes infected with virus following lifting to the air–liquid interface in organotypic raft culture supported replication and spread of these viruses. The 3D models have been used as a platform for screening of antivirals and several compounds that reduced replication and spread of these alphaherpesviruses have been identified.

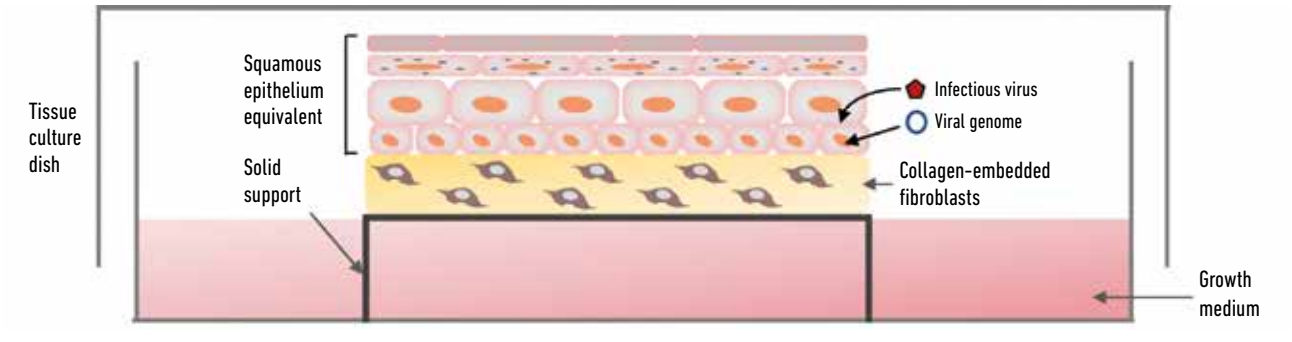


Fig. 2. **Organotypic raft culture.** S. Roberts, University of Birmingham

The gammaherpesvirus Epstein–Barr Virus (EBV) is a common infection that establishes lifelong latency in B lymphocytes. EBV infection in the young is often asymptomatic but if infection is delayed until adolescence, can often manifest as infectious mononucleosis or glandular fever. Establishment of lifelong latency may lead to EBV-associated lymphoid and epithelial cancers. The route of infection of B cells was thought to occur by oral transmission via epithelial cells in the oropharynx, but evidence that EBV could undergo productive replication in epithelia was slight and infection studies using epithelial cells grown in monolayer cell culture only supported a latent EBV infection. Breakthrough came when primary oral keratinocytes grown as 3D rafts were efficiently infected with EBV and the virus underwent a full productive cycle. This EBV infection model showed that the infection of epithelial cells led to the efficient production of new progeny and this tropism was an integral part of EBV spread in the oropharynx. Likewise, a better understanding of the transmission of another herpesvirus, Kaposi sarcoma-associated herpes virus (KSHV), was gained from growing virus-infected tonsil keratinocytes in organotypic raft culture. KSHV is a significant pathogen in the immunocompromised, especially those infected with HIV, and infection is associated with Kaposi sarcoma and several other malignancies. Infected saliva was known to be the route of transmission but the source of the virus in the saliva was unclear. In the rafts, the KSHV lytic cycle was only initiated upon differentiation of the latently infected tonsil cells and newly assembled infectious particles accumulated in the mature epithelial regions; thus infected tonsils could shed new progeny into saliva.

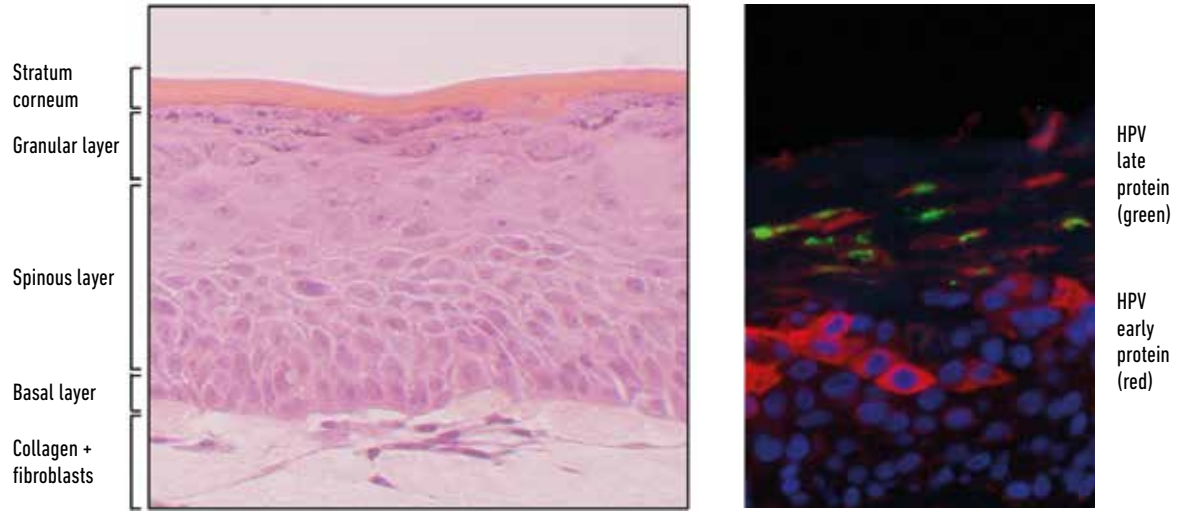


Fig. 3. **Recapitulation of HPV life cycle in organotypic raft culture.** S. Roberts, University of Birmingham

The intimate relationship between human papillomaviruses and epithelial differentiation

The use of epithelium equivalents has been a revolutionary advancement in the study of HPV biology. HPV replication is restricted to keratinocytes and the production of infectious particles is exquisitely dependent upon their differentiation. Infection with the majority of HPV types (there are lots of them) results in benign warty lesions that are subsequently cleared by immune activation. But a small number of HPV types that infect the squamous epithelia of genital and oropharyngeal tracts are the cause of the majority of cervical cancers along with a substantial proportion of other anogenital and oropharyngeal cancers. The virus infects basal keratinocytes and proceeds to manipulate the keratinocyte as it moves up through the layers creating an environment conducive to the productive cycle of the virus.

The virus is dependent on the host cell to replicate and pushes the otherwise postmitotic differentiating keratinocytes back into cell cycle acquiring access to the cellular DNA synthesis machinery. Once the viral genome has been amplified, the delay in differentiation is lifted and the final stages of capsid production and virus assembly take place in the mature regions of the epithelium. This productive cycle can be recapitulated fully in keratinocytes isolated from anogenital and oropharyngeal tissues that harbour the circular HPV genome and grown in organotypic raft culture (Fig. 3). Significant insights into the molecular biology of the HPV life cycle and pathogenesis have come from the use of the 3D culture system.

Future directions

The continuing development of organotypic raft cultures to enable high-throughput screening modalities will enhance the 3D epithelial models of virus infection and replication as platforms for screening antivirals and testing novel therapeutic compounds. Advancement in understanding viral pathogenesis will come from the incorporation of increasingly complex cellular components, e.g. immune cells, into the 3D models to more accurately mimic the site of virus replication.

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Sally Roberts has built a research portfolio studying the molecular biology of human papillomaviruses and a centrepiece of her research is the use of physiological 3D epithelial models of the virus life cycle and virus-driven carcinogenesis. Sally is an associate editor of *Virology Journal*, and was a past member of the Microbiology Society's Virology Division.

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Joanna Parish has studied the molecular biology of HPV for over 20 years and has unravelled mechanisms of HPV genome replication, persistence and epigenetic control of virus transcription utilising 3D epithelial models of HPV infection. Joanna is an Editor of the Microbiology Society publication *Journal of General Virology*, and was a past member of the Microbiology Society's Virology Division.

Why does microbiology matter?

Sally: Over 15% of human cancers are known to have an infectious aetiology and there still may be more associations to discover. Studying these infectious agents not only helps us understand oncogenesis and aids the design of effective vaccine strategies, but also enlightens our knowledge of the basic molecular and cell biology of our cells.

What is the most rewarding part of your job?

Joanna: I have the privilege of working with some of the best academic minds to answer our own important questions about how viruses manipulate cells to cause cancer. My scientific networks are built from those working within my research group (undergraduates, graduates, postdoctoral scientists) to my local, national and international collaborations. I find this 'team science' approach rewarding on many levels.

Human noroviruses and gut bacteria: friends, frenemies or both?

Matthew D. Moore

One does not normally use phrases like 'projectile vomiting' or 'explosive diarrhoea' casually, but in the case of human noroviruses, these terms can often be applied. Norovirus gastroenteritis commonly manifests in the form of vomiting, diarrhoea and abdominal cramping – many times in concert to a degree that would not be forgotten anytime soon.

Human noroviruses: not just cruise ships

Human noroviruses are the leading cause of foodborne illness globally, even though foodborne transmission of noroviruses comprises around 20–30% of all cases. This is no surprise given a number of properties of human noroviruses that makes their control extremely difficult. These viruses are not effectively inactivated by many commercial disinfectants; can survive on surfaces for well over a month; have a very low infectious dose; rapidly evolve to escape host herd immunity; and are asymptomatically and post-symptomatically shed. Although probably most well-known for incapacitating cruise ships, many norovirus outbreaks happen in other settings such as schools, restaurants and long-term care wards. Noroviral illness is so common that (using rough, back-of-the-envelope assumptions) in the US one could fill a little over an Olympic-sized swimming pool of foodborne norovirus diarrhoea

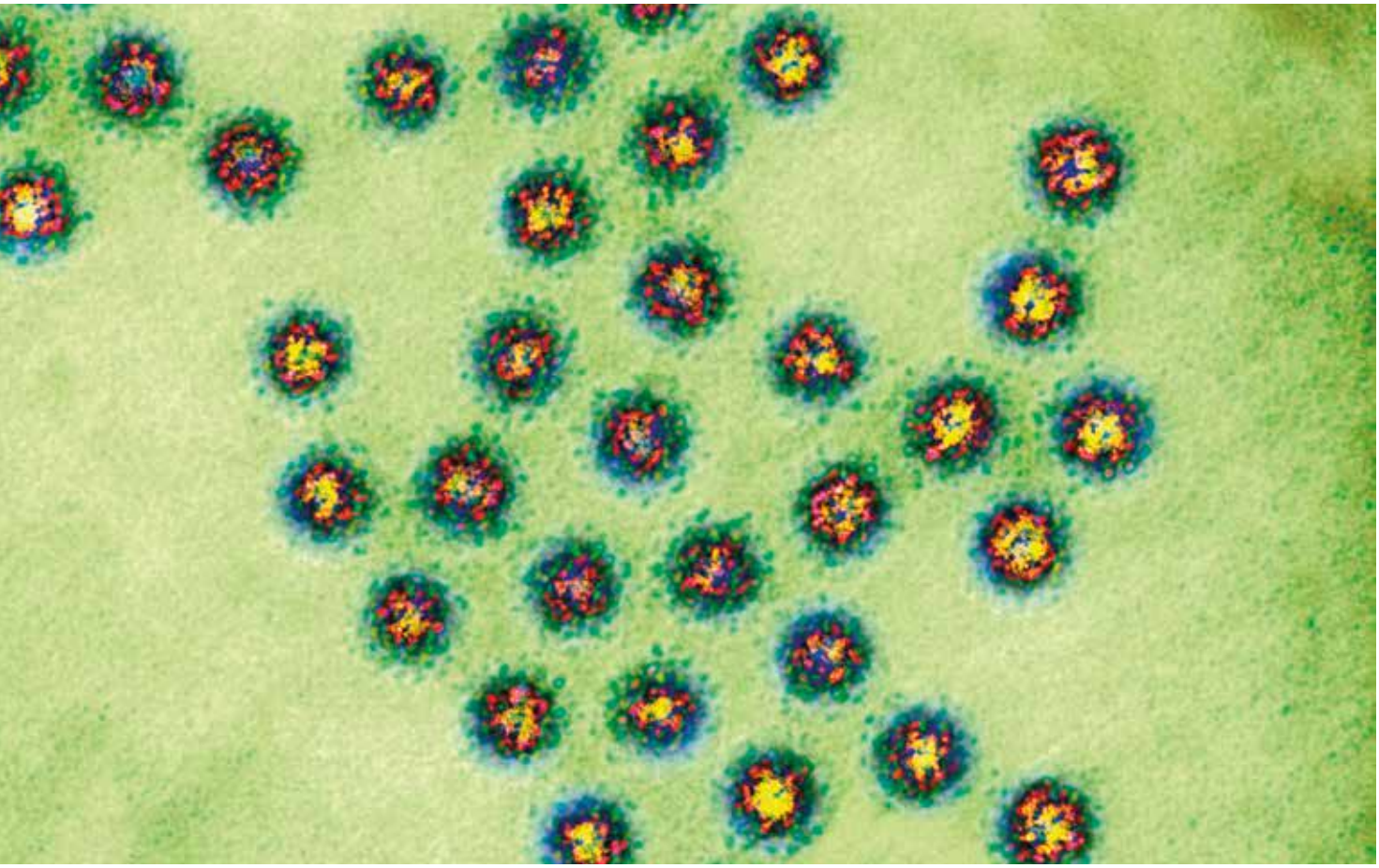
Conversely, a small portion of people shedding norovirus, anywhere from 5-30%, do not display any symptoms despite shedding virus at nearly the same levels for the same duration. Like many questions surrounding human noroviruses, the specific mechanisms for this are not well understood. Despite being generally self-limiting, human noroviruses are still the fourth leading cause of foodborne death and exact a major public health burden on an annual basis.

monthly. That would be nearly 100,000 32 oz (0.95 l) soda cups per day, in case you were wondering.

Trick or treat…or diarrhoea?

The history of human noroviruses as we know them can be traced back to a gastroenteritis outbreak that occurred in an elementary school in Norwalk, Ohio during Halloween in 1968. The agent responsible for the outbreak was not known until 1972, when Dr Albert Kapikian and colleagues reported and visualised noroviruses using immune electron microscopy. Since that time, efforts to cultivate human strains of noroviruses *in vitro* had generally been unsuccessful. The only way to cultivate human strains of the virus was by feeding it to humans (which can still be done today if a study is being conducted and you are desperate for some cash). This forced researchers in the field to rely on related surrogate viruses, including a norovirus that infects mice. Specifically, the major hurdle in human norovirus cultivation appeared to be the uncoating stage of infection. This is because human norovirus genomic RNA could be transfected into cells and go through one stage of replication; however, upon lysing the cell, the virions just bound the outside of neighbouring cells without uncoating. In terms of binding, epidemiological and feeding studies showed that in some cases infection was related to host blood type. Specifically, the majority of human norovirus strains were shown to bind 'histo-blood group antigens (HBGAs)', which are carbohydrates related to blood type that are expressed in a number of tissues in the body, including the intestinal tract. These HBGAs were at least in part suspected of being a co-factor in norovirus infection, but what else was required for *in vitro* cultivation was unclear.

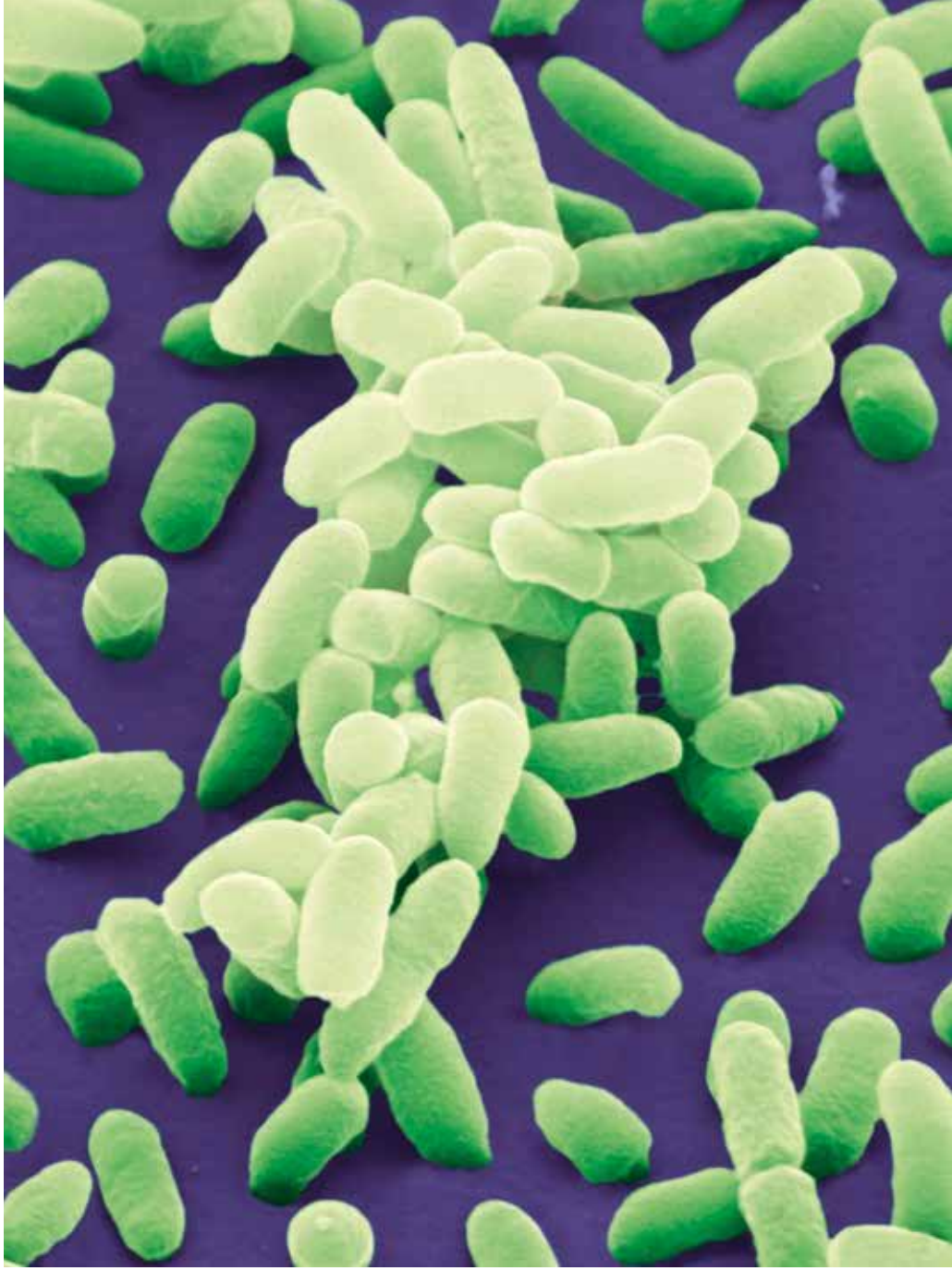
Coloured transmission electron micrograph of a section through several Norwalk virus particles.
Biomedical Imaging Unit, Southampton General Hospital/Science Photo Library



Score one for yogurt?

A major breakthrough came in 2014. Dr Stephanie Karst, Dr Christiane Wobus, Dr Melissa Jones, Dr Jan Vinje and colleagues released a study demonstrating replication of human noroviruses in a human B cell line when enteric bacteria were included as a co-factor. Prior to this, enteric bacteria had been demonstrated to have HBGA-like carbohydrates on their surface, and one had recently had been shown to bind human noroviruses (*Enterobacter cloacae*). The report by Karst and colleagues suggested that enteric bacteria or their HBGA-like carbohydrates promoted norovirus replication in these B cells, in part by aiding viral adhesion to cells. The group was able to demonstrate that inclusion of residual enteric bacteria in norovirus-containing stool or specific doses of heat-killed *Enterobacter cloacae* facilitated replication. Further, the group reported that these enteric bacteria might aid in viral translocation across the epithelial cell layer to get to B cells underneath. Despite this breakthrough, the specific identity of the bacterial proteins or lipids associated with the HBGA-like carbohydrates and the specific effect of norovirus binding on bacteria is still not fully elucidated. A number of studies surveying a broad array of enteric and lactic acid bacteria have demonstrated that numerous norovirus strains bind a number of bacteria to different degrees. Overall, this model has assisted and enabled study of human noroviruses, though with some difficulty in replication. For instance, the use of bacteria has allowed for the study of potential antiviral therapeutics for human norovirus.

Further complicating these findings have been reports that other bacteria may inhibit and inactivate noroviruses. For instance, Dr Changsun Choi and colleagues observed reduction of two human norovirus surrogates during a lactic acid bacterial fermentation, and others have demonstrated antiviral activity of lactic acid bacteria against other enteric viruses (like rotavirus) whose replication has been reported to be enhanced by enteric bacteria. Others have suggested that certain bacteria may reduce viral replication by binding and sequestering potential infectious norovirus particles, thus preventing them from binding and infecting the host cell. Although reports suggesting antiviral effects of certain bacteria on noroviruses are sparse, the issue likely deserves further investigation.



Coloured scanning electron micrograph of *Enterobacter cloacae* bacteria. Juergen Berger/Science Photo Library

Enteric Mini-Mes

Another major breakthrough in the study of human noroviruses came in 2016. Dr Mary Estes, Dr Robert Atmar and colleagues reported successful replication of human norovirus in stem cell-derived human intestinal enteroids. These enteroids are basically made by

> **Although reports suggesting antiviral effects of certain bacteria on noroviruses are sparse, the issue likely deserves further investigation.**

collecting stem cells from a host's small intestine and providing the necessary growth factors to grow a 'mini-gut' with a large number of differentiated intestinal epithelial cells. One major finding from this model was that enteric bacteria were not necessary for human norovirus replication for a number of different human norovirus strains. Evidence from the study did suggest that bile acids enhance infection and may be a necessary co-factor for some human norovirus strains, as well as HBGAs. Further, the study suggested that it was epithelial cells that were being infected and not B cells. Replication was observed in these epithelial cells taken from all three major portions of the small intestine, suggesting that there was no specific localisation of replication in the small intestine. However, the possibility that bacteria may cause localisation of norovirus replication and/or enhance infection still remains a possibility.

More funding please!

All of these interesting developments leave more questions than answers, with numerous areas ripe for investigation. Is infection only occurring in the epithelial layer or could it also be occurring in B cells? What specific bacterial proteins or lipids are responsible for binding to human norovirus? Is there another mechanism through which these bacteria aid infection beyond aiding attachment or aggregation? Are there certain bacteria that may act to inhibit human norovirus infection? What host factors affect this transkingdom interaction? If there is one definitive conclusion that can be drawn from these exciting developments, it is that more research is needed.

Further reading

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Matthew D. Moore

Matthew D. Moore

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Matthew Moore graduated with BSc in Food Science from Cornell University in 2010 and received his PhD in 2016 in Food Science under the supervision of Dr Lee-Ann Jaykus at North Carolina State University. After serving as a postdoctoral fellow under the supervision of Dr Jason Folster at the US Centers for Disease Control and Prevention from 2017–2018, Matt then joined the Department of Food Science at the University of Massachusetts, Amherst as an Assistant Professor.

What is the best career decision you have ever made?

That is really difficult to answer! I feel like I have been unbelievably lucky to end up with amazing mentors and peers throughout my career. Deciding to go into food science and microbiology would be the best, as both communities are full of incredible people – I feel lucky to be a part of these scientific communities!

What is the most enjoyable part of your job?

So many things are enjoyable. I would have to say the daily interaction with the fantastic people in our field as well as getting to work on such interesting topics. Also poop jokes.

The intestinal microbiota in health and disease

Humans coexist with more than 100 trillion micro-organisms, including bacteria, fungi, archaea, viruses and protozoa that reside in multiple sites of the body, including the skin, lungs and reproductive tract. Those with the highest density and diversity are found in the gastrointestinal (GI) tract (the intestinal microbiota) and make up the microbiome.

Katharine Seton and Simon R. Carding

The collective genome of all the micro-organisms that reside in and on the human body encodes approximately 3.3 million genes, which is 100-fold greater than the human genome. Whereas approximately 99.9% of genes within the human genomes of two unrelated humans are identical, only 10–20% of genes within the microbiome are shared by two unrelated humans. This emphasises the importance of the microbiome in defining humans as individuals.

How do we acquire our microbiome?

Microbial colonisation begins during and soon after birth, with the mother being the principal source of microbial pioneers. Depending on mode of delivery, the infant's initial intestinal microbiota will either resemble their mother's vaginal microbiota, rich in *Lactobacillus*, or their mothers skin microbiota, rich in *Streptococcus*. Post-partum, the intestinal microbiota of the infant rapidly changes, increasing in diversity during the first two years, in association with infant feeding. Breast milk, which harbours hundreds of species of bacteria, provides infants with a source of beneficial and health promoting (probiotic) bacteria including *Bifidobacteria* and *Lactobacilli*. By contrast, formula-fed infants have a distinct intestinal microbiota, with fewer probiotic bacteria. Upon introduction of solid food, the intestinal microbiome starts to resemble that of an adult, becoming enriched in genes associated with vitamin biosynthesis and polysaccharide degradation.

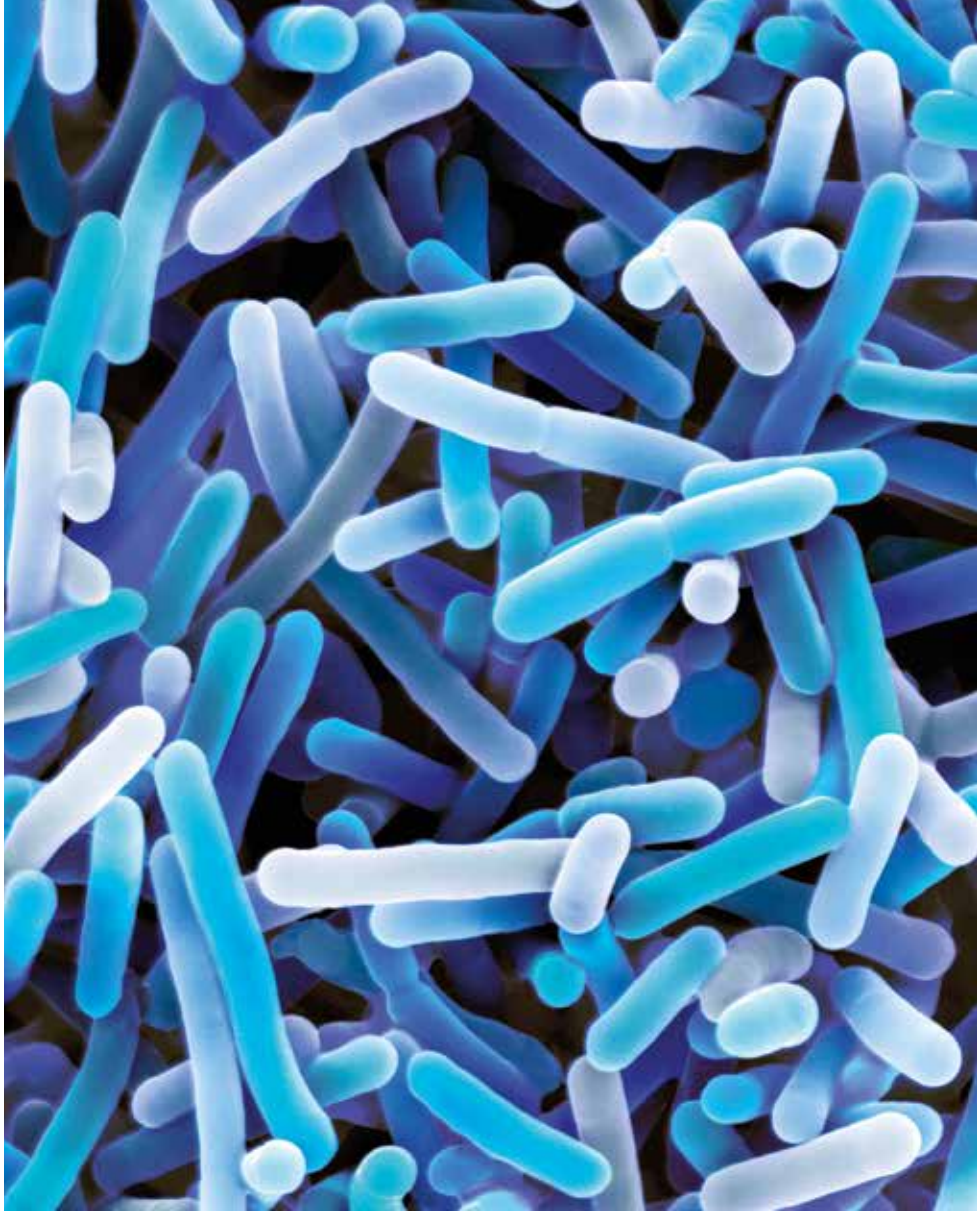
How do we study the microbiome?

The intestinal microbiome makes an important contribution to maintaining human health, with alterations in its make-up and/or function (microbial dysbiosis) being associated with numerous diseases. However, to identify dysbiosis we first need to define a healthy intestinal microbiome. The development of DNA sequencing technologies has significantly advanced and accelerated our understanding

of the intestinal (faecal) microbiota and, in particular, bacterial taxonomy using 16S rRNA based sequencing and the functional capability of the microbiota using whole-genome shotgun sequencing. These culture-independent sequencing methods achieve proportionate analysis of microbial abundances within a complex community of microbes, and the identification of ratios of bacterial families and genera. However, care must be taken when collecting, transporting, storing and processing (faecal) samples to preserve baseline microbial abundances. Some investigators have argued that this analysis should be combined with quantitative microbiome profiling, as microbial load can vary substantially between different samples from the same individual, and between individuals.

What influences the composition of a healthy microbiome?

Difficulties in defining a healthy intestinal microbiome extend beyond limitations of experimental techniques. Both the composition and the temporal stability of the intestinal microbiome are personalised and individual. Performing longitudinal studies on large cohorts, combined with data compilation of environmental, behavioural, genetic and anthropometric measures, enables the dynamics of the microbiota and major covariates of microbiome composition to be identified. Several large-scale microbiome projects, including the Human Microbiome Project, the Flemish Gut Flora Project, the Dutch LLDeep, and the American Gut Project, have identified major covariates that include age, gender, stool frequency and consistency, drug intake and dietary factors such as sugar intake. Among medications, proton pump inhibitors have a strong effect on the gut microbiome, as do antibiotics, metformin, statins and laxatives. Antibiotic-associated changes in the microbiome can extend well beyond course completion. Of note, these covariates together explain less than 20% of variation seen in healthy individuals' microbial compositions.



Scanning electron micrograph of *Bifidobacterium* bacteria. Magnification: x3,000 when shortest axis printed at 25 mm. Dennis Kunkel Microscopy/Science Photo Library

How does the intestinal microbiome promote health?

The major contribution of the intestinal microbiota to maintaining human health is digestion and the processing of food and complex plant-based polysaccharides (fibre). The colon can be considered a large fermentation vessel in which microbes process dietary fibre and resistant starch to generate short-chain fatty acids (SCFAs). SCFAs are an important source of energy for intestinal epithelial cells and they promote local hormone and neurotransmitter production which influences GI motility and appetite control. The microbiome also provides its host with a source of essential vitamins and minerals, such as folates, vitamins K, B2 and B12, and biotin.

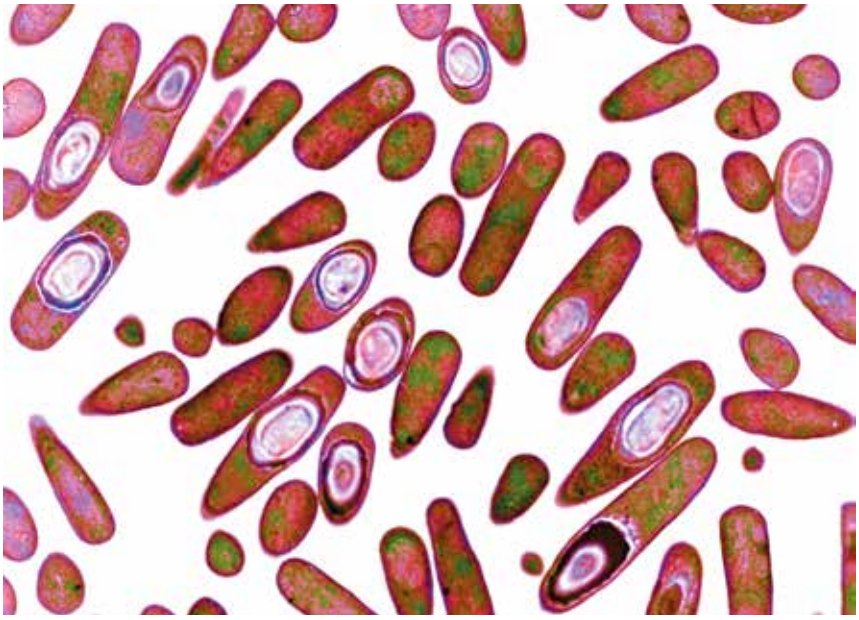
The microbiome promotes the development of both the immune and enteric nervous systems. Mice deficient in key microbial recognition receptors (i.e. toll-like receptors; TLRs) have reduced numbers of enteric neurons and

experience defective intestinal motility. Sterile, germ-free mice are severely immunocompromised with defective development of gut-associated lymphoid tissues and antibody production, in addition to neurological and central nervous system (CNS) deficits. Microbial colonisation in early life promotes the development of the innate immune system and immune tolerance and contributes to host defence against pathogen infection through competitive exclusion and the production of antimicrobial proteins.

In addition to its local effects on intestinal health, the intestinal microbiome has an impact on other organ systems, including the brain, via the bidirectional gut–brain axis, which involves neural pathways as well as immune and endocrine mechanisms. The intestinal microbiome can exploit this axis to influence signalling within the CNS and modulates host behaviour via modification of autonomic sensorimotor connections, influencing the enteric neuroendocrine system by immune activation. Different bacteria within the microbiome are a source of immunomodulators and regulators of endocrine hormone action and can catabolise diet-derived amino acids to synthesise various neurotransmitters including GABA, serotonin, histamine and L-DOPA. Therefore, the microbiome can have an impact on motor control, learning, memory and emotion (primarily stress and depression). If microbiome alterations result in a loss of homeostasis of these systems, then diseases affecting mental health could ensue.

How does the microbiome influence disease?

Intestinal microbial dysbiosis and reduced diversity of bacterial, and increasingly viral, populations is associated with disorders affecting the GI-tract, liver, vasculature, lungs, joints and the brain. However, the majority of human microbiome–disease studies carried out to date are observational and associative providing limited insight into functional causation: cause vs effect of intestinal dysbiosis and disease aetiology is poorly understood. Animal studies can be utilised to explore intestinal dysbiosis and disease pathogenesis. For example, transplanting human faeces from obese patients into germ-free mice resulted in them becoming obese. However, differences in GI anatomy and physiology and in the microbiota of mice versus humans, in addition to obvious differences in lifestyle and behaviour, make it difficult to translate findings from animal studies directly to humans. Relating functionality of bacterial genus/species to the abundance alteration in disease states is another way of exploring intestinal dysbiosis on disease progression. For example, *Faecalibacterium prausnitzii* is a resident intestinal bacterium that possesses anti-inflammatory properties and is less abundant in patients with inflammatory bowel disease (IBD).



Coloured transmission electron micrograph of *Clostridium difficile* drug-resistant bacteria.
Biomedical Imaging Unit, Southampton General Hospital/Science Photo Library

How do we treat microbial dysbiosis to restore health?

Targeting the intestinal microbiome as a therapeutic intervention strategy may be of benefit in diseases associated with intestinal microbial dysbiosis. Three approaches can be considered. First, administration of probiotic micro-organisms. Second, the consumption of prebiotics such as fructans, inulin, fructo-oligosaccharides, galacto-oligosaccharides and lactulose that support the growth of beneficial microbes. Third, wholesale microbiota replacement by faecal microbiota transplantation (FMT). FMT has proven to be a very effective treatment and

cure for recalcitrant *Clostridium difficile* infection (rCDI) and is becoming an established treatment option within the NHS for rCDI. Beyond its use in treating chronic GI infections, several FMT clinical trials are underway exploring its potential use in other disease including IBD, irritable bowel syndrome and myalgic encephalomyelitis.

In summary, humans have evolved with their microbiome, establishing a mutualistic relationship in which the microbiome, in return for being provided a 'home', plays a central role in maintaining life-long health. Further research is now needed to define the nature and molecular basis of microbe–host interactions in the GI-tract and elsewhere, using complimentary culture-dependent and -independent approaches and technologies. Appropriate *in vivo* pre-clinical studies with subsequent human studies and clinical trials can then lead to the development of evidence-based interventions that target the microbiome to promote, maintain or restore health.

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Katharine Seton

Katharine Seton

Gut Microbes and Health Research Programme, Quadram Institute Bioscience, Norwich Research Park, Norwich, Norfolk NR4 7UA, UK

Katharine Seton attained her bachelor's degree in Biomedical Sciences at Newcastle University in 2016. She then moved to Norfolk to undertake a PhD. Her research aims to determine whether there is an abnormal immune response to the microbiota in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients.

Simon Carding

Simon Carding

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Simon Carding is Professor of Mucosal Immunology at the University of East Anglia and leader of the Gut Biology Research Programme at the the Quadram Institute. His research focuses on understanding how gut microbes communicate with their host and the role that this cross-talk plays in establishing and maintaining health, and in diseases affecting the gut and other parts of the body, including the brain.

What do you see as your greatest achievement to date?

Katharine: Looking back, I believe my greatest achievement to date is having been driven and focused enough to complete an undergraduate degree, then undertaking a PhD, despite having myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). In high school, I completed my GCSEs while attending school part-time and pursuing a career in academia seemed unattainable. It feels like a huge achievement to have gotten this far in my research career.

Simon: Having the opportunity to work with and mentor some very talented scientists and seeing them go on to establish successful careers both within and outside of science.

What is the most rewarding part of your job?

Katharine: As part of my PhD 'Defining autoimmune aspects of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)', I am undertaking a human study which involves collecting samples from severe, housebound patients. Interaction with these patients is the most rewarding part of my job, as it enables me to appreciate first-hand the impact my research could have.

Simon: Working in an exciting and dynamic area of biomedical research that is never boring and is both challenging and rewarding.

Annual Conference 2019

8–11 April, ICC Belfast, UK

In April the Microbiology Society welcomed over 1,300 delegates to its flagship Annual Conference, which took place in Northern Ireland for the first time in the Society's history. The line-up of expert speakers from across the globe presented over four days on a wide range of topics. The event included:

- **29 scientific sessions**
- **Talks from 130+ invited speakers**
- **Over 290 offered talks**
- **Over 600 posters**
- **Five sessions dedicated to professional development:**
  - CV workshop
  - Managing a research laboratory
  - Peer review
  - Research and publishing ethics
  - Resilience in careers
- **Two Hot Topics:**
  - Creating a path – how single cells can solve mazes, see round corners, and find out where they ought to go by Professor Robert Insall, Cancer Research Institute, UK.
  - Paralytic disease caused by enteroviruses: the role of non-polio serotypes by Javier Martin, National Institute for Biological Standards and Control (NIBSC), UK.
- **Four Poster Prizes:** Microbiology Society Journals' 'Most Promising Science' Prize, Early Career Microbiologists' Forum Poster Prize, Peoples' Choice Poster Prize , and the Howard Dalton Young Microbiologist of the Year Prize.

If you presented work at our Annual Conference 2019, why not submit your article to one of our journals to continue to support the work of the Microbiology Society and the microbiological community? Visit the Microbiology Society journals platform to find out more (**microbiologyresearch.org**).

Watch some of the videos from year's Annual Conference on the Microbiology Society YouTube Channel (**microbiologysociety.org/YouTube**).

All photos: Ian Atherton

Keep up-to-date with events, follow the Society on Twitter: **@MicrobioSoc**

Annual Conference **2020** #Microbio20

30 March–3 April, EICC Edinburgh, UK

Preparation is now well underway for our Annual Conference 2020 at the Edinburgh International Conference Centre (EICC). The event will take place for an extended five days as part of our 75th anniversary celebrations.

On the first day of Annual Conference 2020, the Microbiology Society will be hosting a special day-long series of Fleming Lectures organised by an appointed committee of previous Fleming Prize winners, chaired by Nobel Prize winner Sir Paul Nurse. The day is designed to provide value to everyone in the microbiology community, including early career scientists. You will be able to attend this day for free when registering for Annual Conference 2020.

Abstracts will open in August 2019 for the Annual Conference sessions running from the Tuesday until the Friday, and the submissions deadline will be **Monday 9 December 2019**.

Destination Edinburgh

Edinburgh is a diverse and vibrant city, steeped in history. The backdrop of Arthur's Seat, the Pentland Hills and Edinburgh's waterfront make the city an exciting event destination. If you extend your stay after Conference, there are plenty of attractions to visit, such as Edinburgh Castle, the National Museum of Scotland, the Scottish Parliament and the Royal Yacht Britannia. Visit **edinburgh.org** for further information.

Accommodation

Edinburgh is a popular destination and we therefore highly recommend you secure your accommodation as soon as possible to ensure you have a place to stay. To support you with this, our booking agent Reservation Highway (**reservation-highway.co.uk/micro20**) has secured a range of accommodation options to suit all budgets throughout Edinburgh, at discounted rates.

Programme

As always, Annual Conference is designed to cover the breadth of microbiology research and its comprehensive scientific programme has over 30 sessions taking place in a range of formats:

Fleming talks

- Genetic control of mosquitoes
- Orchestrating gene regulation across the genome and across the cell
- Palaeomicrobiology: what ancient DNA can tell us about pathogens from the past
- Predatory *Bdellovibrio* bacteria – 58 years of understanding them as allies against AMR infections
- The expanding virosphere
- Visualising bacterial nanomachines *in situ* by electron cryotomography

Main Symposia

- AMR
- Back to the future
- Bacteroidetes
- Bioproduction and biomaterials
- Dynamic cell
- Epigenetics
- Exploring the eukaryotic tree of life
- Genes on the move
- Marine microbiology
- Novel eukaryotic drug targets
- Outer layers of microbiology
- Phage biology
- Public health microbiology
- Skin-full of viruses
- Toxins and antitoxins
- Veterinary microbiology
- Virus modulation of cell stress

Forums

- Environmental and applied microbiology forum
- Genetics and genomics forum
- Microbial infection forum
- Microbial physiology, metabolism and molecular forum

Virology Workshops

- Cell stress and viruses
- Clinical virology
- DNA viruses
- Negative-strand viruses
- Positive-strand and double-strand RNA viruses
- Retroviruses

Professional Development Sessions

- Bioinformatics
- Entrepreneurship
- Fellowship
- Teaching Microbiology in Higher Education Symposium
- Unconscious bias

Sign up to our newsletter and follow the Society on social media to receive regular updates about events and Society news, or visit **microbiologysociety.org/events** for information.

Focused Meetings June 2019

Keep up-to-date with events, follow the Society on Twitter: **@MicrobioSoc**

The first two Focused Meetings of this year's series will take place in June, but there is still time to book your place to attend. Both events will feature a programme of renowned speakers and showcase new and emerging research, while also offering valuable networking opportunities. Microbiology Society members can register at discounted rates and members also have access to Microbiology Society grant opportunities.

Anaerobe 2019: Changing perceptions of anaerobic bacteria; from pathogen to the normal microbiota and back

#Anaerobe19

13–14 June 2019 | Jurys Inn Hotel, Cardiff, UK

microbiologysociety.org/Anaerobe19

Anaerobe 2019 is being held in Cardiff, where the UK Anaerobe Reference Unit is based, in association with the Society for Anaerobic Microbiology and the Welsh Microbiology Association. The meeting will provide insights into the current and future impact of anaerobic bacteria in human health and disease, addressing the implications of recent microbiota studies, as well as the continued threat of emerging and re-emerging anaerobic infection.


Dennis Kunkel Microscopy/Science Photo Library

Anaerobic clinical microbiology remains a challenge due to specialist culture requirements, coupled with the increase in and spread of antimicrobial resistance. The normal human microbiota is primarily composed of anaerobic bacteria and has been recognised as a source of life-threatening anaerobic infection since the early days of microbiology in the late 1800s. More recent metataxonomic and metagenomic sequencing has extended interest in the potential role of the microbiota in a plethora of other aspects of human health, from obesity to mental health. In addition, the successful use of faecal microbiota transplants for the treatment of clostridial infection raises potential unchartered long-term consequences and possibilities.

Follow us on Twitter **@MicrobioSoc** using the hashtag **#Anaerobe19**.

British Yeast Group: Discovery to Impact

#BYG19

26–28 June 2019 | County Hotel, Newcastle, UK

microbiologysociety.org/BYG19

The British Yeast Group (BYG) Focused Meeting is the second event in the Society's 2019 programme and takes place in Newcastle.

Yeasts have been used extensively for over a century to explore fundamental aspects of living systems, and this meeting will focus on the theme of 'Discovery to Impact'. The programme will feature a range of keynote talks from invited speakers and will give early career yeast researchers the opportunity to present their recent research results through a series of posters and offered oral presentations covering the following topics: fundamental cellular processes, including metabolic cycles, chromatin biology, regulation of gene expression and control of quiescence; yeasts as disease models; pathogenic yeasts and biotechnological applications of yeasts.

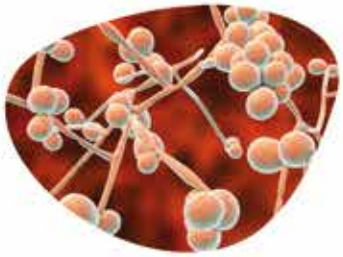

Kateryna Kon/Science Photo Library

Follow us on Twitter **@MicrobioSoc** using the hashtag **#BYG19**.

MICROBIOLOGY SOCIETY

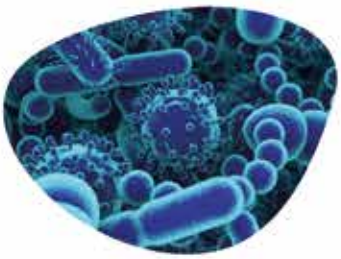
FOCUSED MEETINGS 2019

Anaerobe 2019: Changing perceptions of anaerobic bacteria; from pathogen to the normal microbiota and back
Thursday 13 to Friday 14 June 2019
Jurys Inn Cardiff, UK
microbiologysociety.org/Anaerobe19
#Anaerobe19



British Yeast Group: Discovery to Impact
Wednesday 26 to Friday 28 June 2019
County Hotel Newcastle, UK
microbiologysociety.org/BYG19
#BYG19

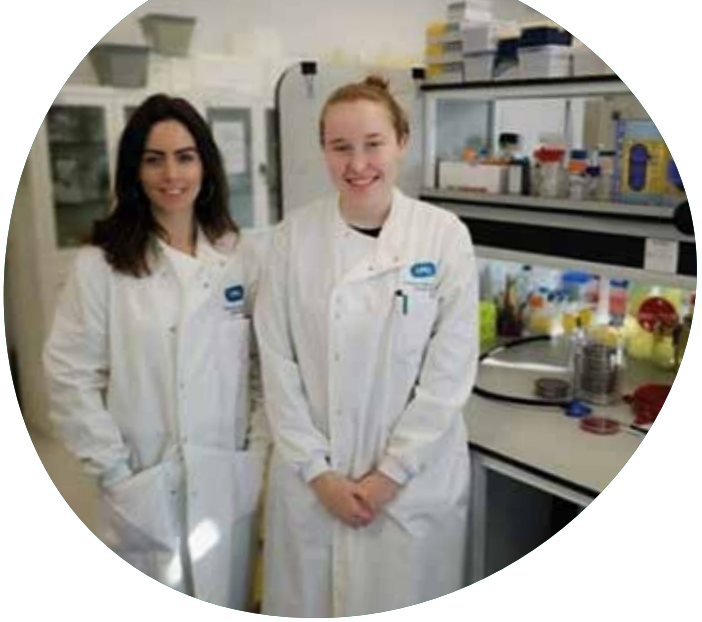
IMAV 2019: International Meeting on Arboviruses and their Vectors
Thursday 5 to Friday 6 September 2019
University of Glasgow, UK
microbiologysociety.org/IMAV19
#IMAV19



Microbes in Medicine: A Century of Microbiology at Trinity College Dublin
Thursday 24 to Friday 25 October 2019
Trinity College Dublin, Ireland
microbiologysociety.org/MicroMed19
#MicroMed19

Antimicrobial drug discovery from traditional and historical medicine
Tuesday 29 October 2019
Ashmolean Museum Oxford, UK
microbiologysociety.org/AMRmeds19
#AMRmeds19

Spotlight on Grants: Colonising the causes of gastric cancer



Helen with Dr Rossiter in the lab. Helen Jordan

Harry Smith Vacation Studentships facilitate short research projects for second year undergraduates during their summer vacation. By funding such opportunities, the Microbiology Society invests in the professional development of budding research scientists and provides opportunities for early career researchers to gain supervision experience.

Last summer, BSc Biomedical Sciences student Helen Jordan was awarded a studentship by the Society, where she worked under the supervision of Dr Amanda Rossiter at the Institute of Microbiology and Infection, University of Birmingham, UK. Helen investigated interactions between *Helicobacter pylori* and the human gastric microbiome, and how changes in frequency of such microbes can be correlated with the development of gastric cancer.

During her studentship, Helen mimicked the conditions of the gastric microbiome environment *in vitro,* so that she could observe the growth of *H. pylori*, before co-culturing with samples of *Actinomyces oris* and *Campylobacter jejuni*. From this co-culture, Helen identified that *A. oris* appeared to be responsible for growth inhibition of *H. pylori* in the gastric microbiome. The data gathered by Helen will contribute to a manuscript that is currently in preparation.

Helen said, "In terms of my academic career, it has cemented for me a drive and desire to pursue a PhD. The project gave me my first experience of research and all that comes with working in a lab. I feel very prepared for my third year dissertation and my PhD applications with this project under my belt."

> **Deciding to undertake a lab project was once of my best decisions at university so far.**

Since Helen left the lab, Dr Rossiter and her research group have been exploring in depth the mechanisms by which cancerous gastric microbes influence the growth of *H. pylori*, and how such behaviour modulates epithelial cell responses in an *ex vivo* organoid model.

Dr Rossiter described Helen as "a great addition to the lab over the summer months. She was able to master a range of culture techniques, independently plan experiments and interpret her results. Her work, and the work of others in my lab, will further our understanding of complex polymicrobial interactions and their role in gastric carcinogenesis."

Helen said: "The highlight of the project for me was seeing my name and data I had produced on a poster Amanda presented at a *H. pylori* conference in Helsingor, Denmark. The skills I have learnt this summer are proving invaluable. I would like to thank the Microbiology Society once again for their support."

Applications for the Harry Smith Vacation Studentship open in December each year. To find out more, visit our website (**microbiologysociety.org/harrysmithvacationstudentships**).

To find out more about the wide range of grants to support Microbiology Society members, visit the grants area of our website (**microbiologysociety.org/grants**).

Kirti Mistry
Grants and Professional Development Officer
k.mistry@microbiologysociety.org

Careers Focus: Putting together your CV

During the Annual Conference 2019, we hosted a CV workshop in collaboration with Miriam Windsor, Pirbright Institute, UK. During the session we covered the purpose of CVs (also known as *résumés*), cover letters which almost always accompany them and what to include to help you get the job. Some of the points that came up during the session are in this article.

For a non-academic CV, there is no perfect, one-size-fits-all CV – there are many ways to structure them and you will find that people will give you slightly different advice. As a scientist, you should work on conveying the transferrable skills you have gained while conducting your research.

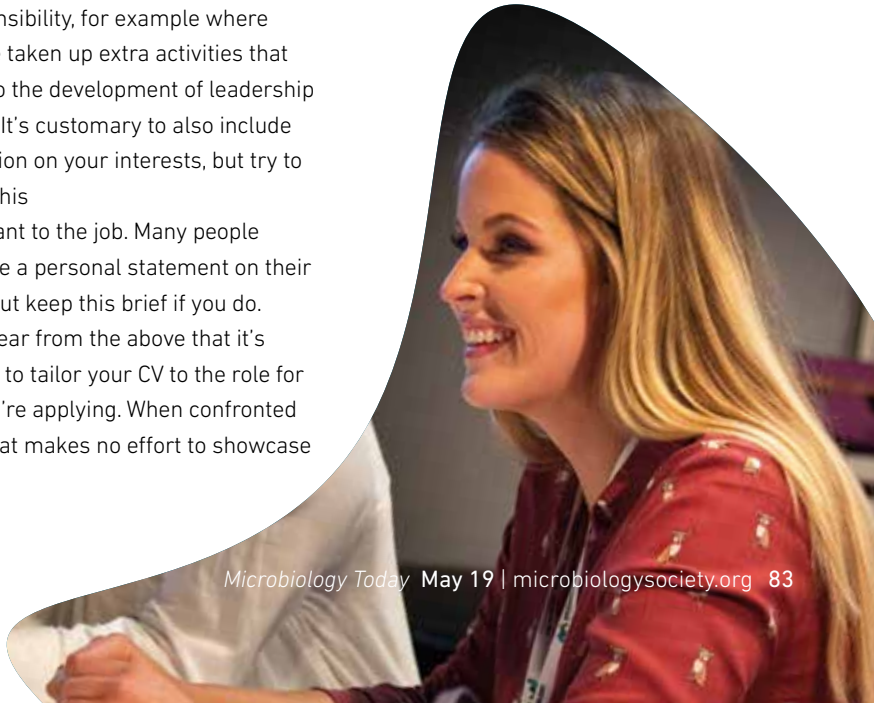
Some common components of a standard, chronological CV are:

- Personal details – to tell readers who you are and how to contact you. You should title your CV with your name (not 'Curriculum Vitae'!) and you could include your LinkedIn URL here too, as long as it's kept up to date. It's not customary to include a photo or information about gender, age or nationality on CVs in the UK.
- Education – with the most recent listed first. Don't include every single school qualification you've had and remember to only include brief details of research degrees, as long as it's appropriate to the potential employer.
- Employment – again, most recent first. You may wish to itemise relevant achievements, skills and responsibilities for each role you've had.
- Competencies – what are you good at? What can you bring to the role? This includes transferrable skills such as project management, analysing data and written and oral communication skills.
- Training and professional development – have you had any training that is relevant to the role you're applying for?
- References – don't forget to check before including up to two people as referees.
- Other things to make sure you include are details to set you apart. This can include positions of responsibility, for example where you've taken up extra activities that lead to the development of leadership skills. It's customary to also include a section on your interests, but try to keep this relevant to the job. Many people include a personal statement on their CV – but keep this brief if you do.

It is clear from the above that it's important to tailor your CV to the role for which you're applying. When confronted by a CV that makes no effort to showcase how the applicant is right for the job, it's unlikely a recruiter will spend time on it. Make sure to use the cover letter too; although some online application portals make these optional, we suggest you always use this opportunity to shine and tell them just how you fit the person specification.

Like any piece you've written, your CV should have a clear objective. In this case, to communicate to an employer just how great you'll be at the job. Make sure you think about your language and audience. CVs and covering letters take a lot of careful time and attention, and lots of reviewing is required too to make sure you are making your point accurately. Don't forget to keep it up to date so that you don't have to start from the beginning again next time!

We have focused on chronological CVs here. For more information on specific items to include in academic CVs, please see the Vitae website (**vitae.ac.uk**).



Open research: it's more than open access

In the last issue of *Microbiology Today* we wrote about open access (OA), copyright, and author rights. In this article we discuss the wider world of open research, also known as open science and open scholarship.

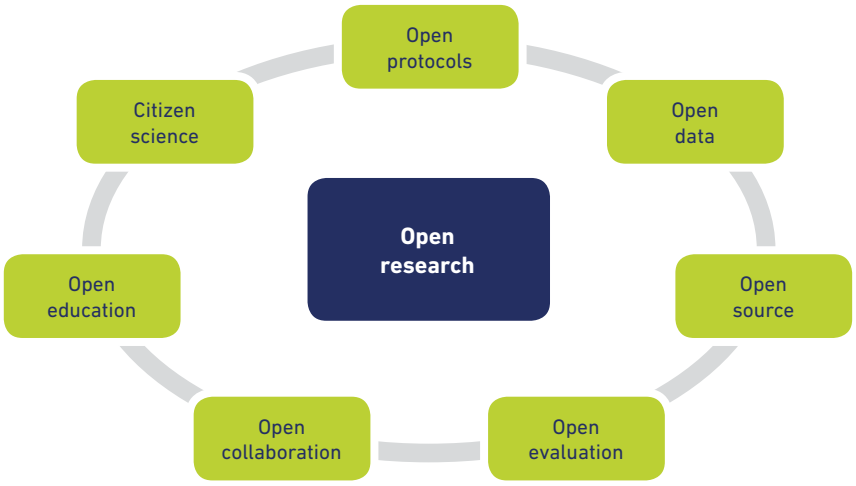
Open research has developed over the last twenty years in response to a combination of factors, including the open access movement, funders' need to map the returns on their research investments, concerns about research reproducibility and research waste, and a desire to properly recognise researchers for all their efforts rather than simply their published output. It covers many aspects of research, from laboratory notebooks and data, to collaboration through scholarly social networks, to citizen science.

Much like open access, open research carries with it benefits for the whole scholarly community. Open methods and open data, in particular, can reduce research waste and aid reproducibility by clearly identifying the precise protocols used in a given lab, and the results associated with that protocol. For individual researchers the increased visibility and engagement associated with open methods, data and code can lead to new collaborations and drive the creation of new research questions. Many organisations and funders are now giving researchers credit for their open research objects, as well as journal articles.

FAIR principles for open research

One of the biggest challenges in open research is good data management, which facilitates discovery and knowledge exchange for both humans and machines. Standing for 'Findable', 'Accessible', 'Interoperable' and 'Reusable', the FAIR principles were launched in 2016 in response to this challenge. Many people assume FAIR applies only to data, but the same principles guide many other aspects of open research, such as open protocols and methodologies, and open source code.

Rich metadata describing research outputs is key in making them 'findable': including items such as keywords, author names, funding data and an abstract will make sure that search engines and other machines will be able to find the research object. 'Accessibility' relies on standard protocols for retrieving research objects – from a researcher's perspective the key to accessibility is to use a compliant repository or platform, such as those described below. For research outputs to be 'interoperable' they need to use community agreed standards and contain links to related information using persistent identifiers like digital object identifiers (DOIs), which allow machines to navigate easily between research objects. Lastly, clear usage licences (such as the Creative Commons licence described in the February issue of *Microbiology Today*: **microb.io/2GTfMtB**) help researchers and machines understand the ways in which they can 'reuse' the research objects.



Components of open research.

Making your research open

The Society's journals work with several FAIR-compliant open research

initiatives* and we encourage you to make use of them. They all offer free services, and every research object in these initiatives has a DOI, so they are easily citable and are usually counted in research evaluation exercises.

First up is protocols.io, a browser-based tool for open methods which meets the FAIR principles. We all know that optimising protocols is time-consuming and that the information is often locked in lab notebooks. One of the things we love about protocols.io is that researchers can follow experiments step-by-step in real time and record their changes, keeping an accurate record of their method and making it easy to write up for publication.

We also work with data repositories such as figshare (**figshare.com**), Dryad (**datadryad.org**), and Zenodo (**zenodo.org**), as well as Microreact for genomic epidemiology (**microreact.org**). These services allow researchers to upload large data sets; being FAIR, these are vastly superior to the older 'supplementary data files' associated with journal articles.

We recommend CodeOcean (**codeocean.com**) for sharing code. Unlike most other services, CodeOcean gives researchers the ability to execute published code without installing anything on their computers – you can even change parameters, modify the code and upload data to see how results change, without needing specialist software.

**We do not receive revenue from these initiatives and are promoting them only because our team truly believes they are useful tools for our members.*

The Global Sustainability Development Report on the Sustainable Development Goals

To celebrate our 75th anniversary in 2020, we are embarking on a project that will demonstrate the value and raise the profile of microbiology in addressing the UN Sustainable Development Goals. In this issue of *Microbiology Today*, we present a major scientific initiative taking place at the international level: The Global Sustainability Development Report.

United Nations

The Global Sustainability Development Report

The United Nations Sustainable Development Goals (UN SDGs) are a call for action by all countries – low-, middle- and high-income – to promote prosperity while protecting the planet. As we write this article, the world has less than 12 years remaining to achieve the ambitions of the 2030 Agenda for Sustainable Development. According to the latest report from the Intergovernmental Panel on Climate Change, we also have less than 12 years left to limit the global average temperature rise to 1.5 °C. In the next few months, the attention of the international scientific community will be focused on the Global Sustainability Development Report (GSDR), a document that aims to provide guidance from a scientific perspective to support policy-makers in striving towards achieving the SDGs.

The Independent Group of Scientists

The next GSDR will be published this year and will be the first of a quadrennial series that will inform the high-level global reviews of the 2030 Agenda at

The Microbiology Society's 'A Sustainable Future' project will promote knowledge exchange by bringing together microbiologists, scientists, industry, NGOs and policy-makers, to champion the importance of microbiology in sustainable development. Microbiological expertise will be used to explore solutions and influence national and international implementation plans. This will drive us towards the Society's vision of a world in which the science of microbiology provides maximum benefit to society. Read our article published in the February issue on the SDGs project for more information (**microb.io/2TmNlee**).

We spoke with Professor Otto Cars, founder of ReAct – Action on Antibiotic Resistance, about the UN's role in devising sustainable and global solutions to tackle AMR. Professor Cars highlighted that the world has failed to keep pace with the issue of AMR, despite many proposals in recent decades. He further explained that, if AMR cannot be eliminated, it can still be managed through concerted efforts to slow down its pace. ReAct recently urged the international community to take up the work on AMR, highlighting that low-income countries experience the combination of the greatest burden of infectious diseases and the weakest healthcare and agriculture systems. It is hoped that the GSDR will acknowledge the need to increase financial and technical support from global funds to support countries in the early phases of implementing National Action Plans on AMR.

the UN. The report is expected to make recommendations 'on the state of global sustainable development from a scientific perspective' and provide the lessons learned during the first four years of implementation of the SDGs, 'while focusing on the challenges, addressing new and emerging issues and highlighting emerging trends and actions that may have an overall effect on sustainable development'. Before leaving office, former Secretary-General Ban Ki-moon appointed 15 experts, representing a variety of backgrounds, scientific disciplines and institutions, to draft the GSDR. Endah Murniningtyas (Indonesia) and Peter Messerli (Switzerland) serve as co-chairs of the Independent Group of Scientists (IGS) supported by a task team co-chaired by six UN entities. The disciplines of biology and microbiology are represented by Katherine Richardson (Denmark), Ernest Foli (Ghana) and Peter Messerli (Switzerland). Scientists from around the world have recognised the IGS's high interdisciplinarity, but have also noted that the group will have to work within the limited resources allocated to the GSDR process.

The GSDR and microbiology

The microbiology community is in a unique position to help tackle many of the SDG targets. Microbiologists have been working for decades on problems like antimicrobial resistance (AMR), a phenomenon that remains a threat to global development at large. Background work on the GSDR highlights that more research and development investments are needed in the field of antimicrobial research and that SDGs should be used as a platform through which AMR's threat to the world's sustainable development can be addressed collaboratively.

Please visit **microbiologysociety.org/SDGs** for further details on the 'A Sustainable Future' project, including opportunities to contribute.

Championing Microbiology and the Microbiology Society

Champions are members who volunteer in their local place of work or study. They get involved in a wide variety of activities and initiatives to help raise awareness of microbiology and the Microbiology Society. Through their actions – and the actions of many others of you who aren't specifically designated 'Champions' but who do similar things – the Society's impact, influence and membership continues to increase.

Ed Cunningham-Oakes, a Society Champion, has said:

> *One of the greatest things about being a Society Champion is being at the frontline of networking and funding for researchers in the field, and being given the opportunity to disseminate useful information at a plethora of networking events. You can travel, meet other researchers, and become a hub of societal information and opportunities. I would highly recommend becoming a Champion to anyone looking to develop holistically, both as a researcher in the field, and an individual.*

Have you ever considered becoming a Society Champion?

Do you not have a Champion based at your institution or in your local area? Being a Champion is a great way to develop new skills, give something back, or you can use your involvement to help advance your own career. As well as access to a budget to support Champion-led initiatives, you'll also benefit from great support and encouragement from the Society in your role. Find out more about the Society Champions scheme and how you can get involved on our website (**microbiologysociety.org/champions**).

If you don't want to be a Champion in the formal sense, you could be one simply by helping spread the word about the Society to a friend or colleague. Word of mouth helps bring the Society to the attention of friends, work colleagues and students who may not yet be members, but could be, and helps to strengthen the microbiology community and networks.

Whatever your involvement – as a formal Champion or an informal one, you make a very significant difference and help bring microbiologists together.

If you have any questions or need any support please contact us at **members@microbiologysociety.org** or call **+44 (0)20 7685 2680**.

Paul Easton
Head of Membership Services,
p.easton@microbiologysociety.org

Society Champions

Find out who the Society Champions are in your institution or local area:

Northern Ireland

Chris Proctor Ulster University
Daniel Storey Queens University Belfast
Georgiana Parau Queens University Belfast
Linda Oyama Queen's University Belfast
Lindsay Broadbent Queen's University Belfast
Sara Pidcock Queens University Belfast
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Republic of Ireland

Gerard Sheehan Maynooth University
Nathaniel Cole Maynooth University
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Ed Cunningham-Oakes Cardiff University
Eleanor Furness University of Aberystwyth
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Jinxin Zhao Monash University, Australia
Manoj Pradhan Nepalese Army Institute of Health Sciences, Nepal
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Nilay Joshi Unique Pharmaceutical Laboratories, India
Sagar Aryal St Xavier's College, Nepal and Kathmandu Center for Genomics and Research Laboratory (KCGRL), Nepal

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Nicola Crewe University of Lincoln

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Sreyashi Basu University College London

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Carl Aston University of Nottingham
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Ethan Iles Chesterfield Royal Hospital
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Rebecca Philp Science Oxford
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Kate Baker University of Liverpool
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Chinyere Okoro University of Surrey
Laura Petch University of Kent
Louisa Wallace University of Surrey
Matthew Herdman University of Oxford
Michael Macey The Open University
Robert Will University of Cambridge

South West
Nigel Brown *retired*, previously University of Edinburgh
Ruth Maclaren Sciencedipity
Tina Joshi University of Plymouth

Yorkshire
Alex Remmington University of Sheffield
Lee Sherry University of Leeds
Omololu Fagunwa University of Huddersfield

MICROBIOLOGY SOCIETY

75 YEARS

ANNUAL CONFERENCE 2020

Monday 30 March to Friday 3 April 2020
EICC Edinburgh,UK
Abstracts go live: 19 August 2019
microbiologysociety.org/annualconference
#Microbio20

MARKETING EDINBURGH

Early Career Microbiologists' Forum Update:

Communications, conferences and careers

April marked the third Annual Conference since the formation of the Early Career Microbiologists' (ECM) Forum. Year on year, the contributions made by early career researchers to the event become more evident. We saw ECMs continuing to play an active role in all aspects of the week, from running the pre-conference networking event to co-chairing many of the sessions. There was also a noticeable increase in the number of offered oral slots across the event, highlighting the effort made by the Microbiology Society to provide a platform for early career researchers to present their work.

I wanted to use this update to promote two fantastic opportunities that the Society offers early career microbiologists. The first is particularly timely. Elections for positions on the ECM Forum Executive Committee open on 3 June, so do keep an eye on the Society's website and social media platforms if you are interested in having your say in how the views of ECMs are represented.

One position that is becoming available is my role as Communications Representative. It is an excellent opportunity for anyone interested in science communication, developing their writing skills or learning more about how the Society communicates with its members and the public. In this role, I sit on the Communications Committee and help to highlight the viewpoint of early career researchers. The position also involves becoming a member of the *Microbiology Today* Editorial Board, allowing you to put forward your suggestions for the quarterly themes and authors. It is a great insight into how the Society runs its communications platforms.

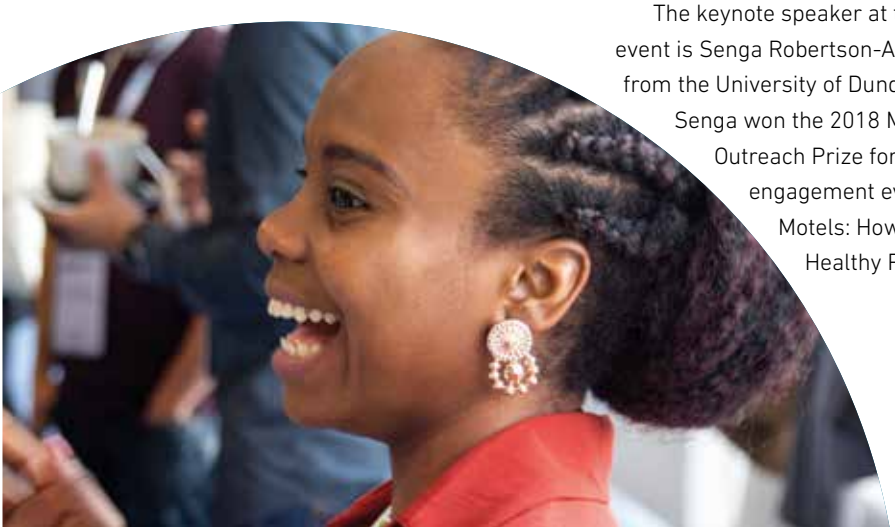
The second opportunity that I wanted to highlight is the return of the ECM Forum Summer Conference, scheduled for 20–21 June at Trinity College Dublin, Ireland. This is back for its second instalment after the inaugural event in 2018 and promises to be even better this year. The Conferences and Division Representatives have worked hard to implement the feedback given by the delegates and I think it now embodies the aims of the ECM Forum more than ever.

The keynote speaker at this year's event is Senga Robertson-Albertyn from the University of Dundee, UK. Senga won the 2018 Microbiology Outreach Prize for her public engagement event 'Microbe Motels: How to Make a Healthy Poo'. It was a real treat to see her demonstrate the activity at the Society Showcase last September – it is an inspired creation. Senga's communication skills and the story behind how she got involved in outreach will make for an excellent talk at the Summer Conference.

The Summer Conference will host invited speakers who will present across a range of microbiology topics. There will also be a careers session that the ECM Forum Conferences Representative Alison MacFadyen believes will be highly beneficial to the attendees, due to the array of different backgrounds included. The panel will include representatives from the Industrial Biotechnology Innovation Centre (IBiolC), Pint of Science and West Cork Distillers. If you are considering a career outside of academia or just want to learn more about the jobs available to early career microbiologists, then this is not to be missed.

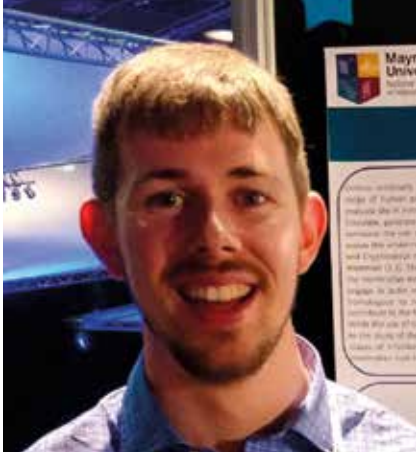
As always, please feel free to get in touch with us with any comments or suggestions. I am particularly happy to answer any questions about running for my role on the committee; I really could not recommend it enough.

Rebecca Hall
ECM Forum Communications Representative



Membership Q&A

This is a regular column to introduce our members. In this issue, we're pleased to introduce Gerard Sheehan.



G. Sheehan

Where are you currently based?

I am currently based in the Medical Mycology laboratory in the Department of Biology at Maynooth University in Ireland.

What is your area of specialism?

Host–fungal pathogen interactions and fungal virulence.

And more specifically?

I am interested in the interplay between fungal pathogens such as *Aspergillus fumigatus* and *Candida albicans* and how they (1) infect their host and (2) respond to the host immune response. I mostly focus on the humoral response and I utilise insect larvae such as *Galleria mellonella* to model infection processes *in vivo*.

Tell us about your education to date

I studied for my BSc in Biomedical Science at Maynooth University and this provided me with an excellent background in microbiology and immunology. I am now in the final year of my PhD and I have loved the whole experience, from designing, performing and analysing experiments, to presenting my work at national and international conferences. I have previously worked on projects ranging from studying the factors affecting biofilm formation in beer lines, to blocking antibiotic resistance in multi-drug resistant (MDR) bacteria.

Where did your interest in microbiology come from?

During my undergraduate degree, our course co-ordinator at the time (now PhD supervisor; Professor Kevin Kavanagh) lectured our class in microbiology. I approached him mid-way through my second year asking about the possibility of getting some lab experience during the summer months. He offered me the opportunity to work in his laboratory and I worked with postgrads on a variety of microbiology projects. I greatly valued this experience and it increased my desire to puruse a career in microbiology. Following on from this I applied for and received a Harry Smith Vacation Studentship from the Microbiology Society to work on an independent project to characterise diseases of honey bees in Ireland. With my time in the laboratory came confidence in my ability and also a love for all things microbiological!

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

Working in academia certainly has its advantages, but it's the drawbacks which are the problem. Job security, difficulty of securing funding, lack of tenured positions, the academia/industry divide. Maybe these will improve in years to come...but the glass is half full and I love working in a laboratory; on a project which needs answers; the idea of being your own 'boss' and teaching in tertiary-level education. Making a difference not only in your field of expertise, but also to society, is really appealing to me

What is the best part about 'doing science'?

I think it's the variety. Nothing is ever the same and everything is fresh. I love working on a project and getting really involved. However, it's a great feeling to finish it and move on to another exciting project.

Who is your role model?

I have been inspired by my lecturers at university and by their dedication to teaching and research. In particular, I have been highly impressed by their ability to inspire undergraduate students and to foster their careers.

What do you do to relax?

Outdoorsy stuff: I like hiking and also play basketball at a high level in Ireland. These things don't sound very relaxing but they are good to clear your head and get away from the lab. To really chill out, I like a good TV series and a cuppa tea.

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

I would either bring a Coldplay greatest hits album, or preferably I would be cheeky and bring my Spotify account. For my luxury item I would have to bring a jar of Nutella!

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

I am lucky that we have a very close-knit community of postgrads in Maynooth and I am extremely close with everyone in the lab, so they know me too well. One thing they won't know about me is I was, at one stage in my early life, an award-winning artist.

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

This is a tough question, as all my college choices involved biology (e.g. biology and PE teaching) but if I had to stray from science it would probably be something practical like an electrician.

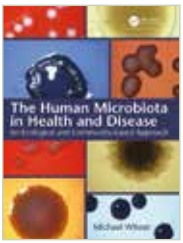
If you would like to be featured in this section or know someone who may, contact Paul Easton, Head of Membership Services, at **p.easton@microbiologysociety.org**.

Exhibition and Sponsorship Opportunities

For further information please contact
exhibitions@microbiologysociety.org
or visit **microb.io/EMay19**

MICROBIOLOGY SOCIETY

Reviews



The Human Microbiota in Health and Disease: An Ecological and Community-Based Approach

Written by Michael Wilson

£148.74 ISBN 978-081534585-5

The Human Microbiota in Health and Disease is the first edition of an extraordinary updated academic resource, which provides an exhaustive description on the nature and diversity of the microbial communities inhabiting the human body.

The first two out of 11 chapters introduce the reader to the molecular features of the host–pathogen interactions and the various methods used to investigate the composition of the human microbiota. Here and throughout the text, the book stresses similarities and, most importantly, differences of microbial data obtained through cultivation-dependent and -independent approaches. The following chapters focus deeply on the indigenous microbiota inhabiting the numerous districts of the human body. In detail, each chapter describes: (i) the anatomy and physiology of the body site; (ii) the environmental determinants dictating the composition of the indigenous microbiota; (iii) the metabolic activities and relationships between host cells and microbes which influence and determine the human health; (iv) the involvement of the microbiota in human diseases; (v) the intervention and manipulation of the microbiota that can result in health effects. The book terminates reporting the most recent studies and hypotheses on possible involvements of microbiota in other human diseases and highlighting questions that still need to be answered.

Each chapter is magnificently illustrated, contains several graphic charts and detailed tables, and terminates with a key concept list, review questions and an updated bibliography divided by topics.

Overall, the book is a valuable resource for students, researchers and anyone interested in the human microbiota and its impact in health and disease.

Dr Fabio Giovannercole

Sapienza University of Rome

For more reviews, please visit the online issue of *Microbiology Today* at **microbiologysociety.org/microbiologytoday**.

Comment

Fungal interactions in health and disease

Courtney Kousser, Farhana Alam and Rebecca Hall

Fungi are important eukaryotic organisms, comprised of more than just mushrooms and moulds, and span beyond environmental saprophytes. Although not all are harmful, from the 100,000 fungal species identified to date, 300 are known to impact human health. These effects can be positive or negative, and this is largely mediated by their interactions with host cells and other resident microbes.

Microbiota: microbiome + mycobiome

The microbiome is a complex community of micro-organisms living on and within humans. The mycobiome represents the fungi present within the microbiota that play important roles in human health. Each anatomical site has a unique microbial fingerprint that can vary with health. For example, the intestinal mycobiome differs between obese and non-obese individuals, as does the oral mycobiome of HIV-positive patients and healthy individuals.

Candida spp. are the most prevalent fungi identified in the mycobiome and, through competition, can act as a protective barrier against invading pathogens. For instance, adapted *Candida albicans* can protect mice against *Aspergillus fumigatus, Pseudomonas aeruginosa,* and *Staphylococcus aureus*. On the other hand, fungi can also have negative effects. For example, colonisation by *Candida* and *Saccharomycetes* is associated with hepatitis B, and the presence of *Candida* can exacerbate disease severity and delay healing of lesions in ulcerative colitis and Crohn's disease patients. Furthermore, *Candida* colonisation is correlated with more severe instances of acute graft-versus-host disease following stem cell transplantation.

A polymicrobial world

Polymicrobial interactions dominate the world around us. Just as humans are social beings, microbes constantly form relationships with other organisms. These can be competitive, where microbes fight for resources and space; or co-operative, where they work together to survive inside the host. These interactions take place in the microbial flora of healthy individuals, and in the context of disease. Many infectious diseases are increasingly recognised as polymicrobial, presenting with aggressive pathologies and increased antimicrobial resistance, leading to poorer patient prognosis.

Most polymicrobial interactions occur within mixed biofilms, i.e. communities of cells ensnared within an extracellular matrix of secreted polymers. For example, the oral cavity hosts a cornucopia of fungal-bacterial interactions, thanks to its moist, nutrient-rich environment. The composition of oral biofilms is relatively similar among healthy individuals, due to the presence of a core microbiome; however, the microbial make-up can vary greatly from one individual to another in cases of disease. It is estimated that around 80% of all microbial infections are in the form of biofilms. Common infection

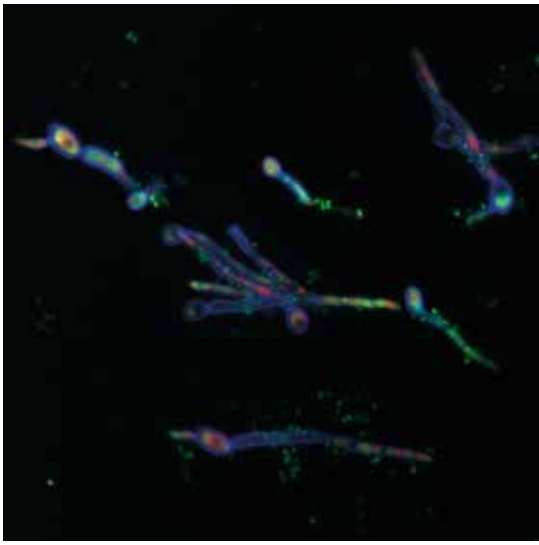


Fig. 1. Microscopic image of *Pseudomonas aeruginosa* attaching to *Candida albicans* hyphae. Dead fungi/bacteria are stained red, fungal chitin is stained purple, and nucleic acids are stained green. Emily Dixon

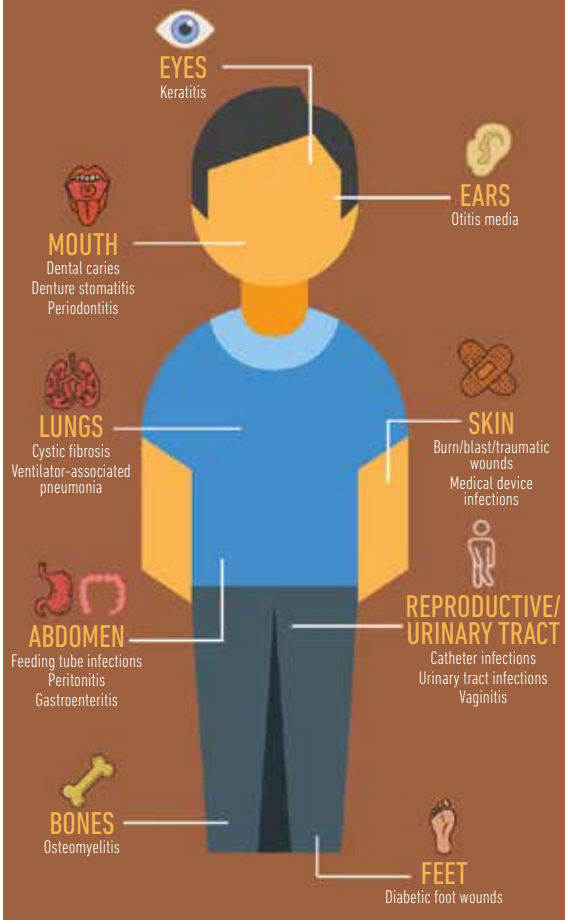


Fig. 2. **Sites of polymicrobial infections and interactions involving fungi.** Courtney Kousser

sites include implanted medical devices, burns, surgical wounds and mucosal surfaces, such as the lung epithelium in cystic fibrosis patients. The prolonged physical proximity of cells within biofilms encourages both intra- and inter-species communication.

The interactions between fungi and bacteria can be physical, chemical or metabolic. Fungal hyphae can provide a scaffold-like structure encouraging formation of fungal–bacterial biofilms or provide a means of transport to enable bacterial dissemination into host tissues. Both types of organism undergo quorum sensing (QS), which is the cell-density-dependent release of signalling molecules that regulate gene expression. The most well-studied cross-kingdom QS interactions are those between *C. albicans* and *P. aeruginosa*, some of which can directly affect virulence.

Antimicrobial resistance

Fungi feature prominently in the fight against antimicrobial resistance. There are currently three main classes of antifungals: azoles, polyenes and echinocandins. The most recent antifungals, anidulafungin and posaconazole, were developed in 2006. The classification, in 2018, of *Candida auris* as the first multi-drug-resistant fungal 'global outbreak pathogen' highlights the urgent need for novel antifungal therapies. As most infections are polymicrobial in nature, this has further implications for antimicrobial drug efficacy. For example, *Streptococcus mutans* has been shown to protect *C. albicans* biofilm cells from the effects of the antifungal fluconazole, via secretion of polymers that sequester the drug. Conversely, *C. albicans* can enhance the tolerance of *Escherichia coli* and *S. aureus* biofilm cells to the antibiotics ofloxacin and vancomycin, respectively. These co-operative interactions suggest that antibiotic–antifungal combination treatments would be clinically more efficacious in many cases.

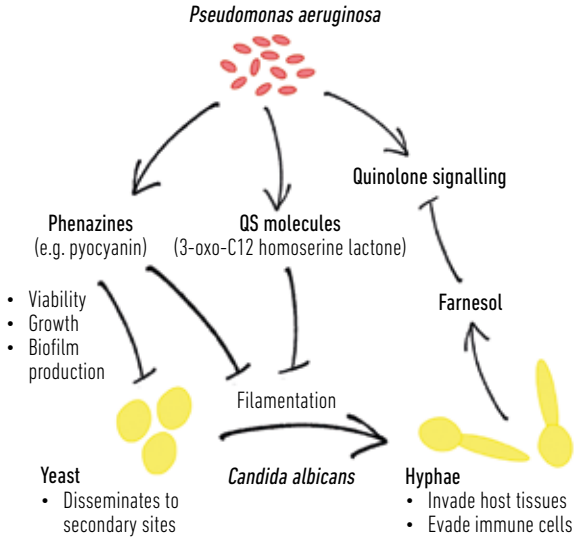


Fig. 3. **Schematic showing the complex ways in which fungi and bacteria can interact, using *Candida albicans* and *Pseudomonas aeruginosa* as an example.** Courtney Kousser and Emily Dixon

Training the immune system

Not all polymicrobial interactions involve direct microbe–microbe communication. Relationships between micro-organisms can also be facilitated by host cells. Fungal interactions with the immune system can influence how the host responds to future microbial invasions. For instance, previous sublethal infections with *C. albicans* can prime the immune system; an interaction mediated by the fungal cell wall component, β-glucan, and the phagocyte surface receptor, Dectin-1. This 'training' leads to enhanced leukocyte recruitment, cytokine production and infection clearance when exposed to secondary pathogens, such as *P. aeruginosa*, or repeated inoculation with *C. albicans*.

Future perspectives

Much is yet to be discovered about the myriad effects of fungi on human health and disease. For example, there is evidence that the fungal QS molecule farnesol can affect human fertility, by modulating sperm motility. The impact of other microbial communication molecules on human

health and disease are yet to be investigated, and who knows what implications these will hold for human health.

Further reading

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Courtney Kousser is a fourth year PhD student in Dr Rebecca A Hall's lab. Courtney's research focuses on the interaction between the deadly fungus, *Rhizopus microsporus,* and the opportunistic bacterium *Pseudomonas aeruginosa* within the host. She has been a member of the Microbiology Society since 2016 and won the 2018 Sir Howard Dalton Young Microbiologist of the Year Prize.

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Rebecca Hall is a current MRC-funded Career Development Award Fellow and Lecturer in Microbial Adaptation at the University of Birmingham. Rebecca is interested in how microbes adapt to the environment of the host and the consequences this adaptation has on disease progression. She has been a member of the Microbiology Society since 2014, and is a member of the Eukaryotic Division.

Why does microbiology matter?

Farhana: Microbes include a hugely versatile range of organisms. They are integral to the functioning of most ecosystems, yet we are still in our infancy in understanding their impact.

Courtney: Micro-organisms coat every surface around us, on us, and in our bodies. By understanding how microbes function and how they can impact us, we can better learn how to work with them or fight them.

Rebecca: Studying all aspects of microbiology is important to enhance our understanding and to make new discoveries. Microbiology has been at the heart of identifying the basic principles of life for decades. Even small pieces of the puzzle provide clarity to the larger picture, and open new avenues of exploration. At heart, everyone is a microbiologist, they might just not know it.

What advice would you give to someone starting out in this field?

Farhana: Read widely and don't limit yourself to your specific research area. There is much to be gained from inter-disciplinary learning; like any other form of life, microbiology does not occur in isolation!

Courtney: Attend conferences, speak to the intimidating Principal Investigator, and step outside of your comfort zone. You'll gain confidence and become an active, well-rounded member of the community.

Rebecca: One of the best ways to get to know people, and the field, is to go to a conference, to hear lots of excellent science, ask questions and share ideas. Also, the fungal community may be small, but we are mighty, collaborative and enjoy a good dance!

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