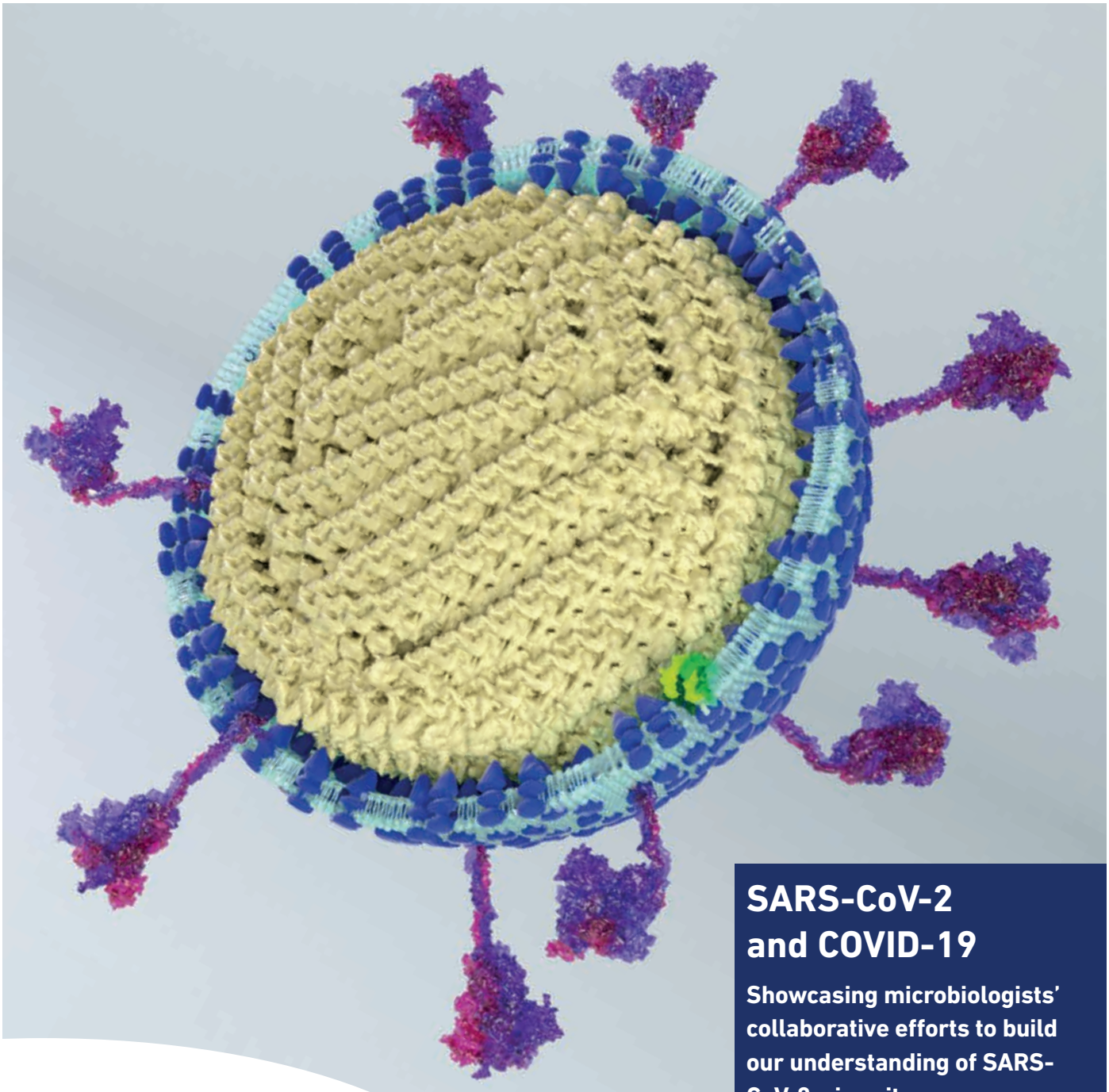
MICROBIOLOGY TODAY

48:2 October 2021



SARS-CoV-2 and COVID-19

Showcasing microbiologists' collaborative efforts to build our understanding of SARS-CoV-2, since its emergence, to improve COVID-19 management and prevention.

MICROBIOLOGY SOCIETY

Editorial

Welcome to the October 2021 issue of *Microbiology Today*! As I write this Editorial in late August, many of us are preparing ourselves for working through a period of yet more uncertainty and volatility as we continue to learn how to deal with the ongoing presence (and consequences) of SARS-CoV-2 in our day-to-day lives. Indeed, as we approach the end of our second year of the COVID-19 pandemic, we have decided to make SARS-CoV-2 and COVID-19 the sole focus of this issue.

I feel that I am understating the matter when I say that SARS-CoV-2 and COVID-19 have had a profound impact on our professional and personal lives. Yet despite this, we have all made incredible efforts to adapt to pandemic life and as professional microbiologists we have shown a captive audience once again why microbiology matters. Many of us have contributed to understanding the virus at a molecular and clinical level, developed diagnostics, treatments and vaccines, and communicated all these aspects and many more to the general populace so they can understand what is happening in the world around them. It is this work that forms the focus of our October issue.

Keith Grehan sets the scene for our issue by providing an overview of the molecular virology of SARS-CoV-2. Keith distils a wealth of information to describe the key features of the SARS-CoV-2 genome. An ongoing concern is the emergence of SARS-CoV-2 variants with altered characteristics. Keith concludes by discussing the consequences of key amino acid substitutions found in several variants of concern.

In the present day we seem to be inundated with requests to have a 'COVID test', and in the UK any suspicion of COVID-19 results in the rapid deployment and turnaround of PCR-based testing. This infrastructure was almost non-existent in early 2020, and in our next article Alan McNally provides us with a fascinating personal insight into these early days of setting up large-scale SARS-CoV-2 testing in the UK. As Alan notes in his article, the advantage of incorporating genomics into infectious disease diagnostics has been highlighted in this epidemic, particularly in using the data generated to monitor the emergence and spread of new variants. Colman O'Cathail expands on this area in his own perspective, by describing the ongoing work of bioinformaticians to rapidly archive and make publicly available the vast quantities of SARS-CoV-2 sequencing data generated around the world.

As an increasing number of COVID-19 cases appeared around the world, we heard of infected individuals suffering from a loss of taste. As these anecdotes gathered an evidence base and became incorporated into criteria for a presumptive diagnosis of COVID-19, work began to understand the mechanistic basis behind the emergence of these symptoms. David Edwards and Alexander Gardner take us through this body of work in our next article, discussing amongst other things the potential for SARS-CoV-2 to replicate within cells of the oral cavity.

Whilst efforts were underway early in the pandemic to develop vaccines effective in *preventing* infection, there was a parallel need to find therapeutics capable of *treating* infection. In our fifth article, Jane Hilton and Catherine Adamson review the challenges faced both in identifying existing agents for repurposing into COVID-19 treatments and in identifying new targets to exploit in the development of new agents.

As we approach the second anniversary of the emergence of COVID-19, our final two articles look at what the future may hold for SARS-CoV-2, and the lessons we can apply to future pandemics. Grace Roberts looks at the challenges of communicating SARS-CoV-2 research to the public, with a focus on perceptions surrounding the introduction of face coverings and the rollout of vaccines. Tim Inglis, who has contributed coronavirus blogs to the Society for most of the pandemic (**microb.io/coronastream**), draws the October issue to a close with his commentary on the future of COVID-19 and the impact of policy and health infrastructure in individual countries on the persistence of this pandemic.

Chris Randall

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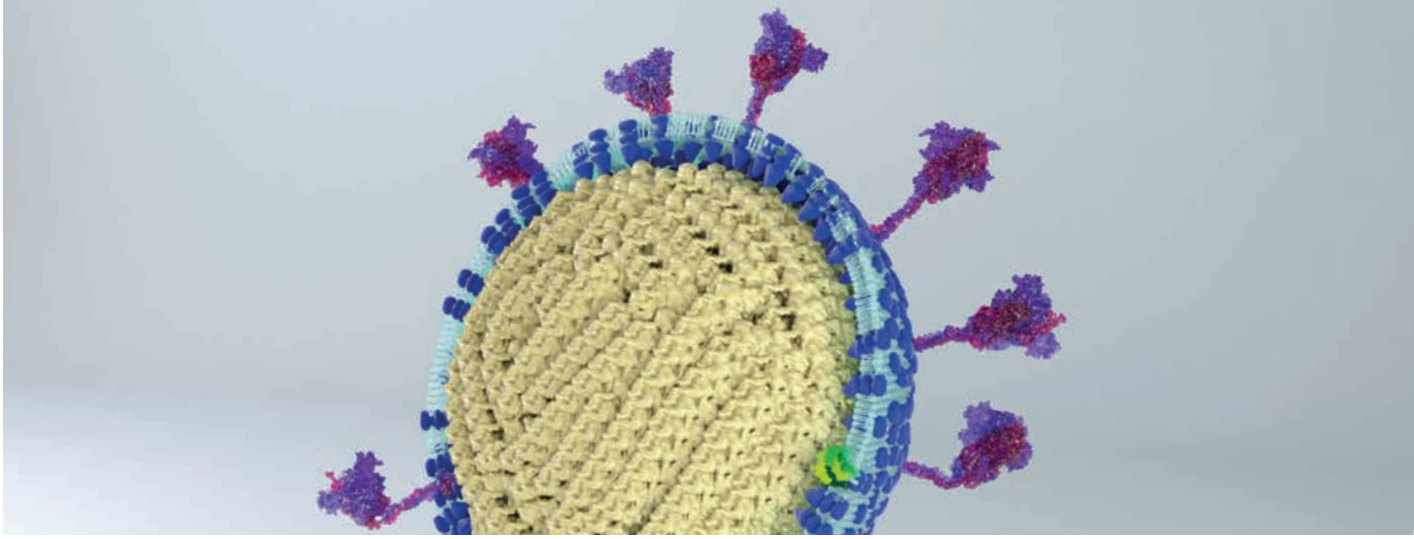

Annabel Slater/MRC-University of Glasgow Centre for Virus Research

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Front cover image: This image is from a collaboration between Annabel Slater, who specialises in science communication and visualisation, and Ed Hutchinson, a virologist at the MRC-University of Glasgow Centre for Virus Research. SARS-CoV-2 virions are irregular structures that cannot be readily resolved by any one method, and this model brings together multiple lines of information about SARS-CoV-2 and other related coronaviruses to provide a clear visualisation of their complex structure.

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From the President

This is the final 2021 issue of *Microbiology Today*, and my final 'From the President' article before Professor Gurdyal Besra FRS begins his term in January. I would therefore firstly like to congratulate Professor Besra on his election and to thank you all for a wonderful three years as President.

To say the least, it has not been quite the three years that I expected. I will always remember the Council meeting in March 2020. We had been intending to discuss the celebrations for the 75th anniversary of the Society and the Annual Conference; instead, we spent two days agonising over the possible trajectory of the newly emerged viral infection, trying to gather as much information as possible and listening to the virologists on Council. No other conferences had been cancelled and large sporting fixtures were still going ahead, but we took the decision to cancel all in-person events.

Hindsight is an amazing thing! A couple of weeks later, the pandemic was declared, followed by the first lockdown. We had to let the staff, who had only just moved into the wonderful new offices, know that the Annual Conference and the 75th celebrations they had been organising for over a year had been cancelled. They were understandably upset, but immediately set about working out how to keep activities going. Working from home, some in bedrooms of house shares, others balancing work with home schooling, they set about mastering virtual platforms and putting together events, including the Fleming Showcase and our first online Annual Conference. I will always remain impressed with the speed and determination with which they all worked together to keep the Microbiology Society not just running, but taking the opportunities the new ways of working threw up to adapt and develop.

This also applies to the membership. I have seen members grapple with presenting outstanding online content, working tirelessly to present the facts as we know them calmly and clearly to the general public, and set up and populate the testing labs. Although SARS-CoV-2 might have stolen the headlines, we haven't ignored the rest of the microbial world. I think we will come out of the pandemic as a better Society with a better understanding of the needs of our membership and new ways to engage.

The President's Roadshow has been a highlight of my time as the Society's President. This was a way to talk to members old and new, as well as potential members, across the country and directly hear about what you wanted from your Society. I so enjoyed meeting those of you who attended in person and was therefore thrilled we were able to continue these events online after the pandemic began. Interestingly, like the online meetings, we had participants from further afield than would have attended in person (The Gambia on one occasion) and there were questions in the chat from people who might have been too unsure to ask in person. This inclusivity is something to try to keep in future formats. Read about the Roadshow on page 41 and at **microbiologysociety.org/roadshow**. Next year, while continuing to offer online opportunities, for example our Scientific Seminar Series, we will be returning to in-person events, which you can find out about on pages 90–94.

Finally, I'd like to remind you about the Society's fundraising project, the Unlocking Potential Fund, which will generate funds to underwrite an Unlocking Potential Grant. It will make funds available to early- and mid-career members who may require an extra level of support to help them deal with a situation that prevents their career developing – I know that a small travel grant transformed my career by giving me access to a rare microscope. We recently published case studies of two people who have made significant contributions to the fund – read Bernard Dixon and Martin Cole's stories on the website (**microbiologysociety.org/UnlockingPotentialFund**).

It has been a great honour to serve as your President in a period covering its 75th anniversary. It might not have been what I expected, but I have had the privilege to see how adversity can really bring out the best in people. While the manner might not have been what we wanted, I think the world now knows that microbiology and microbiologists do really matter.

Judith Armitage

President

president@microbiologysociety.org

From the Chief Executive

Over the past 18 months, we at the Microbiology Society have tried to focus, as we always do, on developing, expanding and strengthening the networks available to you, the Society's members, so that you can generate new knowledge about microbes that can be shared with other communities.

We have held online conferences, brokered relationships with government agencies, published hundreds of papers, given grants, supported early career members and done our best to make sure both that your expertise can help overcome the pandemic and that you can continue to develop your careers.

Many things have made this harder than it used to be, including substantial technological problems, communication difficulties and, of course, health challenges. We have learned a great deal from addressing these conundrums that will stand us in good stead as we come out of the pandemic and look for new ways of supporting the members.

But one aspect of the way we work has proved to be remarkably resilient. Much of the Society's success comes from word of mouth. We in the office email you, tweet, publish blog posts and communicate in a thousand other ways to try to ensure that you can take advantage of all the opportunities that membership of the Society involves. But it is far more influential when your supervisor, your Principal Investigator or a trusted colleague suggests that you submit a paper to one of the Microbiology Society's journals, proposes that you give an offered oral presentation at a Microbiology Society conference or that you attend one of the Microbiology Society's Roadshows or other events.

Word of mouth is our most powerful tool, because we all trust the judgement of colleagues in our professional networks. So your lab-mates, your students and your collaborators will take notice if you tell them that you received rapid, thorough peer reviews on your manuscript and a positive experience of publishing in one of our journals, or if they let you know that they found one of our professional development events useful and productive.

During the pandemic, everyone has seen one another less in person than they otherwise would, and meaningful human contact has been even more important than ever. And where it has not been possible to meet in person, technology has allowed members of the Society to let one another know about all of the opportunities we have been making available. That's why we saw so many people at Annual Conference Online 2021 earlier in the year, it's why we have seen an increase in really interesting papers being submitted to the journals and it's why 2021 saw the largest ever number of members putting themselves forward for the elections to Council, Committees and Divisions.

It is word of mouth among the research community that has enabled the Microbiology Society to remain vibrant and to expand with greater engagement into groups of microbiologists who are less well represented in our activities, such as some parts of the infection science community and researchers in industry.

As we look forward to the rest of 2021 and on into the future, the Microbiology Society will, as always, be trying to ensure the best possible range of opportunities for members. To make it easy for you to let us know the kinds of things you would like to share with your colleagues, we have established our Member Chat series – one-to-one online conversations where we are looking forward to learning more about your research and which microbiology-related topics you find most interesting or relevant. We may not be able to implement every suggestion you make, but we will make every effort to investigate the feasibility of integrating them into our existing programmes. If you would like to speak to us, email **getinvolved@microbiologysociety.org**, and please remember to tell your colleagues about the Microbiology Society, pass on your copy of *Microbiology Today*, encourage them to publish with us, to join as members, to attend our events and to get in touch.

Peter Cotgreave

Chief Executive

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News

Council, Committees and Divisions elections

The change of calendar year marks the turn-over of members who serve on our Council, Committees and Divisions standing down on 31 December, and incoming candidates taking office from 1 January.

As committed as our membership is, we don't expect them all to be working on Society business whilst singing Auld Lang Syne at the turn of the new year. So instead, we take this early opportunity to publicly thank them all for their contributions of time, knowledge and expertise to supporting the Society activities, driving forward its strategy and furthering the crucial and fascinating discipline of microbiology.

It is enormously gratifying to read the long list of names of engaged members who have, and those who will, sit on the groups that make up our governance structure, and it is demonstrative of the unique, collaborative, welcoming community which is at the heart of the organisation. But it is more than a list of names. It is a wealth of diversity, skills and, above all, passion that they all willingly devote in order to support you, the wider membership, and for that we thank them.

Look out for future opportunities to nominate yourself or another member as part of our annual elections which take place every March. Or, if you are keen to get involved but don't know where to start – why not join our Shadowing Scheme? Find more about our governance structures and who currently sits on the Council, Committees and Divisions at **microbiologysociety.org/governance**.

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Microbiology themed collections

In 2022, *Microbiology* will be celebrating its 75th anniversary and so, throughout 2021, the Microbiology Society's founding and flagship journal is launching a series of themed collections celebrating the scope of microbiology and why microbiology matters. Find out more about the collections below:

- **Mycobacteria** collection guest-edited by Dr Riccardo Manganelli (University of Padova, Italy)
- **Metals in Microbiology** collection guest-edited by Dr Jennifer Cavet (University of Manchester, UK) and Dr Karrera Djoko (Durham University, UK).
- **Marine Microbiology** collection guest-edited by Dr Katherine Duncan (University of Strathclyde, UK) and Dr Alex Chase (University of California San Diego, USA).
- **Antimicrobial Resistance** collection guest-edited by Professor Willem van Schaik and Dr Robert Moran (University of Birmingham, UK).
- **Symbiosis** collection guest-edited by Professor Michael Brockhurst (University of Manchester, UK) and Dr Rebecca J. Hall (University of Birmingham, UK)

Keep an eye out for our final collection of this year coming in November!

Find more information about the collections and the current articles in the collections here: **microbiologyresearch.org/content/collections**.

The Microbiology Society is a not-for-profit publisher, supporting and investing in the microbiology community. All journals income is invested back into the Society, be it through providing grants, facilitating policy activities, funding conferences, or other activities.

Microbiology Society members receive a 30% discount on Open Access publishing in Society journals and corresponding authors at Publish and Read institutions can publish fee-free Open Access. Find out if your institution is Publish and Read here: **microbiologyresearch.org/fee-free-open-access.**

News

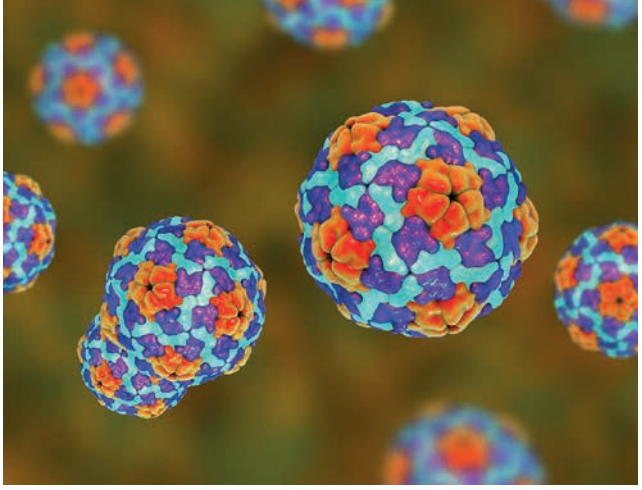
Publishing for the community

Society journals are increasingly supported by Publish and Read deals, offering institutions unlimited usage and frictionless Open Access publishing for faculty and authors. In the move towards Open Science, the Society encourages institutions to adopt Publish and Read deals, allowing fee-free operation in as many organisations as possible to maximise the number of researchers benefiting from Open Access publishing.

By publishing with a Society journal, you will also support funding for our grants, events and activities for the community.

Support your peers.
Benefit from OA.
Publish in our journals.

Find out more about Publish and Read deals in the Scaling up Publish and Read article on p. 98, or visit **microbiologyresearch.org/publish-and-read**.



Dr_Microbe/iStock

Europic 2022

The Microbiology Society is delighted to be hosting Europic 2022, the world premiere virology conference that focuses on studies of picornaviruses. This family of important human and animal pathogens includes enteroviruses (e.g. poliovirus, rhinoviruses, EV-A71, EV-D68), hepatitis A virus and foot-and-mouth disease virus, as well as many other viruses whose number is growing by the day with new discoveries.

The event will take place in the picturesque spa town of Harrogate, UK, on 5–9 June 2022, and will provide a vital forum for the international community to come together to hear about the latest advancements in the field of picornaviruses and enjoy numerous networking opportunities to help strengthen relationships within the scientific community.

News

Winner of the Sir Howard Dalton Young Microbiologist of the Year

The Microbiology Society is pleased to announce that Emma Banks, from University of Nottingham, UK, is the winner of this year's Sir Howard Dalton Young Microbiologist of the Year competition.

Emma is currently studying for a PhD and was awarded the prize for her talk 'Creating curvature to kill: an enzyme that shapes predatory *Bdellovibrio* bacteria, optimising invasion and replication within prey'.

Upcoming grant deadlines

Date	Grant
1 December 2021	Travel Grants for members presenting at conferences or attending short training courses from 1 January 2022. In-person and virtual events will be supported.
17 February 2022	Harry Smith Vacation Studentships to support undergraduate research projects during summer 2022.

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

Connect with the Microbiology Society on social media:

@MicrobioSoc **@microbiosoc**

Gavin Thomas: Editor-in-Chief of *Microbiology*

Gavin Thomas

Please introduce yourself

I am a Professor of Microbiology at the University of York, where I have been now for nearly 20 years. My research interests are quite broad, but are largely on the physiology of how bacteria acquire nutrients from the environment with a focus on transport proteins in their cell membrane. More recently we have been trying to apply this information to different aspects of biotechnology, including the production of sustainable chemicals and a project looking at how bacteria cause body odour in humans.

What motivated you to get involved with *Microbiology*?

Early in my academic position at York, I had taken on the role as Editor of *Microbiology Today*, which was very enjoyable and meant that I sat on Council, in a rather crowded room at Marlborough House, the Society's headquarters at the time, which were near Reading. As well as mixing with my senior colleagues, I could see how important the journals were, and still are, to the income of the Society, supporting all the things that benefit our members, like my first Travel Grant to Aberdeen in 1995 and subsequently as a lecturer, being able to apply for Harry Smith Vacation Studentships. Once my own research was established at York, I was invited to become an Editor for *Microbiology*, which I of course accepted as my way to start putting back into the Society.

Since becoming Editor-in-Chief, in what ways has the journal changed to better serve the microbiology community?

The first change we instigated was creating some clear topic areas within the journal, most of which now are overseen by a Senior Editor. We also appointed four new Senior Editors (Tracy Palmer FRS, Steve Diggle, Martin Welch and Mike Brockhurst) to lead these new sections and a host of new Editors to support both these new areas and existing ones. Our new topic areas also align with some of the UN's Sustainable Development Goals and so fit in with other activities of the Society. What has been fantastic is that Tracy has now joined me as Deputy Editor-in-Chief and is helping drive forward lots of new ideas while still looking after her panel. To help authors and Editors get papers turned around quicker we have revamped our Board of Reviewers and have just created a Rapid-Review Track to attract high-quality papers that have been through peer review at other journals and wish to use those reviewers to get a quick assessment for their suitability for *Microbiology*.

Next year is the 75th anniversary of *Microbiology*. What are some of the highlights you've found in the journal's history?

I have recently been looking through some of the very first issues of *Microbiology*, which was then the *Journal of General Microbiology*, and it has been fascinating to see how many areas of research that started in that period are still being studied to this day, albeit with vastly improved methods and understanding of microbial function. Also, the diversity of people doing microbiology research, despite the limited number of places it was done, is quite striking. We hope to tell some of these stories in a series of articles in 2022, with the main foci on microbiology research at this time and the people and places in which the science was done. There are some great stories we hope you will enjoy reading about next year.

Claudio Ventrella/iStock

Microbiology has been releasing themed collections in the lead up to the anniversary year. What can we expect to see in 2022?

The collections have been running in 2020 and 2021, and we hope they are going to help get more high-quality submissions to the journal, through the hard work of some of our new Editors. One of our collections for 2022 is the Microbial Cell Surface collection and will form a series of excellent Review articles linked to a symposium at Annual Conference in 2022 – the first of our *Microbiology*-linked symposia at our flagship event. There will also be collections on environmental sensing in bacteria and microbial evolution. Each collection has an early career microbiologist (ECM) involved, so talk to the ECM Forum if you are interested in getting involved in a future collection in your area (via **ECM@ microbiologysociety.org**).

Why are Society journals important and how can members get more involved?

A large part of the income that runs the Microbiology Society comes from the publishing arm, and so keeping them healthy and strong is really critical to keep the Society strong. The 'Publishing for the Community' message seems to slowly be getting out as young scientists want to support their learned societies rather than the shareholders of the large for-profit publishers, which is where your article processing charges go when you publish there. Over the next few years, there are going to be big changes to how the Society continues to generate income from publishing, but the best thing you can do is to publish in and promote our journals, especially, of course, *Microbiology*.

What do you think the future holds for microbiology?

The future for microbiology is incredibly exciting, as we gain deeper and broader understanding of the function of microbes in their natural environment and their applications for mankind. For me, the role of communities of microbes is probably the biggest area we are going to start making inroads into in the next few decades, from gut to skin microbiomes, to anaerobic digestors to global chemical recycling in oceans, plant roots and soils. Not much in biology happens in isolation and understanding this complexity is our next big challenge. When writing in 'Microbes and Man', John Postgate discusses the human gut microbiome and it was known to be important for health but was really poorly understood – a 'black box'. Advances in genomics and tools to visualise microbes *in situ*, to name but two, have given us enormous insight that would have seemed impossible when I was at school, and microbiology will continue to advance at a tremendous rate. Being Editor-in-Chief of *Microbiology* and writing the monthly Microbial Musings gives me the privilege of dedicating time to reading about some of these advances outside of my own field within the broad topic areas that we cover.

Microbiology, the founding and flagship journal from the Microbiology Society, showcases the diversity and importance of microbiology by publishing fundamental and applied research across the breadth of the field. Find the latest journal articles on our website: **mic.microbiologyresearch.org**.

Find bonus questions from our Q&A with Gavin Thomas on our website: **microbiologysociety.org/MTOctober2021GavinThomas**.

Molecular virology of SARS-CoV-2

Keith Grehan

Background/description of virus and family

In December 2019, cases of pneumonia were reported in patients in Wuhan, China. These patients were infected with a novel coronavirus of the *Betacoronavirus* lineage, ultimately designated SARS-CoV-2 due to similarities between this virus and the previously identified SARS-CoV. It seems unnecessary to reiterate the impact of this disease; however, at the time of writing, the number of confirmed infections exceeds 218 million, and 4.5 million deaths have been linked to COVID-19, the disease caused by infection with SARS-CoV-2.

Betacoronaviruses are enveloped, positive-sense single-strand RNA viruses, with genomes among the largest for RNA viruses, between 27 kb and 32 kb. Upon infection of a cell, the genome acts as a messenger RNA and initiates translation, polyproteins are produced and two virally encoded proteases process these into the mature protein forms. This processing generates a series of non-structural proteins which coordinate viral replication. One of the more interesting features of coronaviruses is the presence of a 3′-to-5′ exonuclease (ExoN) proofreading enzyme. This ExoN allows the viruses to reduce transcription error often associated with RNA-dependent RNA polymerases. This has allowed coronaviruses to maintain larger genomes than other RNA viruses without the risk of catastrophic mutation accumulation. Studies have demonstrated that mutations that knock out the ExoN greatly reduce coronavirus transcription fidelity and viral fitness.

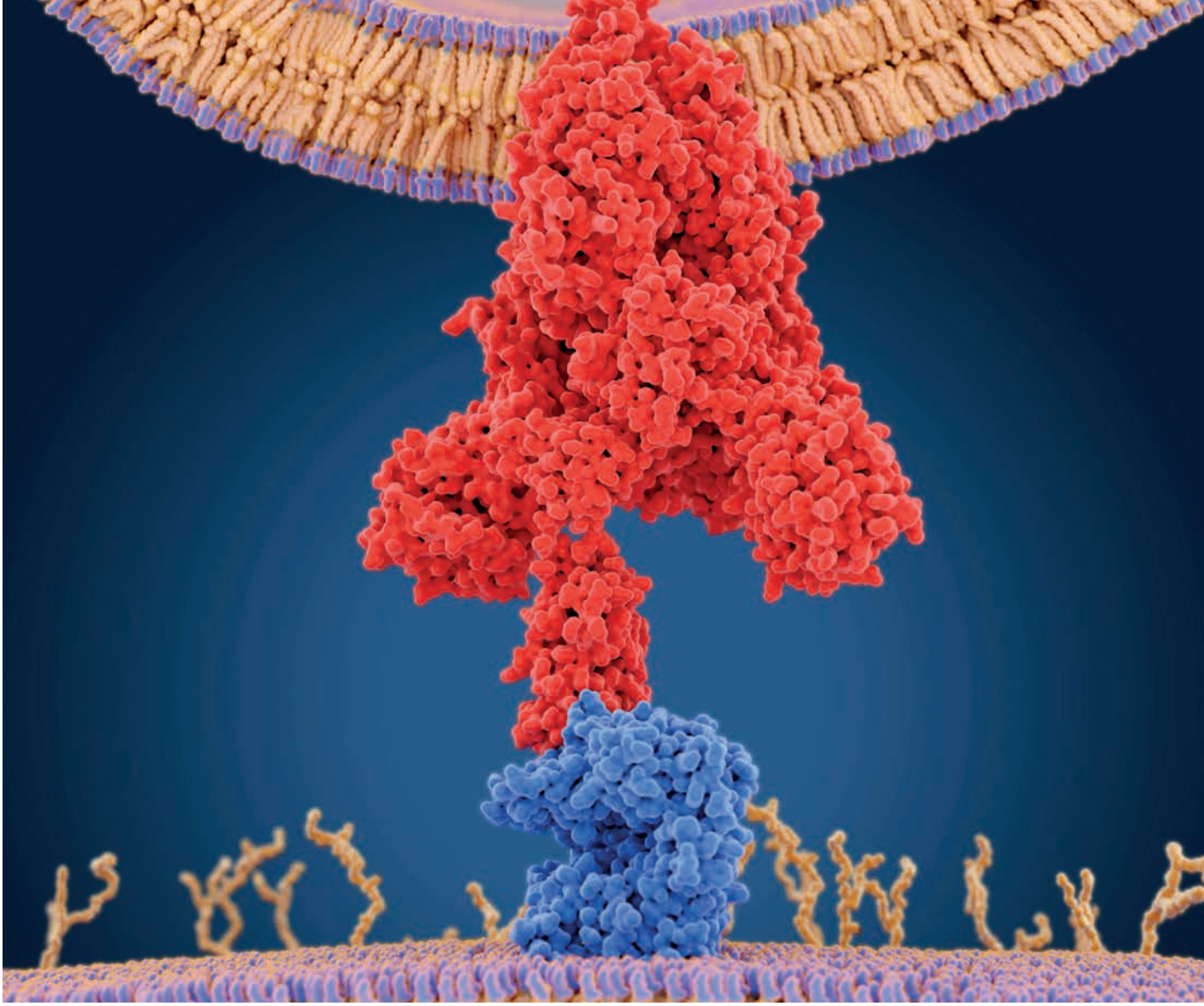
Toward the 3′ end of the genome, coronaviruses encode the structural proteins, comprising the infamous spike protein (S) along with the membrane (M), envelope (E) and nucleocapsid (N) proteins. S proteins are fusion glycoproteins (gp) composed of two distinct parts, S1 and S2. The S1 domain contains the receptor-binding domain (RBD), responsible for engaging the host cell receptor, initiating the conformational changes required for fusion. The S2 domain contains a fusion peptide, which mediates the fusion between viral and cell membranes, allowing the virus to insert its RNA into the host cell.

Before SARS-CoV-2 was identified, betacoronaviruses included the clinically relevant OC43-CoV and HKU1-CoV among others. Both circulate within the human population and are among the 'common cold' viruses. Betacoronviruses also include SARS-CoV and MERS-CoV, diseases of significant public health concern.

What are the traits that make SARS-CoV-2 worse than other coronaviruses?

SARS-CoV-2 has characteristics typical of betacoronaviruses, though the current pandemic highlights the importance of identifying and understanding the traits unique to this virus. The S protein is essential for infection and is the dominant target for antibody responses. Given the functional role of the spike protein in initiating infection, it is possible that the key to the increased transmissibility of SARS-CoV-2 may lie within this region. Both structural and biochemical studies determined that the RBD of SARS-CoV-2 binds to the angiotensin-converting enzyme 2 (ACE2) receptor on human cells. Evidence from the first SARS-CoV outbreak identified six residues critical for effective ACE2-binding. Sequencing of the corresponding region in SARS-CoV-2 showed that five of the six residues were different from those detected in SARS-CoV. While studies are ongoing, it is likely that these changes contribute to the increased affinity of SARS-CoV-2 to ACE2 compared with SARS-CoV.

Cryogenic electron microscopy (Cryo-EM) of SARS-CoV-2 S has captured the flexibility of the S1 domain. The RBD adopts distinct conformational states, with a 'down' state in which the RBD is shielded from receptor binding and an 'up' state in which the RBD is accessible for ACE2-interaction. Interestingly, while it may be assumed SARS-CoV-2 would be more likely



Molecular model of a coronavirus spike (S) protein (red) bound to an angiotensin-converting enzyme 2 (ACE2) receptor (blue) on a human cell.
Juan Gaertner/Science Photo Library

to have its RBD primed for receptor engagement, it appears the RBD of SARS-CoV-2 is more likely to be in the 'down' state. This 'down' state may increase the ability of the virus to evade the host immune system and, coupled with variation in the RBD residues, may have allowed the virus to balance immune evasion with infectivity.

Upon receptor binding, conformational changes in the S are required to bring the S2 region into contact with the cell membrane and initiate fusion. Coronaviruses rely on host proteases to cleave the S protein, a prerequisite for S2-mediated cell fusion. A much-discussed feature of SARS-CoV-2 is the furin-like cleavage site. While not present in other identified SARS-like coronaviruses, related betacoronaviruses (e.g. OC43 and MERS-CoV) do contain a similar furin-like cleavage domain. Given the growing number of SARS-like coronaviruses that have been isolated from animals, it is likely that more SARS-like viruses with furin-like cleavage sites will be identified in the future.

The rise of the mutants

While the ExoN activity of SARS-CoV-2 limits mutation frequency by excising nucleotide mismatches, its activity is imperfect; estimates are that functional ExoN activity can 'repair' 94% of mismatches. Given that an infected individual may carry 10^{11} virions, heterogeneity among circulating viruses is not surprising.

Nonetheless, specific mutations have become fixed within the population, giving rise to the variants we are familiar with. With mutations occurring throughout the genome, those localised to the S region impart clear advantages to the virus. Successful control of SARS-CoV-2 may well depend on our ability to map changes in the S protein as the primary target of vaccines.

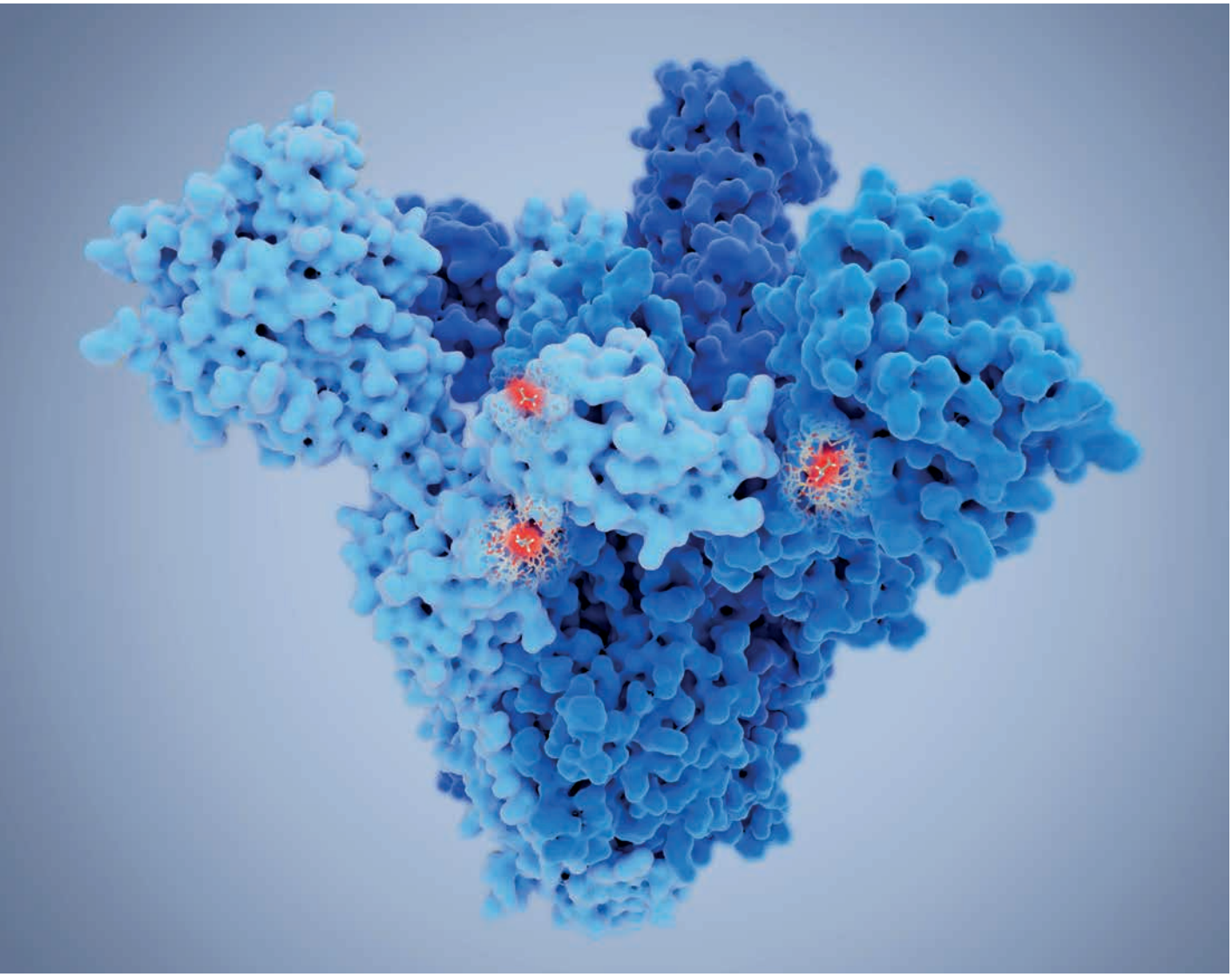
The original SARS-CoV-2 sequence demonstrates a high affinity for the human ACE2 receptor, though computational models show that the RBD sequence was not optimal. These studies determined that asparagine was not the ideal

residue at position 501 for human ACE2-binding. The N501Y substitution was among the first to be identified in what is now characteristic of the Alpha strain. This substitution was one of several changes which allowed infection rates to surge with ongoing adaptation to the human host.

Another early substitution, D614G, lies outside of the RBD, thus the mechanism for increased fitness of this variant was initially unclear. Since then, several studies have shown an increase in entry efficiency associated with the D614G mutation, with structural studies showing more of the RBD in the 'up' (receptor-binding) state. This mutation may represent a trade-off, wherein the virus sacrifices immune evasion for increased receptor binding.

As the pandemic progresses, virologists and public health professionals are concerned that we are now entering a phase where delays in vaccination allow the virus to continue to circulate and evolve. This new paradigm may drive selection of immune evasion mutations. An example may be the Delta variant, associated with decreased vaccine efficacy compared with the previously dominant SARS-CoV-2 strain and the Alpha

SARS-CoV-2 virus spike protein and mutation. Juan Gaertner/Science Photo Library



variant. However, it is worth noting that all vaccines remain >60% effective at preventing infection with the Delta strain and have >90% efficacy against disease leading to hospitalisation.

The Delta variant genome has several mutations, four of which are in the S region. This includes D614G, providing increased infectivity, along with T478K and L452R. The latter two reside within the RBD, altering binding to ACE2 and providing immune evasion. These changes may represent an adaptation to the more challenging immunological landscape. The other characteristic Delta mutation is P681R, located within the furin cleavage site of the S protein. The role of this substitution is unclear, though preliminary data suggest an improved fusion efficiency and an immune evasion phenotype.

Individually, these mutations are not unique to the Delta variant; however, their simultaneous occurrence has made the Delta variant distinctive. The presence and variability of immune evasion mutations is a reminder that SARS-CoV-2 remains a significant threat; if infection numbers remain high, the virus will evolve and spread.

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Keith Grehan

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Keith currently works at the University of Leeds as part of a team developing a virus-like particle (VLP)-based polio vaccine produced in yeast for use as a post-eradication vaccine. His other work focuses on the use of HBc as an antigen presentation system for more effective vaccine development.

What inspired you to become a microbiologist?

I started my academic life with no intentions of becoming a microbiologist. In 2012, I began an MSc studying the genetics of the innate immune system of bats. Over the course of this project, I became more and more interested in the viruses that seemed benign in bats but devastating for humans. I was struck by the impact some of these diseases have and, in some cases, how little can be done to prevent them. I was fortunate to find a PhD seeking to examine the relationship between bats and the viruses that infect them. This was my first step into microbiology, but I was hooked. The idea that understanding of viruses would lead to better treatments and prevention of disease has continued to motivate me since I first began to wonder about all these viruses that seemed to exist so well with bats.

What do you love most about your job?

This is tricky. I love research and the sense of being the first person to know something, a feeling with which most scientists are probably familiar. I also love the novelty that comes from constantly learning new things; while always challenging, the diversity of my job is one of its greatest charms. Whenever possible, I try to balance my research with teaching and science outreach. Several of my proudest accomplishments in academia have been seeing people whose training I have had a role in achieving their goals; these goals can be describing their work in a group meeting or successfully completing a PhD. Playing a role in helping someone accomplish their goals is a rare privilege that most careers don't provide. But I think what I love most about my job is the idea that research I am involved in can be used to help people. Microbiologists at every level can be justifiably proud that their work forms part of a field that directly helps improve the lives of people all over the world.

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A personal perspective on SARS-CoV-2 testing in the United Kingdom

Alan McNally

Like most of the UK microbiology community, I watched in horror as the nation stumbled its way towards an uncontrollable rise in COVID-19 cases in January and February of 2020. The failure to monitor borders led to multiple introductions of the virus into the UK, seeding numerous transmission chains. As cases increased, the government made the decision to test only those who attended hospital with respiratory infection symptoms for the virus, effectively destroying any ability to truly determine the scale of the epidemic in the UK. Along with many of my colleagues, I was very vocal in the press and media as to why this was a terrible idea, and that testing capacity in the UK had to be dramatically increased in a very short space of time. I was amongst those advocating the deployment of university labs with the capability to do so to switch over to performing community SARS-CoV-2 testing to determine the scale of the epidemic.

In early March, I was invited to a teleconference organised by the Office for Science, to discuss how the UK may ramp up its testing capacity. The upshot of that meeting was that rather than a flotilla of small regional university labs being established, a small number of 'mega-labs' would be created across the UK to allow the creation of large-scale

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symptomatic community testing. On 16 March 2020, I received an email asking if I would be able to take a secondment to help establish the first of those testing labs at the UK Biosample Centre in Milton Keynes, and if I could help in recruiting volunteers to work in the facility. A quick email to the Microbiology Society's Chief Executive, Peter Cotgreave, saw the Society swing into action, coordinating messaging to relevant university schools and departments and willing volunteers. A call to arms on Twitter also led to a number of volunteers being recruited, including a number of PhD students and postdocs from Birmingham.

I arrived at Milton Keynes for the first time on Thursday 26 March 2020, along with 12 other scientists, including Dr Maddy Seale from Oxford and Dr Joana Viana from Birmingham. We were met by Dr Mike Hill, Dr Stewart Moffat and their team from Oxford who had been ***in situ*** for 10 days setting up the lab, its equipment and reagents. On that first day, we tested 500 samples manually and worked a 14-hour shift, troubleshooting and identifying protocols to allow us to reach the capacity being requested by the government of some 50,000 tests per day. Within three weeks, we had 240 people split into four teams, operating 12-hour shift patterns, with the lab functioning 24/7, and with staff given free accommodation in a closed hotel in central Milton Keynes. The Royal Army Logistics Corps were drafted in to solve the hugely complex logistics issues of ordering, storing and stock taking all the equipment and reagents needed to run a lab of that scale. Liquid handling robots were acquisitioned to allow us to automate almost all lab processes, and by the first week in April the lab was operating non-stop at maximum capacity of around 50,000 tests per day. Much of the equipment, of course, was donated by universities, but most importantly, the entire workforce of the facility was composed of quite incredible university researchers who put their careers and lives on hold to provide the testing capacity the country so greatly needed. From professors to undergraduate students, everyone chipped in and gave their all in what was one of the greatest experiences and achievements of my career.

As the lab became established and operating to an excellent level of standard, I felt I was no longer needed at Milton Keynes, and on 1 June 2020 I ended my secondment and returned to Birmingham, naively thinking my time working on viral diagnostics was over once again, having not actually worked in the field since my final postdoc with Professor Ian

Brown on H5N1 in 2006. However, in July I was contacted once again, this time to set up a testing lab at the University of Birmingham, to cope with the anticipated surge in cases and demand for testing as autumn 2020 loomed. On 1 September, our university testing lab went live, delivering 5,000 tests per day for the Pillar 2 programme, including testing of swabs taken at our campus testing site and helping local public health teams with outbreak investigations. It was of course a tragic few months for the country as COVID-19 devastated our hospitals, but it was also exhilarating and exhausting to be working on the front line of the pandemic. We were heavily involved in the discovery of the B.1.1.7 Alpha variant in the UK, working closely with Professor Nick Loman's CoG-UK lab in the university to rapidly test and then sequence the S gene target failures which came to represent the variant in testing labs.

The other area of testing I found myself deeply involved in was the rollout of lateral flow (LFD) testing for SARS-CoV-2. It is fair to say this was one of the most controversial aspects around testing for the virus, with often bitter arguments over their value and merit. From my perspective, I saw them as another valuable tool in an arsenal of weaponry to deal with

David Benito/iStock

the pandemic, and alongside wonderful colleagues across the University of Birmingham, we converted our famous Great Hall into a large-scale asymptomatic LFD testing site for SARS-CoV-2 in December 2020, which was overseen by Dr Jack Ferguson and Dr Steven Dunn. Regardless of opinions on the rights and wrongs of mass-scale LFD testing, our experience was that they identified people walking around shedding detectable SARS-CoV-2 without any idea of being infected, and undoubtedly interrupted potential transmission chains on our campus.

What has been quite incredible during the pandemic is the level of interest that has been generated towards infectious disease (ID) diagnostics. For years diagnostics has been massively neglected by both funding bodies and journals. My first ever grants as a principal investigator (PI) in 2006 and 2008 were on rapid diagnostic research, but the level of interest in that work was minuscule and so I developed my genomics and antimicrobial resistance (AMR) interests instead. My hope is that the pandemic opens the microbiology community's eyes to how important the innovation and development of ID diagnostics is. This is our opportunity to truly solidify the clear value and sustained use of genomics in ID diagnostics, surveillance and epidemiology. We must also now think about how the democratisation of infection testing to self-administered home tests may impact our desire for collections of clinical isolates, and how we do ID epidemiology in the future.

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Alan McNally

Professor of Microbial Evolutionary Genomics, Institute Director, Institute of Microbiology and Infection, College of Medical and Dental Science, University of Birmingham, UK

Professor and Institute Director at Birmingham, Alan McNally began his scientific career studying molecular microbiology at the University of Glasgow. He then went on to do a PhD studying gene regulation in *Escherichia coli* O157 at the University of Edinburgh. A short postdoc in microbial biochemistry at Bristol was followed by two postdoctoral projects at the Veterinary Laboratories Agency in Surrey. It was here that Alan developed an interest in phylogenetics and evolution, which he developed in his first academic PI position at Nottingham Trent University. During 10 successful years, Alan established his group as an internationally renowned group studying microbial genomics and evolution. During the COVID-19 outbreak, Alan was seconded to the Milton Keynes Lighthouse Lab as Infectious Disease lead at the Government's first flagship COVID-19 testing facility.

What inspired you to become a microbiologist?

I applied to do medicine at university but a mix of grades saw me offered an unconditional place to study Biological Sciences at Glasgow. The first two years were an amazing mix of disciplines, from immunology to human anatomy and, of course, microbiology. I loved the micro teaching and became fascinated by how such simple organisms could have such a devastating effect on human health. A year's work placement at the microbiology labs at SmithKline Beecham sealed it for me that I wanted to do microbiology research for a living.

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

Don't let anyone tell you there is only one sure path to success in microbiology research. Follow your heart and your interests wherever they might take you. I hopped from molecular microbiology to biochemistry to population microbiology, then virology and finally genomics. My best mentor told me that you do the very best science with a smile on your face, and I absolutely believe that and still preach it. So make sure you love and enjoy what you are doing, and if you don't, find something else that you do.

COVID-19: a new era for microbial genomics

Colman O'Cathail

"The COVID-19 pandemic has changed the world …" is probably how 90% of the articles about the topic have started since SARS-CoV-2 burst so unceremoniously onto the scene in late 2019. You will hear no disagreement from me in that regard, but we do need to discuss a significant change that has been heralded by the pandemic, and that is in the field of bioinformatics.

Even very early on in the pandemic, it was clear genomics was going to have a big role to play, not only because it was an available technology but also because of its cost effectiveness. Make no mistake, sequencing has been around a while now and cost-effective pathogen sequencing certainly isn't novel by any standards. It is the fact that the skills, knowledge and infrastructure are far more ubiquitous now than they were in the previous decade. This is, I believe, what made all the difference. The paper describing the genome of SARS-CoV-2 was received by *Nature* on 7 January 2020 and subsequently published on 3 February shortly thereafter. On the face of it, most scientists reading this will be aghast with how quick a publication this was, but there is a far more astounding story within this.

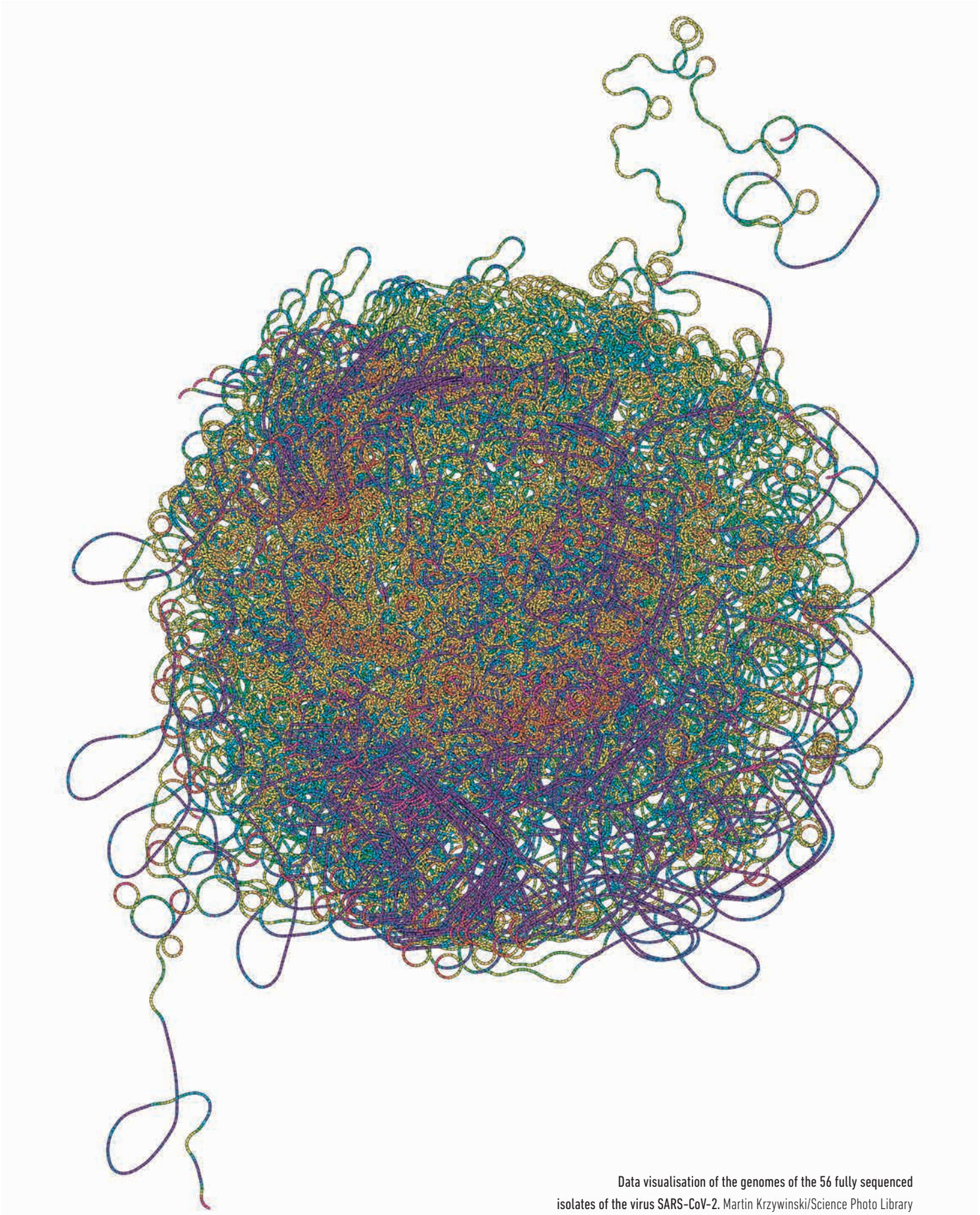
The patient from whom this novel coronavirus genome was elucidated was admitted to hospital on 26 December 2019. Within 12 days of admission, the genome of the novel coronavirus responsible for causing the patient's disease was assembled from a metagenomic sequencing run of a bronchiolar lavage, a paper was written and submitted to *Nature*, describing the genome, illustrating where it sat in the evolutionary framework of other coronaviruses and identifying its possible origins as a spillover event from bats. This was an early marker that genomics and bioinformatics were going to play a huge role in this pandemic.

By March 2020, SARS-CoV-2 had spread far across the globe. Many countries entered lockdowns of some form. On 11 March, the World Health Organization (WHO) Director General declared that COVID-19 was indeed a pandemic. The rapid spread of the pandemic was quickly met with the swift mobilisation of scientists in response. Thousands of scientists were committing themselves to the fight against SARS-CoV-2, whether that be as the labour force processing PCR tests or changing their research focus. Importantly, as this is about bioinformatics, many consortia popped up in countries dedicated to one goal: to sequence positive COVID-19 samples. The most notable of which popped up in the UK: the COVID-19 Genomics UK Consortium, COG-UK for short.

COG-UK was, and continues to be, a collaborative effort unlike any other. A plethora of scientists working across 22 universities, institutes and health agencies to deliver on the singular goal: sequence, analyse and report on the genomes of SARS-CoV-2 samples in the UK. At the time of writing, COG-UK has sequenced more than 800,000 SARS-CoV-2 genomes, meaning it has sequenced more genomes per head of population than any other on the planet. More importantly, and what, for me, is the true cultural shift in this field, is the rapid archival of these data publicly for use by the wider scientific community.

Before I continue, I should be clear that I currently work as a bioinformatician with the European Nucleotide Archive (ENA) at EMBL's European Bioinformatics Institute (EMBL-EBI) as part of the team responsible for the archival and mobilisation of SARS-CoV-2-related data. I can offer my perspective as someone working with the immense volume of data and give a professional view as to why I feel this pandemic has been such a major cultural shift for the microbial genomics community and bioinformatics.

There are currently two primary routes to archive your SARS-CoV-2 data as a scientist: GISAID and the International Nucleotide Sequence Database Collaboration (INSDC);



Data visualisation of the genomes of the 56 fully sequenced isolates of the virus SARS-CoV-2. Martin Krzywinski/Science Photo Library

consisting of the European Nucleotide Archive [ENA], National Center for Biotechnology Information [NCBI] and DNA Data Bank of Japan [DDBJ]). The latter of the two will be well known to many scientists, as the INSDC has been archiving digital biological data for many years. GISAID is a newer service that initially focused on the rapid sharing of influenza data but adapted to also take in SARS-CoV-2 genomes when the pandemic struck. Initially, genomic consortia responsible for sequencing the virus submitted primarily to GISAID, mainly due to their strong desire to get genomes available to the wider community as fast as possible, which is a key advantage of GISAID as a service. This enabled many decisions early in the pandemic to be informed by genomics and helped get a sense of how the pandemic spread across the globe. The rapid sharing of genomes allowed the rapid development of tools for genome analysis, such as the PANGOLIN lineage assignment tool and CoV-GLUE for exploring amino acid mutations, and genomes could be picked up and analysed by services like Nextstrain. All of these tools are now ubiquitous in the fight against the pandemic, all powered and enabled by rapid sharing of genomes.

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However, GISAID currently only archives assembled genome sequences, which gives limited options for researchers looking to do more in-depth analyses of the SARS-CoV-2 data or those who would like to control how those genomes were constructed from the raw data. This is where the INSDC is of enormous importance to researchers, as you can also archive raw read data and sequences, along with a myriad of other data types.

For context, at the time of writing (August 2021), SARS-CoV-2 reads make up 7.7% of all the raw reads archived within the ENA (by accession, not in terms of storage), which I think contextualises just how enormous the sequencing efforts by the UK and the rest of the world have been. So important is this flow of data, a consortium of European partners including EMBL-EBI, ELIXIR, Erasmus MC, ELTE and DTU have a dedicated service for exploring SARS-CoV-2 data, the European COVID-19 Data Platform. Even more astonishing is the fact that the median turnaround time from sample collection date to the raw data going public in the ENA is 25 days at its peak. There is an extraordinary amount of manpower involved in this feat, one that we should be celebrating.

The advantage of archiving these data, especially with the INSDC, is that it will be archived to provide the maximum utility to any scientists wishing to repurpose the data for as long as possible. However, in order to provide the maximum utility of the data, the metadata surrounding each of the samples needs to be as rich as possible. At a bare minimum, collection date, species and geography are the metadata of utility in public health genomics, but much of the data is capturing more than this. Ct values from qRT-PCR runs being captured, or the number of days hosts were symptomatic for are just two examples of the kind of detailed metadata I'm talking about. This, for me, is where we are witnessing the true culture shift in public health genomics. Yes, the volume of data being produced is a feat to behold. But there is great depth to the metadata, and this is what makes the public data so useful. Not just now, but long into the future, scientists will be able to analyse these data in detail and we, as a society, will be learning from this pandemic for years to come. All thanks to the bioinformaticians and scientists across the globe who have been committed to sequencing, archiving and making available all the data.

This is the unsung cultural change in the science of the pandemic. We are heralding a new era of open science. We

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know we can sequence pathogens at scale. We know we can archive and contextualise genomic data robustly and quickly. Now we just have to keep doing it, because in this new era of open science, robust, public and accessible, digital, biological data will be the key to fighting infectious diseases.

Further reading

International Nucleotide Sequence Database Collaboration (insdc.org)
GISAID (gisaid.org)
European Nucleotide Archive (ebi.ac.uk/ena/browser/home)
National Center for Biotechnology Information (ncbi.nlm.nih.gov)
DNA Data Bank of Japan (ddbj.nig.ac.jp/index-e.html)
Cov-lineages (cov-lineages.org)
CoV-GLUE (cov-glue.cvr.gla.ac.uk)
Nextstrain (nextstrain.org)

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Colman currently works as a bioinformatician at the ENA dealing with SARS-CoV-2 data. He has been a member of the Society since 2014 and is currently Chair of the ECM Forum Executive Committee and a member of Council.

Could you describe one of your typical workdays?

Typical feels so unjust to use as I think my workdays can be very varied. But broadly speaking, my workday would include an internal team meeting or two relating to data archiving or analysis at the ENA. Generally, I would usually meet with our international partners across Europe or even further afield, which is one of my favourite parts of working at EMBL-EBI! In between, I'll be working on helping users submit data, delivering support for ongoing SARS-CoV-2 work and collaborating on coding projects within the ENA team.

Which parts of your job do you find most challenging?

I think the most challenging part of my job can be being stumped by coding problems. Although, that incidentally makes it one of the more satisfying parts of my job too! Hard to beat the feeling of solving a problem that's stumped you for a while.

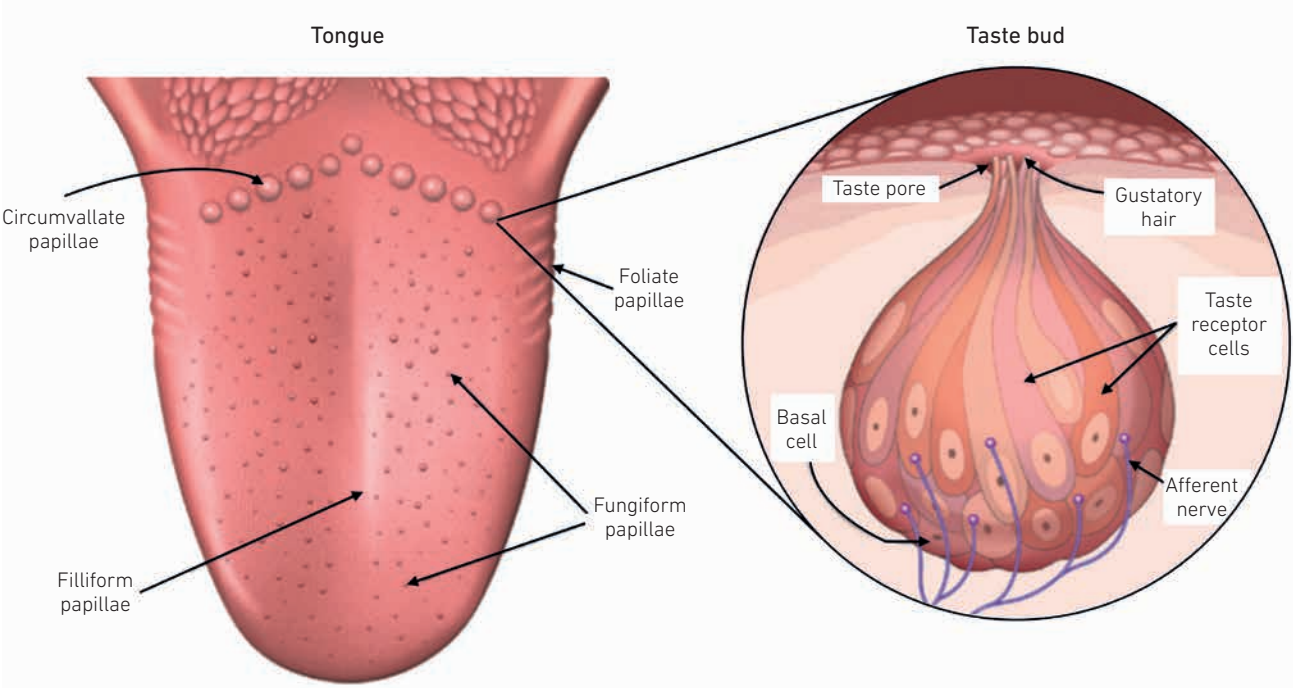
The role of the oral cavity in SARS-CoV-2 detection, dissemination and disease

David H. Edwards and Alexander Gardner

Early in the COVID-19 pandemic, anecdotal reports of the loss of smell (anosmia) and taste (ageusia) were reported as potential symptoms of SARS-CoV-2 infection. The diagnostic significance of these characteristics resulted in the publication of revised guidance in May 2020. Subsequent studies have suggested 65% of all infections may generate a disturbance to one or both of these sensory processes, but clear links between these symptoms and how they vary according to age, sex and ethnicity or impact clinical outcome have yet to be established. However, what these sensory disturbances did highlight was the significance of the nose and mouth in the infection and proliferation of SARS-CoV-2.

The ability to perceive taste involves groups of approximately 50 chemosensory cells, organised into structures on the tongue, called buds. Each bud consists of three types of taste cells and a renewing population of basal cells that are capable of detecting one of five distinct flavours: sweet, sour, bitter, salt and umami. The perception of salt and sour is achieved via receptors that respond to sodium or hydrogen ions, while the other tastes require receptors tuned to specific molecules such as sugars in the case of

Anatomy of the tongue and taste buds. Dr Alexander Gardner

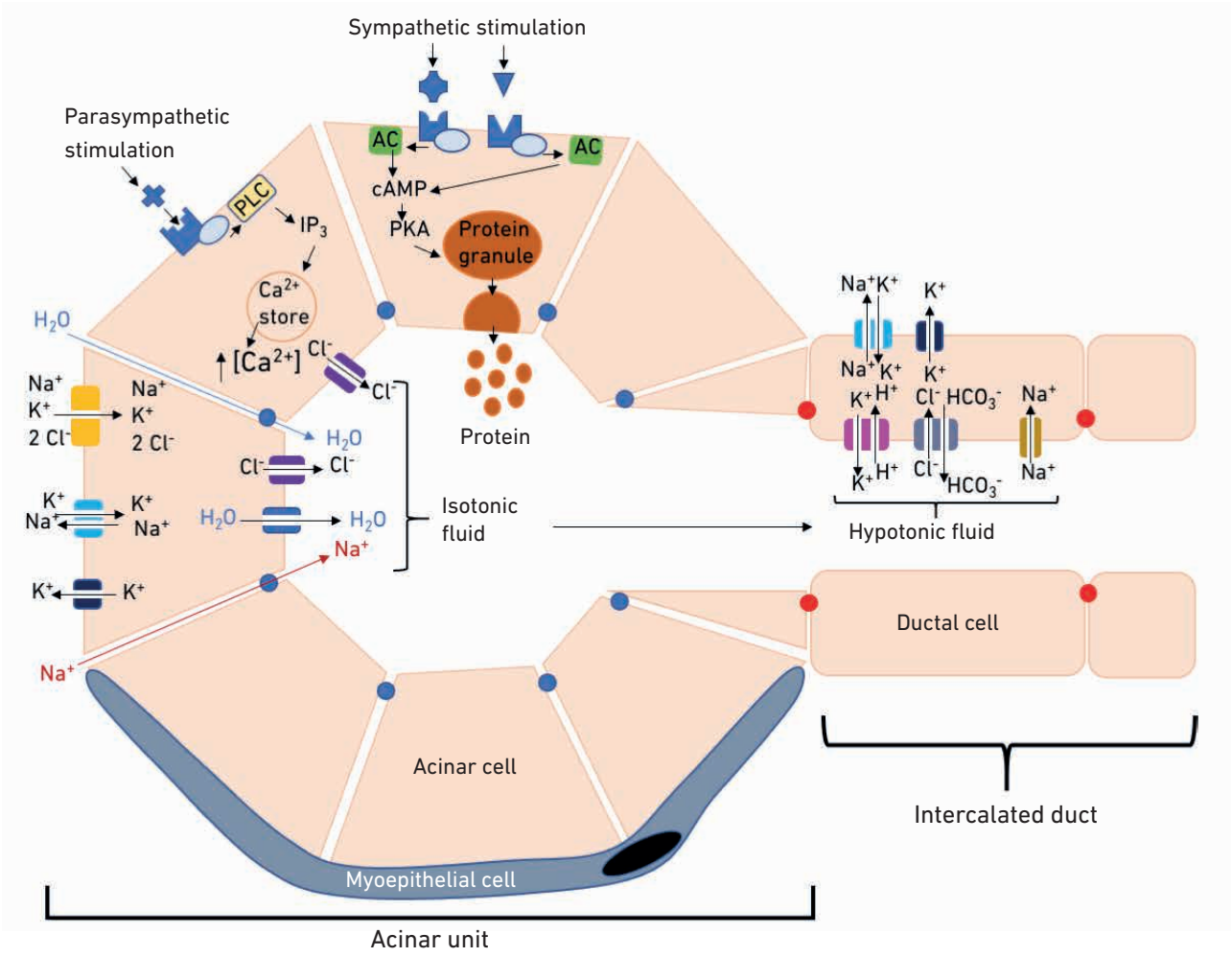


sweet, glutamate in the case of umami, and a diverse set of molecules including many plant alkaloids for the perception of bitter. Following receptor activation, signals are relayed via dedicated nerves assigned to individual taste buds, then onward to the brain where the responses are integrated with other sensory determinants, including smell, to assign a particular sensation. Each taste bud contains multiple papillae, with fungiform papillae associated with the surface of the tongue and circumvallate and foliate papillae located on the underside or dorsum. True ageusia (loss of taste) is a relatively uncommon phenomenon, believed to be caused by severe nerve damage. Taste disruption (dysgeusia) is considerably more prevalent and can arise from several mechanisms including damage to taste bud cells via direct injury or interventions such as chemotherapy. For viral illnesses such as the common cold, much of the taste disruption experienced is attributed to the absence of smell due to nasal congestion. In the case of COVID-19, where taste dysfunction is prevalent but congestion absent, the cause is currently unclear. Possible mechanisms include direct damage to taste cells during angiotensin-converting enzyme 2 (ACE2) mediated viral entry, indirect damage and impaired turnover of taste cells by localised inflammation, and damage to cells associated with the peripheral and central nervous system. Impaired salivary flow and changes in its composition following viral salivary gland damage has also been proposed as a contributing factor in the taste disruption reported by COVID-19 patients.

Understanding the basis of these sensory disruptions may have broader significance for SARS-CoV-2-mediated disease since several cell lineages expressing taste receptors can be found in the epithelium of the upper and lower respiratory tract and therefore may also be sensitive to disruption. Interestingly, these include solitary chemosensory cells (SCCs) that in the lower respiratory tract are proposed to be involved in modulating the immune response during challenge and supporting the mucociliary clearance of pathogens. In one study, a unique population of SSCs was shown to proliferate in post-influenza virus-damaged lungs, and it would be fascinating to know if a similar process occurs in severe COVID-19 pathology.

To understand the ability of SARS-CoV-2 to infect taste buds and other potentially susceptible oral tissues, initial investigations utilised publicly available databases. The examination of mRNA levels indicated the viral receptor ACE2 to be enriched in several oral epithelial cells, including those associated with the periodontium and the tongue. The salivary glands proved particularly interesting as they appeared to combine significant levels of *ACE2* expression with the transcription of both *furin* and *TMPRSS2*, encoding key proteases that are important for efficient viral entry. Subsequent studies using cell lines and tissue samples from both humans and animals confirmed the presence of proteins that facilitate SARS-CoV-2 infection in a variety of oral contexts. However, although questions remain about the precise amount and accessibility of these proteins for the infection of specific tissue types, the isolation of 10^8 viral particles per millilitre of saliva and the detection of virions in the gingival pocket that surrounds the tooth has confirmed that SARS-CoV-2 has the potential to replicate at several sites within the mouth.

As oral COVID-19 research progressed, the focus shifted to the salivary glands and the secretion they produce, saliva. The oral cavity is serviced by four salivary glands that are composed of a variety of associated cell types including serous and mucous acini, basal epithelial, myoepithelial and neuroendocrine cells. Saliva both lubricates and protects hard and soft tissue, determining key features of the oral environment that impact its colonisation by micro-organisms. Its complex mix of components has been extensively studied and shown to have properties that range from promoting wound healing to controlling remineralisation of the tooth surface and, importantly within the context of COVID-19, a number of anti-viral properties. The associated mechanisms include the secretion of salivary glycoproteins that can act as decoy receptors able to bind to the surface of enveloped viruses and therefore both block cell entry and facilitate clearance from the mouth. This mechanism has been proposed for SARS-CoV-2, with several salivary constituents including mucin-7, mucin 5B and salivary gp-340 reported to bind the spike protein *in vitro*. The direct inactivation of



Key:

- = Acetylcholine (Ach)
- = Ach receptor
- = Noradrenaline
- = β1-Adrenergic receptor
- = Vasoactive intestinal peptide (VIP)
- = VIP receptor
- = G-proteins
- AC = Adenylate cyclase
- cAMP = Cyclic AMP
- PKA = Protein kinase A
- = Protein
- PLC = Phospholipase C
- IP_3 = Inositol triphosphate
- = Calcium-activated Cl^- channel
- = Aquaporin
- = $Na^+/K^+/Cl^-$ co-transporter
- = Na^+/K^+ ATPase
- = K^+ channel
- = Permeable intercellular junction
- = Impermeable intercellular junction
- = Na^+ channel
- = K^+/H^+ ion exchanger
- = Cl^-/HCO_3^- ion exchanger

Salivary gland secretion mechanisms. Dr Alexander Gardner

viral membranes by cationic peptides, including histatins 1, 3 and 5, has not been established for SARS-CoV-2 but it is interesting to note that one of these molecules has been shown to inhibit furin *in vitro* and therefore could interfere with priming of the spike protein. Other salivary constituents such as cystatin S are considered important factors in controlling periodontal disease via their ability to inhibit serine proteases, a feature that has potential implications for TMPRSS2 activity. In this context, it interesting to note that during active periods of periodontal disease a related

protein, cystatin C, can accumulate in the oral cavity, and this molecule has been reported to inhibit the replication of other coronaviruses in tissue culture experiments. Post-infection, the presence in saliva of IgA and IgG antibodies that recognise spike glycoprotein has been reported, with one study recording virus neutralising levels of salivary IgA persisting for up to 73 days post-infection. These antibody results highlight the single most significant anti-viral property of saliva and one which will impact not only possible protection from infection but also the efficiency of onward transmission. However, for context, it should be remembered that all these anti-viral features exist alongside the presence of furin and TMPRSS2 and high levels of calcium, an ion that is involved in the stabilisation of the ACE2 fusion peptide,

At this stage of the pandemic, we still don't understand why sensory disturbance occurs during some infections and not others or how the balance of salivary constituents varies or impacts susceptibility due to age, sex or ethnicity. Similarly, it is not clear how much the relative expression of the viral receptors in the mouth determines susceptibility. What is clear is that from disease to dissemination the study of the oral cavity's response to SARS-CoV-2 infection continues to be an important element in understanding the development of the COVID-19 pandemic.

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Alex studied dentistry at the University of Dundee and spent time working as a general dentist in Glasgow before undertaking a PhD at the Centre for Host–Microbiome Interactions at King's College London Dental Institute. Alex currently works at Dundee Dental School as a clinical lecturer in restorative dentistry.

How did you enter this field?

David: I relocated to the Dental School in Dundee 14 years ago and developed an interest in anaerobic bacteria and salivary components that control colonisation and growth. At the start of the pandemic, the developing story on the loss of taste and smell lead to us forming a small team of cell biologists, microbiologists and clinicians who were funded for a seed project to examine how salivary proteins interfere with the SARS-CoV-2 spike protein.

Alex: My PhD studied salivary metabolite composition and function. Oral bacteria are critical in shaping the metabolite composition of saliva, and the idea of using metabolomics as a functional measure of microbiome activity is a growing area of research.

What do you find most enjoyable about your work?

David: One of the nicest aspects of oral biology is the crossover of interest with material scientists, clinicians, cell biologists and microbiologists. Consequently, it has been an easy environment to set up multidisciplinary groups and, in particular, I have found salivary biology to be an underappreciated and fascinating area of research.

Alex: This is an exciting time for microbiology, and there is a lot of variation every day, so there's no risk of getting bored.

The quest for COVID-19 treatments

Jane Hilton and Catherine S. Adamson

Treatments for coronavirus disease 19 (COVID-19) were not available at the outset of the pandemic caused by severe acute respiratory coronavirus 2 (SARS-CoV-2), which emerged as a new pathogenic human respiratory virus in late 2019 and reached pandemic status by March 2020 (Fig. 1). The urgent need for COVID-19 treatments was quickly recognised, as 5–10% of patients develop a severe disease that requires hospitalisation/intensive care and around 4 million deaths have been recorded by the World Health Organization (WHO) to date.

Scientists around the world rapidly began the quest for effective COVID-19 treatments. In the first instance, efforts focused on clinical trials to test existing drugs in the hope that they could be rapidly repurposed for treatment of COVID-19 patients. Examples of these clinical trials include the UK-led RECOVERY trial and WHO-led Solidarity trial. A small number of treatments have now been deemed safe and offer some therapeutic benefits against COVID-19, and have thus been granted approval or emergency use authorisation (EUA) by regulatory bodies such as the US Food and Drug Administration (FDA). A huge number of other prospective therapeutic agents are currently undergoing investigation as potential COVID-19 treatments.

In this article, we highlight key treatment successes and failures and review different virus-targeted and host-targeted treatment strategies (Fig. 1). We discuss ongoing and future COVID-19 treatment research approaches and perspectives, as despite the ongoing successful rollout of COVID-19 vaccines, effective treatment options will continue to be vital for patients who succumb to serious disease and to tackle the clinical consequences of long-COVID.

Targeting the virus

Antiviral drugs have been successfully developed and used against a handful of clinically important viruses and are an essential approach for viral disease treatment. Typically, antiviral drugs are highly optimised to act against a specific virus by directly targeting a viral component or step in the virus replication cycle. Unfortunately, prior to the pandemic, no specific antiviral drugs had been approved for clinical use against human coronaviruses.

The quickest strategy to identify antiviral drugs to treat COVID-19 is investigation of existing compounds with known broadly acting antiviral activity against a range of RNA viruses including other coronaviruses. The leading candidate fitting these criteria was remdesivir (Veklury), which belongs to the established drug class nucleos(t)ide analogue inhibitors. Drugs in this class target the viral RNA-dependent RNA polymerase, preventing viral RNA genome replication. Laboratory/animal studies demonstrated that remdesivir exhibits anti-SARS-CoV-2 activity, but clinical trials have reported mixed results with respect to its therapeutic effect in COVID-19 patients. Despite this, remdesivir is currently the only directly acting small-molecule antiviral drug to receive FDA approval for COVID-19 treatment. To build on a potentially successful strategy, other nucleos(t)ide analogues are also under investigation, such as favipiravir (Avigan), an antiviral drug licenced in Japan to treat influenza.

The concept of repurposing existing drugs for fast discovery of COVID-19 treatments was also applied to the HIV protease inhibitor lopinavir, based on evidence from laboratory/animal studies that the drug exhibits activity against SARS-CoV and MERS-CoV. Clinically, lopinavir is administered in combination with ritonavir, to boost lopinavir's plasma half-life. Unfortunately, numerous clinical trials demonstrated no benefit from lopinavir–ritonavir (Kaletra) treatment in COVID-19 patients and this line of investigation has largely been abandoned.

A probable explanation for HIV protease inhibitor failures in COVID-19 treatment is their high specificity for the HIV- encoded aspartic protease, whereas coronaviruses encode two cysteine proteases. Protease inhibitors are, however, a highly successful class of antiviral drugs, and both SARS-CoV-2 proteases are considered attractive drug targets as their activity is essential for virus replication. Previous extensive drug discovery efforts targeting SARS-CoV/MERS-CoV proteases, combined with the rapid elucidation of the X-ray structure of both SARS-CoV-2 proteases, provides

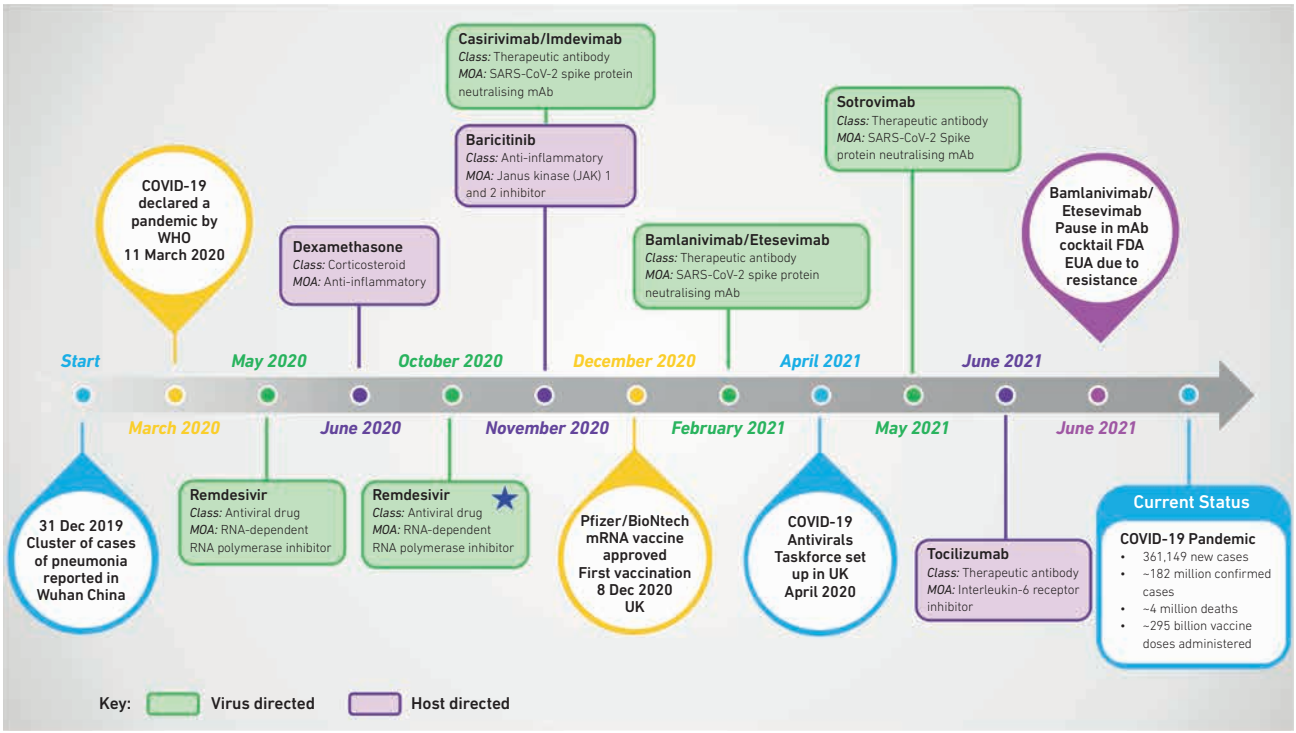
an excellent starting point that is driving a large research effort to develop SARS-CoV-2 protease inhibitors, with multiple lead compounds under active investigation.

In addition to the key RNA-dependent RNA polymerase and protease enzymatic targets, multiple other steps in the SARS-CoV-2 replication cycle are being intensively investigated as potential drug targets. The research effort ranges from highly targeted approaches, such as those briefly discussezd above, to high-throughput screening of large compound libraries. A robust drug discovery research pipeline is essential as there is no guarantee that leading drug candidates currently in advanced clinical trials will ultimately yield a positive outcome.

Safety and efficacy are essential criteria, but several other challenges must be overcome. Time of antiviral treatment is critical and should be as early as possible to halt virus replication before disease progression, as the short therapeutic window for treatment of acute respiratory viruses limits antiviral effectiveness. Ideally, the antiviral drug should be in the form of an oral pill, which can be administered in a variety of settings. Currently, remdesivir can only be given in hospital, as it is administered intravenously due to its poor bioavailability and short half-life, limiting its usefulness. Acquisition of drug resistance is a widely documented challenge in the use of antiviral drugs against RNA viruses and is typically overcome via combination therapy consisting of two or more antiviral drugs with different mechanisms of action.

Antiviral drug discovery and development is expensive and time consuming. However, the magnitude of the COVID-19 pandemic is sufficient to drive the global research effort, financial investment and political will required to deliver effective antiviral treatments with accelerated clinical testing and rapid manufacturing scale-up. For example, in April 2021 the UK government launched the COVID-19 Antivirals Taskforce, which aims to identify at least two effective treatments, either in tablet or capsule form, that the public

Fig. 1. Timeline of COVID-19 Treatments. The timeline depicts key milestones in the COVID-19 pandemic and successful treatments that have been awarded Emergency Use Authorization (EUA) or Approval (highlighted by a blue star) by the US Food & Drug Administration (FDA), with the exception of Dexamethasone, which has been approved for COVID-19 treatment by the UK Medicines & Healthcare Products Regulatory Agency (MHRA). Statistics on the current status of the pandemic were sourced from the World Health Organization (WHO). MOA, mechanism of action; mAb, monoclonal antibody.



can take at home to combat any future increase in infections and limit the impact of new viral genetic variants. The stated timeline is rollout by the end of 2021; it remains to be seen if this ambitious goal can be achieved.

Therapeutic antibodies targeting SARS-COV-2 are being rapidly developed for COVID-19 treatment. The starting point for using neutralising antibodies (nAbs) to treat COVID-19 is the use of convalescent plasma, donated by patients who have survived SARS-CoV-2 infection by producing these protective antibodies. Although the use of convalescent plasma has received an FDA EUA, clinical trial data has been disappointing, along with difficulties associated with standardising the potency of plasma doses. Instead, the development of monoclonal antibodies (mAbs) has proven more advantageous in COVID-19 treatment.

Several mAbs have been rapidly developed and all target the SARS-CoV-2 spike protein, which mediates virus entry via interaction with host cell receptor angiotensin-converting enzyme 2 (ACE2). The vast majority of these mAbs target epitopes within the receptor-binding domain (RBD) of the spike protein. The principal mechanism of virus neutralisation is blocking infection of target cells by antibody binding to the viral spike protein and preventing ACE2 interaction.

Clinical investigation of mAbs has thus far resulted in a small number being granted FDA EUA; at the current time, FDA EUAs exist for REGEN-COV, a combination of two mAbs administered together (casirivimab and imdevimab), and sotrovimab, administered as a monotherapy. Clinical trials are investigating mAbs' effectiveness in different patient scenarios; however, existing EUAs are for the treatment of mild–moderate COVID-19 patients who are at high risk for progressing to severe COVID-19 and/or hospitalisation.

A second mAb combination therapy (bamlanivimab and etesevimab) had its FDA EUA paused in June 2021, due to evidence that both mAbs are not active against certain circulating SARS-CoV-2 genetic variants of concern (VOC). Indeed, several mutations found in VOC have been shown to abolish the neutralisation activity of multiple mAbs. Monitoring the resistance of mAbs to circulating variants will be critical for their therapeutic use and will guide future development strategies.

Targeting the host

The severity of COVID-19 depends on many factors, but a common hallmark of severe disease is dysregulation of the immune/inflammatory response. Immune factors can be impaired or downregulated; a key example is the interferon (IFN) response, a vital part of the innate immune response to counteract virus spread in the early stages of infection. Elevated levels of several proinflammatory cytokines, often referred to as a cytokine storm, is also a signature of severe COVID-19. The consequence of this immune dysregulation is robust virus regulation and inflammatory damage to tissues within the body, both of which are linked to disease severity. Host-targeted strategies are required to relieve the symptoms caused by dysregulation of the immune/inflammatory response, and repurposing of existing immunomodulatory and anti-inflammatory agents has been utilised for the discovery of host-directed COVID-19 treatments.

One therapeutic strategy is the replacement of host factors that have been impaired or downregulated during infection. Administration of purified IFN has been used in the clinic against several viruses, most notably hepatitis C virus (HCV), on the rationale that treatment with this vital cytokine will stimulate the IFN signalling pathway, activating expression of IFN-stimulated genes (ISGs) to induce an antiviral state to block virus infection and spread within the body. Multiple clinical trials are being evaluated for the effect of IFN treatment in COVID-19 patients. To date, the results are mixed and indicate that IFN treatment may only be beneficial for a subset of patients with a minimal IFN response that are treated early in infection.

Another strategy is inhibition of COVID-19 elevated cytokines. IL-6 is one of the signature cytokines that is excessively upregulated in the cytokine storm. Treatment with a mAb (tocilizumab [Actemra]) which binds to the IL-6 receptor, inhibiting IL-6 mediated signalling, has recently been granted an FDA EUA for use in certain hospitalised COVID-19 patients. The Janus kinase 1 and 2 (JAK 1/2) inhibitor baricitinib (Olumiant) in combination with remdesivir also has an FDA EUA for treatment of certain hospitalised COVID-19 patients. JAK 1/2 signalling plays an important role in the cytokine-mediated host inflammatory response to infection and disease.

Early in the pandemic, anti-parasitic drugs chloroquine and hydroxychloroquine were tested as potential COVID-19 treatments. The mechanism of action of these drugs is not clearly understood, but antiviral and immunomodulatory activities have been proposed. In June 2020 the FDA revoked the EUA for these drugs on the basis that they are unlikely

to be effective in treating COVID-19, together with ongoing serious side effects.

Dexamethasone is a corticosteroid that is widely used for its anti-inflammatory and immunosuppressant effects. In June 2020 the RECOVERY trial announced that dexamethasone reduces death by one third in hospitalised patients with severe respiratory complications of COVID-19. Given that dexamethasone is off-patent, cheap and widely available, it provides the capacity for a global treatment option, which is already being translated into saving lives.

Summary

The COVID-19 pandemic has brought into sharp focus our lack of treatments that can be rapidly deployed upon emergence of a new pathogenic virus. A remarkable global research effort is underway to discover, develop, test and manufacture new treatments against COVID-19. The continued success of this research effort is dependent upon sustained financial investment together with coordinated political will to tackle the current COVID-19 pandemic, but also so that we are better prepared for the emergence of the next deadly virus.

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Jane Hilton undertook her PhD in Neuroscience at the University of St Andrews, before transitioning into industry and advancing as a screening scientist in Drug Discovery. In 2020, Jane moved back to academia, working in Dr Catherine Adamson's lab to contribute to the fight against coronavirus at the University of St Andrews.

Catherine S. Adamson

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Catherine Adamson is Senior Lecturer in Molecular Medicine in the School of Biology at the University of St Andrews. Catherine's area of research expertise is antiviral strategies against viruses including HIV and RSV. Catherine is currently the virology lead on multiple interdisciplinary projects to combat SARS-CoV-2/Covid-19. Catherine has been a member of the Microbiology Society for 28 years.

What do you love most about your job?

Catherine: First and foremost, I love biology and science in general. I enjoy the huge variety of work that I conduct on a daily basis and the opportunity to interact with a diverse range of talented colleagues. The real joy of the job comes from learning something new almost every day.

Jane: I feel privileged to work on SARS-CoV-2 in a BSL3 facility and to be part of a multidisciplinary team of physicists and biologists working together to meet the challenge of identifying novel engineered surfaces that could potentially be used to supress the transmission of SARS-CoV-2 in public spaces.

How did you enter this field?

Catherine: I became interested in virology as an undergraduate student. At that time, during the 1990s, we were in the midst of the HIV/AIDS pandemic. I conducted doctoral and postdoctoral research into HIV, and now as Principal Investigator I am conducting research that will contribute to tackling the 2nd major viral pandemic that has affected humanity in my lifetime, the SARS-CoV-2/COVID-19 pandemic.

Jane: During the COVID-19 pandemic, an opportunity became available to work in Dr Catherine Adamson's lab on SARS-CoV-2; I was already interested in virology and the research that was being conducted in Dr Adamson's lab. As a scientist, I was keen to be involved and utilise my skills and experience to contribute to the field of SARS-CoV-2 research.

Improving public understanding of scientific issues on a pandemic scale

Grace Roberts

Most scientists have dabbled in science communication at some point in their careers. Now, in the midst of a pandemic, many of us are doing more than ever. But why do we do outreach? Personally, I find it really fun, but I think it's a really important part of being a scientist. The public has a right to know what we get up to in the lab – particularly if we are publicly funded, (e.g. by government or charities). Another aspect is inspiring the next generation of scientists in order to make sure we will continue to have passionate and creative young people pursuing scientific careers and increasing the diversity in these professions.

A hugely important reason is to increase the scientific exposure and knowledge of our fellow citizens. Sensationalist news stories about science are relatively common, and were even prior to the COVID-19 pandemic. Stories such as the breakthrough of 'three-person' IVF or GM foods have caused many waves, often emotive ones, but the actual science behind these stories is often neglected. If the public had a good understanding of the scientific process or basic understanding of biology, these 'controversial' stories may have seemed less, well, controversial. The more scientific exposure we provide to the public, the better equipped the public will be in making decisions in everyday life – from decisions such as choosing a healthy diet and living more sustainably, to life-or-death decisions like consenting to medical procedures.

The way science has been communicated since the pandemic started has been vastly different from any other time in history. As a 'new' virus, there was very little data available on SARS-CoV-2 and any new data was quickly reported on by the media. The public was watching the science unfold in real time, often including preliminary or non-peer reviewed studies. This led to conflicting information being disseminated, preliminary data being presented as fact and a general sense of confusion around the science of the

Drazen Zigic/iStock

pandemic. In some instances, this sadly led to distrust and fear. I'm going to take two major topics of the pandemic – masks and vaccines – and will discuss how better outreach may have aided the public's understanding of these areas.

Face coverings

Wearing of 'face coverings' became mandatory in indoor public places in the UK in the summer of 2020, with similar mandates appearing in other countries around the world. Prior to this, the public had been advised against wearing face masks for multiple reasons. Understandably, there were concerns that if the public started using masks, there would be further pressures on the availability of PPE for healthcare workers. There were also concerns that wearing masks would provide a false sense of security, potentially inducing wearers to engage in risky behaviours that would increase virus spread. There was also limited evidence that non-surgical masks reduced viral spread – not because this wasn't true, but because this wasn't a particularly widely studied area.

Many studies concerning masks prior to the pandemic were addressing very specific questions, for example efficacy of specialised masks in healthcare settings, or with particular attention to certain diseases (e.g. influenza). In addition, this is a practically challenging area of study due to difficulties in experimental design and ethical concerns of using human subjects.

Early on in the pandemic, due to a lot of pandemic planning being based on the influenza virus, there was a large emphasis on fomite transmission. People were advised to not touch their face, avoid touching surfaces and frequently wash their hands. Although this is sound advice, we now have mounting evidence that SARS-CoV-2 spreads predominantly via droplets and aerosols and, therefore, as we re-entered workplaces, public transport, school and other indoor environments, masks became mandatory.

This dramatic change in policy was met with confusion and, occasionally, anger. Why did the message about masks change so drastically? Simply put, the research showed that it was likely to be beneficial in preventing SARS-CoV-2 transmission.

In the modern world, people want clear cut answers quickly. Scientists were questioned whether they were 'wrong' before on the matter of masks. And if they were wrong on this, what else were they wrong about?

In science, we know that all the knowledge we hold true isn't necessary 'true', it's simply the best explanation we have based on the evidence available to us at the time. When new research comes to light, we change our ideas and theories. Therefore, when data became available that masks were likely to significantly reduce virus spread, the policy changed. If the general public were more familiar with the scientific process, perhaps there would have been less backlash to this particular issue.

Vaccines

I am still, to this day, astounded and impressed that we had approved vaccines in clinical use just over a year after the virus had been identified. The amount of effort put in by huge multidisciplinary teams to realise this goal is astronomical. Yet many people are still distrustful of them.

There is confusion as to why we have a vaccine for SARS-CoV-2, a virus first identified in 2019, but we still don't have a vaccine for viruses we've known about for a long time, e.g. HIV. This, as many readers will be aware, is down to the many complex biological differences between these different viruses; how they spread, infect and evolve. The general public are not virologists, and at the start of the pandemic many wouldn't have known the differences between viruses and bacteria, let alone the many types and pathologies of different viruses. The general public can't be expected to have a profound and deep understanding of virology, but if most had a good understanding of biology in general, these misconceptions and concerns would have been easily mitigated.

A major reason for vaccine hesitancy is the speed at which the vaccine was developed, tested and approved. Most people who don't work in clinical trials research probably don't have a particularly good understanding of the process for a new vaccine approved for clinical use. Clinical trials are often long and laborious, but most of this time is not spent on the actual testing of the vaccine, it is spent liaising with medical staff, recruiting volunteers and applying for further funding for each stage of testing. However, in the pandemic, huge chunks of time were saved by multiple research teams coming together, funding being rapidly approved and a monumental national effort in patient recruitment and clinical coordination. If the public were better informed of how clinical trials are conducted, perhaps this would have alleviated some of the worries people had in terms of the speed at which they have been conducted this past year.

Grace Roberts

Finally, an often-overlooked part of why outreach is important is that scientists are normal people too. Too many people imagine scientists to be eccentric Einstein-types, detached from society. As most readers will know, this is far from true, but it didn't stop a lot of hate being directed at scientists for supporting strict virus-control measures, whether this be abusive comments on social media or fully fledged protests. We have families we want to visit too, pubs and cafes we love to frequent, activities we love to participate in – just because we advised against visiting the places and people we love, didn't mean that we didn't miss these aspects of our 'normal' lives.

For many of us, this pandemic has been a crash course in science communication, but if we had sown the seeds of science outreach further and more regularly, we may have mitigated some of the misconceptions and confusions that arose throughout this global pandemic. Our scientific studies and findings are useless without communicating them outside our research groups. In order to have an impact, we share our findings to the scientific community, through talks and publications, but often no further. Perhaps now is the time we

Grace Roberts

include journalists and the public in this process on a regular basis. Many publications support the inclusion of a lay abstract in addition to the standard scientific one. Some researchers do excellent explainers of their work to the public, such as through Twitter threads, YouTube videos – even colouring books! I personally write articles in *The Conversation*, who publish lay articles for general readers that are heavily utilised by media to report on these stories; *The Conversation* regularly contact the authors for further pieces. In all of these methods, we, the scientists, directly communicate our scientific findings to the public, and with more exposure, we can, hopefully, form a world where everyone thinks more scientifically, and sensibly.

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How did you get started in scientific outreach?

The first time I heard of 'outreach' as a term and a concept was when I was a technician working in cancer pathology in Leeds. Cancer Research, who funded many research projects in the centre, had an annual visit day where any patients who had involvement in the research (e.g. donated tissue samples) could visit the centre for a day of talks and a tour around the labs. It was well received by the attendees, and I thought it was a great idea! Then when I went on to do my PhD, I got involved in outreach through the annual Leeds Festival of Science, which introduces school children to hands-on science, where I helped design and run a stall about microbiology and the importance of handwashing. I loved how what seemed like basic science to me induced such enjoyment and intrigue in young minds. Since then, I've been regularly involved in outreach and have seen its importance in inspiring the next generation, but also informing the general public of scientific research.

What advice would you give to others who want to get started in outreach?

Definitely ask someone who has some experience who can help you develop your ideas. Hands-on experience of what worked well in the past is valuable to designing new outreach activities. When designing a new activity, I think the two most important things to establish are your main message and your target audience. Once you have established your 'main message' for your outreach activity, make sure every aspect of your activity contributes to the communication of the message, regardless of the outreach format. When considering your target audience, it's important to consider things such as the audience's age (which can affect what is appropriate to include in the activity) and prior knowledge of your subject. Importantly, however, never underestimate or patronise your audience – often, I have found non-scientists to be fully capable of understanding vastly complex concepts, they often just lack the technical vocabulary that scientists use every day.

Annual Conference 2022

Monday 4 April–Thursday 7 April 2022

Annual Conference 2022 will see the Society return to its in-person annual meeting format following a two-year hiatus due to the global health crisis.

The Society is delighted to be going back to Belfast and its International Convention Centre that will host the organisation's flagship meeting next April.

Destination Belfast

Belfast is the capital of Northern Ireland and home to the Microbiology Society Annual Conference 2022. Next year's flagship event features an extensive programme designed to cover the breadth of microbiology, as well as professional development sessions, social activities and lots of face-to-face networking opportunities.

Belfast is a city rich in culture and history and is the perfect destination if you're looking to extend your stay. Whether you enjoy historic landmarks, attractions or want to experience some new culinary delights, there is a lot waiting to be discovered. To help plan your visit there are a number of guides, available in different languages, to download on the Visit Belfast website (**visitbelfast.com**).

Popular Belfast attractions include the Titanic Museum, the Alexandra Graving Dock and Belfast City Hall, one of Belfast's most iconic buildings.

Abstracts

Annual Conference regularly attracts over 1,600 attendees for the UK's largest annual gathering of microbiologists. It is designed to cover the breadth of microbiology research and its oral abstracts and posters reflect this comprehensive scientific programme.

Abstract submission for Annual Conference 2022 is now open and the key abstract deadlines are as follows:

Abstracts close:	**10 January 2022**
Notification of acceptance:	**w/c 7 February 2022**

See the event's webpage (**microbiologysociety.org/microbio22**) for further information and specific abstract submission categories.

Registration

Bookings are now open for next year's Conference.

See the event's webpage for further booking details (**microbiologysociety.org/microbio22**).

Early bird discount ends:	**28 February 2022**
Bookings close:	**28 March 2022**

Travel and accommodation

Travel to Belfast is easy and fast. The city is well connected by road, rail and sea transport, and with 2 local airports the city is accessible by air from both Great Britain and overseas destinations.

To support you in securing your accommodation we have provided links to our booking and accommodation services on the Annual Conference 2022 website, where we have secured negotiated rates at hotels to suit a wide range of budgets.

Follow **@MicrobioSoc** on Twitter to keep up with the latest Annual Conference 2022 updates, using the hashtag **#Microbio22**.

ICC Belfast

FIS 2021

5 November 2021 and 8–9 November 2021

The British Infection Association (BIA) is hosting the Federation of Infection Societies 2021 Annual Conference (FIS 2021) in Manchester (5 November) and online (8 and 9 November 2021).

FIS is the largest gathering of the UK infection community and includes societies, groups and individuals who are interested in all aspects of infection, from basic science and clinical infection to infection prevention and control.

The two online dates (8–9 November) will include sessions hosted by the Microbiology Society:

- Future Proofing Antibiotic Resistance: Alternatives to Antibiotic Discovery
- Understanding Emerging Biocide and Antibiotic Co-resistance

Have you got an idea for a Microbiology Society event?

Our busy programme of activities is developed from event proposals from the Society's members and we're currently calling for suggestions for our events programme in 2023 and beyond. All Society members are invited to submit proposals covering any topic relating to microbiology, which will be considered by the Scientific Conferences Panel.

Visit **microbiologysociety.org/events** to find out more.

Focused Meetings 2022

Following disruption to our Focused Meetings programme due to the COVID-19 pandemic, the Society is planning to organise one of its most ambitious and varied meetings programmes in 2022.

The schedule will feature a variety of in-person meetings that were scheduled to take place in 2020 and 2021, alongside some newly planned meetings, covering the depth and breadth of microbiology.

Microbial Cycling of Volatile Organic Compounds

7–8 February 2022
John Innes Centre, Norwich, UK

The first Focused Meeting of the year will bring together those working within the field of biogenic volatile organic compounds (BVOCs). The meeting will address recent advances in the field of BVOC microbiology, such as the discovery of new degradation pathways, the role of BVOCs in inter- and intra-species signalling, new techniques to explore the volatile metabolome and synthetic biology approaches to create novel BVOC biosynthetic pathways.

Europic 2022

5–9 June 2022
Harrogate Majestic Hotel & Spa, UK

Europic is the world premier virology conference that focuses on studies of picornaviruses, a family of important human and animal pathogens including enteroviruses (e.g. poliovirus, rhinoviruses, EV-A71, EV-D68), hepatitis A virus and foot-and-mouth disease virus, as well as many other viruses whose number is growing by the day with new discoveries.

The Microbiology Society is delighted to be hosting the meeting in 2022 to bring together the international community to hear about the latest advancements in the field of picornaviruses and enjoy numerous networking opportunities to help strengthen relationships within the scientific community.

What's New in Cryptosporidium?

4–5 July 2022
Swansea University, UK

Cryptosporidium is the most common parasitic cause of gastroenteritis in the UK and one of the most important contributors to the burden of childhood diarrhoea morbidity and mortality globally.

This one-and-a-half-day meeting will provide an opportunity to those working in clinical, industrial, veterinary and agricultural settings to hear about advances in the field. The event will share good practice and establish collaborations with others across science, industry, environmental health and clinical and veterinary practice.

British Yeast Group 2022: From Genomes to Cells

Date to be confirmed
University College London, UK

Yeasts are very versatile, model unicellular eukaryotes that have been extensively used for over a century to explore fundamental aspects of living systems. Annual gatherings of the British yeast community have taken place since the 1980s, and the Microbiology Society is pleased to be incorporating the BYG meeting in its Focused Meeting Programme for the fifth time next year.

The programme will incorporate a broad range of talks from invited speakers and will provide plenty of opportunities for early career researchers to present their research through posters and offered oral presentations.

The meeting will include a varied social agenda providing opportunities to make new connections and strengthen the yeast community in Britain and beyond.

Cell–Cell Communication in Bacteria – Fundamental and Applied Aspects

28–30 June 2022
University of Cambridge, UK

Communication between single species and within polymicrobial communities has profound impacts on host–microbial interactions in the context of health and disease and its understanding offers diverse translational opportunities in medicine, agricultural and industrial contexts.

The Cell–Cell Communication in Bacteria (CCCB) Focused Meeting will bring together a multidisciplinary audience of microbiologists, structural, systems, evolutionary and synthetic biologists, mathematicians, chemists, biochemists and ecologists. The event will provide a vital forum for the dissemination and exchange of new information and will look to foster the next generation of scientists working within this area.

Genomes of Microbiomes

Date and venue to be confirmed

The field of microbial genomics is progressing rapidly and has attracted growing interest within the research community of microbiologists. This meeting will bring together an audience of researchers who are keen to hear about how advances in sequencing technologies and computational methods can be best exploited to understand the microbial world.

This meeting will provide a forum for the discussion of the impact of metagenome-assembled genomes (MAGs), including how they should be incorporated into public databases. It will focus on metagenomics advances and the contributions technologies are making toward more readily achieving complete microbial genome sequence assemblies.

Mining the Microbiome for Antimicrobials and New Therapeutics

Date to be confirmed
Venue to be confirmed, Ireland

With the emergence of antibiotic resistance and the decreasing effectiveness of antibiotics, there is growing interest in the potential of mining the gut microbiome for new antimicrobials.

This Focused Meeting will provide an insight into the current state of research on the exploration of the interactions between the gut microbiota, pathogens and the mucosal immune system in the search for new alternatives for the treatment of infectious disease.

Protein Secretion at the Host–Pathogen Interface

Date to be confirmed
Queen's University Belfast, UK

Bacterial infections remain one of the top causes of human suffering and death globally and have a huge economic impact on agriculture and animal production. The ability to cause disease of nearly all important bacterial pathogens depends on secretion systems, which deliver virulence factors to the surface or directly into host cells, where they modulate host processes to the benefit of the bacteria. There have been plenty of new scientific discoveries pushing our understanding of the molecular basis of host–pathogen interactions to new levels, and this meeting has been organised to foster the exchange of information, networking and new collaborations across the research community.

Understanding and Predicting Microbial Evolutionary Dynamics

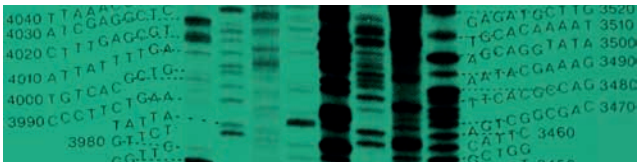
Date and venue to be confirmed

This Focused Meeting will bring together leading researchers working on microbial evolution from across varied disciplines, including infectious diseases, genomics, environmental microbiology, biotechnology and mathematical modelling.

It has been designed to provide a unique opportunity to allow this multidisciplinary community to identify the common themes and shared approaches for understanding and predicting microbial evolutionary dynamics across these diverse systems and applications.

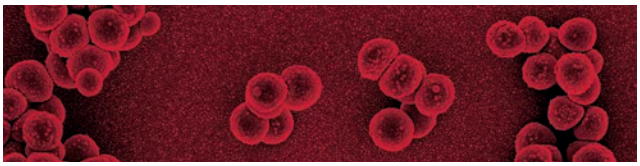
Scientific Seminar Series

The Scientific Seminar Series is designed to reach a priority microbiology community to support it in disseminating knowledge across its professional networks. The events are designed as a regularly repeated series of short (typically 1–2 h) online meetings.



Microbial Genomics Seminar Series

This monthly seminar series from *Microbial Genomics* will bring together the community of microbiologists using genomic approaches to discover more about viruses, bacteria, archaea and microbial eukaryotes. Centred around the journal's key section areas, this series will highlight the latest research in Microbial Communities, Pathogens & Epidemiology, Genomic Methodologies, Functional Genomics, Microbe–Niche Interactions, and Evolution and Responses to Interventions, and provide a forum for networking and exchange of knowledge.



JMM Seminar Series

A monthly seminar series from the *Journal of Medical Microbiology* (JMM) that is designed to disseminate high-quality and timely research from the journal's key authors. JMM is the go-to interdisciplinary journal for medical, dental and veterinary microbiology. It welcomes everything from laboratory research to clinical trials, including bacteriology, virology, mycology and parasitology.

Further details and information on how to register to participate in the Scientific Seminar Series can be found at **microbiologysociety.org/ScientificSeminarSeries**.

Roadshow 2020 and 2021: an opportunity to meet our President, Professor Judith Armitage

Following the success of the President's Roadshow events held in-person since 2019, which brought local communities of microbiologists together, in 2020 we moved them online to offer microbiologists in several local areas the chance to virtually meet each other and listen to our President, Professor Judith Armitage, talk about her career journey. The President took delegates through her achievements and great moments, but also provided examples of challenging situations that she had to overcome.

The first two Microbiology Society Online Roadshow events were held in Manchester, hosted by Dr Chloe James, University of Salford; and in Cardiff, chaired by Dr Helen Brown at Cardiff University. We continued this into 2021, successfully running a virtual Roadshow in Norwich in May, led by Professor Lindsay J. Hall, from Quadram Institute Bioscience.

> The stories of Professor Armitage were very interesting and a perfect example of persistence in science. It is an example of how to have a great career.
>
> I enjoyed the question and answer session, as I like the spontaneity of the speaker's ideas. The format and timing was great.
>
> *Dr Teagan Brown*
> *Postdoctoral Researcher, Quadram Institute Bioscience, UK*

All of the virtual Roadshow events received positive feedback, highlighting the great opportunity that they provided for attendees to network with microbiologists in their local area, and how inspiring it was to hear about our President's career. It was great to see members from around the world drop in to the calls too – an unexpected benefit of moving online. Some of those that attended commented that they found the Roadshow event to be a great opportunity to find out about how they can be more involved with the Society and to talk about the issues they are currently facing in their careers.

Take a look at what our delegates have said about the Roadshows:

> It was a great forum, and the talk was excellent.
>
> *Dr Melissa Lawson*
> *Postdoctoral Scientist, University of Manchester, UK*

To find out more about the Microbiology Society Roadshow, visit our website at **microbiologysociety.org/roadshow**.

How can you increase the rigour and transparency in your research? Submit to our open research platform

Over the past year during the pandemic, there has been a complete overhaul of the way research is undertaken and shared. Researchers need to rapidly share their work, often before publication, and are increasingly being required to share the underlying results of their research too.

This has put the open science agenda at the forefront for the Microbiology Society, and we recognised the need for a trusted place for researchers to disseminate their work rapidly, rigorously and transparently. Using a grant awarded by the Wellcome Trust and the Howard Hughes Medical Institute (HHMI), the Microbiology Society is converting our sound science, Open Access journal, *Access Microbiology*, into an open research platform. The platform will launch and be open for submissions at the beginning of 2022.

How will the platform work?

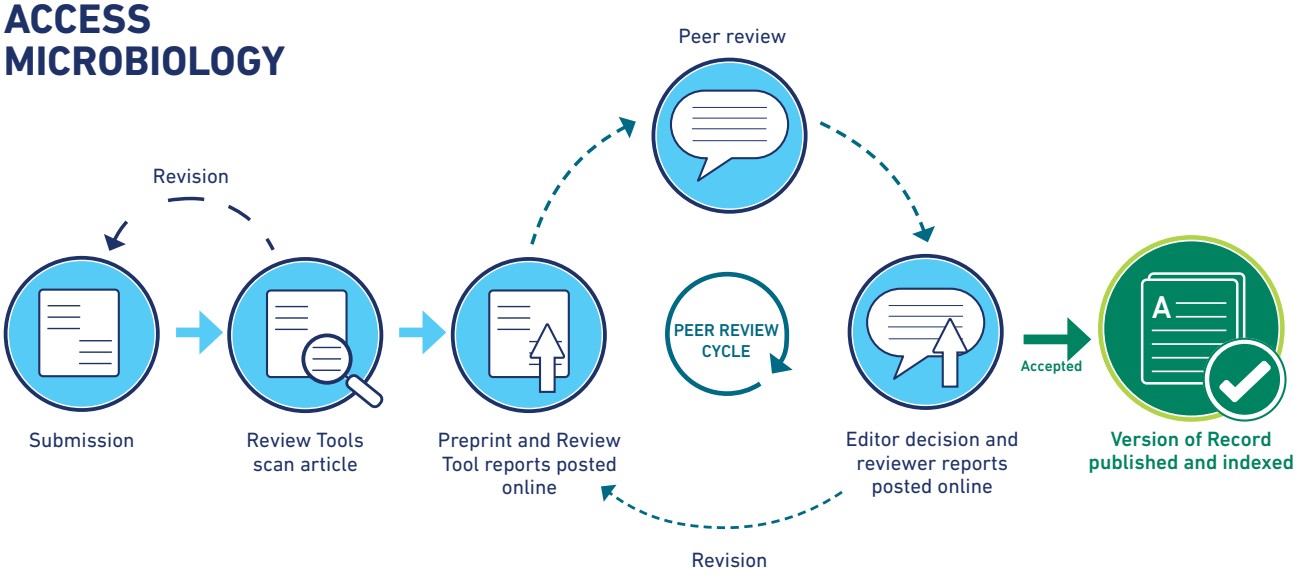
The *Access Microbiology* open research platform will become a home for the entire life cycle of an article, from the author's very first preprint all the way to the published Version of Record. Authors will submit to our peer review system as usual and will be given the opportunity to improve their article using feedback from three manuscript review tools, Penelope.ai, SciScore and iThenticate. Once the authors are happy with their article and it complies with the platform's ethical and editorial policies, the article is posted online as a preprint with a digital object identifier (DOI), giving authors the opportunity to start to receive community feedback on their work. The reports from the manuscript review tools will also be posted alongside the preprint, allowing readers to perform their own 'health check' on the preprint prior to completing peer review. In an effort to increase the rigour and reproducibility of the research, the platform will adopt an open data policy, so all articles will include links to open data, code and methods, allowing readers to access the underlying data of the work.

Meanwhile, the preprint is assigned to an Editorial Board Member (EBM) and will undergo full, transparent peer review. We recognise that reviewers might not always want to put their name to their review, so whilst the content of all reviews will be posted alongside the article, reviewers can choose to remain anonymous if they wish. Once the Editor makes their recommendation, the reviewer reports and Editor's decision and comments will be posted online. Reviewers can therefore receive public recognition of their work, if they wish, and readers can assess these reviews themselves, promoting trust in the publishing process. Articles that are considered acceptable for publication will then be fully typeset in our platform style and branding, published on the platform in full-text HTML and PDF, and deposited in PubMed, the open access repository PubMed Central, and other indexing services.

What are the benefits over traditional journal publishing?

There are various unique and innovative aspects to the platform that mean authors will benefit more than if they were to submit to a normal preprint server and journal. Firstly, during submission authors can choose to receive immediate feedback from three manuscript review tools (**microb.io/3fwM79o**) and revise their article based on these before it is posted on the platform as a preprint.

Penelope.ai can be used prior to submission to ensure the article complies with the platform's ethical guidelines and policies. Running an article through this tool means authors are far less likely to miss key requirements and have their article returned to them at the very first hurdle. During the submission process, SciScore scans the methods for a variety of rigour criteria which have been shown to contribute to the reproducibility of research. It also detects elements such as sequencing data, plasmids, cell lines and software tools, and assesses how uniquely identifiable and accessible these are. These are elements that authors can easily include but may not have been trained in the importance of, and as such their work is less reproducible. Lastly, iThenticate scans the



article for language, picking up on text that may have been unknowingly reused from previously published work. Our testing of this tool identified that a surprising number of authors do this, but it is easily rectifiable, and making these changes will improve the originality and scholarship of an author's work.

A second unique advantage of our platform is the single location of all your article versions. Whilst many authors' articles are posted on a preprint platform and subsequently published on a separate journal website, all preprint versions and the final published article will be together in one location on the *Access Microbiology* platform, with clear and easy links to navigate between them.

What do I need to know for the launch?

The funding from Wellcome Trust and the HHMI means that it will be completely free for authors to post and publish for the first 12 months after launch at the beginning of 2022, so we encourage early submission to take advantage of this. The sound science nature of the platform provides microbiologists with a place to publish all their work, as long as it is related to microbiology and the work is sound. We welcome any original research (including null, negative and replication studies), descriptions of large datasets, case reports, a new tool or code used to help researchers in their research, or even the description of a useful technique used in microbiology teaching or outreach. To read more on why sound science research is important and the types of research the *Access Microbiology* platform will publish, read our recent blog on Microbe Post (**microb.io/3d2ONLw**).

We are living in a fast-paced and ever-changing period, and the Microbiology Society is embracing this with the *Access Microbiology* platform in the hope that we can provide a unique, transparent and trusted place for our community to publish their work.

Alex Howat
Open Research Platform Project Manager

a.howat@microbiologysociety.org

jakkaje808/iStock

Scaling up Publish and Read

"*Charting the progress of our journals as they transition to more Open Access (OA) has been fascinating,*" says Gaynor Redvers-Mutton, who is leading the business model transformation underpinning the Society's publishing programme from subscriptions to a Publish and Read model, "*and the next three years will be key in determining whether the route we have adopted will fly globally, as it has done in the UK and Australia/New Zealand since first piloted in 2020.*"

The Society's OA business model, created in collaboration with other membership organisations that formed Society Publishers' Coalition, is a unique way for institutions to repurpose subscription spend. Offering researchers from a Publish and Read institution unlimited OA publishing and full access to all content on the platform, the model removes the administration involved in similar commercial models that operate paydown funds and article processing charge (APC) discounts.

Pilot years (2020–2021) enabled us to listen to customers, learn how to deliver Publish and Read and, crucially, gave us time to develop the model so that it could be extended beyond the early adopter institutions and consortium groups. The London School of Hygiene and Tropical Medicine, for instance,

Society Publishers' Coalition

Unlimited Open Access

offered this feedback: "*All institutions should try using P&R deals as opposed to just read only deals* ***if they can afford it****. It increases the amount of research which isn't closed off behind paywalls*." This new phase in Publish and Read addresses a key obstacle that many of our subscribers face in a budget climate impacted by the pandemic.

From 2022, Unlimited Publish and Read will be offered to a broader range of subscribing institutions with a tiered structure to help bridge the gap from current subscription spend to Publish and Read. Allowing for a period of adjustment to the new model, re-tiering according to article output will be introduced using a transparent formula designed to smooth out peaks and troughs in research output. By doing this, we hope to avoid any yo-yoing between tiers and provide greater budget predictability for our librarian customers.

Why are we doing it and why should you care?

As the subscription business model continues to crumble and the tidal wave of Open Science initiatives carries us along to a new future, the Society will prioritise the following areas:

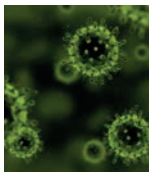
- Ensuring the quality and relevance of the research it publishes on behalf of its community.
- Putting its full force and energy behind the most inclusive OA business model of all those that we've reviewed and analysed – one that removes the burden of publication costs from researchers.
- Working proactively to make the new model a success through outreach to researchers.

The publishing programme has financially underwritten many great activities – events, grants, prizes and professional development resources – that the Society undertakes on behalf of microbiologists. A key objective in pursuing more OA is to maintain our muscle power to provide these resources: it's a win-win for authors looking to make an impact with OA and support their community. Publishing in one of the Society journals will throw weight behind our OA transformation. This is how you can support us in this:

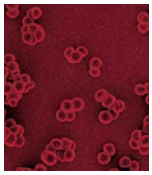
- Take advantage of the benefits of Publish and Read if in participating institutions.
- Ask your library to sign up if in non-participating institutions.
- In either case, publish your research in Society journals and on the new open research platform.
- Spread the word to colleagues.

Publishing for the community
microbiologyresearch.org

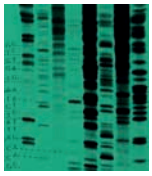
MICROBIOLOGY
mic.microbiologyresearch.org
#MicrobioJ



JOURNAL OF
GENERAL VIROLOGY
jgv.microbiologyresearch.org
#JGenVirol

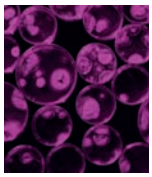


JOURNAL OF
MEDICAL MICROBIOLOGY
jmm.microbiologyresearch.org
#JMedMicro



MICROBIAL GENOMICS
mgen.microbiologyresearch.org
#MGen

INTERNATIONAL JOURNAL OF
SYSTEMATIC AND EVOLUTIONARY MICROBIOLOGY
ijs.microbiologyresearch.org
#IJSEM



ACCESS MICROBIOLOGY
acmi.microbiologyresearch.org
#AccessMicro

We hope that you're finding these articles useful. If there is a topic you would like us to address, email us at **journals@microbiologysociety.org**.

Equality, diversity and inclusion at the Microbiology Society

One of our core values is that we are welcoming to anyone interested in microbes, their effects and their uses. Diversity is important – it brings different perspectives and creativity to what we do. Over the years we have paid attention to our membership's gender diversity and, thanks to the efforts of all decision-making groups, the representation of women has improved and now reflects the wider membership. It took a lot of hard work from organisers and decision makers to do this, paying consistent attention to many things including invited speakers and Prize nomination processes to ensure they were as fair as they could be.

Since 2018, we have asked members to anonymously tell us about themselves. This helps us to paint a picture each year of who is a member of the Society, and the results help us to determine if the Society's activities properly reflect the community it represents. From that point, we expanded our data collection to ethnicity, disability and career stage, and in 2021 we started to ask members if they identified as LGBTQIA+, as we know that there is far more to diversity than gender. In addition to this annual survey, we welcome suggestions from members on more specific surveys; in late 2020, Champion Michael Pascoe led a survey asking LGBTQ+ members what more the Society could do to support them.

These insights have allowed us to put measures in place across all our activities to make them as welcoming as possible. In addition to specific welcoming efforts at all our events including nursing rooms, childcare, prayer rooms, accessibility improvements and support grants for members with any caring responsibilities, we have introduced the Council and Committees Shadowing Scheme as we know our decision-making bodies do not reflect the wide diversity of our membership. We introduced a Code of Conduct to protect members and ensure everyone is aware of the Society's values and our expectations of participants in Society activities. We partner with other organisations to hold ourselves accountable and ensure we are working together as part of the wider scientific and publishing communities.

While we are proud of how far we've come since 2013, we know that there is so much more to do and progress takes time and effort. We want to make sure we are accountable to you, our members, on how we can be inclusive to all with an interest in microbes. So, we have established a new Members Panel, to bring the voice of our members even closer. We invite members from under-represented groups and those who are allies who want to make a real difference to the Society's efforts to be more inclusive to join the Members Panel.

We are committed to the continuous process of improving inclusion and we hope that by getting more members involved, we can ensure our thriving membership feels welcome in everything we do.

Representation (%) of women at the Society across membership, Council, Divisions, Committees, Editorial boards and Annual Conference (AC) Speakers. Marker lines for 33% and 50% are provided for comparison.

To find out more about equality, diversity and inclusion at the Microbiology Society, including data for 2020 and information on how to join our new Members Panel, please visit **microbiologysociety.org/equality-diversity**.

Spotlight on Grants: International Development Fund

The International Development Fund offers support to assist microbiologists in countries with low-income or lower-middle-income economies.

2020–2021 Biomedical Science Undergraduate Students at Mzuzu University. Okazaki Graphics, Malawi

Earlier this year, Pizga Kumwenda organised diagnostic training for students at Mzuzu University, Malawi. Pizga was already working at the university, in the Medical Microbiology department, before coming to the University of Birmingham, UK, to study for a PhD. Due to the COVID-19 pandemic, Pizga returned to Malawi to write up his thesis, and during this time he ran an outreach project to help level 3 biomedical sciences undergraduate students develop practical skills in clinical microbiology.

The aim of the training was to provide the students with a general understanding of medical microbiology that they could then apply when learning how to practically isolate and identify bacterial and fungal pathogens from clinical samples, performing antimicrobial susceptibility testing and interpreting results. In addition, students learned about aseptic techniques, lab safety and quality assurance, as well as how to collect and process microbiology samples.

Pizga noted that "most of our graduates in biomedical sciences go to work in government and private hospitals as laboratory technicians, hence the skills gained will be of great use in clinical microbiology departments. Apart from limited resources, most hospitals in Malawi do not offer routine culture and sensitivity testing because of inadequate skills. Hence this project will at least try to address this challenge."

> The highlight of the project was to see students confidently demonstrating what I taught them.

Going forward, Pizga hopes that the resources that remained after the training will be used to support new students. The university is currently considering integrating similar training into the clinical microbiology course curriculum in the future.

Applications for the International Development Fund open twice a year, in January and June, with deadlines in April and October, respectively. To find out more about the wide range of grants available to support Microbiology Society members, visit the grants area of our website (**microbiologysociety.org/grants**).

Careers Focus: careers in SARS-CoV-2

During recent times, the importance of microbiologists in society and the impact of their contributions to the overall health of the wider community have become clearer than ever. As we have begun to move forward from the COVID-19 pandemic, we interviewed our members to see how they have been involved, demonstrating the diversity of microbiology-related careers.

Lindsay Broadbent, from Queen's University Belfast, is a Wellcome Trust Institutional Strategic Support Fund (ISSF) Fellow researching respiratory viruses. As well as working on SARS-CoV-2, looking at virus–host interactions and drug repurposing, Lindsay works to educate the public through outreach and media engagement.

What was your role during the pandemic?

Outside of the day job, I have been doing a lot of outreach and media about COVID-19. My first media appearance was in February 2020 and I have now taken part in over 1000 media appearances (or syndications).

How did your career path lead you to this role?

I have been involved with science outreach throughout my career. Before 2020, that mostly involved science festivals and school events, but now I do much more general science communication (although events with kids are still my favourite – they ask the best questions!). I turned down a lot of the media requests that I received at the start of 2020. I was worried I wouldn't be taken seriously because I am not a professor, but it was actually a journalist that told me that was a good thing – they wanted a variety of voices discussing the pandemic.

Can you describe a typical day/activity related to this role?

First, coffee! Then I have my day job as a scientist to think about: planning and carrying out experiments, writing papers, helping students, teaching, meetings. Throughout the day I get phone calls or emails from media producers asking for my availability. Our Communications Department at Queen's is

fantastic – if things get too much, they help manage the requests I receive.

I reply to the producers to figure out what their story is. If it is something I am unable to comment on I will suggest a colleague with the right expertise. I'll then set aside half an hour to make sure I am up to date on the current facts and figures, and any other relevant infomation that could be useful. I usually spend two minutes before the interview walking around my office to get rid of the nervous energy!

What do you most enjoy about this role?

On a more personal note, I have received some very kind letters and emails from people thanking me for my contribution to science communication. Including someone that told me her daughter now wants to be a virologist!

What is one of the most challenging aspects of your engagement activities?

Without a doubt, social media has been one of the hardest aspects of science communication over the past year and a half. Social media can be such a useful tool to communicate with a lot of people, but the more you engage with people the more you will experience the downsides of sites such as Facebook or Twitter. There have been times I have had to take a break from Twitter for my own mental health. I am learning to deal with it much better; a combination of blocking abusive accounts and laughing at some of the ridiculousness!

At the start of the pandemic, Andrew Bosworth, now a Senior Clinical Scientist at University Hospitals Birmingham, was undertaking training in microbiology as a pre-registration clinical scientist. Andrew later moved into clinical virology to assist with providing routine clinical services whilst continuing his research into dangerous viruses.

What was your role during the pandemic?

I was temporarily state registered while still in training, and suddenly found myself as the first point of call for hundreds of doctors arranging testing for their patients at a time where lack of information became a real problem in the health service. We were all learning on the fly. I worked with the University of Birmingham, supporting research and development (R&D) activities to develop new diagnostics for COVID-19 and to develop surge capacity across Birmingham. Later in the pandemic I completed my training, becoming one of the few virologists at my NHS trust in Birmingham, helping to set up rapid testing laboratories in emergency departments, and developing new services for COVID testing. My work during the pandemic on new test development led to being approached by Test and Trace to join the national Technologies Validation Group, providing input and support to the validation and roll-out of new tests of every shape and form.

How did your career path lead you to this role?

My first job was as an Anthrax Research Scientist at Porton Down, working for the then Health Protection Agency. I then joined the Rare and Imported Pathogens Laboratory, helping to diagnose dengue virus infections, chikungunya, scrub typhus and of course highly dangerous viral haemorrhagic fevers (VHF), such as Crimean-Congo haemorrhagic fever and Ebola virus. I had the opportunity to be deployed alongside

many colleagues to West Africa, working for Public Health England (PHE) and the World Health Organization (WHO) to diagnose patients in the field for the Ebola virus. I completed a PhD focusing on the biology of the Ebola virus before moving into Clinical Scientist training. Since working in the NHS, I have continued to be involved in research into dangerous viruses.

What do you most enjoy about your role?

I enjoy how varied my role is. It is a mixture of developmental, educational and clinical responsibilities, with room to explore my own scientific interests. I also enjoy seeing patients' health improve because of the clinical advice given, and seeing patients receive the care they need because of the testing our laboratory performs. A safe and effective NHS service relies on the work of thousands of scientists and technicians.

What is the most challenging aspect of your role?

A key aspect of the role is being required to make some quite important decisions with sometimes unclear, unavailable or incomplete information. This can have significant impact on patients and it can be stressful under pressure.

The pandemic has mobilised microbiologists and demonstrated the need for their expertise and knowledge throughout the journey to pandemic recovery. We must emphasise the importance of microbiologists in society more to inspire the next generation of scientists.

For more interviews with those working in the field of SARS-CoV-2 and COVID-19, visit our SARS-CoV-2 and COVID-19 hub (**microbiologysociety.org/covid19hub**).

Early Career Microbiologists' Forum update

Welcome to the October Early Career Microbiologists' (ECM) Forum Update. Firstly, an introduction from me. I'm Rebecca McHugh, a Postdoctoral Researcher from the University of Strathclyde. I will be taking over the writing of our ECM Forum updates from Robert Will, as his time on the ECM Forum Executive Committee comes to an end. On behalf of the ECM Forum, I would like to thank Robert for his excellent contributions over the previous years.

Rebecca McHugh

This period saw a significant milestone for the Microbiology Society holding its first virtual Annual Conference. The meeting was a great success, with large numbers of ECMs contributing to the conference in a variety of ways, including posters and some outstanding offered oral presentations. The committee was involved in organising the ECM workshop titled 'Coping with the pandemic'. This session was organised by the Virology Division in response to the concerns of many ECMs about the impact of COVID-19 on their research careers. Some of the concerns raised included the lack of funded extensions, reduced productivity and 'gaps' in publication records. Although the solutions to these problems remain complex, feedback from ECMs indicated that having a platform to discuss their issues with other ECMs and panel members was beneficial overall.

ECMs were also encouraged to complete the Society's survey to determine the impact of the pandemic on early career researchers, and they responded in large numbers. The Microbiology Society will launch a position statement and action project intended to address the effect of the pandemic on ECMs. As a committee, we have been working with the Society to ensure that the feedback provided by our members is at the centre of these plans. If you are struggling with the effects of the pandemic and need someone to talk to, you can find a comprehensive list of organisations here on the NHS website (**nhs.uk/conditions/stress-anxiety-depression/mental-health-helplines**).

As the UK and Ireland's vaccination programme has made significant progress, we are beginning to benefit from a little more normality. Behind the scenes, the ECM Forum Executive Committee has been working hard to develop our events programme for the coming year. We are hopeful

PrathanChorruangsak/iStock

that this will involve the continuation of the annual ECM conference, with some smaller training events online. We look forward to Annual Conference 2022 going ahead in person in Belfast next year, while also ensuring that we maintain some of the accessibility benefits associated with this year's Annual Conference.

Finally, thanks to everyone who contributed to the ECM Forum events during this years' Annual Conference, and to those who continue to interact with our forum. Your participation allows us to be the voice of ECMs within the Society so please keep getting involved. Thanks again, stay safe everyone!

Rebecca McHugh
ECM Representative for Impact and Influence Committee, ECM Forum Executive Committee

Donate to the Unlocking Potential Fund

This year, the Society launched its first fundraising campaign after feedback from our community. The campaign aims to fund a new grant, called the Unlocking Potential Grant, to help members progress in their careers and reach their full potential. This is a call to those in our community who are in a position to help others, to support those who would benefit from the interventions this grant would enable.

Our members have said that there is more we could do to support their professional development, to ensure that they are enabled at key points in their career. Our existing grants programme already provides support, but the Society recognises the wide variety of issues many members face in their professional lives and bespoke support addressing a specific need could be vital to help a member succeed. The pandemic has added to the pressure many of our members are facing. Microbiologists are stretched within their place of work or study, with less contact time and with fewer opportunities for guidance and support. Members in the later stages of their careers have also said they would like a way to give back and support others to progress:

> "In 1952 I was awarded a State Scholarship and later a Research Studentship from the Department of Scientific and Industrial Research (DSIR), I won a State Scholarship to pay the fees to go to College [Royal College of Science, now part of Imperial College London] and had fantastic teachers and facilities. I had opportunities to go to labs at Rothamsted Experimental Station, John Innes Horticultural Institute and DSIR Ditton. I would like others to have the same opportunities to go to labs to learn from other scientists, as working in these labs broadened my experience. I also went to conferences and finding out about the work of others helped me decide where to take my career." *Dr Martin Cole, Society member since 1961*

> I would like others to have the same opportunities to go to labs to learn from other scientists, as working in these labs broadened my experience.

The Unlocking Potential Grant will be used to support members who may face barriers to career progression for a variety of reasons. Overcoming certain issues requires a variety of routes to the right support. It may be in the form of a careers coach, resilience expert, or mentor or it may be a career development package. Whatever form it takes, it will be tailored to the grant recipient and unique to their needs. The grant will:

- help those facing issues of confidence
- provide mentoring/partnering support
- give access to career support
- support those with leadership potential to achieve their goals
- support those facing workplace issues associated with discrimination, access, bullying, or other related issues
- support with other issues that require bespoke help

If you are in a position to give back, consider donating to the Unlocking Potential Fund fundraising campaign. Help early and mid-career members to get the support they need to move forward.

Find out more about the fund and how to donate on our website (**microbiologysociety.org/UnlockingPotentialFund**).

The coronavirus crisis: how are early career microbiologists impacted?

A recent survey conducted by Vitae and the Student Mental Health Research Network highlighted that around two-thirds of early career researchers (ECRs) are very worried about their future and finances, with only 10 per cent of those whose contracts end in 2020 having been granted extensions in the context of the pandemic.

In June 2020, the Microbiology Society ran a series of focus groups bringing together ECRs in the UK and Ireland to consider the impact of the coronavirus pandemic on their careers and opportunities to bring about culture change. Inputs from these discussions and recommendations for funders and policy-makers will soon be articulated in a position statement. In this article, we hear from three members of the Microbiology Society about the challenges they have been facing since the pandemic started.

Rebekah Penrice-Randal started her PhD in 2018 evaluating the impact of therapeutic mutagens on viral replication using reverse genetic systems *in vitro*. Her work evolved into working on clinical samples from patients with MERS-CoV in Saudi Arabia, where she was part of a research group that designed an amplicon sequencing approach compatible with Oxford Nanopore technologies to facilitate phylogenetic and genomic surveillance studies. When the pandemic started, the group were involved in setting up containment level 3 facilities to receive clinical samples

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Goran13/iStock

from COVID-19 patients for the investigation of the host response and viral evolution through sequencing methodologies. Rapidly, the COVID-19 research response became a full-time endeavour during which a shift occurred from independent research to team science. Projects that may have taken an individual months to complete were now being achieved in weeks. Despite enjoying the intensified collaboration with colleagues, Rebekah is unsure how this shift will translate into the future; will the collaborative efforts be maintained and will coronavirus researchers be expected to continue working with this level of urgency? These questions, amongst others, have led to what she describes as "ECRs feeling stretched, unsure and working through imposter syndrome". Rebekah also highlights that the pandemic facilitated the abandonment of many research projects that had a successful trajectory and that it is important for those who hire and fund ECRs to recognise the impact that the pandemic is having on researchers' lives and careers.

Dr Sariqa Wagley is a postdoctoral researcher and Co-Principal Investigator on a BBSRC–Industry partnership award on bacterial dormancy. In March 2020, Sariqa had nine months of grant funding left and was forced to abandon her experiments that had taken months to set up. Since then, she has faced a number of challenges. For example, by the time she was allowed back in the lab, staff allocated on the project had moved on to other positions due to the uncertainty around whether grants would receive a extension. Despite receiving a no-cost grant extension eventually, Sariqa was left to carry out the lab work alone: "a lack of research jobs and funding has meant that postdocs around me have had to take technician or lower-salaried posts". Lab restrictions also meant that she had to work in short blocks of time and only carry out a few key experiments with the constant threat of another lockdown being announced. Prior to the pandemic, Sariqa had been advised to publish to support fellowship applications. Whilst lockdown gave her an opportunity to write and publish manuscripts, her application to the UKRI fellowship scheme did not get past the internal round, as she is now facing tougher competition with many established researchers applying for the same scheme. Sariqa notes that funding applications should include a statement where scientists can explain how COVID-19 has impacted them and reduced their outputs and productivity.

A postdoctoral researcher who wishes to remain anonymous has been facing additional stress juggling childcare and working from home. With family abroad and financial challenges due to the pandemic, her husband, who is currently completing a PhD, has had to take on childcare responsibilities and delay the completion of his thesis. She sees similarities between current pressures and those that she experienced whilst on maternity leave and when returning to work, with the pandemic bringing into sharp relief issues that have been present in academia for years. She is unsure whether she will pursue a career within a system that "evaluates people in terms of outputs of papers and number of grant acquisitions whilst offering no long-term job security". Given the widespread impact of COVID-19 on the research community, she explains that researchers have an opportunity to change the overall narrative in the research culture: "It would be great to have open conversations and reflections on how, as a collective, we can change and establish what kind of research culture we want to have and take it from there, but it will be a long road".

Eva Scholtus

Head of Policy and Engagement

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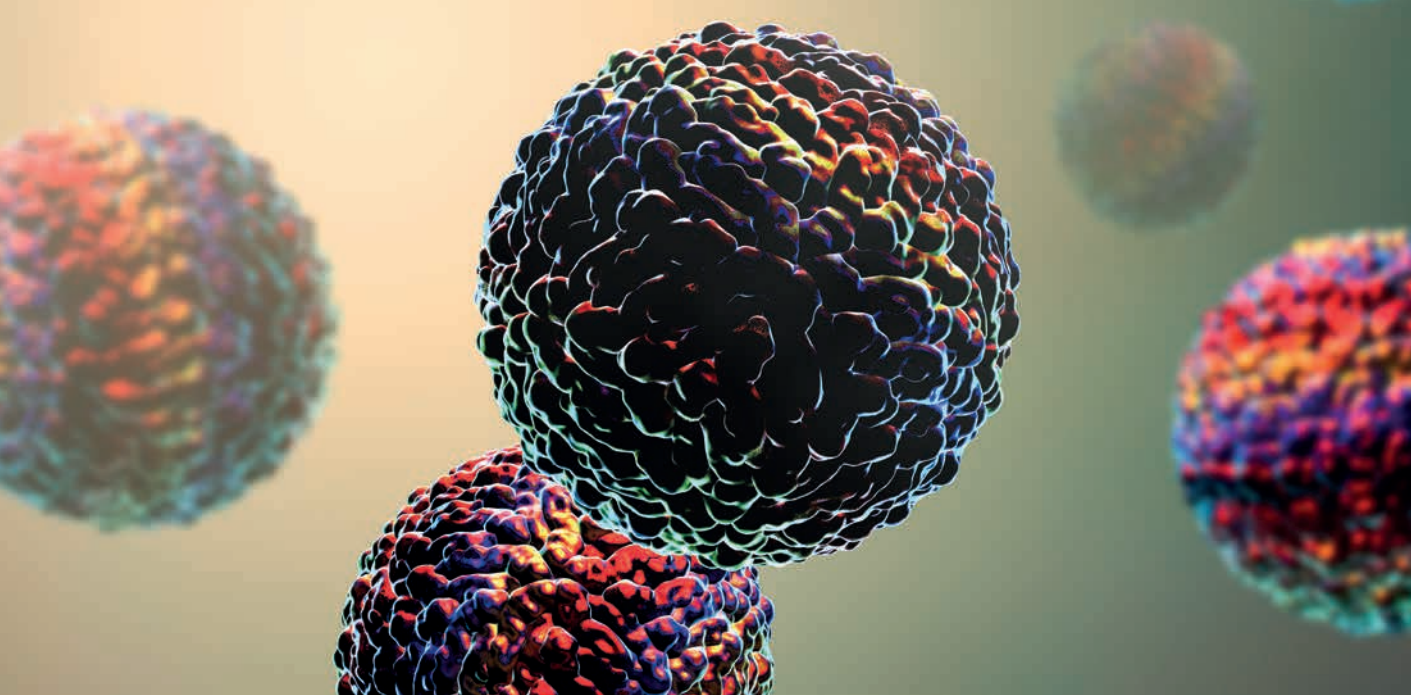

Zika virus. Dr_Microbe/iStock

The National Collection of Pathogenic Viruses – a dynamic repository for viral strains

The National Collection of Pathogenic Viruses (NCPV), established in 1999 with funding from the Wellcome Trust, curates and supplies pathogenic viruses to scientists around the world.

Operated by Public Health England (PHE) and based in Porton Down, UK, the collection includes Advisory Committee on Dangerous Pathogens (ACDP) hazard group 2 and 3 viruses, and viruses classified under the Specified Animal Pathogens Order (SAPO). All banks of viruses that are produced are independently cultured and authenticated. As a dynamic collection, new strains are regularly added to the catalogue and NCPV encourages deposits from scientists around the globe. Deposits are checked for identity, viability and contamination, stored in monitored cold storage and made available to the virology community for scientific use.

The importance and relevance of a viral repository that houses both modern and historical strains is of immense scientific value. Viruses can spend years circulating in obscurity and it is always difficult to predict which may become clinically significant. This was well illustrated during 2015–2016, when the Zika virus gained worldwide attention due to its links with microcephaly and other neurological disorders, resulting in the WHO declaring it a Public Health Emergency of International Concern. NCPV had within its existing catalogue a Zika strain from 1962, which had been isolated from *Aedes africanus* mosquitoes captured in Zika Forest, Uganda. This strain had been available to the scientific community since 2013 (NCPV 1308258v). In order to meet the growing public health demand, the NCPV catalogue was then rapidly updated to include a more recent clinical isolate, sourced from a semen sample and accompanied with rich metadata including full genomic sequence information (NCPV 1609021v). During the Zika outbreak, NCPV distributed live Zika or Zika RNA to 50 labs in 16 countries. These reference materials were essential for scientific research, underpinning a number of important studies that advanced our knowledge of the Zika virus. These ranged from NCPV Zika strains used to identify a small animal model suitable for *in vivo* Zika research, to comparing virulence differences between African and Asian Zika virus lineages, to

methods for Zika virus inactivation. NCPV was also featured on a Brazilian TV show and in *Focus* science magazine (Italy) due to its provision of Zika reference materials and the importance of using authenticated viruses in research, respectively.

During the present SARS-CoV-2 pandemic, NCPV scientists have been supporting PHE's outbreak response by monitoring the prevalence of SARS-CoV-2 antibodies in UK population sera, processing patient respiratory sample swabs, and testing vaccine and drug efficacy using plaque neutralisation assays. NCPV also accessioned and whole-genome sequenced the betacoronavirus OC43 (2008103v) and alphacoronaviruses 229E (2008101v and 0310051v) and NL63 (2008102v). NCPV is actively looking to access the betacoronavirus HKU-1 strain and would be interested in hearing from any virologists who would like to deposit this important strain within the collection. These seasonal human coronaviruses, related to SARS, MERS and SARS-CoV-2, are ADCP hazard group 2, and are currently being used worldwide in pandemic-response research (for example, in research to understand tissue tropism, dynamics and pathogenesis, and in assessing the specificity of rapid diagnostics and point-of-care tests). In addition, related viruses from NCPV have been used to investigate the broad antiviral activity of specific compounds and have been used in research conducted to support the SARS-CoV-2 outbreak responses.

In total, NCPV has over 300 catalogue items available on the Culture Collections website (**phe-culturecollections.org.uk**). Advantages to virologists looking to deposit into the collection include the ability to independently authenticate virus identity, sterility and mycoplasma testing, for which a Certificate of Analysis is provided. NCPV is certified to ISO 9001; shipping is compliant with global biosecurity regulations, and deposited viral strains are made available to scientists globally. Flexible release dates (for example ensuring the strain is only available after the publication of a given manuscript) are also available.

The value of biological resources such as NCPV to the scientific community is far reaching, and there is a recognised need for the conservation of organisms for future use. The importance of such collections is evidenced by the diversity and quality of the organisms and associated data they hold, the research they support and contribute to, the advances in industrial processes and biotechnology as a result of their use, as well as the role that they play in addressing global public health, societal and economic challenges.

As NCPV enters its third decade of operation and its parent organisation transfers from PHE to the United Kingdom Health Security Agency (UKHSA), it is anticipated that the collection will continue to expand to meet the ever-growing needs of the global virology community.

Further reading

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Ellie Drinkwater

NCPV Virologist

Dr Sarah Alexander

Lead Microbiologist

Connect with us

Twitter: **@NCPV**

Latest news: **phe-culturecollections.org.uk/signup**

Member Q&A: Phillip Yates


Phillip Yates

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

What is your job title?

The title itself is 'Clinical Biomarker Lead' but I am a specialist in Clinical Virology.

Have there been any discoveries in clinical microbiology that inspired you?

I was involved in the development of Relenza, generically known as *Zanamivir*, which is similar to Tamiflu, both of which are anti-influenza drugs. The project I am currently involved in is the Vir-GSK monoclonal antibody sotrovimab which is directed against the spike protein of SARS-CoV-2 and will be used for the treatment of COVID-19. I have found this work very inspiring because the drug will have a direct impact on people's lives. The development of this drug has been carried out under challenging conditions because just over a year ago we didn't even know the virus existed!

What are you working on at the moment?

Since March 2020, we have been working on the human monoclonal antibody that is directed against the spike protein of SARS-CoV-2. The first phase monoclonal antibody development required us to isolate the B-cells (a type of white blood cell that makes antibodies) from an infected individual. This would help us find out which monoclonal antibody was the best one for our purposes; directing high neutralisation activity against a conserved region of the spike protein. The antibody was isolated from a patient who was infected with the original 2004 SARS-CoV-1 and it was found that this antibody cross reacts with the new SARS-CoV-2.

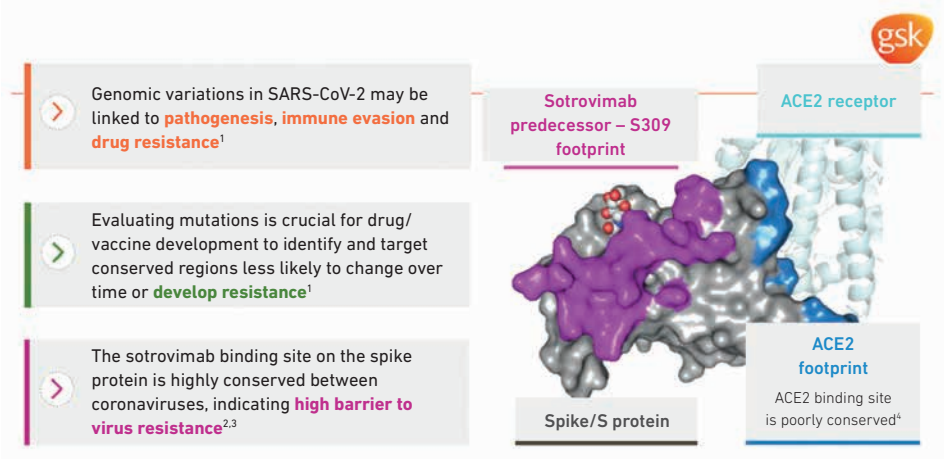
What skills are important to do your job?

Apart from the scientific knowledge, I need to keep up with the scientific literature, as it is constantly developing, particularly in a pandemic. Problem solving is also important, for example in clinical trials there is always something that does not work out smoothly so you would need to work out the problem and solve it. You need to work well with people within the team and be able to think on your feet.

Tell us about some of your professional challenges and how you managed to overcome them?

I think that the biggest professional challenge for the last year was that we collaborated with people we had never worked with before. Building a relationship with other professionals typically takes some time, so it was difficult getting used to the different working practices, but in the end, it worked out!

Find bonus content from our Q&A with Phillip Yates in the online version of the magazine: **microbiologysociety.org/MicrobiologyToday**. If you would like to be featured in this section or know someone who may, contact our Membership team, at **members@microbiologysociety.org**.



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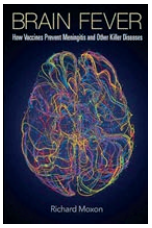
Reviews

Read excerpts from the latest book reviews below. To read the full reviews, and for more reviews, please visit our website: **microbiologysociety.org/MTOctober2021Reviews**



Brain Fever: How Vaccines Prevent Meningitis and Other Killer Diseases

By Richard Moxon
World Scientific Publishing (2021) £19.99
ISBN: 978-1-80061-001-9

Meningitis affects hundreds of thousands of people each year. This is an 'insider's' story of the heartbreaks and triumphs that resulted in the development of vaccines to prevent the major forms of meningitis. Brain Fever is an intimate and forthright account of the brilliant scientists who have brought about a milestone in medical practice. As we are learning from the COVID-19 pandemic, it is vaccines that we rely on to fight and overcome the devastation caused by virulent pathogens.

Richard Moxon
University of Oxford, UK

Legionellosis Diagnosis and Control in the Genomic Era

Edited by Jacob Moran-Gilad and Rachel E. Gibbs
Caister Academic Press (2020) £199
ISBN: 978-1-913652-53-1

This book focuses on the pathogen from the standpoints of its bacteriology, ecology, epidemiology, public health and clinical medicine. Newer research techniques including the use of genomics have revolutionised the research on *Legionella*, which is reflected throughout the book.

Chapters in this book are written in lucid language with adequate illustrations to engage the readers. This volume will serve as a useful reference for scholars, researchers and academicians interested in or working with *Legionella* and will be a valuable addition for libraries in colleges and universities.

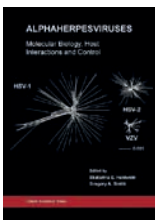
Arindam Mitra
Adamas University, India

Lyme Disease and Relapsing Fever Spirochetes: Genomics, Molecular Biology, Host Interactions and Disease Pathogenesis

Edited by Justin D. Radolf and D. Scott Samuels
Caister Academic Press (2021) £199
ISBN: 978-1-913652-61-6

Lyme disease is on the rise in the Northern Hemisphere. It is steeped in controversy, and most definitely in need of rigorous scientific understanding. As such, Lyme Disease and Relapsing Fever Spirochetes provides an excellent reference for students, scientists and clinicians alike. It provides clear overviews of the evolutionary biology, physiology, pathogenicity and immune evasion of *Borellia*, meanwhile also contextualising current contentious debates involving chronic Lyme disease and post-treatment Lyme disease. A truly fascinating and invaluable resource for the modern microbiologist!

Rachel Patel
Royal Devon and Exeter NHS Foundation Trust, UK



Alphaherpesviruses: Molecular Biology, Host Interactions and Control

Edited by Ekaterina E. Heldwein and Gregory A. Smith
Caister Academic Press (2020) £199
ISBN: 978-1-913652-55-5

The book has a practical and appealing approach to conveying information on herpes viruses and will benefit a wide range of readership. The book features convenient tables, for example, summarising the clinical trial results of the HSV (herpes simplex virus) vaccine candidates and fluorescently labelled alphaherpesvirus tracing recombinants. Multiple colourful illustrations in each chapter are convenient for visual learners. The book abolishes the need to consult additional molecular references as each chapter provides comprehensive information and comparative scientific evidence in *in vitro* and animal models.

Afrinash Ahamad
Stony Brook Medicine New York, USA

Comment: SARS-CoV-2; the unwelcome guest

When SARS coronavirus 2 (SARS-CoV-2) burst onto the scene, it arrived as an uninvited guest at the party, sneaking in with genuine invitees. Our indifference gave way to a sense of foreboding as SARS-CoV-2 reached into our lives. More than a year into the pandemic and the uninvited guest has become the constant companion who elbows past family, friends or close colleagues, and is incapable of recognising when it's time to go.

Tim Inglis

We have learned so much about the behaviour of this virus that you would have thought we would have sent it packing by now, but no, there is still no end in sight. All our predictions of pandemic decline have been frustrated by this insubordinate coronavirus.

Our best pandemic models have wide confidence limits that broaden the further out you care to go. There is no recognisable vanishing point. On the contrary, the unpredictably recurrent epidemic waves appear to favour divergence as SARS-CoV-2 continues on its erratic

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Ridofranz/iStock

evolutionary path. The evil logic of this virus favours accumulation of transmission-enabling features where the pandemic is already at its most intense, resulting in the generation of new variants. The molecular biology that brought us this insight also gave us the vaccines on which so many now pin their hopes. Sadly, the challenge of COVID vaccine delivery to the global population has exposed fault lines in vaccine supply, distribution, delivery and acceptance. Social distancing, public health restrictions, border closures, sanitiser and personal protective equipment are likely to remain with us for some time to come as we strive for that elusive herd immunity.

If we take an evidence-based approach to mapping out the next six to twelve months in pandemic time, it is reasonable to consider the fast and slow extremes, the most likely and most dangerous outcomes. From recent experience in the USA, where vaccine rollout has been rapid and comprehensive, suppression of epidemic spread is plausible in a matter of months. However, this may fall short of the near elimination achieved in New Zealand and parts of Australia through favourable geography, stringent border controls, quarantine and other public health measures. Continuing a global fast track assumes similar rollout in low- and middle-income countries that lack the public health infrastructure of wealthy countries. The coordination of disease prevention on this scale will be a monumental task but has to be given serious consideration because the alternative is very unattractive.

So what of the slow path to pandemic's end? Some have suggested five years or more, but this is only an informed guess. It could be longer, if repeated stop-start controls provide SARS-CoV-2 with the evolutionary bottlenecks that encourage transmission enhancements, vaccine escape mutations and diagnostic test evasion. At a strategic level, a methodical and therefore slower approach would start with pockets of disease elimination which are then expanded until they join up.

Adam Webb/iStock

The most likely path for the COVID pandemic will probably be the consequence of vaccination bias that favours wealthy countries, and wealthier people in lower-income countries. The vaccine-advantaged will surround their disease-free havens with border controls, quarantine and ever-improving vaccination regimes. The most dangerous course will be a protracted series of pandemic waves due to new variants of concern, arising in populous newly industrialised countries such as the BRIC group. No amount of vaccine imperialism will stop further waves of vaccine-escape COVID from burning through well-heeled communities with a strong attachment to freedoms they lost to SARS-CoV-2.

The first few weeks of the pandemic saw a cessation of ineffectual peacetime bureaucracy, interdisciplinary communication, pragmatic decision-making and rediscovered community cooperation. There is a pressing need to rediscover that common language and sense of purpose. SARS-CoV-2 is able to change its fundamental behaviour faster than public administration can adapt. Agile administration is a step in the right direction, but if we want to put a confident date on the end of the pandemic, we need to use microbiology's moment on stage to re-engage everyone outside coronavirology, from vaccine refusers to exhausted politicians. The conversation must start with what life beyond the pandemic will look like before we can move onto how we might get there. Only then will we be confident that the end is nigh.

Tim Inglis

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Tim Inglis is a UK-trained medical microbiologist, who migrated via Singapore to Australia, and Deputy Editor-in-Chief of *Journal of Medical Microbiology*. His work on emerging infectious diseases in Western Australia has emphasised capability building in regional, rural and remote locations where pathology support is lacking. Currently, much of his time is taken up on COVID laboratory activities, and if it weren't for the pandemic, he would be working flat out on new methods for rapid diagnosis of systemic, drug-resistant infections in regional Australia. In his spare time, he enjoys trail running and looking after a smallholding.

What parts of your job do you find the most challenging?

The part of the job I find most challenging is finding the patience needed to handle public-sector administration!

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

Our discipline is in the spotlight: do micro, think global.