Applied Microbiology International

POLICY BRIEFING

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Supporting microbiology to prevent the next global catastrophe

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Applied Microbiology International is a global membership organization that seeks to bring the international microbiology community together to advance scientific impact. We are the oldest microbiology society in the UK and with more than half of our membership outside the UK, we are truly global, serving microbiologists based in universities, private industry and research institutes around the world.

Due to COVID-19, research and development in fields not directly related to COVID-19 have suffered substantial losses in support and funding.

If sufficient support for research and development is not provided now, many scientific challenges will worsen and will be harder to remedy later, resulting in potentially even more devastating consequences.

This report highlights five microbiology areas:

1 Antimicrobial resistance (AMR)
2 Food security
3 Preserving and protecting oceans
4 Microbiome
5 Future applications of microbiology

to exemplify the severe risks posed by the absence of research and the lost opportunities to eradicate current global challenges.

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INTRODUCTION

While scientists continue to battle COVID-19 and develop vaccinations at record pace, other significant areas of scientific research, reeling from disruptions due to COVID-19, threaten to become the next global catastrophe. As a result of COVID-19, many vital research and development projects have been delayed, halted or substantially altered due to various repercussions, including lab closures, loss of funding, reduced staff members and delays in obtaining testing resources, to name a few. The current pandemic has exacerbated pre-existing challenges that the scientific community already faced, such as underfunding, while also presenting new challenges, such as restricted access to fieldwork.

These setbacks have long-term, devastating implications so it is vital that they are remedied and protected from further loss. However, funding cuts to many research and development areas are already alarming scientists throughout the UK. With the uncertainty surrounding the UK's continued association with Horizon Europe and an announced £120 million cut to UKRI's Global Challenge Research Fund, the future of many vital UK research programmes with global impacts is at risk.[1] Similarly, medical research programmes, dependent on private funding, are already suffering severe setbacks, with the Association of Medical Research Charities estimating an average 41% decrease in their research spend for 2021 and Cancer Research UK reducing its annual research spend by £150 million a year over the next 3–4 years.[2, 3]

These cuts not only threaten to delay developments and reverse progress already achieved, but also threaten to deter future scientists from pursuing careers in these priority fields. The Applied Microbiology International (AMI) December 2020 end-of-year membership survey found that when members were asked whether they had considered changing research area, sector (academic, industry etc.) and/or career due to the impact of COVID-19, 18.6% of the 217 survey respondents answered 'yes'.

By highlighting risks and opportunities in the five microbiology areas listed below, this brief demonstrates why continued support for research and development is critical:

1. **Antimicrobial resistance (AMR)**
2. **Food security**
3. **Preserving and protecting our oceans**
4. **Microbiomes**
5. **Future applications of microbiology**.

While these are just some of the research fields suffering severe funding cuts, AMI has focused on these five areas as they illustrate the significant risks posed from discontinuing research support. Since their remits are far reaching and urgent, the implications from cancelling or even postponing their programmes threaten the future of our planet and its inhabitants. Moreover, these areas are interrelated, with developments in one area often affecting developments in another. For example, increasing temperatures in oceans because of climate change can lead to an increase in the spread of pathogens (Preserving and protecting our oceans) that could result in increases in foodborne illnesses (Food security). While this interrelation will require greater support for collaboration across sectors, it also means that successful solutions discovered in one field may be applicable to another field. Discoveries in microbiome manipulation, for example, may prove a suitable alternative to antibiotic treatment, thus reducing the spread of AMR infections.

All five of these microbiology fields have promising potential and indicate numerous opportunities for both eradication of current challenges and prevention of future ones. With adequate and sustained support, both financially and collaboratively, these research and development areas can continue to solve current crises while also providing innumerable benefits to the UK's economy, particularly as it recovers from the current pandemic.

1 ANTIMICROBIAL RESISTANCE

Background

Prior to COVID-19, AMR was already a high priority for public health, featuring in the global action plan in 2015[4], the O'Neill report in 2016[5] and the basis for founding the UN Interagency Coordination Group (IACG) on AMR.[6] With no new classes of antibiotic having been discovered since the 1980s and increasing resistant pathogens, the UK recognised the significance of this growing concern in 2019 by committing to ambitious targets to combat the spread of AMR via the UK's five-year action plan for antimicrobial resistance.[7]

Since the emergence of COVID-19, there has been a substantial increase in the use of antibiotics, further exacerbating these concerns. Hospitalised individuals with serious cases of COVID-19 infection often have secondary infections such as pneumonia, for which

antibiotic treatment is vital.[8] Because of this, antimicrobial treatments have been more heavily used within healthcare settings; however, microbiology testing has decreased over the same period. Moreover, uncertainty around COVID-19 and its effects have resulted in increased use of broad-spectrum antibiotics for patients who may not require them. The increased use of antibiotics, in addition to conditions increasingly exposing individuals to AMR, such as the increase of vulnerable patients in riskier healthcare environments, are all factors that enable resistant pathogens to thrive and spread more easily.

Current AMR research follows a global, multifaceted One Health approach that includes strategies to tackle the numerous areas that AMR affects, including monitoring transmission of resistance genes and developing new diagnostic tools and treatment products. If this strategy and AMR research is not sustained and not expanded, then drug-resistant infections will increase, and future generations will have to grapple with even more dire consequences.

Antimicrobial use in the healthcare setting

Hospitalised COVID-19 patients presenting with mild infection and no signs of pneumonia, or moderate infection with signs of pneumonia, are often prescribed antibiotics without confirming whether antibiotics are necessary.[9] This amounted to 72% of patients who received antibiotics to treat COVID-19-related secondary bacterial or fungal infections, but of these only 8% were subsequently confirmed to need antibiotic treatment, signifying an overuse of antibiotics during the current pandemic.[8]

Further to this is the increased risk of exposure to healthcare-associated infections (HAIs) and multidrug-resistant microorganisms for hospitalised individuals.[10] Antimicrobial treatments are routinely used as a preventative measure for high-risk patients admitted to intensive care units. Of those admitted, 70% typically receive antimicrobial treatment despite only 54% presenting with bacterial infection.[11] The increased admittance to intensive care units of patients who have complicated COVID-19 infections has consequently increased the use of antimicrobial treatments as a preventative and protective measure. Despite this, it is known that prophylactic use of antimicrobial treatments promotes AMR.[12] To counter this inevitable problem, the need for alternative therapeutics, new antimicrobial formulations, the following of antimicrobial stewardship guidelines and predictive prevention of bacterial or fungal infection is more urgent than ever.

Increased use of biocides

Biocides, which are used to decontaminate skin and surfaces, have been pivotal for the management of COVID-19 in healthcare settings, the agriculture and food sectors and the community. These include disinfectants to clean rooms, surfaces associated with food production, equipment and instruments, and hand gels. Hand gel dispensers are now commonplace in a variety of public places from schools, restaurants and hairdressers to dental surgeries and supermarkets to name a few, whereas previously they were primarily used in healthcare settings. While biocides are effective, they also carry the risk of contributing to AMR as a number of studies have revealed cross-resistance between some unrelated biocides and antibiotics.[13] It is understood that the increased use of biocides during the COVID-19 pandemic could result in higher levels of detectable biocide in the environment and low levels of environmental biocides may encourage AMR. Given the current and likely continued ubiquitous use of biocides, it is paramount that their potential role as a driver of AMR is better understood.

AMR: a future pandemic

Estimates by the World Health Organization (WHO) indicate that 700,000 people die annually from antibiotic-resistant infections;[14] this number will continue to increase, accelerated by COVID-19. In Europe alone, excess deaths caused by AMR infections in hospitals exceeds 25,000, with an annual cost of €1.5 billion.[15] It is predicted that within the next 35 years 300 million people will die prematurely as a consequence of antimicrobial-resistant infections, which has led to the suggestion that AMR will be the next global pandemic. The key to preventing this scenario lies in preparedness and global collaboration to avoid uncontrolled AMR with consequent human suffering and impact on economic outputs. It has been suggested that if uncontrolled, AMR could see the predicted global GDP 2%–3.5% lower than it should be in 2050.[16]

Antibiotics play a key role in every part of the health system. Following their introduction, the average life expectancy in the UK rose by over 20 years. A future where antibiotics no longer work would undo decades of medical gains and present unprecedented challenges for healthcare, far greater than those currently experienced with COVID-19.

Protecting antimicrobial stewardship

Antimicrobials have facilitated a wide range of medical advancements, but the COVID-19 pandemic could curb this progress. Antimicrobial stewardship aims to promote the appropriate use of antimicrobials to reduce AMR, decrease the spread of multidrug-resistant microorganisms and improve patient outcomes.[17] Increased antimicrobial prescribing during the pandemic and pressures within the healthcare system could lead to the breakdown of established stewardship programmes.

It is prudent to consider how plans to manage infectious disease pandemics and AMR might complement each other. Some strategies implemented in healthcare settings for the control of COVID-19 could support the management of AMR. For example, increased diligence with regard to hygiene, and additional cleaning and sterilisation of rooms and surfaces could prevent the transmission of antibiotic-resistant healthcare infections. Better understanding of AMR issues such as emergence and transmission, rapid diagnosis and innovative technologies has the potential to contribute to the management of infectious disease outbreaks and AMR in future.

2 FOOD SECURITY

Background

Since the 1980s a series of bacterial foodborne illnesses (*Salmonella* in poultry and eggs; *Listeria monocytogenes* in meat and dairy products; *Campylobacter* in poultry; *E. coli* O157:H7 in meat) have caused a serious health and economic burden on society. In the UK in 2018, there were 2.4 million foodborne illness cases, costing the UK £9.1 billion in both financial (e.g. medical, disturbance to business, lost earnings) and non-financial (e.g. long-term complications, grief/loss) costs.[18] The risks of foodborne pathogens contaminating food products are far reaching, from farm to fork, and thus require a thorough understanding of pathogens and control measures throughout the food production process.

Following extensive research and industry action, some of these foodborne pathogens have been brought under control, for example decreasing *Salmonella* in eggs and chickens through flock vaccination. However, there are still many unresolved issues, as well as newly emerging pathogens, as new sources of food are accessed. Without more research on areas of pathogen ecology such as animal colonisation, conducive physiological systems in food production and constantly evolving

environmental conditions that support pathogen growth, it will continue to be difficult to identify and control contamination of food products. Without this knowledge, foodborne illnesses will continue to negatively impact mortality and morbidity along with their associated financial and non-financial costs.

Animal-to-human (zoonotic) transmission

Zoonotic transmissions are diseases or infections that transfer from animals to humans, such as through consumption of food products from infected animals. Some of the most virulent examples include *Salmonella* in chickens and eggs and *Campylobacter* in poultry and raw milk and cream. *Campylobacter* is still the most commonly reported human gastrointestinal pathogen in the UK, with 63,946 cases in the UK in 2017 and recent figures suggesting a rise in incidence.[19] Likewise, *Salmonella* accounted for 94,625 confirmed cases in the EU and 125 deaths in 2015.[20]

Research has identified better practices for mitigating the spread of foodborne diseases such as novel feed additives (e.g. bacteriocins, prebiotics, probiotics). However, since there are no effective interventions to fully eliminate pathogens from animals and their food products, there is still a need for more knowledge on detecting and preventing colonisation in animals so that pathogens cannot enter animals in the first place.

Food production transmission

Food processing and manufacturing environments continue to present significant risks to food safety as pathogens can persist in factories over prolonged periods of time. As AMI's 2019 policy report on food security *Food Manufacturing and Processing* explains, harmful bacteria can develop in the form of biofilms that stick to production machines and thus contaminate food products.[21] These biofilms can be incredibly difficult to remove since they can be resistant to chemicals or grow in hard-to-reach places. Despite thorough mitigation measures such as processing and routine cleaning procedures, pathogens can persist. For example, studies have found *L. monocytogenes* can grow on fresh-cut produce even after control measures were implemented, such as modified atmosphere packaging (MAP) and refrigeration.[22]

While scientists have continued to develop techniques to prevent outbreaks, such as using whole-genome sequencing to trace outbreaks to their original source, increasing automation in production processes designed to meet increasing supply demands has resulted in new food safety challenges. Moreover, supply shocks from COVID-19 exposed the UK's already fragile food system as surges in demand, disruptions to supplies and labour shortages placed additional pressure on processors and manufacturers to find rapid and safe production solutions. These newly emerging challenges stress the need for further research on the physiological systems that allow bacteria to persist and to identify innovative mitigation measures.

Climate change transmission

The effects of climate change, including deforestation, extreme weather events such as floods and droughts, changes in temperature and availability of water can affect the growing conditions of crops, aquaculture, livestock, diseases and pests. These effects can alter the persistence and distribution of pests and diseases to new areas where crops lack resistance or livestock has no prior exposure to pests. For example, *Vibrio parahaemolyticus* and *Vibrio vulnificus* are waterborne pathogens found in marine environments such as estuaries, brackish ponds or coastal areas of particular temperature and salinity ranges. These pathogens are transmitted through consumption of raw or undercooked shellfish or exposure of wounds to contaminated water, causing an invasive infection that progresses to septicaemia and necrotising fasciitis in the extremities, with a case fatality rate of ~35% for *V. vulnificus*. Environmental changes in water

temperature and salinity are resulting in greater geographical spread of these organisms, with the average annual incidence of all *Vibrio* foodborne illnesses in the USA increasing by 41% between 1996 and 2005.[23] Further research is needed to understand how changing climate conditions can encourage and spread pathogens as well as identify new mitigation measures to prevent further increases in foodborne illness-related deaths.

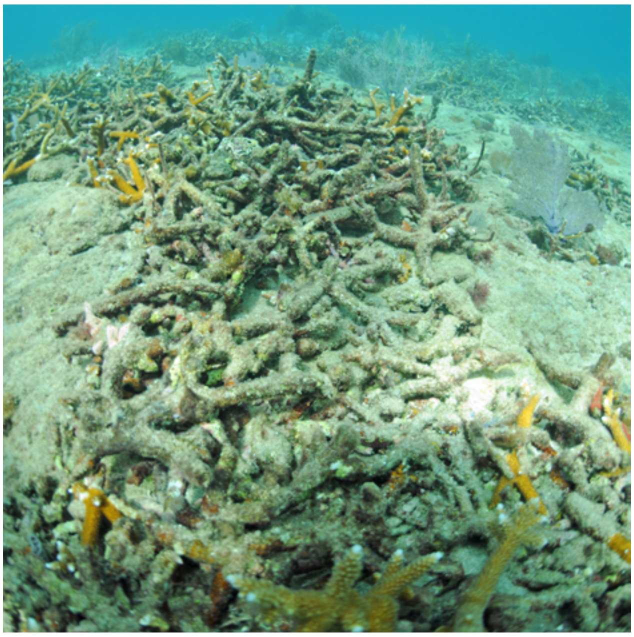
3 PRESERVING AND PROTECTING OCEANS

Background

Oceans account for about 50%–80% of Earth's oxygen and 97% of Earth's drinking water.[24] Yet these precious resources and the biodiversity and habitats that produce and maintain them are threatened by numerous challenges resulting from pollution and climate change. With changes in temperature, oxygen and carbon dioxide levels, and salinity, many aquatic organisms are dying out, new and existing pathogens are spreading to new areas, and extreme weather events are increasing. If left unaddressed, these challenges will worsen and new problems will arise.

The United Nations has already recognised how significant these challenges are by initiating the Decade of Ocean Science for Sustainable Development from 2021 to 2030.[25] The decade has been commissioned in order for scientists to globally collaborate to identify and fill many existing knowledge gaps about the vast mysteries of the ocean and subsequently produce a framework for action to preserve and protect those areas.

As the Decade of Ocean Science recognises, it is crucial that marine scientists continue their research. However, COVID-19 and ensuing lockdowns have already severely disrupted marine microbiologists' ability to monitor the impact of climate change and its effects on ocean biodiversity. The implications from these disruptions are long-lasting as they impede our ability to anticipate and adequately mitigate fatal, irreversible disturbances to ecosystems. Likewise, many investigative missions have been delayed or halted, resulting in the delay of discovering solutions to many medical, environmental and diagnostic issues we currently struggle with. Without adequate support for further investigation, mitigation and exploration today, we risk facing even bigger challenges in the future and losing opportunities to fix and prevent many existing ones.



Lost data

Long-term microbiological studies rely on consistent collection of data that are captured at precise times and locations. Consistent observation enables marine scientists to study how the environment is changing and impacting organisms and microbial diversity. With these data, scientists can map and reduce the risk of extreme weather events, monitor oxygen and carbon dioxide levels and their impacts on aquatic microbes, and track and mitigate the spread of exotic pathogens to new areas because of increasing water temperatures.[26] Numerous industries, from farming to global shipping, also rely on these data sets daily.[27]

Prior to COVID-19, scientists heavily relied on commercial activities to collect data sets to reduce operational costs. The Surface Drifting Buoy Programme and Ships of Opportunity Programme, for example, use commercial container ships to deploy buoys that measure climate variables, including surface pressure, salinity or ocean temperature. However, the buoys need to be replaced at precise times and locations to sustain these programmes and often require frequent maintenance due to the corrosive conditions of seawater. As Dr Johannes Karstensen from OceanSITES explains, the loss of just one moored buoy would result in a gap of 2 to 5 years of data.[28]

Due to failure to collect vital samples, coupled with delays in procuring testing materials, many microbiologists have struggled during COVID-19 to collect critical monitoring information, such as data on harmful algal bloom events (HABs). HABs, where microorganisms rapidly grow in large quantities, can produce toxins and deplete nutrients in water sources. These pose a risk to not only aquatic organisms and seabirds, but also to humans through contaminated seafood, drinking water and crops that have been irrigated by contaminated water. In 2014, the city of Toledo in Ohio, USA suffered an HAB that resulted in 110 people developing disease and more than 400,000 people were without drinking water for days.[29] Therefore, many water facilities that manage municipal drinking water and seafood industry stakeholders rely on this testing to ensure their products are safe for human consumption.

HABs can be very difficult to manage and treat, so mitigation measures, such as data collection and sampling, are vital to their prevention. The costs of not preventing these incidents can be significant, with an

estimated overall economic impact of HABs in the EU costing €919 million per year.[30]

Missed opportunities in biomedical and bioremediation applications

Since scientists have only studied about 10% of Earth's oceans, ocean research presents substantial opportunities.[24] Due to its extreme conditions, the ocean hosts structurally unique natural products that can withstand the ocean's various temperatures and pressure ranges, offering promising applications in drug discovery and bioremediation.

Marine-derived medical drugs and therapeutics are already showing promising results. For example, marine actinomycete bacteria have already been proven useful for new antibiotics and biocompounds, which are used to treat nerve damage, inflammation and diseases like cancer or AIDS.[31] In addition to biomedical applications, marine bacteria are an excellent source for bioremediation of contaminants from both land and water environments, including toxic heavy metals and petrol spills.

Perhaps most relevant to the current pandemic, marine research has helped progress diagnostic tools including testing for COVID-19, as well as AIDS and SARS. These tests were developed from an enzyme isolated from a microbe found in marine hydrothermal vents.[32] Without prior marine research's identification of this enzyme, the current pandemic would likely be in a more dire state. It is therefore critical that scientists are able to continue exploratory research now, as their findings may prove vital for the next global disaster.

4 MICROBIOMES

Background

Complex, balanced communities of microbes (viruses, bacteria, fungi, protozoa etc.) living in a particular ecosystem, known as microbiomes, are vital components for the health of humans, animals and the environment. Due to the prevalence of microbiomes, which exist in, on and around us, they play a crucial role in many life processes, such as building resistance to infection in humans or decontaminating soil through bioremediation. Consequently, disruption of these communities, such as pollution in water systems, antibiotics that disturb the normal microbiome in humans, or waste run-off from agriculture that could contain antibiotics or biocides, can all adversely affect individuals and the environment, including agriculture, water sources and global warming.

Since microbiome research is a relatively new field, scientists have only just begun to develop techniques for better understanding its applications. So far, microbiome research has unearthed many benefits such as improving gut microbiota through probiotics or improving crop yield and resilience through microbiome breeding. Moreover, microbiomes are widespread, with great manipulation potential for multidisciplinary applications in medicine, agriculture and industry. As such, impediments to microbiome research not only hinder microbiome work but hamper other research fields from reaching their full potential.

Microbiomes in human health

Our bodies each contain unique microbiome populations that are vital to maintaining good health because they support our immune system and provide resilience to a variety of health problems. Gut microbiomes are known to be especially important for multiple facets of human health including immunity, metabolic health and neurobehavioural traits such as Parkinson's disease and dementia. For example, gut microbiome research in patients with *Clostridioides difficile* infection (CDI), which was responsible for 4056 deaths in the UK in 2007, has found that disruptions to the gut microbiome from multiple antibiotic treatments resulted in harmful bacteria dominating the gut.[33] Application of microbiome-based therapeutic approaches, such as faecal microbiota transplantation (FMT), whereby microbes of a healthy gut are transplanted to the infected gut, have shown promising results, with an efficacy rate of nearly 90% in multiple recurrent CDI cases.[34]

Researchers are only just beginning to understand how the human microbiome can be understood and applied to improve health. But as we learn more about the role of the microbiome in human health, this knowledge can be exploited to support a healthier society, with far-reaching gains.

Microbiomes and the environment

Rivers, oceans and soils all contain microbiomes that are integral to sustaining Earth's many ecosystems. Microbiome communities are key for removing contaminants and pollutants from the environment through biodegradation, bioremediation and nutrient recycling. This also includes carbon cycling, where carbon dioxide is removed from the environment and stored as an organic molecule. Disrupting these microbiomes ultimately disrupts some of the natural processes that protect the planet from global warming. Further, microbiomes in the soil are critical to sustaining wildlife and food security, such as promoting biodiversity or supporting crops through water retention/drainage. But these microbial populations are at risk from pollutants, including those containing

antibiotics, that can disrupt the delicate balance of crucial environmental microbes and spread antibiotic resistance.

Much is still unknown of these complex microbial communities, but they have immense potential to meet global food security and climate change commitments. With the UK government's 25 year environmental plan including a target of managing all of England's soils sustainably by 2030, microbiome research and innovation have the potential to play a significant role in diagnosing, improving and managing soil health through sustainable practices.[35]

5 FUTURE APPLICATION OF MICROBIAL BIOTECHNOLOGY

Background

Microbes inhabit every environment on earth, delivering critical ecosystem services and playing vital roles in human and environmental health. Thanks to technological advances, microbes and their products have immense potential as they have wide applications across areas, including medicine, industry and agriculture. Previous examples include yeast for producing beer, penicillin (antibiotics from moulds) and the anti-malarial drug artemisinin (a synthetic biology product).[36] With such far-reaching uses, microbial biotechnology will likely play a crucial role in identifying sustainable living solutions.

There is global consensus that now is a critical point in ecosystem damage. Urgent remedial action is needed to avoid a terminal spiral of decreasing soil quality with concurrent decreasing food production, increasing energy and resource demand, irreparable pollution of freshwater reserves and overwhelming plastic pollution. As the United Nations' Sustainable Development Goals (SDGs) emphasise, global actors are committed to ensuring a holistic approach is taken to reduce the negative environmental impact of climate change while improving living conditions for both current and future generations. With the SDG's 17 ambitious goals and each of their corresponding targets set to be delivered by 2030, microbiological innovation can play a pivotal role in helping the UK meet those commitments.[37]

How microbes can save the world

It is imperative that governments address bioremediation of global ecosystem damage and pollution, but solutions should not be viewed in isolation. Recent developments mean that not only can microbes

be used extensively for remediation of a range of pollutants, but these processes can now be engineered to enhance the economic and environmental value of the end-products. For example, the use of anaerobic digesters, whereby microorganisms break down materials in the absence of oxygen, in wastewater treatment has enabled safe treatment of sewage on a large scale while simultaneously producing renewable green energy, known as biogas.[38] Likewise, the development of microbial fuel-cell systems, whereby the catalytic activities of microbes produce electricity from organic and inorganic substrates in wastewater, offer similar multi-issue solutions.[39] Research in this field is now investigating ways to recover nutrients from this process and use it for single-celled protein production, which could contribute toward feeding an increasing population in a sustainable way.

Plastic contamination of soil and freshwater and marine ecosystems presents another challenge, with widespread consequences to both animal and human health. Many microbes have indicated potential for degrading plastic polymers, and developments have already demonstrated that the microbial degradation process may yield further reusable compounds. Likewise, microbes can produce renewable, fully degradable plastics as an alternative to oil-derived plastic polymers that are highly recalcitrant to breakdown. These technologies are still in their infancy but offer hope, both of bioremediation and of an alternative, sustainable route forward for plastic-dependent livelihoods.

These examples are by no means the limit of microbial potential. Microbial processes could play key roles in rebalancing the nitrification of soil and freshwater, reduction of greenhouse gases in the atmosphere, protection of food production through sustainable pesticide and herbicide development as well as maintaining soil integrity, and the production of bioenergy and biomaterials.

What is needed?

The promising products and developments that microbial biotechnology could generate require further research, resources and collaborative opportunities. While many microbial processes are demonstrable in the lab (including bioremediation, biopolymer, bioenergy, biocontrol etc.), funding and increased industrial partnerships are key to turning microbial potential into large-scale industrial solutions.

6 THE FUTURE OF MICROBIOLOGY RESEARCH

As these five microbiology areas exemplify, maintaining research support is vital for the eradication, prevention and remediation of global challenges. Many of the previously described research areas have a significant role to play in helping achieve the United Nations' 17 SDGs, such as zero hunger and climate action.[37] However, to successfully achieve these goals, scientific research requires sufficient and sustained support that includes not only increased funding, but also provision of a means for strong collaborations across academics, industries and sectors (e.g. health, agriculture, environment etc.). For example, developing resilient crops for food security will benefit from research collaborations and developments in microbiome applications and ocean monitoring and mitigation.

Lastly, there are huge knowledge gaps still to be filled, presenting both risks and opportunities. More research is needed to identify innovative solutions as well as potential challenges that may arise in the future. This research requires long-term funding and investment in areas where the results are unknown and may not produce returns. However, the information discerned from that research is invaluable in progressing discovery and development.

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