Estimates suggest that less than 1% of the microorganisms present in most habitats on Earth are culturable,¹ which means that our current view of the structural and functional diversity of the microbial world is severely limited and its vast emporium of potential medicines and useful industrial products lies virtually untapped. Furthermore, our historical reliance on culture means that we have a limited, and in some cases, somewhat biased view of infectious disease pathogenesis.

Metagenomics, defined as the culture-independent genomic analysis of microbial communities, has emerged as a powerful new field of research in microbiology over the last two decades. The power of this technique lies in the fact that microbial DNA is isolated directly from the environmental sample enabling access to the entire microbial community, including the majority that have not been cultured in the laboratory. Metagenomics can take one of two approaches: (1) a sequence-based approach in which either the entire DNA sample is sequenced, assembled, and annotated, or a more targeted approach in which a particular gene or gene family of interest or a phylogenetically useful marker, for example, the 16S rDNA, is sequenced, or (2) a functional approach in which metagenomic libraries are constructed in a heterologous host and screened for an activity of interest. In their article in this special focus, Culligan and colleagues consider the methods of DNA isolation for metagenomics and then comprehensively discuss both sequence-based and functional approaches which have been used.² Integration of the information derived from both sequence-based and functional metagenomics enables a more comprehensive analysis of the structure and function of microbial communities than ever before.

The revolution in metagenomics has been instrumental in changing our view of microbial interactions with the human host from a strictly “one pathogen one disease” concept to a more ecological view of microbe-host interactions in which the bacterial composition and diversity of the microbiota is perturbed by environmental factors leading to a shift in equilibrium to a “dysbiotic” state. It appears that the pathogenesis of several important diseases of humans, including for example, inflammatory bowel disease and bacterial vaginosis, results from ecosystem destruction rather than the action of a single etiological agent, and the contribution of metagenomics in achieving this understanding is reviewed in the article by Martin and co-authors.³ Although ecological principles were applied to the pathogenesis of the oral infectious diseases, dental caries and periodontal disease, before the metagenomics era,⁴ application of these techniques in oral microbiology has defined the dysbiosis concept in oral infectious disease and led to the “keystone pathogen hypothesis”,⁵ which is discussed in this special focus by Ping Xu.⁶ The article by Xu also reviews interesting literature which has identified associations between specific genes or metabolic pathways and oral health and disease.

As well as the associations between the human microbiota or its products and health or disease, metagenomics can also be applied to assessing the phylogenetic diversity of gene/gene products and the article by Nobutada Kimura reviews the contribution made by metagenomics in investigating the phylogenetic diversity of quorum sensing (QS) systems present within microbial communities.⁷ In this context, the application of metagenomics has not only identified new potential QS signals and signal transduction systems but has also identified new inhibitors of QS, some of which may be useful therapeutically as anti-virulence or anti-biofilm agents (see Kimura, in this issue).⁷ In this age of ever-increasing resistance to conventional antibiotics, new approaches to discovering novel antibacterial agents are of the utmost importance.

The role of metagenomics in discovery of new therapeutic agents theme is continued in the review by Culligan and colleagues.² These authors describe the impact that both sequence-based and functional metagenomics studies have had in discovering new antimicrobial and anti-cancer drugs as well as the application of “meta-biotechnology” in the identification of novel genes with application in biotechnology and in the creation of bio-engineered probiotics. The role of metagenomics in opening up new avenues within the biotechnology and therapeutic arenas is an exciting and rapidly progressing area.

Finally, the impact of functional metagenomics and its limitations in investigating antibiotic resistance in bacteria is explored by Peter Mullany.⁸ Given the current global threat from antibiotic resistant bacteria, as well as the potential to discover new antibacterial agents, functional metagenomics is a powerful tool which enables a comprehensive understanding of the prevalence of different types of antibiotic resistance genes, and their distribution in the microbiota of a particular ecosystem. By isolating the mobile genetic elements which harbor these antibiotic resistance genes, metagenomics also allows us to understand the
mechanisms by which antibiotic resistance genes are transmitted between bacteria and how they evolve within communities.

The articles presented in this special focus demonstrate that it is an exciting time in microbiology as the refinement of metagenomics techniques, including new heterologous host and vector systems and further progress in sequencing technologies, continues to expand our knowledge of the diversity of the microbial world that lies within and all around us. These articles show how the metagenomics revolution is enabling us to pry ever deeper into the functional attributes of microbial communities in both the pursuit of basic knowledge and to discover new microorganisms and microbial products potentially of benefit for human use.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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