Natural products have been a prolific source of antibacterial and anticancer drugs in the pharmaceutical industry. However, despite the pressing need for new drugs, the rate of natural product discovery has been diminishing. Fortunately, the genomics revolution has made it clear that natural product-producing microorganisms have the genetic capacity to produce a far greater number of natural products than have been isolated to date. Recent technological developments in bioinformatics and synthetic biology are now making it feasible to harness this rich biosynthetic diversity through the identification and prioritization of biosynthetic gene clusters and their (re-)engineering for expression in heterologous hosts. In this special issue of *Natural Product Reports*, we present eight articles that describe these developments, and discuss their applications for discovery and production of novel natural products.

Synthetic biology can be simply defined as the use of engineering principles to design biological systems with new or improved functions. In recent years, synthetic biology has been increasingly explored for natural product research. One of the hallmarks of synthetic biology is standardization. In their Viewpoint article, Zhao and Medema (DOI: 10.1039/c6np00030d) discuss the role of standardization in natural product research, with a focus on standardization of data on biosynthetic pathways and gene clusters. In addition, they emphasize the role of standardization in the process of biosynthetic gene cluster engineering.

Another hallmark of synthetic biology is the use of the design–build–test cycle. In their Highlight article, Carbonell, Takano and coworkers (DOI: 10.1039/c6np00018e) discuss how the design, build and test components of the synthetic biology cycle can be integrated by powerful bioinformatics tools for natural product discovery and production. These bioinformatics tools include design and build tools for the selection, synthesis, assembly and optimization of parts (enzymes and regulatory elements), devices (pathways) and systems (chassis), as well as test tools for screening, identification and quantification of metabolites for rapid prototyping.

The raw material for natural product synthetic biology is formed by enzyme-coding genes and their corresponding biosynthetic pathways and gene clusters. In their Review article, Ziemert, Alanjary and Weber (DOI: 10.1039/c6np00025h) provide a comprehensive overview of various computational tools for the mining of microbial genomes to discover genes involved in natural product biosynthesis and connect them to their molecular products. Enabled by the development of next-generation DNA sequencing technologies, genome mining tools have evolved from homology-based detection of biosynthetic genes (classical approaches) to phylogeny- or resistance/target-based methods during the past decade. Future developments may include integrative application of several different genome mining strategies simultaneously in a high-throughput manner.

Because the majority of the natural product biosynthetic gene clusters are inactive under common cultivation conditions, synthetic biology strategies have been developed to activate these silent gene clusters. In most of these strategies, target silent gene clusters are refactored using well-characterized regulatory elements including promoters and terminators. Therefore, the availability of well-studied constitutive and inducible promoters is critical for identifying natural products encoded by silent gene clusters. In addition, as discussed in the reviews by Zhao and co-workers (DOI: 10.1039/c6np00017g) and Kim, Weber and coworkers (DOI: 10.1039/c6np00019g), the availability of well-characterized promoters is also important for microbial production of natural products using metabolic engineering.

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and synthetic biology tools. Myronovskyy and Luzhetskyy (DOI: 10.1039/c6np0002a) provide a comprehensive overview of known promoters for streptomycetes, one of the most prolific natural product producers, and their successful applications in refactoring silent gene clusters.

Microbial fermentation has been widely used to produce natural products. However, production titers are typically low and need to be significantly improved for compound identification and/or commercial production. In their Review article, Zhao and co-workers (DOI: 10.1039/c6np00017g) discuss recent developments and challenges in the engineering of native and heterologous microbial hosts for the production of bacterial natural products, with a focus on the genetic tools and strategies for strain improvement of actinomycetes. Similarly, in their Highlight article, Kim, Weber and coworkers (DOI: 10.1039/c6np00019c) discuss recent metabolic engineering studies with emphasis on host selection and engineering approaches for optimal production of bacterial natural products: native versus heterologous hosts (e.g., *Escherichia coli*) and rational versus random approaches. In addition, they discuss systems biology tools that have been used in the study on optimization of natural product production.

Dereplication of known natural products is essential for efficient discovery of novel natural products. Mass spectrometry (MS) is the most powerful tool to achieve robust and high-throughput dereplication. In their Highlight article, Henke and Kelleher (DOI: 10.1039/c6np00024j) discuss some recent examples of how modern mass spectrometry can be applied to synthetic biology and structure-based discovery of natural products, and recent methods for dereplication and correlation of substructures using tandem MS data.

Similar to actinomycetes, plants are also a rich source of bioactive natural products. Due to recent technological breakthroughs in the assembly of complex genomes, the number of available plant genomes is now growing rapidly. In their Review article, Medema and Osbourn (DOI: 10.1039/c6np00035e) discuss various computationally driven strategies for the discovery of plant biosynthetic pathways encoded by both chromosomally clustered and non-clustered genes. Besides the identification of biosynthetic gene clusters, this involves the use of data on co-expression, co-evolution and co-regulation of biosynthetic genes. Predicted plant biosynthetic pathways can subsequently be functionally reconstituted and experimentally characterized in heterologous hosts using synthetic biology tools.

In conclusion, these eight reviews have highlighted the recent advances in natural product discovery and production using synthetic biology and bioinformatics tools. This is a rapidly developing field, which will have to show its worth to society in the coming years; we await further developments with excitement. We thank the authors for their contributions to this issue of *Natural Product Reports* and hope that the readers will enjoy their work as much as we have.