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POTENTIAL APPLICATIONS OF SYNTHETIC BIOLOGY IN MARINE MICROBIAL FUNCTIONAL ECOLOGY AND BIOTECHNOLOGY

Guangyi Wang[1] and Juanita Mathews[2]

[1]*Department of Oceanography, University of Hawaii at Manoa, 1000 Pope Road, Honolulu, Hawaii 96822*

[2]*Department of Molecular Biosciences and Bioengineering, University of Hawaii at Manoa, Honolulu, Hawaii 96822*

18.1 INTRODUCTION

The oceans cover 70 percent of the earth's surface and are the most complicated and dynamic of all the earth's ecosystems; they provide the largest inhabitable space for living organisms, particularly microbes [1–3]. Microbes are well known to live in every corner of the oceans. Their habitats are extremely diverse and include, but not limited to, open water, sediment, estuaries, and specialized niches like hydrothermal vents and symbiotic hosts [1,4]. Microbial cells may account for more than 90 percent of the total oceanic biomass [5]. For more than 3 billion years, these microscopic creatures have mediated critical physical, chemical, and biological processes that have shaped the planet's habitability [2,6]. Marine microbes are responsible for about 50 percent of global primary productivity and play a major role in global nutrient cycles, which

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can directly or indirectly impact global climate change [6–9]. Due to their unique living environments in the oceans, marine microbes must adjust metabolically and physically to escape predators and adapt to harsh environments. Accordingly, intensive evolutionary pressures have forced marine microbes to evolve a wide range of metabolic abilities for regulatory function and the production of diverse molecules. Therefore, it comes as no surprise that the microbial diversity of the ocean is vast and a rich source of interesting biological materials for biotechnological applications [3,4,10].

Prior to the 1990s, our understanding of the diversity, ecological function, and biomedical potential of microbial communities was limited by the complexity of marine ecosystems. Recent developments in microbiological oceanography, high throughput screening methods and genomics have revealed new marine microbes and the natural compounds that they produce. However, in marine ecosystems, less than 0.1 percent of the indigenous microorganisms can be readily recovered by standard cultivation techniques. Therefore, our understanding of the ecological function and biotechnological potential of most marine microbes has been greatly limited [11,12]. At present, most studies of marine ecology still focus on mining genetic materials from diverse marine habitats and the understanding of the diversity and structure of marine microbial consortia [2,7,8,11,13–17]. Particularly, molecular approaches have opened the door to the understanding of ecological functions and the discovery of novel metabolic pathways and natural compounds. Because most marine microbes are not amenable to genetic manipulation, little work in synthetic biology has been done using marine microbes.

There are two broad goals for synthetic biology. One is the design and fabrication of biological components and systems using unnatural molecules, and the other is the redesign and fabrication of existing biological systems using interchangeable parts from natural biology [18]. Among the applications of this new field is the creation of bioengineered microbes and possibly other life forms that produce pharmaceuticals, detect toxic chemicals, break down pollutants, repair defective genes, destroy cancer cells, and generate hydrogen for the postpetroleum economy. Synthetic biology is chiefly an engineering discipline, but the ability to design and construct simplified biological systems offers life scientists a useful way to test their understanding of the complex functional networks of genes and biomolecules that mediate life process [19]. In this chapter, we review the use of genetic material from marine microbes to engineer conventional hosts for biotechnological and ecological benefits. The major goal is to illustrate the application of synthetic biology in oceanography and marine biotechnology research.

18.2 MARINE QUORUM SENSING AND SYNTHETIC REGULATORY NETWORK

Many accomplishments have already been made in synthetic biology, including diagnostic tools and diverse regulatory genetic circuits [18,20]. In this section, we only summarize utilization of genetic elements of marine quorum sensing for synthetic cell communication systems.

18.2.1 Quorum Sensing of the Marine Symbiotic Bacterium *Vibrio fisheri*

Quorum sensing is the regulation of gene expression in response to fluctuations in cell population density [21]. Quorum-sensing bacteria synthesize and release chemical signal molecules called autoinducers that increase in concentration as a function of cell density. The detection of a minimal threshold concentration of an autoinducer leads to change in gene expression. Quorum sensing was first described in two symbiotic luminous marine bacteria, *Vibrio fischeri* and *Vibrio harveyi* [22]. In both species, enzymes responsible for light production are encoded by the luciferase structural operon *luxICDABEG*, and light emission only occurs at high cell population density in response to the accumulation of the secreted autoinducer molecules [22–25]. The LuxI/LuxR quorum sensing system of *V. fisheri* is the first and the most thoroughly studied system in quorum sensing. *V. fisheri* is a Gram-negative bacterium that can be free living or can form a symbiotic relationship with a variety of invertebrate and vertebrate marine organisms [25,26]. In these symbiotic associations, the eukaryotic host supplies the bacterium with a nutrient-rich environment so that the bacterial culture can grow to extremely high cell densities, reaching 10^{11} cells/mL and emitting light [26,27]. The quorum sensing of *V. fisheri* depends on the synthesis and recognition of the autoinducer, *N*-(3-oxohexanoyl) homoserine lactone, also called *V. fischeri* autoinducer or VAI. This molecule freely diffuses across the cell membrane, triggering the formation of the enzymes necessary for bioluminescence [28]. The gene product of *luxI*, an acylhomoserine lactone synthase, can use acyl-ACP from the fatty acid metabolic cycle and *S*-adenosylmethionine (SAM) from the methionine pathway to synthesize the autoinducer [24,31].

The quorum sensing mechanism of *V. fisheri* is illustrated in Figure 18-1 and involves several products encoded by *lux* operon and *luxR* gene. The regulatory protein encoded by the *luxR* gene has two binding domains, one that interacts with the autoinducer and the other that binds to the promoter region of the *lux* operon and also to the promoter region of the *luxR* gene itself. The amino terminus contains the binding site for the autoinducer and the carboxyl terminus possesses a helix-turn-helix binding motif, typical of many DNA binding domains. In the absence of the autoinducer, the

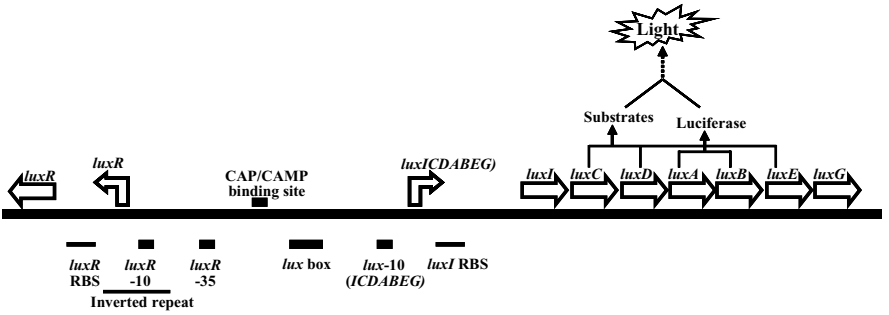

Figure 18-1 Genetic organization of genes and regulatory elements within lux operon on the chromosome of *V. fisheri*.

amino terminus is able to mask the carboxyl terminus, preventing the luxR protein from binding to the *lux* operon promoter region. Once the autoinducer binds to the luxR protein, the newly formed complex binds upstream of the *luxICDABEG*, promoting transcription of all the necessary components of the luciferase system [21]. The complex also acts as a negative autoregulator of the luxR transcriptional unit, by binding near the *luxR* promoter. The genes contained within the *lux* operon encode for several enzymes; *luxAB* encode the subunits of the luciferase enzyme, *luxCDE* encode proteins required for biosynthesis of the aldehyde substrate, and another open reading frame (*luxG*) exists downstream, but its function is still unknown [30]. The two regulatory *lux* genes (*luxR* and *luxI*) exist adjacent to each other, but unlike *luxI*, *luxR* is transcribed divergently from the *lux* operon (Fig. 18-1). At low population density, the *luxICDABEG* operon is transcribed at a basal level. Hence, a low level of autoinducer is constantly produced along with a low level of light [32]. When the autoinducer concentration reaches a threshold level (about 1–10 μg/mL), the cytoplasmic LuxR can detect and bind to it [31]. Interaction of LuxR and the autoinducer unmasks the DNA binding domain of LuxR, allowing LuxR to bind with the *luxICDABEG* promoter and activate its transcription [33]. This reaction causes an exponential increase in both autoinducer production and light emission. In addition, the LuxR and autoinducer complex represses the expression of *luxR*. This negative feedback loop is a compensatory mechanism that decreases *luxICDABEG* expression in response to the positive feedback circuits [21,34]. In the quorum sensing system, the autoinducer functions as a communication signal for the bacteria ''inside'' the host as opposed to ''outside'' in the seawater. The quorum sensing system enables *V. fisheri* to produce light only under conditions in which there is a positive selective advantage for the light [21].

The regulatory region of *lux* operon is complicated and contains two divergently transcribed promoters, as illustrated in Figure 18-1. The left promoter P_{luxL} constitutively transcribes the *luxR* gene. This promoter has a standard δ^{70} binding region, consisting of the -10 and -35 sequences, and a CRP/CAMP binding site, which is involved in catabolic repression of LuxR transcription. The right promoter P_{luxR} controls the expression of the *luxICDABEG* transcript [35]. Interestingly, the lux box, a 20 bp inverted palindromic repeat, allows dimeric binding of the LuxR protein in the presence of the autoinducer. This dimeric binding results in a nonlinear concentration response, a transcriptional control behavior of DNA binding proteins that is an essential element of signal restoration and digital control of expression [35,36]. These complicated genetic regulatory elements of quorum sensing allow populations of bacteria to simultaneously regulate gene expression in response to changes in cell density. Quorum sensing has broad biotechnological applications, including pathogen/pest management, recombinant gene expression, food preservation, and drug design [37–39]. Quorum sensing also exists in other bacteria and has been extensively discussed in several reviews [21,29,38–44].

18.2.2 Synthetic Cell Communication Network

Engineering of multicellular systems that utilize cell-to-cell communication to achieve coordinated behavior has been one of the foci for synthetic biology. This type of

engineered system can be used to study multicellular phenomena ranging from synchronized gene expression in homogenous populations to spatial patterning in developmental processes [20]. Recently, the genetic elements of *V. fisheri* quorum sensing have been successfully used to engineer several cell–cell communication systems (Fig. 18-2) [45–48].

First, genetic elements of the quorum sensing system are separated into sender and receiver components that are integrated into two different *E. coli* populations (Fig. 18-2a) [20,35]. The sender cells contain the genetic elements responsible for autoinducer production. The receiver cells are engineered with the control element of the *lux* operon, a reporter gene (GFP), and the *luxR* gene. The free diffusion of the autoinducer within the medium and across the cell membranes allows the establishment of chemical gradients and the controlled expression of the reporter gene. For good control, the expression level of the *luxI* gene is placed under the control of the $P_{Ltet0\text{-}1}$ promoter, which is upregulated by the *tetR* gene product in the presence of tetracycline [49,50]. The *tetR* gene under the control of the constitutive promoter P_{N25} is chromosomally carried in a special strain of *E. coli*, which harbors the spectinomycin resistance gene. The $P_{Ltet0\text{-}1}$ promoter allows the controlled expression of the *luxI* gene using a varying amount of a nongrowth inhibitory version of tetracycline, anhydrotetracycline (aTc). Therefore, the level of the autoinducer in the sender cells can be controlled by varying the aTc concentrations [35]. The autoinducer diffused into the receiver cells can regulate the expression of *luxR* and therefore the reporter gene (GFP). In this engineered system, the levels of fluorescence in the receiver cells are successfully controlled via aTc concentration.

In another synthetic system, positive and negative regulations of gene expression are integrated into multicellular bacterial systems to obtain a transient response in cell-to-cell communication [47] (Fig. 18-2b). Using aTc, the sender cells in the system are induced to produce the autoinducer, which then diffuses to the nearby pulse-generating receiver cells. In response to a long-lasting increase in the autoinducer concentration, the receiver cells are engineered to transiently express a GFP. This is accomplished by a feedforward motif, which is placed in the genetic circuit of the receiver cells and allows them to display an initial excitation followed by a delayed inhibition in the presence of the autoinducer [51]. The feedforward motif is made up of two transcriptional regulators, LuxR and the lambda repressor (CI) that act on the GFP promoter. The LuxR protein when combined with the autoinducer from the sender cells, acts as an activator of CI production, and also acts as an activator of GFP transcription. CI acts as an inhibitor of GFP transcription, but because it has a lower affinity for the promoter than the LuxR and autoinducer complex, it is only able to repress GFP transcription after it has accumulated a threshold concentration. Thus, the receiver circuits can distinguish between various rates of increase in the autoinducer levels and gain ability to generate a spatiotemporal behavior so that the receiver cells only respond transiently to signal from the nearby cells but ignore signal from sender cells, which are farther away.

Using the same cell-to-cell communication mechanism, a ‘‘population control’’ genetic circuit is engineered to program the dynamics of cell population despite variability in the behavior of individual cells by coupling quorum-controlled gene

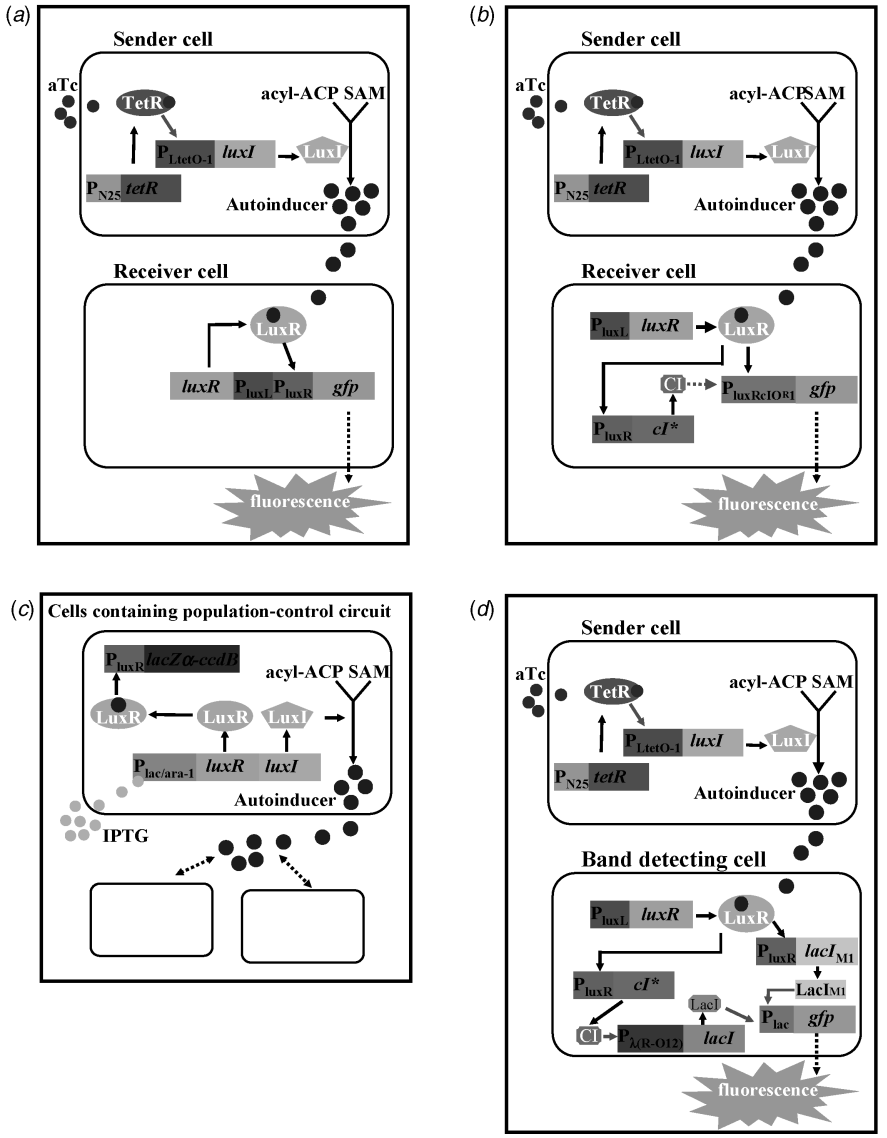

Figure 18-2 Engineered cell-to-cell communication networks using genetic elements of lux operon from *V. fisheri.*(a) diagram of gradient communication system [20,35]; (b) genetic network for pulse signal generation [47]; (c) design of "cell population control"" genetic circuit [48]; (d) design of "band-detect"" gene network [46]. Red arrow means suppression and black arrow induction. See text for abbreviations and details.

expression to cell survival and death [48]. This synthetic circuit can autonomously control the density of an *E. coli* population through a quorum-sensing system and can set a stable steady state in terms of cell density and gene expression that is easily tunable by varying the autoinducer signal. As illustrated in Figure 18-2c, the *luxI* and

luxR genes are placed under the control of a synthetic promoter Plac/ara^{-1} in the "population control" system [52]. When isopropyl-β-D-thiogalactopyranoside (IPTG) is present, LuxR is produced along with the autoinducer. The activated LuxR transcriptional regulator activates the promoter P_{luxR} from the *lux* operon that controls the expression of the killer gene *lacZα-ccdB*. The killer gene product is a fusion protein containing LacZα and CcdB. The LacZα portion of the fusion protein allows the measurement of fusion protein levels using a LacZ assay. The CcdB portion still has the toxicity of native CcdB, which kills susceptible cells by poisoning the DNA gyrase complex [53]. Therefore, in the presence of IPTG, cells harboring the genetic circuit will produce enough killer protein to maintain a stable cell density.

Another synthetic system utilizes "band-detect" gene networks that are engineered to allow the receiver cells to form diverse patterns around the sender cell colony (Fig. 18-2d) [46]. As in the above two systems, the sender cells produce LuxI protein for the biosynthesis of the autoinducer, which forms a chemical gradient around the sender cell colony. The LuxR protein in the receiver cells activates the expression of lambda repressor (CI) and Lac repressor ($LacI_{M1}$, a product of a codon-modified *lacI*), which are under the control of P_{luxR}. CI then binds to the $P_{\lambda(R\text{-}012)}$ promoter and represses the expression of the wild-type LacI. The GFP reporter gene is under the control of the promoter $P_{lac,}$ which is repressed by $LacI_{M1}$ and LacI. Receiver cells proximal to the senders encounter high concentrations of the autoinducer and produce high levels of CI and $LacI_{M1}$. Hence, receiver cells near the sender cells will not express GFP. The receiver cells that are far from the sender cells will express $LacI_{M1}$ and CI at basal levels. Thus, the wild-type LacI will be expressed and again suppress the expression of GFP. At intermediate distances from the senders, both CI and $LacI_{M1}$ are expressed in moderate levels in the receiver cells. However, due to the different repression efficiency of CI and $LacI_{M1}$, CI effectively represses LacI expression while the $LacI_{M1}$ concentration is below the level required for GFP production. Hence, the GFP is produced. Overall, this feedforward loop, including LuxR, CI, $LacI_{M1}$, LacI, and GFP, attributes the desired nonmonotonic response to the autoinducer concentrations to the genetic circuit [54,55]. By deliberately arranging sender cells on solid-phase media containing a mixture of receiving cells, diverse spatial patterns including bull's-eyes, ellipses, hearts, and clovers can be produced using the system [46].

18.3 RECONSTRUCTING NATURAL SYSTEM OF UNCULTURABLE MARINE MICROBES IN MICROBIAL HOST

One of the potential applications of synthetic biology is testing our understanding of the functions involved in biological systems [56]. Overall, research on this aspect of synthetic biology is rare. In this section, we will briefly discuss the potential application of synthetic biology in a marine functional ecology study. The example described below may be relatively simple, but it illustrates how the concept of synthetic biology can be used to understand the ecological function of unculturable marine microbes.

Major efforts have been made to investigate marine microbial diversity in many different natural habitats [2,6,8,15,16]. However, our current understanding of the ecological function of marine microbes in their natural environments is minimal. The major reason for this lack of understanding can be ascribed to our limited ability to cultivate and to genetically manipulate these marine microbes for physiological and metabolic characterization. The vast majority (>99 percent) of marine microbes are unculturable and therefore their ecological roles in marine natural environments remain largely unknown. Some molecular techniques such as the FISH (fluorescence *in situ* hybridization) have revealed the identity, abundance, and distribution of selected unculturable microbes in natural marine habitats. However, the ecological function of these marine microbes cannot be understood in this way. Genetic materials from unculturable microbes can be recovered using an environmental genomic strategy. Functional biological components or pathways encoded in the genetic materials can then be fabricated using the principles of synthetic biology. Large genomic DNA fragments of uncultured marine microbes are usually recovered from environmental genomic libraries, which are constructed using fosmid or BAC (bacterial artificial chromosome) vectors [57,58]. Recently, a new phototroph in the sea was identified by characterization of new type of rhodopsin from a picoplankton bacterial artificial chromosome library [57]. Analyses of a 130 kb environmental clone revealed a new class of genes for the rhodopsin family (named proteorhodopsin) that has not been observed in bacteria before. Proteorhodopsin (PR) proteins were found to be bacterial retinal-binding membrane pigments that function as light-driven proton pumps in the marine ecosystem [56]. Subsequent investigations indicated that proteorhodopsin occurs in many marine bacteria and evolves for various light wavelengths at different ocean depths [59–66]. However, it is a great challenge to prove bacteria containing proteorhodopsin, are a novel group of marine phototroph. To that end, *E. coli* cells were engineered to use the proteorhodopsin genes. The engineered cells acquired the net-outward transport of protons in the presence of retinal and light [57]. Recently, analysis revealed that PR genes are linked to a carotenoid biosynthesis gene cluster, which encodes proteins responsible for converting geranylgeranly diphosphate to β-carotene [67]. In addition, a gene coding for a homologue of the bacteriorhodopsin-related-protein-like homologue protein (Blh) from the archaeon *Halobacterium* sp. NRC-1 was also found in the marine bacteria BAC clone. Blh has been shown to be involved in the retinal biosynthesis [68]. This indicates that bacteria possessing PR proteins also carry the ability to synthesize the retinal chromophore and to potentially form functional PR holoproteins. Indeed, expression of *blh* in the β-carotene producing *E. coli* cells results in the loss of the yellow color of these cells because β-carotene is converted into a colorless all-*trans* retinal by Blh. When the colorless retinal binds PR protein, the resulting complex becomes red colored and can function as an active proton pump [67]. Thus, proteorhodopsin is proved to have the ability to couple light energy harvesting with carbon cycling through nonchlorophyll-based pathways in the ocean.

In addition, the environmental genomic approach has been used to study methane-oxidizing microbial consortia in deep sea methane seeps [69] and resulted in the identification of the methanogenic pathway of the ANME-1 archeal groups [70].

Unfortunately, no further functional analysis of the pathway was carried out. It is believed that a methanogenic *E. coli* strain could be constructed by using this archeal pathway. Overall, application of synthetic biology in the understanding of marine microbial ecology is still in its infancy. Close collaboration between marine microbial ecologists and synthetic biologists may greatly benefit the development of both fields.

18.4 METABOLIC ENGINEERING FOR THE PRODUCTION OF MARINE NATURAL PRODUCTS

The production of natural compounds through metabolic engineering has been one of the major foci in synthetic biology [18,19]. Tremendous progress has been made in the production of natural compounds of terrestrial origins and is summarized in many excellent reviews [71–76]. In this section, we review the progress of metabolic engineering for the production of marine natural compounds. Production of valuable marine natural products in engineered microbial hosts has been an active research area. Some engineered hosts have shown promise in pharmaceutical and nutraceutical industries. Like terrestrial natural products, marine natural compounds are often produced by enzymes coded in gene clusters. Polyunsaturated fatty acids (PUFAs) are of biotechnological interest for their beneficial properties to human health and their importance in infant development [77]. The most important PUFAs are eicosopentaenic acid (EPA) and docosahexaenic acid (DHA). The 38 kb genomic fragment, which includes all genes responsible for the production of EPA, was recovered from the marine bacterium *Shewanella putrefaciens* strain SCRC-2738 [78]. Engineered *E. coli* cells, with the foreign gene cluster cloned into them, produced EPA in low yield. Also, the same gene cluster was cloned into the marine cyanobacterium *Synechococcus* sp. using a broad host cosmid vector, pJRD215. The engineered cyanobacterial cells produced EPA up to 0.56 mg/g dry cells at 23°C [79]. In addition, the production yield of EPA was further improved by stabilizing the expression and maintenance of the cluster in the host cells [78]. Thus, these studies provide the first examples of EPA production in bioengineered hosts. Also, the increased understanding of PUFA-related genes offers the possibility for the engineering of microbial cell factories suitable for an alternative production of EPA and DHA.

Most microalgae are obligate photoautotroph and their growth strictly depends on the generation of photosynthetically derived energy. *Phaeodactylum tricornutum* is a unicellular nonsilicate diatom and can accumulate EPA up to 30 percent of the total fatty acid content. Furthermore, astaxanthin is an efficient antioxidant and produced by a number of marine bacteria and microalgae. It can be synthesized from β-carotene by the addition of two keto groups to carbons C4 and C4' and two hydroxyl groups to C3 and C3' [81]. The gene *crtO* encoding β-C-4-oxygenase from the green alga *Haematococcus pluvialis* can convert β-carotene to astaxanthin. The cyanobacterium *Synechococcus* PCCC7 can produce astaxanthin as well as other keto-carotenoids [82]. After the introduction of a single gene for glucose transporters *glut1* or *hup1*, the microalga *P. tricornutum* was genetically engineered to thrive on exogenous glucose

in the absence of light [80]. The trophic conversion of microalgae has provided an important platform for large-scale production of PUFAs and carotenoids using engineered microalgal cells. Metabolic engineering of conventional noncarotenogenic bacteria and yeasts using carotenoid metabolic pathways genes (e.g., *crt* genes or IPP synthetic genes) from marine microbes has been intensively studied (for reviews, see Refs [83,84]).

Marine invertebrates such as sponges, ascidians, and bryozoans are well known for their production of bioactive natural products, several of which are currently undergoing clinical trials [85,86]. These marine invertebrates also harbor diverse symbiotic microbes [64,87,88]. Because many marine natural products from these marine invertebrates resemble bacterial compounds, some of their natural chemicals have long been proposed to be produced by their bacterial symbionts [88]. Several studies have demonstrated that microbial isolates associated with sponges produced the same compounds formerly isolated from sponges [89–93]. However, these results do not rule out the possibility that substances might be transported between bacterial symbionts and their hosts via export or sequestration mechanisms [94]. Recently, several biosynthetic pathways for anticancer compounds have been isolated from marine invertebrates using molecular approaches [87,95,96]. Particularly, the patellamide A and C biosynthetic pathway was identified from *Prochloron didemni*, a cyanobacterial symbiont of *Lissoclinum patella*. *E. coli* cells that were engineered to harbor this biosynthetic pathway and its regulatory region produced patellamide A at the level of 20 μg/L. Although the production yield is low, it represents the first successful case of the production of marine natural compounds in a synthetic microbial host.

18.5 CONCLUSION

The world's oceans cover the largest portion of the global surface and contain the most complicated ecosystems. They are home to different biota ranging from tiny planktonic organisms that comprise the base of the marine food web (i.e., phytoplankton and zooplankton) to large marine mammals like the whales, manatees, and seals. It has been estimated that the oceans harbor 3.6×10^{29} microbial cells with a total cellular carbon content of about 3×10^{17}g [97]. These microbial cells are responsible for the vast majority of primary production and mediate all biogeochemical cycles in the oceans [5]. Considering the enormous number of microbes, their interaction with other hosts, and their vast metabolic diversity, marine environments can be an enormously rich source for novel molecular regulatory networks and pathways for new natural compounds.

Further environmental genomic investigation of marine microbes will contribute to the development of synthetic biology by providing novel genetic regulatory networks and pathways. On the other hand, synthetic biology can also benefit marine microbial ecology by providing techniques for the functional characterization of unculturable marine microbes. Particularly, the synthetic biology approach can provide a viable solution for the development of interesting marine natural compounds. For example, the valuable and powerful antimalarial drug artemisinin (a sesquiterpene lactone) is

isolated from the sweet wormwood, *Artemisia annua*, at very low yield. Recently, its immediate precursors artemisinic acid and amorphadiene have been successfully produced at a significantly high level in engineered *Saccharomyces cerevisiae* and *E. coli*, respectively [98,99]. Thus, metabolically engineered microbial hosts are likely to solve the supply and affordability issues for this effective antimalarial drug. Therefore, many valuable marine terpenoids such as cytotoxic eleutherobin and sarcodictyins could also be produced in engineered microbial hosts using similar strategies because most terpenoids use the same building blocks IPP (isopentenyl diphosphate) and DMAPP (dimethylallyl diphosphate) for their biosynthesis. Unfortunately, most of the key genes responsible for the production and modification of these valuable marine compounds are still not available. At present, the application of synthetic biology to the understanding of marine microbial ecology and marine biotechnology is mainly limited by the availability of the novel genetic materials from the marine environments.

The quorum-sensing system of *V. fisheri* has been successfully used to engineer several cell-to-cell communication systems. It is reasonable to believe that diverse and novel genetic regulatory systems will be found in marine microbial genomes using an environmental genomics approach. Thus, these marine regulatory systems will provide the platform for bioengineers to synthesize novel genetic circuits and cell communication systems for diverse biotechnological applications. Collaborative research of interdisciplinary scientists and researchers from oceanography, microbiology, metabolic engineering, computer science, mathematics, informatics, and marine biology can provide greater progress in understanding marine ecosystems and the discovery of new techniques in synthetic biology.

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