Chapter 17
Beach to Bench to Bedside: Marine Invertebrate Biochemical Adaptations and Their Applications in Biotechnology and Biomedicine

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Abstract The ocean covers more than 70% of the surface of the planet and harbors very diverse ecosystems ranging from tropical coral reefs to the deepest ocean trenches, with some of the most extreme conditions of pressure, temperature, and light. Organisms living in these environments have been subjected to strong selective pressures through millions of years of evolution, resulting in a plethora of remarkable adaptations that serve a variety of vital functions. Some of these adaptations, including venomous secretions and light-emitting compounds or ink, represent biochemical innovations in which marine invertebrates have developed novel and unique bioactive compounds with enormous potential for basic and applied research. Marine biotechnology, defined as the application of science and technology to marine organisms for the production of knowledge, goods, and services, can harness the enormous possibilities of these unique bioactive compounds acting as a bridge between biological knowledge and applications. This chapter highlights some

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M. Kloc, J. Z. Kubiak (eds.), *Marine Organisms as Model Systems in Biology and Medicine*, Results and Problems in Cell Differentiation 65,
https://doi.org/10.1007/978-3-319-92486-1_17

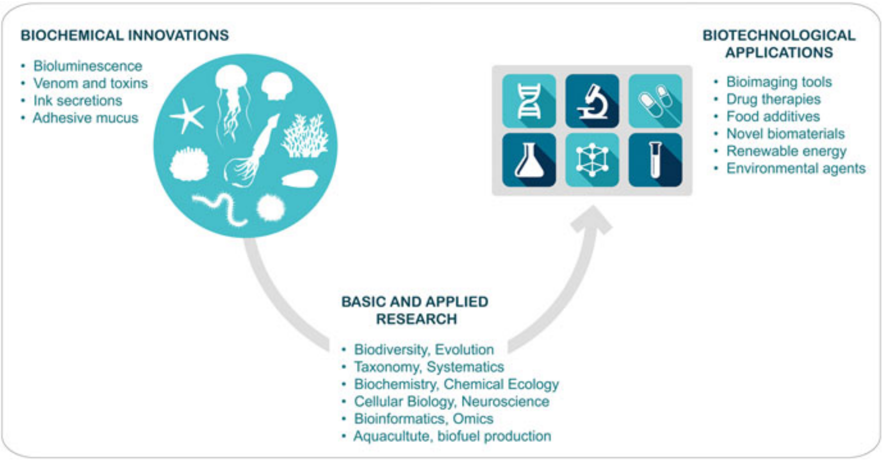

Fig. 17.1 Marine biotechnology workflow. Marine (blue) biotechnology relies on unique bioactive products derived from marine invertebrate biochemical innovations. These products and the animals that produce them are investigated using a biotechnological toolbox that applies basic and applied research methods such as biodiversity assessments and aquaculture production to develop a wide range of biotechnological applications

of the most exceptional biochemical adaptions found specifically in marine invertebrates and describes the biotechnological and biomedical applications derived from them to improve the quality of human life.

17.1 Marine Biotechnology and the Ocean as a Source of Chemical Diversity

Life on earth began in the ocean billions of years ago, and most organisms that exist today on land, or in freshwater and ocean ecosystems, originated in the sea. The ocean covers more than 70% of the Earth's surface and has high phylogenetic diversity, as it is home to 34 of the 36 known animal phyla that currently inhabit the planet. Because of its immense breadth and high degree of biodiversity, the ocean is arguably the ecosystem with the greatest potential for biodiscovery, and it is therefore a very promising source of innovation (Evans-Illidge et al. 2013). Marine biotechnology—broadly defined as the application of science and technology to marine organisms for the production of knowledge, goods, and services—can harness the enormous possibilities of marine biological resources, acting as a bridge between biological knowledge and applications to improve the quality of human life (Querellou 2010) (Fig. 17.1). However, despite the great potential of marine ecosystems to provide solutions to address global challenges, such as food scarcity, sustainable energy, and environmental and human health, the ocean remains largely unexplored (Trincone et al. 2015). In fact, we know more about the moon's surface than we know about the depths of our oceans. But this can change. We are at a confluence in time where advances in the last 40 years have spearheaded technological breakthroughs above and below the seas. These innovations enabled new approaches for collecting marine organisms, using methods like remotely operated underwater vehicles (ROVs) and gliders, and for leveraging the twentieth-century revolution in molecular biology to decipher the genetic and chemical composition of marine organisms in a relatively fast and cost-effective manner.

The marine biotechnology enterprise (blue biotechnology) has grown exponentially in the last few decades, and with less than 5% of the vast oceanic environment explored, it has already delivered an array of innovations such as new medicines, chemicals, nanomaterials, nutritional supplements, bioenergy resources, and strategies for the sustainable use and management of the world oceans (e.g., Hannon et al. 2010; Livett et al. 2004; Schmidtko et al. 2010). Starting in the 1980s, there has been a significant increase in the number of marine compounds discovered each year, with annual numbers peaking at 400–500 novel compounds (Greco and Cinquegrani 2016). The biomedical industry has particularly benefited from the discovery of novel marine chemicals, with nine therapies derived from marine organisms currently approved for treating disease and disorders, namely, Adcertis®, Carragelose®, Cytosar-U®, Halaven®, Lovaza®, Retrovir®, Prialt®, Vira-A®, and Yondelis® (Arrieta et al. 2010) (Table 17.1). The applications of these compounds are as diverse as the organisms from which they were discovered. For example, Prialt® is a pain therapy developed from the venom of the marine snail *Conus magus*, while Adcertis® is an antibody-drug conjugate derived from the sea hare *Dolabella auricularia* that treats Hodgkin lymphoma (Hart 2015; Miljanich 2004). Halaven® is a breast cancer therapy derived from the sponge *Halichondria okadai*, while Retrovir®, also derived from a marine sponge, is an antiretroviral medication used to prevent and treat HIV/AIDS (Chiba and Tagami 2011; Rachlis 1990). As these successful cases illustrate, the great diversity of chemical compounds found in the ocean is a highly valuable but yet untapped resource for the discovery of novel bioactive agents with unique structures and diverse biological activities that can greatly improve human life (Evans-Illidge et al. 2013).

Marine habitats range from tropical coral reefs to ocean trenches and include ecosystems with the most extreme conditions of pressure, temperature, and light. As a consequence, marine organisms have evolved a plethora of remarkable adaptations that serve a variety of vital functions to survive in different habitats. For example, toxic secretions such as those produced by venomous marine organisms are in some cases used as a defensive mechanism against predators and in others as a weapon to subdue prey (Casewell et al. 2013; Verdes et al. 2018). Like venom, several other adaptations developed by marine organisms, such as bioluminescence and ink, represent biochemical innovations where the animals have attained novel and unique bioactive molecules that often show considerably greater potency than their terrestrial counterparts (Schroeder 2015; Trincone et al. 2015). Marine organisms have perfected these biochemical adaptations through millions of years of evolution, providing an immense reservoir of bioactive compounds with enormous potential for both basic and applied research (Schroeder 2015; Trincone et al. 2015) (Fig. 17.1). In this chapter, we provide an overview of some of the exceptional

Table 17.1 Therapeutics derived from marine organisms. Examples of some successful, currently approved therapies derived from bioactive compounds isolated from marine organisms

Marine organism		Drug	Treatment	Company	References
	Sea hare *Dolabella auricularia*	Adcetris	Hodgkin lymphoma	Seattle Genetics (Bothell, WA, USA)	Hart (2015)
	Seaweed *Rhodophyceae*	Carragelose	Antiviral respiratory diseases	Marinomed (Vienna, Austria)	Li et al. (2014)
	Sponge *Tectitethya crypta*	Cytosar-U (Ara-C)	Leukemia	Bedford Laboratories (Ohio, USA)	Sullivan (1982)
		Vira-A	Antiviral herpes simplex	King Pharmaceuticals (NJ, USA)	Privat de Garilhe and de Rudder (1964)
	Sponge *Halichodria okadai*	Halaven	Breast cancer	Eisai (Tokyo, Japan)	Chiba and Tagami (2011)
	Fish	Lovaza	Hypertriglyceridemia	GlaxoSmithKline (Brentford, UK)	Halade et al. (2010)
	Marine snail *Conus magus*	Prialt	Chronic pain	Perrigo (Dublin, Ireland)	Miljanich (2004)
	Sea sponge	Retrovir	HIV/AIDS	ViiV Healthcare (NC, USA)	Rachlis (1990)
	Tunicate *Ecteinascidia turbinata*	Yondelis	Liposarcoma and leiomyosarcoma	PharmaMar (Madrid, Spain)	Erba et al. (2004)

biochemical innovations found in marine organisms, specifically marine invertebrates, and the biotechnological and biomedical applications derived from them to advance and improve human life.

17.2 Biochemical Innovations of Marine Invertebrates

To survive in the varied ocean ecosystems they occupy, marine invertebrates have evolved an array of biochemical innovations that allow them to adapt and thrive in often extreme environments. These biochemical innovations, which range from secretions of mucus and toxins to light-producing molecules, play fundamental roles in marine ecological interactions, acting as pheromones, feeding deterrents, mediators of spatial competition, site recognition cues, antifouling agents, UV sunscreens, and facilitating reproduction (Harper et al. 2001). In a journey from the shallow intertidal to the abyssal depths, marine invertebrates display effortless biochemical innovations that humans have labored to reproduce in laboratories. In the following paragraphs, we describe a few examples of biochemical wonders produced by marine invertebrates, including toxins, ink secretions, adhesive gels, and light-producing compounds that have been translated to advance the blue biotechnology enterprise.

17.2.1 Marine Invertebrate Toxins

Many marine organisms defend themselves from predators by using toxic substances, including harmful secondary metabolites, poisonous molecules, and venomous secretions. These types of chemical defenses are particularly common among sessile and soft-bodied invertebrates such as sponges, corals, and ascidians that often dominate subtidal habitats with intense rates of predation (Lindquist 2002). For instance, venoms, which are generally defined as toxic secretions produced by one animal and delivered to another animal through the infliction of a wound, have evolved independently many times throughout the Metazoa (Casewell et al. 2013; Fry et al. 2009). Animal venoms are composed of a mixture of bioactive toxins and represent one of the most complex biochemical natural secretions known to date (Norton and Olivera 2006; Vonk et al. 2013). Venomous marine invertebrates are found in many phyla, from cnidarians such as sea anemones and jellyfish, which are the oldest venomous sea creatures recorded (Macek 1992; Ponce et al. 2016), to echinoderms such as starfish and sea urchins (Lee et al. 2015; Nakagawa et al. 1991); mollusks, such as cone snails and octopuses (Gorson et al. 2015; Olivera and Teichert 2007); annelids, including fireworms and bloodworms (Verdes et al. 2018; von Reumont et al. 2014a, b); and arrow worms (Thuesen et al. 1988) (Fig. 17.2a–c).

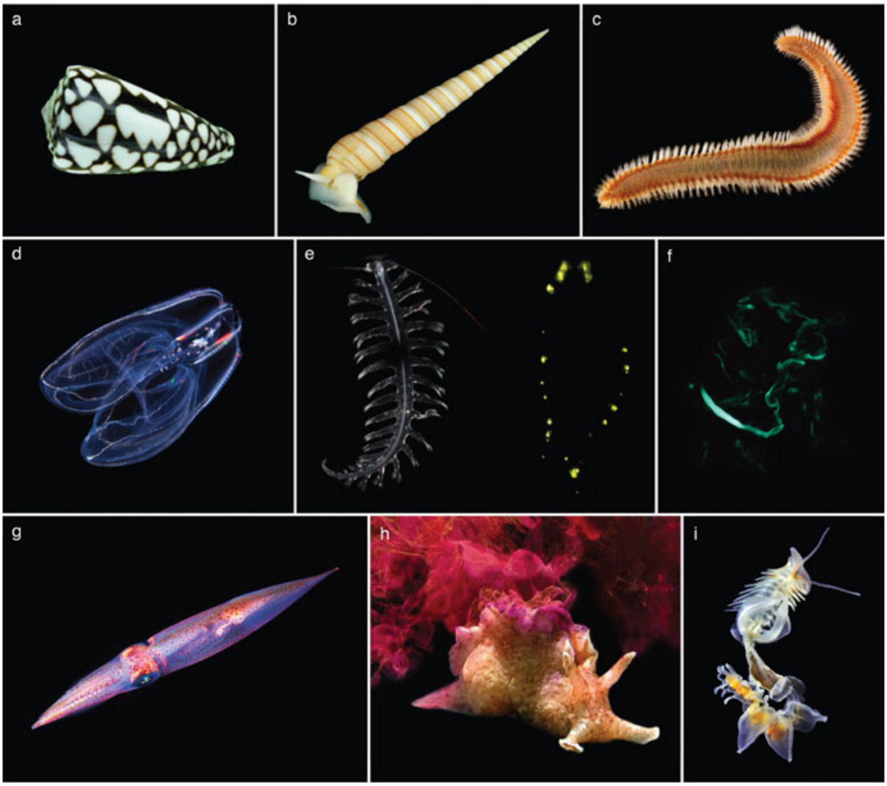

Fig. 17.2 Biochemical innovations of marine invertebrates. Venomous conoidean snails (**a**) *Conus marmoreus* and (**b**) *Terebra tricolor*; (**c**) venomous fireworm *Eurythoe complanata*; (**d**) bioluminescent comb jelly *Bolinopsis infundibulum*; bioluminescent annelids (**e**) *Tomopteris helgolandica* under natural light (left) and in the dark after induced bioluminescence (right); and (**f**) *Odontosyllis enopla* bioluminescent display; inking mollusks (**g**) squid *Loligo vulgaris* and (**h**) sea hare *Aplysia californica*; (**i**) mucus-producing annelid *Chaetopterus variopedatus*. Images courtesy of Yves Terryn (**b**), Denis Riek (**c**), Alexander Semenov (**d**, **g**, **i**), Anaïd Gouveneaux (**e**), and John Sparks (**f**)

A particularly prolific group in terms of venom is the predatory marine neogastropods of the Conoidea superfamily that includes cone snails (Conidae), auger snails (Terebridae), and turrids (Turridae) (Fig. 17.2a–b). The Conoidea represents one of the most diverse groups of venomous marine organisms with numerous lineages characterized by a venom apparatus used for predation (Gonzales and Saloma 2014; Gorson et al. 2015; Gorson and Holford 2016; Holford et al. 2009; Puillandre et al. 2014). The genus *Conus* is the most comprehensively studied and includes species that produce complex venoms with hundreds of unique peptide toxins, referred to as conotoxins (Kaas et al. 2012; Puillandre et al. 2012). While cone snail venom has been studied for more than 40 years, less than 2% of their venom peptides have been characterized to identify their functional molecular targets. Similarly, beyond cone snails, the venoms of terebrids and turrids are largely unknown. Recent efforts have begun to characterize the venom peptides of terebrids and turrids relying largely on advances in next-generation sequencing and other analytic techniques such as proteomics (Gonzales and Saloma 2014; Gorson et al. 2015). In fact, small, harder to collect, and often neglected venomous marine invertebrates are now being investigated in record numbers, thanks to what is sometimes referred to as the "rise of the omics" (Gorson and Holford 2016; von Reumont et al. 2014a, b). Given that venomous conoidean snails can conservatively produce between 50 and 200 peptides in their toxic arsenal and there are more than 10,000 species of conoideans, there is an amazing repertoire of venom peptides to be discovered. Whether in cnidarians, echinoderms, or mollusks, the venom peptides produced by these organisms are extremely potent, fast acting, and very specific, targeting hematic and neurotic pathways (Fry et al. 2009; Verdes et al. 2018).

17.2.2 Marine Mollusk Ink Secretions

Some mollusks, including sea hares (*Aplysia*) and coleoid cephalopods (octopuses, squid, and cuttlefishes), produce an ink secretion that functions as a chemical antipredator defense (Fig. 17.2g–h). Sea hares, in particular, have risen to scientific acclaim for their use in neuroscience to determine the mechanisms of learning and memory. These herbivorous animals, when threatened, release toxins sequestered from their diet of red algae (Kicklighter et al. 2007; Paul and Pennings 1991). Both sea hares and cephalopods secrete their chemically laden ink from two distinct glands. In the case of the sea hare, the products of the ink gland and the opaline gland are released into the mantle cavity and then pumped through the siphon toward the predator (Love-Chezem et al. 2013; Prince 2007). Opaline is a viscous substance that contains a high concentration of free amino acids and sticks to the chemosensory appendages of the predator, inactivating them and thus influencing its capacity to detect prey (Kicklighter et al. 2007; Love-Chezem et al. 2013). In addition to acting through sensory inactivation, ink secretion of sea hares can also act as an unpalatable repellent and as a decoy that misdirects and confuses the predator (Nolen et al. 1995; Nusnbaum and Derby 2010). Cephalopod ink functions as antipredatory visual stimuli, acting either as a smoke screen or as a distracting decoy and possibly also disrupting the predator's chemical sensors (Caldwell 2005). It is composed of a black ink containing melanin produced by the ink gland and a viscous mucous produced by the funnel organ (Derby 2014). Ink secretions of both sea hares and cephalopods represent a successful biochemical innovation that has enabled the organisms to survive and thrive.

17.2.3 Viscoelastic Adhesive Gels

A variety of marine invertebrates produce viscoelastic adhesive gels such as mucus secretions that consist of a network of polysaccharides and proteins entangled to form a gel with more than 95% of water content (Stabili et al. 2015). These mucous secretions are essential for the survival of many marine invertebrates as they are used for a variety of functions including protection against pathogens and parasites, to coat vulnerable organs, reduce drag forces, prevent sedimentation, enhance adhesion, limit water loss, and aid in locomotion and feeding (Smith 2002; Stabili et al. 2015; Weigand et al. 2017).

Sessile marine invertebrates, in particular, which are permanently attached to the sea floor with limited mobility, are more vulnerable to predation and use mucus secretions as an antipredator mechanism. In addition to mechanical protection, the mucus of many of these species contains toxic compounds that make the animal poisonous or distasteful (Iori et al. 2014). In many cases, the mucus also serves as an immune response system, producing a considerable amount of defensive compounds such as bioactive antimicrobials, toxins, and cytolytic molecules (Derby 2007; Iori et al. 2014; Stabili et al. 2015).

Numerous filter-feeding sessile organisms, such as the marine annelid *Chaetopterus* (Fig. 17.2i), use mucus to trap and filter food, to deter prey, and to gather sand particles to build protective tubes (Weigand et al. 2017). Other marine invertebrates, most notably mollusks, use mucus as an adhesive to attach to the substratum during locomotion. Some of these mollusks such as limpets and mussels are well-known for the extraordinary adhesive power of their mucus secretions (Smith 2002; Stewart et al. 2011).

17.2.4 Light-Producing Compounds

Bioluminescence, the ability to produce light by living organisms, is another outstanding biochemical innovation that has independently evolved in many lineages across the tree of life (Haddock et al. 2010). Bioluminescent light is the product of a chemical reaction involving the oxidation of a light-emitting molecule—luciferin—by a specific enzyme, luciferase (Shimomura 2012). In some cases, the luciferin is strongly bound to the luciferase and oxygen, forming a stable complex referred to as a photoprotein (Deheyn and Latz 2009; Shimomura 1985). Bioluminescent forms are found in many taxonomic groups, ranging from bacteria to vertebrates, but the great majority of luminous organisms are marine taxa (Shimomura 2012; Widder 2010). In fact, a recent study based on observations of more than 350,000 individuals in the water column reported that 76% of them were bioluminescent (Martini and Haddock 2017). A great number of these luminous marine organisms are invertebrates, including cnidarians, ctenophores, annelids, mollusks, and arthropods (Haddock et al. 2010) (Fig. 17.2d–f). The ecological diversity of bioluminescent marine invertebrates is remarkable, with species occupying a great range of habitats, from coastal waters to the deep sea, in benthic and pelagic waters, from polar to tropical regions. This outstanding diversity is matched by the wide array of bioluminescent colors—including yellow light emitters (Fig. 17.2e), which are extremely rare in marine environments—as well as varying light patterns and chemistries (Verdes and Gruber 2017). Likewise, bioluminescence is associated with a variety of different functions, including defense, predation, and intraspecific communication (Bassot and Nicolas 1995; Gouveneaux and Mallefet 2013; Haddock et al. 2010; Oba et al. 2016).

Although all bioluminescent organisms convert the chemical energy of an oxidation reaction into light, their independent evolutionary origins have resulted in a great diversity of chemistries and biological systems (Conti et al. 1996). The luciferases characterized so far from different organisms have extremely diverse structures, substrate specificities, and mechanisms and do not generally share sequence similarities (Viviani 2002). Luciferins are also quite diverse; however, in many cases the same compound has been independently co-opted in unrelated organisms. For instance, coelenterazine is the light emitter in at least nine phyla including jellyfish, crustaceans, mollusks, and vertebrates, even though their luciferases are unrelated in sequence and structure (Gimenez et al. 2016; Haddock et al. 2010).

17.3 Biotechnological and Biomedical Applications

Recent scientific breakthroughs and technological advances such as next-generation sequencing, proteomics, and bioinformatics are accelerating our capacity to harness marine bioactive compounds for biotechnological and biomedical applications that have significant potential to improve human life and advance scientific knowledge. In the following sections, we describe some of the novel applications that have been developed from bioactive compounds isolated from marine invertebrate biochemical adaptations.

17.3.1 Pharmacological Applications of Venom Peptides

Many compounds derived from marine invertebrate biochemical innovations, in particular venom toxins, have become major sources of drug leads driving research efforts in the pharmaceutical industry and greatly advancing drug discovery and development efforts. The only drug derived from venomous marine snails, Prialt®, is based on a venom peptide from the species *Conus magus*, and it is used to treat chronic pain in HIV and cancer patients (Miljanich 2004). Prialt® (ziconotide; MVIIA) is a breakthrough drug as it not only realized the potential of venomous marine snails for drug discovery, but it also provided a new paradigm for treating pain because it targets N-type calcium channels instead of opioid receptors (Fusetani et al. 2000; McGivern 2007). Until the discovery and development of Prialt®, most pharmaceutical companies looking for analgesic remedies investigated compounds that target opioid receptors, such as morphine. Prialt® revolutionized chronic pain treatment as it demonstrated that a peptide that modulates ion channels can be just as effective, or even more, than the gold standard morphine, with the additional benefit of not causing the undesirable side effect of drug addiction. However, Prialt® does not cross the blood-brain barrier, and it is currently administered via intrathecal injection, which represents a major drawback limiting its widespread application (Staats et al. 2004). Recent efforts to overcome the invasive delivery method of Prialt® involve a Trojan horse strategy in which the peptide is encapsulated in a viral nanocontainer and shuttled across the blood-brain barrier (Anand et al. 2015; Kelly et al. 2015). The Trojan horse strategy mimics how venom is stored and delivered by venomous snails in nature. Conoidean snails produce venom in a special gland referred to as the venom gland, where toxins are stored in capsule-like structures similar to a nanocontainer and later delivered to a hollow radular harpoon for injection into the prey (Holford et al. 2009; Terlau and Olivera 2004). The potential applications of conoidean venom peptides go well beyond pain management and include treatment of other disorders such as epilepsy and cancer, to name a few (Petras et al. 2015; Vetter and Lewis 2012). Most drug therapies being developed from marine snail venom peptides target ion channels and receptors (King 2011; Lewis and Garcia 2003; Olivera 1997; Ortiz et al. 2015; Vetter et al. 2011). Conoidean venom peptides are short disulfide-rich peptides with a characteristic structure consisting of a signal peptide, followed by a propeptide region and a terminal cysteine-rich mature peptide, and therefore they share some features of other peptide therapeutics, namely, poor pharmacokinetics and not being orally active (Uhlig et al. 2014). As a consequence, there are key areas pertaining to drug delivery that must be addressed to truly advance the potential of marine snail venom peptides for drug development.

17.3.2 Applications of Light-Producing Molecules in Biophotonics

Light-emitting compounds have also been widely used for biotechnological applications. The discovery of the green fluorescent protein from the bioluminescent jellyfish *Aequorea victoria* revolutionized the biological field leading to a variety of novel imaging tools and reporters (Chalfie et al. 1994; Tsien 1998). In a similar way, the constituents of bioluminescent systems, luciferin and luciferases, have been widely used in biotechnology for three primary applications: as probes for cellular biology, as tools to map and identify genes, and to track the progression of disease in laboratory animals (Widder and Falls 2014).

Bioluminescent molecules have been widely used in cell biology because many enzymes and metabolites can be measured by coupling them to bioluminescence cofactors such as ATP or H_2O_2 (Widder and Falls 2014). For instance, the firefly luciferin-luciferase system can use the ATP produced by a reaction catalyzed by a kinase to produce light in proportion to the kinase (Lundin et al. 1976). This assay is the most sensitive detection method available, and because all living cells contain ATP, it has been used in a wide range of applications, from determining the impact of antibiotics on bacterial growth to the search for life on Mars (Widder and Falls 2014). In addition, many calcium-activated photoproteins isolated from marine invertebrates such as cnidarians and ctenophores have played a major role in understanding the function of calcium, a ubiquitous intracellular messenger in cell regulation (Bonora et al. 2013; Ottolini et al. 2013).

Bioluminescent proteins have also been used to replace fluorescent markers in genetic engineering experiments, to determine if a gene of interest inserted into a particular cell is actually being expressed. For this purpose, a luciferase gene is incorporated into the DNA region adjacent to the gene of interest, and both genes are expressed together when luciferin and any necessary cofactors are added (Contag and Bachmann 2002; Mezzanotte et al. 2017). The luciferases most commonly used for monitoring gene expression are those isolated from the North American firefly *Photinus pyralis* and from two marine invertebrates, the sea pansy *Renilla reniformis* and the copepod *Gaussia princeps* (Widder and Falls 2014).

Bioluminescent imaging reporters have also revolutionized the study of disease progression, for example, enabling the tracking of an infection in a single animal. Transforming pathogenic bacteria with luciferase and monitoring its bioluminescence made it possible to track the course of an infection in a single host; observe cell migration, proliferation, and apoptosis; and evaluate the effectiveness of antibiotics (Contag et al. 1995; Kim et al. 2015). Bioluminescence imaging has also greatly contributed to advances in cancer research, allowing to visualize tumor cells in living animals and making possible to evaluate the efficacy of chemotherapies and immune cell therapies in vivo (Madero-Visbal et al. 2012; Sweeney et al. 1999).

17.3.3 Biomaterials Derived from Marine Invertebrates

In recent decades, marine-derived biomaterials have gathered increased attention from the medical, pharmaceutical, and biotechnology industries for a variety of applications ranging from food additives to biodegradable plastics and bio-adhesives.

Cephalopod ink, for example, has been widely used by humans for many practical and commercial purposes, especially in medicine, cuisine, and art (Derby 2014). Several cosmetic products such as mascara or eyeshadow have been developed using squid ink, with the goal of developing products that are effective but also sustainable, safe, and respectful with the environment (Neifar et al. 2013). The food industry has also used cephalopod ink in various ways, including food flavoring, food coloring, and even curing and preserving cuttlefish meat, due to its antimicrobial properties (Derby 2014; Xu et al. 2009).

Adhesive gels and their constituents, such as mussel adhesive proteins, are also being investigated as attractive biomaterials for various applications including electronic skin and wound dressings or to develop biomimetic analogues that function as antifouling coatings (Kord Forooshani and Lee 2017; Li and Zeng 2016). For example, the adhesion mechanism of mussels has inspired a freestanding, adhesive, tough, and biocompatible hydrogel that might be more convenient for surgical applications than currently used adhesives (Han et al. 2017).

17.4 Future Prospects

As outlined in this chapter, there are numerous biochemical adaptions that marine organisms have developed which could lead to important scientific advances, such as nonaddictive pain therapies as an alternative to opioids or novel surgical hydrogels. However, to realize the immense potential of marine invertebrate bioactive molecules for both basic research and biotechnological applications, much more must be done to support the study and discovery of the numerous secrets hidden in our oceans.

The Earth's oceans are a scientific phenomenon, full of amazing creatures that have evolved to master their domain and in doing so have provided a roadmap for discovery and innovation. While there are many ways to investigate the oceans, the path that puts the conservation of the environment and the organisms first should be the preferred one. As extinction rates increase, we are losing more than we can characterize with existing technologies. It would be a catastrophic human failure to treat our oceans as factories and not as a source of inspiration. To effectively develop applications based on successful marine products provided by nature, we need to invest in basic research to identify the most promising compounds and the best environmentally safe methods for extracting them. When discussing the biotechnology enterprise, the tendency is to highlight the human applications but not the relevance of the basic research that led to them. However consider, for example, the great scientific advances being achieved and conceived with CRISPR-Cas9 technology (Mei et al. 2016). Had it not been for the thoughtful and thorough investigations of the adaptive immune system of *Streptococcus thermophilus*, the powerful genome editing tool CRISPR-Cas9, as we know it, might not have happened (Lander 2016; Mojica and Rodriguez-Valera 2016). In the attempt to translate ocean products to goods and services to advance society, we must practice the concept of identifying the "usefulness of useless knowledge" (Flexner 1955). It is imperative that we bring to the table the inherent value of basic fundamental research in evolution and biodiversity, to allow the blue biotechnology enterprise to act as a true bridge between basic knowledge and applications to improve the quality of human life.

Acknowledgments MH acknowledges funding from the Camille and Henry Dreyfus Teacher-Scholar Award and NSF awards CHE-1247550 and CHE-1228921.

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