NATURAL PRODUCTS FROM MARINE MICROORGANISMS

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Contents

Summary

An enormous diversity of microorganisms is found in the ocean. It is approximated that 10^2 fungi, 10^3 bacteria, and 10^7 viruses exist in a single milliliter of seawater. They exist throughout the marine environment including in estuaries, suspensions of seawater and sediment, within or on the surfaces of macroorganisms and benthic structures. Microorganisms are fully adapted to survive in extreme marine environments from the frigidity of sub-zero Antarctic waters to deep sea hydrothermal vents, where temperatures are greater than 100 °C and highly acidic conditions exist. We now know that these marine microorganisms are able to produce secondary metabolites, which are defined as molecules that are unnecessary to the normal growth and development of their life cycle, but are now thought to facilitate long-term survival. Secondary metabolites, or natural products, can serve as both initiators and regulators of a diverse set of ecological relationships and processes. This review serves to provide the reader with a brief history of secondary metabolites that have been isolated from marine microorganisms, and to demonstrate a growing distinction between the microbial

products of terrestrial and marine environments. It will also emphasize that distinct microhabitats drive the biodiversity found within, and this results in niches of microbial diversity that are currently being exploited for their ability to produce an assortment of structurally unique secondary metabolites.

1. Introduction

History of Microbial Drug Discovery:

In the late 1930's, stimulated by the discovery of penicillin by Alexander Fleming, terrestrial microorganisms became the focal point for one of the most prolific drug discovery efforts ever recognized. The discoveries of penicillin and later actinomycin (1940), led to the "Great Antibiotic Era", which yielded more than 120 drugs for the treatment of infectious diseases, cancer, elevated cholesterol, immunomodulation and others. Some of the most important of these discoveries came from studies of the filamentous actinomycete bacteria, which because of their growth forms were at one time considered to be fungi (hence the suffix "mycetes"). The actinomycetes are responsible for the majority of the antibiotics in clinical use today. From the period 1950 to 1990 most of the pharmaceutical companies invested heavily in microorganism-based drug discovery with financial commitments that reached in the vicinity of $10B per year. The intensity of these explorations led to discoveries of new microorganisms from virtually all accessible terrestrial environments from arctic, and cold temperate regions to tropical environments.

Interestingly, although the world's oceans occupy more than 70% of the surface of the Earth, this massive resource was never explored. Convinced by some that the ocean was a simple repository for terrestrial strains, and that cultivation of true marine microbes was difficult if not impossible, this component of planet Earth never received serious consideration. However, in 2009 microorganisms are no longer the focus of most drug industries, even though marine researchers are now demonstrating the enormous drug discovery potential of microorganisms isolated from this source.

Given the growth in this field, it is important to emphasize the unambiguous criteria that separate marine microorganisms from their terrestrial counterparts. Three such traits that help define *some* of the more distinctly marine microorganisms are their ability to display barophily (adaptation to high pressures), halophily (adaptation to high salt environments), and chemoautotrophic growth (ability to use CO_2 as a carbon source and derive energy from chemicals rather than light) properties. One tool that has been essential to define distinctions between marine and terrestrial microbes is the use of 16S ribosomal RNA analysis (16S rRNA). Many true marine microorganisms from oceanic environments contain previously unobserved 16S signatures; this is especially true in the case of invertebrate microbial symbionts, as the phenomenon of symbiosis is prevalent in the ocean. Given the aforementioned properties, it remains difficult to prove whether a microorganism collected from an oceanic environment is truly 'marine' or whether it is simply a terrestrial strain that has been rinsed into the ocean. Over decades of study, one must simply illustrate that microbes are regularly found in the ocean and not in terrestrial environments. For example, fungi are cosmopolitan organisms that are incredibly adaptive to new environments. Several investigators

mistakenly label fungi collected from the ocean as "marine fungi". This label is unwarranted until it is demonstrated that a fungal species has an obligate requirement for life in the sea. Until more can be learned, a more appropriate label is "marine-derived fungi".

Oceanic Microhabitats Drive Biodiversity:

The ocean was formed sometime after the birth of our 4.5 billion year old planet. Evaporation of water from Earth's crust and return as precipitation from the atmosphere, and the accumulation of ice from colliding comets, afforded us with massive collections of water that dispersed to become today's ocean. Water, along with moderate temperatures, the development of a unique atmosphere, and other factors provided the foundation for increasingly complex carbon-based life forms to develop.

Despite the outward appearance of the ocean as a uniform aquatic tapestry, the regions that lie at the poles and beneath the sea are anything but homogenous, and in each of these oceanic niches a specific set of physical conditions selects for the existence of an incredible diversity of life. Although the terrestrial environment is limited to a relatively thin crust on its surface, life in the sea is distributed in three dimensions to a depth in excess of 13,000 meters. This region is divided into several unique microhabitats that contain a largely unknown microbial diversity. One microhabitat that is known for supporting microbial life is marine sediment. Marine sediment and mud are nutrient-laden surfaces that invite microbial colonization and growth. The organic content of these benthic surfaces differs greatly by region and displays geological diversity that consequently selects for a wealth of microbial taxa. However, surface microbes are not limited to sediment; microorganisms colonize virtually every inanimate and living surface in the ocean, including man-made structures, plants, invertebrates, and larger organisms. These microbial colonizers are known as epibionts. In addition to epibionts, microbes are also found living within marine organisms (endobionts). Some are crucial to their host's survival (symbionts), whereas others are pathogenic. Unlike its occurrence in terrestrial organisms, the phenomenon of endobiosis is the rule rather than the exception in the largely nutrient-limited ocean. Lastly, a remotely explored diversity of microorganisms is found within the water column, a microhabitat that is the most abundant of all in the marine environment and is the epitome of the nutrient-limiting conditions that broadly exist in the ocean. Recently, the Sorcerer II global ocean sampling expedition set out to attain a preliminary assessment of the genetic diversity in the world's oceans. While shotgun sequencing samples from the North Atlantic to the South Pacific (via the Panama Canal), 16S rDNA species analysis indicated the presence of distinct microbial communities. It was reported that only a handful of species (ribotypes) were ubiquitously abundant. Further analysis of these metagenomic data confirmed that taxonomic diversities were distinct between coastal, estuarine, and open-ocean environments. Although this was not the first study to show that microbial diversity varied with geographic location, it was certainly the most elaborate and extensive.

Geographic location is not the only determining factor for microbial diversity. Physical parameters such as depth are an integral part of microbial selection. One study utilized genomic analyses of planktonic microbial communities in the North Pacific Subtropical

Gyre as a function of seawater stratification. Samples in the photic zone of the water column (10, 70, 130 meters) harbored sequences associated with photosynthesis, porphyrin and chlorophyll metabolism, and other functions. Conversely, samples greater than 200 meters in depth, and consequently at pressures exceeding greater than 20 atmospheres, exhibited significantly different sequences. As illustrated in the following examples, other physical parameters that select for microbial taxa are temperature, mineral composition of the surrounding water, and salinity.

The structure of the ocean floor varies as distance from the continents into the deep ocean increases. Stretches of sediment 5 km thick are covered by hills, volcanoes, trenches, actively spreading seafloor, and mountain chains known as oceanic ridges. One of the most intriguing of these marine environments was seen for the first time in 1977. Using a submersible remotely operated vehicle (ROV) in the Galapagos mountain range of the eastern Pacific, scientists discovered tall chimney-like structures known as hydrothermal vents. These vents spew mineral-rich water at temperatures as high as 400 °C, and are known to exist along actively spreading plates of every major ocean ridge system on the planet; it is the dispersion of these plates that allows lava to rise, cool, and form elevated seafloor. Seawater penetrates cracks in the ocean crust and is eventually superheated and thrust out of chimneys nearby these ridge systems. Astonishingly, the area surrounding these extreme environments is teeming with life from tube worms to crabs, all of which readily survive in a toxic, sunlight deprived habitat. Studies have shown that it is the chemical makeup of this environment that ultimately drives the distribution of taxa. Unlike photosynthetic organisms, the various vent invertebrates are dependant on large populations of symbiotic bacteria that utilize chemosynthetic processes, in some cases the oxidation of hydrogen sulfide, to generate a supply of carbon-based nutrients that are the basis for the existence of this vent population. Contrary to the notion of life beginning in primordial ‘organic soup’, some believe that life’s origins evolved from ancient chemosynthetic microorganisms that benefited from mid-temperature zones above hydrothermal vents.

In addition to harboring hot environments, Earth is home to extreme cold environments as found near the continent of Antarctica. Located in the southernmost point on the globe, Antarctica is widely believed to have broken off from a massive supercontinent named Gondwanaland approximately 180 million years ago. It is an ice-laden landmass nearly twice the size of Western Europe and harbors approximately 90% of the world’s ice. Its surrounding ocean can be as cold as 1.9 °C, yet still the Antarctic is rich in biodiversity. Most of the ecosystem is reliant upon copious summer blooms of phytoplankton, which serve as food for larger species such as fish, seals, whales, and penguins. In addition, studies have determined contiguous benthic communities to be rich in sessile feeders such as sponges and soft corals. Some have postulated that predation constraints and competition for limited resources in this frigid underwater environment have selected for organisms that produce chemical defenses. However, many aspects of this marine ecosystem remain relatively unexplored, including those involving psychrophilic microorganism occurrence and function.

Salt marshes represent another category of extreme marine environments. They may exist across all temperature gradients, though many are found on the Atlantic coast of North America and near the Gulf of Mexico. These environments are protected from

strong ocean currents and are an intermediate point between land and sea. Their salinity level typically ranges from 5 to 40 parts per thousand and is at times greater than that of the open ocean. Many salt marshes form in estuaries, shallow areas where fresh water from a flowing river meets a body of salt water. Small plants such as sea grasses are abundant in this habitat and often root themselves deep into muddy sediment. The decomposition of salt-tolerant plants in addition to nutrient deposits from incoming rivers are critical components of estuarine food chains. The microorganisms (such as photosynthetic sulfur bacteria) and other small animals that contribute to these chains are part of a unique environment whose biomass per unit of surface area is among the greatest of all marine environments.

One of the most densely populated oceanic environments is the coral reef, a structure made as a result of the symbiosis between coral polyps and zooxanthellae (phototrophic dinoflagellates). Formed with tough calcium carbonate skeletons, corals grow best in waters with temperatures above 21 °C and depths from 5 to 10 meters deep, so as to harness the power of sunlight for optimal growth. Considering the very low nutrients present in tropical seawater, microorganisms have often adapted to live within the tissues of invertebrates. Sponges, for example, can be as high as 50% microorganisms by weight.

The aforementioned marine habitats were briefly described in order to illustrate a point: Earth's ocean is capable of sustaining a wide variety of living conditions, and these environments ultimately select for their associated biodiversity. Furthermore, the circumstances that support this delicate balance of life involve ecologically significant populations of microorganisms. The occurrence of microbes in the ocean is massive. As previously discussed, they occur in the open water column and in sediment, in the tissues of marine organisms and on benthic surfaces, in mid-ocean ridge hydrothermal vents and freezing temperatures of Antarctic waters, and in hyper-saline pools at the junction of rivers and the sea. Given this array of marine habitats, little is known about the overall quantitative diversity of marine microorganisms. New species are discovered daily. And, research expeditions such as the Sorcerer II further emphasize that exploration of this elusive complexity has only just begun.

Secondary Metabolite Production by Marine Microorganisms:

Finally, one very important aspect of these microorganisms is their capacity to produce secondary metabolites. The ecological significance of these naturally-occurring compounds has been mostly overlooked, predominantly because we have lacked the sensitive analytical tools to actually measure the presence of these compounds under natural conditions. Consequently, little is known about the origin, diversity, and role that secondary metabolites fulfill in their surrounding microenvironments. This review provides a brief history of the structurally interesting secondary metabolites that have been isolated from cultured marine microorganisms, and hopefully will demonstrate a growing distinction between the microbial products of terrestrial and marine microorganisms. Due to the expanse of the topic, it is beyond the scope of this chapter to provide a comprehensive review of the metabolites produced by all marine microorganisms (*e.g.* phototrophic eukaryotes such as dinoflagellates and diatoms, yeasts, etc.). Instead, an overview of those metabolites produced by various taxa of

marine bacteria and marine-derived fungi is offered. For each category of marine microorganisms, a few highlights will be shared of the more interesting environments, methods, or structures found within. For further information on specific topics the reader is referred to more comprehensive review articles located in the bibliography. With a few exceptions, the articles published after January 2009 have not been included.

This overview is organized by taxon, beginning with unicellular Gram-negative bacteria and increasing in complexity to end with eukaryotic fungi. This chapter is written with a focus on chemistry and the environments, and not from the perspective of microbial taxonomy. We chose to organize this chapter following the taxonomic classifications of Bergey's Manual of Determinative Bacteriology and of "The Prokaryotes – A Handbook on the Biology of Bacteria".

2. Secondary Metabolites from Gram-negative Marine Bacteria

In this section, bacteria have been broken down into two classifications: Gram-negative and Gram-positive bacteria. This is based on their ability to retain a purple dye (the Gram stain). In brief, Gram-negative bacteria do not retain this dye due to the structure of their cellular envelope. They possess a tough outer membrane that consists of lipopolysaccharides in addition to a thinner peptidoglycan cell wall. In the following sections, the chemistry of marine Proteobacteria and Bacteroidetes are demonstrated to be the most prolific of the Gram-negative strains.

2.1. Proteobacteria

The Proteobacteria, formerly known as purple bacteria, constitutes the largest and most physiologically diverse phylum of all bacteria. Indicative of this diversity, the phylum was named after the Greek god Proteus, son of Poseidon, who had the ability to assume different shapes. This phylum comprises the majority of medically and agriculturally significant Gram-negative bacteria. The chemically prolific gliding bacteria are found within the Proteobacteria but are restricted to the β-, δ-, γ-divisions. It is home to a large group of gliding bacteria called the myxobacteria, which are aerobic, chemoorganotrophic, typically rod-shaped, and which form fruiting bodies under low-nutrient conditions. In the following two sections proteobacterial secondary metabolites are organized by class.

2.1.1. Alpha- and Delta-Proteobacteria

Categorized within the broad phylum Proteobacteria are the classes α- and δ-Proteobacteria. The mitochondria, found in the eukaryotic cell, are believed to have originated from α-Proteobacteria, a class that is crucial to the regulation of Earth's carbon, sulfur and nitrogen cycles. The majority of α-proteobacteria are rod-shaped and contain strains that are prokaryotic predators (*Bdellovibrio*), strains that have the ability to glide (myxobacteria), and those that can reduce sulfur. To date, relatively few secondary metabolites have been identified from marine representatives of these classes.

From the cells of an undescribed species of the unicellular marine α-proteobacterium *Agrobacterium*, agrochelin A (1), a cytotoxic thiazole alkaloid was isolated. This strain

was cultivated from a tunicate collected in the Mediterranean Sea, off the east coast of Spain. It displayed inhibitory activity against a panel of tumor cell lines and was shown to form a complex with $[Zn]^{2+}$ ions. In the search for endothelin-converting enzyme (ECE) inhibitors, B-90063 (2), a dimeric oxazole-pyridone analog was isolated from an undescribed species of the marine α-proteobacterium *Blastobacter*. This strain was isolated from the water column on the coast of Ojika Peninsula, Japan, and required seawater for growth. It exhibited antagonistic activities toward endothelins, peptides responsible for the constriction of blood vessels. In addition to the two aforementioned metabolites from α-proteobacteria, two polyketide-derived metabolites were discovered from two marine-derived myxobacterial strains. An ethylated polyene-substituted pyrone metabolite (phenylnannolone A, 3) was isolated from the marine δ-proteobacterium *Nannocystis exedens*. Though polyene pyrones have been reported from various terrestrial sources, the presence of an ethyl group on the polyene chain represented a novel deviation from this class of molecules. Biosynthetic studies suggested unprecedented biochemical reactions are employed to form phenylnannolone A. In a program designed to isolate true marine myxobacteria, the δ-proteobacterium *Haliangium luteum*, was isolated from a seaweed in Kanagawa, Japan. This myxobacterium required approximately 2–3 % NaCl for growth and production of the metabolite haliangicin (4). Compound 4 was found to display antifungal activity toward a number of fungi, including the pathogenic strain *Phytophthora capsici*.

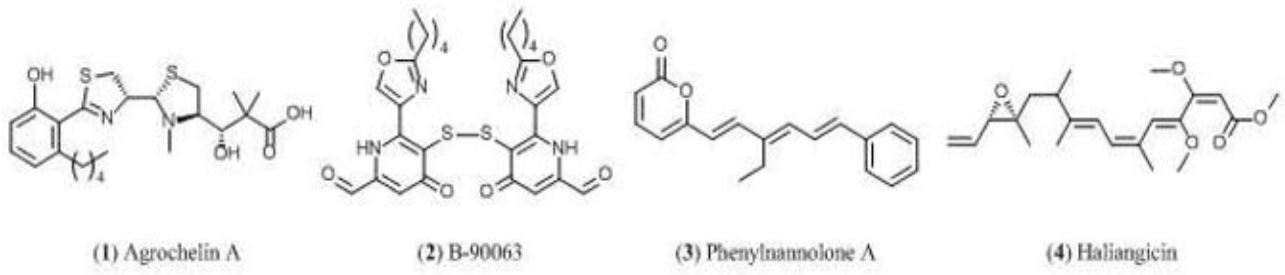

Figure 1. Secondary metabolites from α- and δ- Proteobacteria.

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Bibliography

Introduction (1.0.)

Arp, A. J. (2008) Hydrothermal vent fauna, physiology of. *Encyclopedia of ocean sciences*, second edition, (ed. JH Steele, KK Turekian, SA Thorpe), 1242-1246. Elsevier. [This chapter describes the basic environmental contitions that exist in hydrothermal vents.]

Biers, E. J., Sun, S. & Howard, E. C. (2009). Prokaryotic genomes and diversity in surface ocean waters: Interrogating the global ocean sampling metagenome. *Applied and Environmental Microbiology* 75(7), 2221-2229. [This study used data from the Sorcerer expedition to analyze microbial populations in distinct habitats.]

Bowman, J. P., Mccammon, S. A., Brown, M. V., Nichols, D. S. & Mcmeekin, T. A. (1997). Diversity and association of psychrophilic bacteria in antarctic sea ice. *Applied and Environmental Microbiology* 63(8), 3068-3078. [This study describes the phylogenetic analysis of microbial populations in both Antarctic sea ice and the water found beneath.]

Day, T. (1999). Oceans, 216 pp. New York, NY, USA: Facts On File, Inc. [This textbook offers a general introduction to the topic of oceanography.]

Delong, E. F., Preston, C. M., Mincer, T., Rich, V., Hallam, S. J., Frigaard, N. U., Martinez, A., Sullivan, M. B., Edwards, R., Brito, B. R., Chisholm, S. W. & Karl, D. M. (2006). Community genomics among stratified microbial assemblages in the ocean's interior. *Science* 311(5760), 496-503. [This study provides an analysis of microbial communities as a function of ocean depth.]

Dworkin, M. (2006) *The Prokaryotes: A Handbook on the Biology of Bacteria*, third edition, (ed. M Dworkin, S Falkow, E Rosenberg, K-H Schleifer, E Stackebrandt). Springer Science + Business Media, Inc. [This book is a thorough examination of the taxonomy, classification, and physical characteristics of bacteria.]

Garrison, T. (2007). *Oceanography: An invitation to marine science*, sixth edition, 588 pp. Belmont, CA, USA: Thompson Brooks/Cole. [This textbook offers a general introduction to the topic of oceanography.]

Luther, G. W., 3rd, Rozan, T. F., Taillefert, M., Nuzzio, D. B., Di Meo, C., Shank, T. M., Lutz, R. A. & Cary, S. C. (2001). Chemical speciation drives hydrothermal vent ecology. *Nature* 410(6830), 813-816. [This study discusses the speciation surrounding hydrothermal vents.]

McManus, J. W. (2008) Coral Reefs. *Encyclopedia of ocean sciences*, second edition, (ed. JH Steele, KK Turekian, SA Thorpe), 524-534. Elsevier. [This serves as an introductory chapter to coral reefs.]

Pommier, T., Canback, B., Riemann, L., Bostrom, K. H., Simu, K., Lundberg, P., Tunlid, A. & Hagstrom, A. (2007). Global patterns of diversity and community structure in marine bacterioplankton. *Molecular Ecology* 16(4), 867-880. [This study reports the comparative analysis of marine bacterioplankton communities from various geographic locations worldwide.]

Rusch, D. B., Halpern, A. L., Sutton, G., Heidelberg, K. B., Williamson, S., Yooseph, S., Wu, D., Eisen, J. A., Hoffman, J. M., Remington, K., Beeson, K., Tran, B., Smith, H., Baden-Tillson, H., Stewart, C., Thorpe, J., Freeman, J., Andrews-Pfannkoch, C., Venter, J. E., Li, K., Kravitz, S., Heidelberg, J. F., Utterback, T., Rogers, Y. H., Falcon, L. I., Souza, V., Bonilla-Rosso, G., Eguiarte, L. E., Karl, D. M., Sathyendranath, S., Platt, T., Bermingham, E., Gallardo, V., Tamayo-Castillo, G., Ferrari, M. R., Strausberg, R. L., Nealson, K., Friedman, R., Frazier, M. & Venter, J. C. (2007). The Sorcerer II global ocean sampling expedition: Northwest Atlantic through Eastern Tropical Pacific. *PLoS Biology* 5(3), e77. [This study analyzed the diversity of marine microbial plankton via a metagenomic study.]

Teal, J. M. (2008) Salt marshes and mud flats. *Encyclopedia of ocean sciences*, second edition, (ed. JH Steele, KK Turekian, SA Thorpe), 2490-2495. Elsevier. [This chapter describes the diversity of life that exists in hydrothermal vents.]

Van Dover, C. L. (2008) Hydrothermal vent ecology. *Encyclopedia of ocean sciences*, second edition, (ed. JH Steele, KK Turekian, SA Thorpe), 1234-1241. Elsevier. [This chapter describes the basic environmental conditions that exist in salt marshes.]

Venter, J. C., Remington, K., Heidelberg, J. F., Halpern, A. L., Rusch, D., Eisen, J. A., Wu, D., Paulsen, I., Nelson, K. E., Nelson, W., Fouts, D. E., Levy, S., Knap, A. H., Lomas, M. W., Nealson, K., White, O., Peterson, J., Hoffman, J., Parsons, R., Baden-Tillson, H., Pfannkoch, C., Rogers, Y. H. & Smith, H. O. (2004). Environmental genome shotgun sequencing of the Sargasso Sea. *Science* 304(5667), 66-74. [This was a pilot study for the Sorcerer II global sampling expedition; it used whole genome shotgun sequencing to analyze en masse microbial communities.]

Williamson, S. J., Rusch, D. B., Yooseph, S., Halpern, A. L., Heidelberg, K. B., Glass, J. I., Andrews-Pfannkoch, C., Fadrosh, D., Miller, C. S., Sutton, G., Frazier, M. & Venter, J. C. (2008). The Sorcerer II

global ocean sampling expedition: Metagenomic characterization of viruses within aquatic microbial samples. *PLoS One* 3(1), e1456. [This study describes the abundance and diversity of viruses found in ocean water samples collected around the globe.]

Secondary Metabolites from Gram-negative Marine Bacteria (2.0.)

Acebal, C., Canedo, L. M., Puentes, J. L., Baz, J. P., Romero, F., De La Calle, F., Gravalos, M. D. & Rodriguez, P. (1999). Agrochelin, a new cytotoxic antibiotic from a marine agrobacterium. Taxonomy, fermentation, isolation, physico-chemical properties and biological activity. *Journal of Antibiotics* 52(11), 983-987. [This study presents fermentation and bioactivity data of agrochelin.]

Andrianasolo, E. H., Haramaty, L., Rosario-Passapera, R., Bidle, K., White, E., Vetriani, C., Falkowski, P. & Lutz, R. (2009). Ammonificins A and B, hydroxyethylamine chroman derivatives from a cultured marine hydrothermal vent bacterium, *Thermovibrio ammonificans*. *Journal of Natural Products* 72(6), 1216-1219. [This study presents the isolation, structure elucidation, antimicrobial and anticancer activity of the ammonificins.]

Bassler, B. L., Wright, M., Showalter, R. E. & Silverman, M. R. (1993). Intercellular signalling in *Vibrio harveyi*: Sequence and function of genes regulating expression of luminescence. *Molecular Microbiology* 9(4), 773-786. [This study identifies a number of genes responsible for the bioluminescence of *Vibrio harveyi*.]

Bassler, B. L., Wright, M. & Silverman, M. R. (1994). Multiple signalling systems controlling expression of luminescence in *Vibrio harveyi*: Sequence and function of genes encoding a second sensory pathway. *Molecular Microbiology* 13(2), 273-286. [This study reports the identification of genes responsible for a second sensory pathway in *Vibrio harveyi* that regulates bioluminescence.]

Bell, R., Carmeli, S. & Sar, N. (1994). Vibrindole A, a metabolite of the marine bacterium, *Vibrio parahaemolyticus*, isolated from the toxic mucus of the boxfish ostracion cubicus. *Journal of Natural Products* 57(11), 1587-1590. [This study presents the isolation, structure elucidation, and antibacterial activity of vibrindole A.]

Boehler, M., Jensen, P. R. & Fenical, W. (1997). Bahamamide, an unusual cyclic bis-amide produced by an undescribed marine bacterium. *Natural Product Letters* 10(1), 75-78. [This study presents the isolation and structure elucidation of bahamamide.]

Burkholder, P. R., Pfister, R. M. & Leitz, F. H. (1966). Production of a pyrrole antibiotic by a marine bacterium. *Applied Microbiology* 14(4), 649-653. [This study presents the isolation and structure elucidation of pentabromopseudilin from *Pseudomonas bromoutilis*.]

Canedo, L. M., Fuente, J. A. D. L., Gesto, C., Ferreiro, M. J., Jimenez, C. & Riguera, R. (1999). Agrochelin, a new cytotoxic alkaloid from the marine bacteria *Agrobacteria* sp. *Tetrahedron Letters* 40, 6841-6844. [This study presents the structure elucidation of agrochelin.]

Chen, X., Schauder, S., Potier, N., Van Dorsselaer, A., Pelczer, I., Bassler, B. L. & Hughson, F. M. (2002). Structural identification of a bacterial quorum-sensing signal containing boron. *Nature* 415(6871), 545-549. [This study presents the structure elucidation of the elusive autoinducer AI-2 via a crystal structure with its sensor protein.]

De Rosa, S., De Giulio, A., Tommonaro, G., Popov, S. & Kujumgiev, A. (2000). A beta-amino acid containing tripeptide from a *Pseudomonas-Alteromonas* bacterium associated with a black sea sponge. *Journal of Natural Products* 63(10), 1454-1455. [This study presents the isolation and structure elucidation of a tripeptide from a marine *Pseudomonas – Alteromonas* species.]

Fedorov, R., Bohl, M., Tsiavaliaris, G., Hartmann, F. K., Taft, M. H., Baruch, P., Brenner, B., Martin, R., Knolker, H. J., Gutzeit, H. O. & Manstein, D. J. (2009). The mechanism of pentabromopseudilin inhibition of myosin motor activity. *Nature Structural & Molecular Biology* 16(1), 80-88. [This study presents the biological mechanism of action of pentabromopseudilin as an inhibitor of myosin.]

Fudou, R., Iizuka, T., Sato, S., Ando, T., Shimba, N. & Yamanaka, S. (2001). Haliangicin, a novel antifungal metabolite produced by a marine myxobacterium. 2. Isolation and structural elucidation. *Journal of Antibiotics* 54(2), 153-156. [This study presents the structure elucidation of haliangicin.]

Gandhi, N. M., Nazareth, J., Divekar, P. V., Kohl, H. & De Souza, N. J. (1973). Letter: Magnesidin, a novel magnesium-containing antibiotic. *Journal of Antibiotics* 26(12), 797-798. [This study presents the original isolation and structure elucidation of magnesidin A from a marine *Pseudomonas* sp.]

Gil-Turnes, M. S. & Fenical, W. (1992). Embryos of *Homarus americanus* are protected by epibiotic bacteria. *The Biological Bulletin* 182, 105-108. [This study presents the isolation of an epibiotic bacterium from lobster embryos and identification of an antifungal chemical subsequently produced by the microorganism.]

Gil-Turnes, M. S., Hay, M. E. & Fenical, W. (1989). Symbiotic marine bacteria chemically defend crustacean embryos from a pathogenic fungus. *Science* 246, 116-118. [This study describes the isolation of an epibiotic bacterium and identification of its antifungal chemical defense.]

Hugenholtz, P. & Stackebrandt, E. (2004). Reclassification of *Sphaerobacter thermophilus* from the subclass Sphaerobacteridae in the phylum Actinobacteria to the class Thermomicrobia in the phylum Chloroflexi. *International Journal of Systematic and Evolutionary Microbiology* 54(Pt 6), 2049-2051. [This study describes some physiological characteristics of the phylum Chloroflexi.]

Iizuka, T., Fudou, R., Jojima, Y., Ogawa, S., Yamanaka, S., Inukai, Y. & Ojika, M. (2006). Miuraenamides A and B, novel antimicrobial cyclic depsipeptides from a new slightly halophilic Myxobacterium: Taxonomy, production, and biological properties. *Journal of Antibiotics* 59(7), 385-391. [This study presents the isolation, structure elucidation and antibiotic activity of miuraenamides A and B.]

Imamura, N., Adachi, K. & Sano, H. (1994). Magnesidin A, a component of marine antibiotic magnesidin, produced by *Vibrio gazogenes* atcc29988. *Journal of Antibiotics* 47(2), 257-261. [This study presents the first structure elucidation of magnesidin A as a single component.]

Kanoh, K., Matsuo, Y., Adachi, K., Imagawa, H., Nishizawa, M. & Shizuri, Y. (2005). Mechercharmycins A and B, cytotoxic substances from marine-derived *Thermoactinomyces* sp. YM3-251. *Journal of Antibiotics* 58(4), 289-292. [This study presents the isolation, structure elucidation and bioactivity of the mechercharmycins.]

Kobayashi, M., Aoki, S., Gato, K., Matsunami, K., Kurosu, M. & Kitagawa, I. (1994). Marine natural products. XXXIV. Trisindoline, a new antibiotic indole trimer, produced by a bacterium of *Vibrio* sp. Separated from the marine sponge *Hyrtios altum*. *Chemical & Pharmaceutical Bulletin* 42(12), 2449-2451. [This study presents the isolation and structure elucidation of trisindoline.]

Kundim, B. A., Itou, Y., Sakagami, Y., Fudou, R., Iizuka, T., Yamanaka, S. & Ojika, M. (2003). New haliangicin isomers, potent antifungal metabolites produced by a marine myxobacterium. *Journal of Antibiotics* 56(7), 630-638. [This study presents the stereochemical determination and the antifungal activity of haliangicin and its analogs.]

Nett, M., Erol, O., Kehraus, S., Kock, M., Krick, A., Eguereva, E., Neu, E. & Konig, G. M. (2006). Siphonazole, an unusual metabolite from *Herpetosiphon* sp. *Angewandte Chemie International Edition* 45(23), 3863-3867. [This study reports the isolation and structure elucidation of siphonazole.]

Ohlendorf, B., Leyers, S., Krick, A., Kehraus, S., Wiese, M. & Konig, G. M. (2008). Phenylnannolones A-C: Biosynthesis of new secondary metabolites from the myxobacterium *nannocystis exedens*. *Chembiochem* 9(18), 2997-3003. [This study presents the structure elucidation, biosynthesis, and bioactivity of phenylnannolones.]

Oku, N., Adachi, K., Matsuda, S., Kasai, H., Takatsuki, A. & Shizuri, Y. (2008). Ariakemicins A and B, novel polyketide-peptide antibiotics from a marine gliding bacterium of the genus *Rapidithrix*. *Organic Letters* 10(12), 2481-2484. [This study presents the structure elucidation and antibacterial activity of the ariakemicins.]

Oku, N., Kawabata, K., Adachi, K., Katsuta, A. & Shizuri, Y. (2008). Unnarmicins A and C, new antibacterial depsipeptides produced by marine bacterium *Photobacterium* sp. Mbic06485. *Journal of Antibiotics* 61(1), 11-17. [This study presents the structure elucidation and antibacterial activity of unnarmicins A and C.]

Reysenbach, A. L., Hamamura, N., Podar, M., Griffiths, E., Ferreira, S., Hochstein, R., Heidelberg, J., Johnson, J., Mead, D., Pohorille, A., Sarmiento, M., Schweighofer, K., Seshadri, R. & Voytek, M. A. (2009). Complete and draft genome sequences of six members of the Aquificales. *Journal of Bacteriology*

191(6), 1992-1993. [This study provides a description of marine and terrestrial bacterial strains from Aquificales.]

Shigemori, H., Bae, M.-A., Yazawa, K., Sasaki, T. & Kobayashi, J. (1992). Alteramide a, a new tetracyclic alkaloid from a bacterium *Alteromonas* sp. Associated with the marine sponge *Halichondria okadai*. *Journal of Organic Chemistry* 57(15), 4317-4320. [This study reports the isolation and structure elucidation of alteramide A.]

Shindo, K., Asagi, E., Sano, A., Hotta, E., Minemura, N., Mikami, K., Tamesada, E., Misawa, N. & Maoka, T. (2008). Diapolycopenedioic acid xylosyl esters A, B, and C, novel antioxidative glyco-C30-carotenoic acids produced by a new marine bacterium *Rubritalea squalenifaciens*. *Journal of Antibiotics* 61(3), 185-191. [This study reports the isolation, structure elucidation, and antioxidant activity of a long-chain acid from *R. squalenifaciens.*]

Shiozawa, H., Kagasaki, T., Torikata, A., Tanaka, N., Fujimoto, K., Hata, T., Furukawa, Y. & Takahashi, S. (1995). Thiomarinols B and C, new antimicrobial antibiotics produced by a marine bacterium. *Journal of Antibiotics* 48(8), 907-909. [This study describes the isolation, structure elucidation, and bioactivity of two thiomarinol analogs.]

Sobik, P., Grunenberg, J., Boroczky, K., Laatsch, H., Wagner-Dobler, I. & Schulz, S. (2007). Identification, synthesis, and conformation of tri- and tetrathiacycloalkanes from marine bacteria. *Journal of Organic Chemistry* 72(10), 3776-3782. [This study reports the isolation, structure elucidation and GCMS analysis of seven thiacycloalkanes from a *Cytophaga* strain.]

Speitling, M., Smetanina, O. F., Kuznetsova, T. A. & Laatsch, H. (2007). Bromoalterochromides A and A', unprecedented chromopeptides from a marine *Pseudoalteromonas maricaloris* strain kmm 636t. *Journal of Antibiotics* 60(1), 36-42. [This study presents the structure elucidation and cytotoxic effects of bromoalterochromide and its analogs.]

Spyere, A., Rowley, D. C., Jensen, P. R. & Fenical, W. (2003). New neoverrucosane diterpenoids produced by the marine gliding bacterium *Saprospira grandis*. *Journal of Natural Products* 66(6), 818-822. [This study presents the structure elucidation of neoverrucosane diterpenoids.]

Takaishi, S., Tuchiya, N., Sato, A., Negishi, T., Takamatsu, Y., Matsushita, Y., Watanabe, T., Iijima, Y., Haruyama, H., Kinoshita, T., Tanaka, M. & Kodama, K. (1998). B-90063, a novel endothelin converting enzyme inhibitor isolated from a new marine bacterium, *Blastobacter* sp. Sank 71894. *Journal of Antibiotics* 51(9), 805-815. [This study presents the structure elucidation and bioactivity of B-90063.]

Wang, L., Grosse, T., Stevens, H., Brinkhoff, T., Simon, M., Liang, L., Bitzer, J., Bach, G., Zeeck, A., Tokuda, H. & Lang, S. (2006). Bioactive hydroxyphenylpyrrole-dicarboxylic acids from a new marine *Halomonas* sp.: Production and structure elucidation. *Applied Microbiology and Biotechnology* 72(4), 816-822. [This study reports the isolation, structure elucidation, and bioactivity of a number of small molecule aromatic pyrrole derivatives, including HPPD-1.]

Yoshikawa, K., Adachi, K., Nishida, F. & Mochida, K. (2003). Planar structure and antibacterial activity of korormicin derivatives isolated from *Pseudoalteromonas* sp. F-420. *Journal of Antibiotics* 56(10), 866-870. [This study presents the structure elucidation and antibacterial activity of korormicin analogs, including a brominated derivative.]

Yoshikawa, K., Nakayama, Y., Hayashi, M., Unemoto, T. & Mochida, K. (1999). Korormicin, an antibiotic specific for gram-negative marine bacteria, strongly inhibits the respiratory chain-linked Na^+-translocating NADH: Quinone reductase from the marine *Vibrio alginolyticus*. *Journal of Antibiotics* 52(2), 182-185. [This study presents the original bioactivity of korormicin.]

Secondary Metabolites from Marine Cyanobacteria (3.0.)

Cardellina, J. H., 2nd, Marner, F. J. & Moore, R. E. (1979). Seaweed dermatitis: Structure of lyngbyatoxin A. *Science* 204(4389), 193-195. [This study presents the isolation and structure elucidation of lyngbyatoxin A.]

Cardellina, J. H., Ii, Marner, F. J. & Moore, R. E. (1979b). Malyngamide A, a novel chlorinated metabolite of the marine cyanophyte *Lyngbya majuscula*. *Journal of the American Chemical Society* 101(1), 240-242. [This study presents the isolation and structure elucidation of malyngamide A.]

Edwards, D. J., Marquez, B. L., Nogle, L. M., Mcphail, K., Goeger, D. E., Roberts, M. A. & Gerwick, W. H. (2004). Structure and biosynthesis of the jamaicamides, new mixed polyketide-peptide neurotoxins from the marine cyanobacterium *Lyngbya majuscula*. *Chemistry & Biology* 11(6), 817-833. [This study presents the isolation, structure elucidation, and identification of the biosynthetic gene cluster for jamaicamides A-C.]

Gerwick, W. H., Proteau, P. J., Nagle, D. G., Hamel, E., Blokhin, A. & Slate, D. L. (1994). Structure of curacin A, a novel antimitotic, antiproliferative and brine shrimp toxic natural product from the marine cyanobacterium *Lyngbya majuscula*. *Journal of Organic Chemistry* 59(6), 1243-1245. [This study presents the isolation, structure elucidation, and bioactivity of curacin A.]

Gu, L., Wang, B., Kulkarni, A., Geders, T. W., Grindberg, R. V., Gerwick, L., Hakansson, K., Wipf, P., Smith, J. L., Gerwick, W. H. & Sherman, D. H. (2009). Metamorphic enzyme assembly in polyketide diversification. *Nature* 459(7247), 731-735. [This study presents the biochemical studies of enzymes involved in the biosynthesis of curacin A and the jamaicamides.]

Hamada, Y., Shibata, M. & Shioiri, T. (1985). New methods and reagents in organic synthesis. 58. A synthesis of patellamide A, a cytotoxic cyclic peptide from a tunicate. Revision of its proposed structure. *Tetrahedron Letters* 26(52), 6501-6504. [This study presents the synthesis of patellamide A and revision of its structure.]

Ireland, C. M., Durso, A. R., Jr., Newman, R. A. & Hacker, M. P. (1982). Antineoplastic cyclic peptides from the marine tunicate *Lissoclinum patella*. *Journal of Organic Chemistry* 47(10), 1807-1811. [This study presents the original isolation and (incorrect) structure elucidation of patellamides A-C from *Lissoclinum patella*.]

Kato, Y. & Scheuer, P. J. (1974). Aplysiatoxin and debromoaplysiatoxin, constituents of the marine mollusk *Stylocheilus longicauda* (quoy and gaimard, 1824). *Journal of the American Chemical Society* 96(7), 2245-2246. [This study presents the isolation of aplysiatoxin and debromoaplysiatoxin from *Stylocheilus longicauda* and original structure elucidation.]

Liu, Y., Law, B. K. & Luesch, H. (2009). Apratoxin a reversibly inhibits the secretory pathway by preventing cotranslational translocation. *Molecular Pharmacology* 76(1), 91-104. [This study presents the identification of mechanism of action of apratoxin A.]

Luesch, H., Moore, R. E., Paul, V. J., Mooberry, S. L. & Corbett, T. H. (2001). Isolation of dolastatin 10 from the marine cyanobacterium *Symploca* species vp642 and total stereochemistry and biological evaluation of its analogue symplostatin 1. *Journal of Natural Products* 64(7), 907-910. [This study presents the isolation of dolastatin 10 for the first time from a cyanobacterium, stereochemical determination, and biological evaluation.]

Luesch, H., Yoshida, W. Y., Moore, R. E., Paul, V. J. & Corbett, T. H. (2001). Total structure determination of apratoxin A, a potent novel cytotoxin from the marine cyanobacterium *Lyngbya majuscula*. *Journal of the American Chemical Society* 123(23), 5418-5423. [This study presents the isolation, structure determination, and cytotoxicity of apratoxin A.]

Mynderse, J. S., Moore, R. E., Kashiwagi, M. & Norton, T. R. (1977). Antileukemia activity in the Osillatoriaceae: Isolation of debromoaplysiatoxin from *Lyngbya*. *Science* 196(4289), 538-540. [This study presents the first isolation of debromoaplysiatoxin from *Lyngbya* and characterization of its antileukemia activity.]

Pettit, G. R., Kamano, Y., Fujii, Y., Herald, C. L., Inoue, M., Brown, P., Gust, D., Kitahara, K., Schmidt, J. M., Doubek, D. L. & Michel, C. (1981). Marine animal biosynthetic constituents for cancer chemotherapy. *Journal of Natural Products* 44(4), 482-485. [This study presents the original isolation of dolastatins 1-9 from *Dolabella auricularia*, and a nice history of the bioactivity of *Dolabella*.]

Pettit, G. R., Kamano, Y., Herald, C. L., Tuinman, A. A., Boettner, F. E., Kizu, H., Schmidt, J. M., Baczynskyj, L., Tomer, K. B. & Bontems, R. J. (1987). The isolation and structure of a remarkable marine animal antineoplastic constituent: Dolastatin 10. *Journal of the American Chemical Society* 109, 6883-6885. [This study presents the original isolation of dolastatin 10 from *Dolabella auricularia*.]

Proteau, P. J., Gerwick, W. H., Garcia-Pichel, F. & Castenholz, R. (1993). The structure of scytonemin, an ultraviolet sunscreen pigment from the sheaths of cyanobacteria. *Experientia* 49(9), 825-829. [This study presents the structure elucidation of scytonemin.]

Sakai, S., Hitotsuyanagi, Y., Aimi, N., Fujiki, H., Suganuma, M., Sugimura, T., Endo, Y. & Shudo, K. (1986). Absolute configuration of lyngbyatoxin A (teleocidin A-1) and teleocidin A-2. *Tetrahedron Letters* 27(43), 5219-5220. [This study presents stereochemical studies of the teleocidins.]

Schmidt, E. W., Nelson, J. T., Rasko, D. A., Sudek, S., Eisen, J. A., Haygood, M. G. & Ravel, J. (2005). Patellamide A and C biosynthesis by a microcin-like pathway in *Prochloron didemni*, the cyanobacterial symbiont of *Lissoclinum patella*. *Proceedings of the National Academy of Science U S A* 102(7315-7320. [This study presents the identification of *Prochloron didemni* as the source of the patellamides using genome sequence analysis and cloning.]

Secondary Metabolites from Gram-positive Marine Bacteria (4.0.)

Asolkar, R. N., Jensen, P. R., Kauffman, C. A. & Fenical, W. (2006). Daryamides A-C, weakly cytotoxic polyketides from a marine-derived actinomycete of the genus *Streptomyces* strain CNQ-085. *Journal of Natural Products* 69(12), 1756-1759. [This study describes the isolation, structure elucidation, antitumor and antifungal activity of the daryamides.]

Asolkar, R. N., Freel, K. C., Jensen, P. R., Fenical, W., Kondratyuk, T. P., Park, E. J. & Pezzuto, J. M. (2008). Arenamides A-C, cytotoxic NF-κB inhibitors from the marine actinomycete *Salinispora arenicola*. *Journal of Natural Products* 72(3), 396-402. [This study describes the isolation, structure elucidation, and chemopreventative properties, such as NF-κB and nitric oxide inhibition.]

Azumi, M., Ogawa, K.-I., Fujita, T., Takeshita, M., Yoshida, R., Furumai, T. & Igarashi, Y. (2008). Bacilosarins A and B, novel bioactive isocoumarins with unusual heterocyclic cores from the marine-derived bacterium *Bacillus subtilis*. *Tetrahedron* 64(6420-6425. [This study describes the isolation, structure elucidation, and bioactivity of the bacilosarcins.]

Bae, M.-A., Yamada, K., Ijuin, Y., Tsuji, T., Yazawea, K., Tomono, Y. & Uemura, D. (1996). Aburatubolactam A, a novel inhibitor of superoxide anion generation from a marine microorganism. *Heterocyclic Communications* 2(4), 315-318. [This study describes the isolation, structure elucidation, and bioactivity of aburatubolactam A.]

Barsby, T., Kelly, M. T., Gagne, S. M. & Andersen, R. J. (2001). Bogorol A produced in culture by a marine *Bacillus* sp. reveals a novel template for cationic peptide antibiotics. *Organic Letters* 3(3), 437-440. [This study describes the isolation, structure elucidation, and antibiotic activity of bogorol A.]

Barsby, T., Warabi, K., Sorensen, D., Zimmerman, W. T., Kelly, M. T. & Andersen, R. J. (2006). The bogorol family of antibiotics: Template-based structure elucidation and a new approach to positioning enantiomeric pairs of amino acids. *Journal of Organic Chemistry* 71(16), 6031-6037. [This study describes a peptide sequence identification technique for the cationic peptide antibiotics the bogorols.]

Bernan, V. S., Montenegro, D. A., Korshalla, J. D., Maiese, W. M., Steinberg, D. A. & Greenstein, M. (1994). Bioxalomycins, new antibiotics produced by the marine *Streptomyces* sp. Ll-31f508: Taxonomy and fermentation. *Journal of Antibiotics* 47(12), 1417-1424. [This study describes the isolation and antimicrobial activity of the bioxalomycins.]

Boonlarppradab, C., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2008). Marineosins A and B, cytotoxic spiroaminals from a marine-derived actinomycete. *Organic Letters* 10(24), 5505-5508. [This study describes the isolation, structure elucidation, and cytotoxicity of the marineosins.]

Buchanan, G. O., Williams, P. G., Feling, R. H., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2005). Sporolides A and B: Structurally unprecedented halogenated macrolides from the marine actinomycete *Salinispora tropica*. *Organic Letters* 7(13), 2731-2734. [This study describes the isolation and structure elucidation of the sporolides.]

Canedo, L. M., Fernandez-Puentes, J. L. & Baz, J. P. (2000). IB-96212, a novel cytotoxic macrolide produced by a marine *Micromonospora*. II. Physico-chemical properties and structure determination. *Journal of Antibiotics* 53(5), 479-483. [This study describes the isolation and structure elucidation of IB-96212]

Charan, R. D., Schlingmann, G., Janso, J., Bernan, V., Feng, X. & Carter, G. T. (2004). Diazepinomicin, a new antimicrobial alkaloid from a marine *Micromonospora* sp. *Journal of Natural Products* 67(8), 1431-1433. [This study describes the isolation and structure elucidation of diazepinomicin.]

Cho, J. Y., Kwon, H. C., Williams, P. G., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2006). Actinofuranones A and B, polyketides from a marine-derived bacterium related to the genus *Streptomyces* (Actinomycetales). *Journal of Natural Products* 69(3), 425-428. [This study describes the isolation and structure elucidation of actinofuranone metabolites.]

Cho, J. Y., Kwon, H. C., Williams, P. G., Jensen, P. R. & Fenical, W. (2006). Azamerone, a terpenoid phthalazinone from a marine-derived bacterium related to the genus *Streptomyces* (Actinomycetales). *Organic Letters* 8(12), 2471-2474. [This study describes the isolation and structure elucidation of azamerone.]

Cho, J. Y., Williams, P. G., Kwon, H. C., Jensen, P. R. & Fenical, W. (2007). Lucentamycins A-D, cytotoxic peptides from the marine-derived actinomycete *Nocardiopsis lucentensis*. *Journal of Natural Products* 70(8), 1321-1328. [This study describes the isolation, structure elucidation, and cytotoxicity of the lucentamycins.]

Choi, I. K., Shin, H. J., Lee, H. S. & Kwon, H. J. (2007). Streptochlorin, a marine natural product, inhibits NF-κB activation and suppresses angiogenesis in vitro. *Journal of Microbiology and Biotechnology* 17(8), 1338-1343. [This study describes the isolation, structure elucidation, and antiangiogenic activity via NF-κB inhibition of streptochlorin.]

El-Gendy, M. M., Shaaban, M., Shaaban, K. A., El-Bondkly, A. M. & Laatsch, H. (2008). Essramycin: A first triazolopyrimidine antibiotic isolated from nature. *Journal of Antibiotics* 61(3), 149-157. [This study describes the isolation, structure elucidation, and antibacterial activity of essramycin.]

Erba, E., Bergamaschi, D., Ronzoni, S., Faretta, M., Taverna, S., Bonfanti, M., Catapano, C. V., Faircloth, G., Jimeno, J. & D'incalci, M. (1999). Mode of action of thiocoraline, a natural marine compound with anti-tumour activity. *British Journal of Cancer* 80(7), 971-980. [This study describes the DNA polymerase-α activity of thiocoraline.]

Feling, R. H., Buchanan, G. O., Mincer, T. J., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2003). Salinosporamide A: A highly cytotoxic proteasome inhibitor from a novel microbial source, a marine bacterium of the new genus *Salinispora*. *Angewandte Chemie International Edition* 42(3), 355-357. [This study describes the isolation, structure elucidation, and bioactivity of the proteasome inhibitor salinosporamide A.]

Fiedler, H. P., Bruntner, C., Riedlinger, J., Bull, A. T., Knutsen, G., Goodfellow, M., Jones, A., Maldonado, L., Pathom-Aree, W., Beil, W., Schneider, K., Keller, S. & Sussmuth, R. D. (2008). Proximicin A, B and C, novel aminofuran antibiotic and anticancer compounds isolated from marine strains of the actinomycete *Verrucosispora*. *Journal of Antibiotics* 61(3), 158-163. [This study describes the isolation, structure elucidation, and bioactivity of the proximicins.]

Ford, P. W., Gadepalli, M. & Davidson, B. S. (1998). Halawanones A-D, new polycyclic quinones from a marine-derived streptomycete. *Journal of Natural Products* 61(10), 1232-1236. [This study describes the isolation and structure elucidation of the halawanones.]

Ravel, J. & Fraser, C. M. (2005). Genomics at the genus scale. *Trends in Microbiology* 13(3), 95-97. [This article provides a genomic analysis of various species of *Bacillus*.]

Gerard, J. M., Haden, P., Kelly, M. T. & Andersen, R. J. (1999). Loloatins A-D, cyclic decapeptide antibiotics produced in culture by a tropical marine bacterium. *Journal of Natural Products* 62(1), 80-85. [This study describes the isolation, structure elucidation, and antibacterial activity of the loloatins.]

Gontang, E. A., Fenical, W. & Jensen, P. R. (2007). Phylogenetic diversity of Gram-positive bacteria cultured from marine sediments. *Applied and Environmental Microbiology* 73(10), 3272-3282. [This study provides insight into the unexplored diversity of Gram-positive bacteria from marine sediments.]

Gustafson, K., Roman, M. & Fenical, W. (1989). The macrolactins, a novel class of antiviral and cytotoxic macrolides from a deep-sea marine bacterium. *Journal of the American Chemical Society* 111(19), 7519-7524. [This study describes the isolation and structure elucidation of macrolactins A-F.]

He, H., Ding, W. D., Bernan, V. S., Richardson, A. D., Ireland, C. M., Greenstein, M., Ellestad, G. A. & Carter, G. T. (2001). Lomaiviticins A and B, potent antitumor antibiotics from *Micromonospora lomaivitiensis*. *Journal of the American Chemical Society* 123(22), 5362-5363. [This study describes the isolation, structure elucidation, DNA damaging activity, and cytotoxicity of the lomaiviticins.]

Hernandez, D., Altuna, M., Cuevas, C., Aligue, R., Albericio, F. & Alvarez, M. (2008). Synthesis and antitumor activity of mechercharmycin A analogues. *Journal of Medicinal Chemistry* 51(18), 5722-5730. [This study presents the synthesis and antitumor activity of analogs of mechercharmycin A.]

Hohmann, C., Schneider, K., Bruntner, C., Irran, E., Nicholson, G., Bull, A. T., Jones, A. L., Brown, R., Stach, J. E., Goodfellow, M., Beil, W., Kramer, M., Imhoff, J. F., Sussmuth, R. D. & Fiedler, H. P. (2009). Caboxamycin, a new antibiotic of the benzoxazole family produced by the deep-sea strain *Streptomyces* sp. NTK 937. *Journal of Antibiotics* 62(2), 99-104. [This study describes the isolation, structure elucidation, antimicrobial and antitumor activity of caboxamycin.]

Hughes, C. C., Prieto-Davo, A., Jensen, P. R. & Fenical, W. (2008). The marinopyrroles, antibiotics of an unprecedented structure class from a marine *Streptomyces* sp. *Organic Letters* 10(4), 629-631. [This study describes the isolation, structure elucidation, anti-MRSA activity of the marinopyrroles.]

Hughes, C. C., Macmillan, J. B., Gaudencio, S. P., Fenical, W. & La Clair, J. J. (2009a). Ammosamides A and B target myosin. *Angewandte Chemie International Edition* 48(4), 728-732. [This study describes the biological mechanism of action of the ammosamides, targeting the protein myosin.]

Hughes, C. C., Macmillan, J. B., Gaudencio, S. P., Jensen, P. R. & Fenical, W. (2009b). The ammosamides: Structures of cell cycle modulators from a marine-derived *Streptomyces* species. *Angewandte Chemie International Edition* 48(4), 725-727. [This study describes the isolation and structure elucidation of actinofuranone metabolites.]

Imada, C., Okami, Y. & Hotta, K. (2002). Production of selenohomocystine as an antibiotic by a marine *Bacillus* sp. No. 14 with selenomethionine resistance. *Journal of Antibiotics* 55(2), 223-226. [This study describes the isolation and structure elucidation of selenohomocystine.]

Jensen, P. R., Dwight, R. & Fenical, W. (1991). Distribution of actinomycetes in near-shore tropical marine sediments. *Applied and Environmental Microbiology* 57(4), 1102-1108. [This study was the first to provide evidence for marine-obligate actinomycetes.]

Jeong, S. Y., Shin, H. J., Kim, T. S., Lee, H. S., Park, S. K. & Kim, H. M. (2006). Streptokordin, a new cytotoxic compound of the methylpyridine class from a marine-derived *Streptomyces* sp. Kordi-3238. *Journal of Antibiotics* 59(4), 234-240. [This study describes the isolation, structure elucidation and cytotoxicity of streptokordin.]

Kanoh, K., Matsuo, Y., Adachi, K., Imagawa, H., Nishizawa, M. & Shizuri, Y. (2005). Mechercharmycins A and B, cytotoxic substances from marine-derived *Thermoactinomyces* sp. YM3-251. *Journal of Antibiotics* 58(4), 289-292. [This study describes the isolation, structure elucidation and cytotoxicity of the mechercharmycins.]

Kwon, H. C., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2006). Marinomycins A-D, antitumor-antibiotics of a new structure class from a marine actinomycete of the recently discovered genus "*Marinispora*". *Journal of the American Chemical Society* 128(5), 1622-1632. [This study describes the isolation, structure elucidation, antitumor, and antibacterial activity of the marinomycins.]

Kwon, H. C., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2009). Marinisporolides, polyene-polyol macrolides from a marine actinomycete of the new genus *Marinispora*. *Journal of Organic Chemistry* 74(2), 675-684. [This study describes the isolation and structure elucidation of five marinisporolides.]

Li, F., Maskey, R. P., Qin, S., Sattler, I., Fiebig, H. H., Maier, A., Zeeck, A. & Laatsch, H. (2005). Chinikomycins A and B: Isolation, structure elucidation, and biological activity of novel antibiotics from a marine *Streptomyces* sp. Isolate M045. *Journal of Natural Products* 68(3), 349-353. [This study describes the isolation, structure elucidation, and antitumor activity of the chinikomycins.]

Macherla, V. R., Liu, J., Bellows, C., Teisan, S., Nicholson, B., Lam, K. S. & Potts, B. C. (2005). Glaciapyrroles A, B, and C, pyrrolosesquiterpenes from a *Streptomyces* sp. isolated from an Alaskan marine sediment. *Journal of Natural Products* 68(5), 780-783. [This study describes the isolation and structure elucidation of the glaciapyrroles.]

Macherla, V. R., Liu, J., Sunga, M., White, D. J., Grodberg, J., Teisan, S., Lam, K. S. & Potts, B. C. (2007). Lipoxazolidinones A, B, and C: Antibacterial 4-oxazolidinones from a marine actinomycete isolated from a guam marine sediment. *Journal of Natural Products* 70(9), 1454-1457. [This study describes the isolation, structure elucidation, and antibacterial activity of the lipoxazolidinones.]

Maldonado, L. A., Fenical, W., Jensen, P. R., Kauffman, C. A., Mincer, T. J., Ward, A. C., Bull, A. T. & Goodfellow, M. (2005). *Salinispora arenicola* gen. Nov., sp. Nov. And *Salinispora tropica* sp. Nov., obligate marine actinomycetes belonging to the family Micromonosporaceae. *International Journal of Systematic and Evolutionary Microbiology* 55(Pt 5), 1759-1766. [This study provides the formal description of the genus *Salinispora* along with two of its species, *S. arenicola* and *S. tropica*.]

Maloney, K. N., Macmillan, J. B., Dipasquale, A., Kauffman, C. A., Jensen, P. R., Rheingold, A. & Fenical, W. (2009). Lodopyridone, an unprecedented alkaloid from the marine bacterium *Saccharomonospora* sp. *Organic Letters*, In press. [This study describes the isolation, structure elucidation, and bioactivity of lodopyridone.]

Manam, R. R., Teisan, S., White, D. J., Nicholson, B., Grodberg, J., Neuteboom, S. T., Lam, K. S., Mosca, D. A., Lloyd, G. K. & Potts, B. C. (2005). Lajollamycin, a nitro-tetraene spiro-beta-lactone-gamma-lactam antibiotic from the marine actinomycete *Streptomyces nodosus*. *Journal of Natural Products* 68(2), 240-243. [This study describes the isolation, structure elucidation, antimicrobial and antitumor activity of lajollamycin.]

Martin, G. D., Tan, L. T., Jensen, P. R., Dimayuga, R. E., Fairchild, C. R., Raventos-Suarez, C. & Fenical, W. (2007). Marmycins A and B, cytotoxic pentacyclic C-glycosides from a marine sediment-derived actinomycete related to the genus *Streptomyces*. *Journal of Natural Products* 70(9), 1406-1409. [This study describes the isolation, structure elucidation, cytotoxicity and apoptotic activity of the marmycins.]

Maskey, R. P., Sevvana, M., Uson, I., Helmke, E. & Laatsch, H. (2004). Gutingimycin: A highly complex metabolite from a marine streptomycete. *Angewandte Chemie International Edition* 43(10), 1281-1283. [This study describes the isolation, structure elucidation, and possible biosynthesis of gutingimycin.]

Mcarthur, K. A., Mitchell, S. S., Tsueng, G., Rheingold, A., White, D. J., Grodberg, J., Lam, K. S. & Potts, B. C. (2008). Lynamicins A-E, chlorinated bisindole pyrrole antibiotics from a novel marine actinomycete. *Journal of Natural Products* 71(10), 1732-1737. [This study describes the isolation, structure elucidation, and antibacterial activity of the lynamicins.]

Mcglinchey, R. P., Nett, M., Eustaquio, A. S., Asolkar, R. N., Fenical, W. & Moore, B. S. (2008). Engineered biosynthesis of antiprotealide and other unnatural salinosporamide proteasome inhibitors. *Journal of the American Chemical Society* 130(25), 7822-7823. [This demonstrates the use of genetic engineering to produce unnatural derivatives of a natural product.]

Miller, E. D., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2007). Piperazimycins: Cytotoxic hexadepsipeptides from a marine-derived bacterium of the genus *Streptomyces*. *Journal of Organic Chemistry* 72(2), 323-330. [This study describes the isolation, structure elucidation, and screening against an NCI 60-cell line tumor panel of the piperazimycins.]

Mitchell, S. S., Nicholson, B., Teisan, S., Lam, K. S. & Potts, B. C. (2004). Aureoverticillactam, a novel 22-atom macrocyclic lactam from the marine actinomycete *Streptomyces aureoverticillatus*. *Journal of Natural Products* 67(8), 1400-1402. [This study describes the isolation, structure elucidation, and cytotoxicity of aureoverticillactam.]

Negri, A., Marco, E., Garcia-Hernandez, V., Domingo, A., Llamas-Saiz, A. L., Porto-Sanda, S., Riguera, R., Laine, W., David-Cordonnier, M. H., Bailly, C., Garcia-Fernandez, L. F., Vaquero, J. J. & Gago, F. (2007). Antitumor activity, x-ray crystal structure, and DNA binding properties of thiocoraline A, a natural bisintercalating thiodepsipeptide. *Journal of Medicinal Chemistry* 50(14), 3322-3333. [This study describes the DNA intercalating ability of thiocoraline.]

Okazaki, T., Kitahara, T. & Okami, Y. (1975). Studies on marine microorganisms. IV. A new antibiotic SS-228 Y produced by *Chainia* isolated from shallow sea mud. *Journal of Antibiotics* 28(3), 176-184. [This study describes the isolation, structure elucidation, and antibacterial activity of the quinone metabolite SS-228 Y.]

Oh, D. C., Williams, P. G., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2006). Cyanosporasides A and B, chloro- and cyano-cyclopenta[*a*]indene glycosides from the marine actinomycete "*Salinispora pacifica*". *Organic Letters* 8(6), 1021-1024. [This study describes the isolation, structure elucidation, bioactivity, and potential biosynthetic origin of the cyanosporosides.]

Oh, D. C., Gontang, E. A., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2008). Salinipyrones and pacificanones, mixed-precursor polyketides from the marine actinomycete *Salinispora pacifica*. *Journal*

of Natural Products 71(4), 570-575. [This study describes the isolation, structure elucidation, and potential biosynthetic origin of the salinipyrones and pacificanones.]

Pathom-Aree, W., Stach, J. E., Ward, A. C., Horikoshi, K., Bull, A. T. & Goodfellow, M. (2006). Diversity of actinomycetes isolated from challenger deep sediment (10,898 m) from the Mariana trench. *Extremophiles* 10(3), 181-189. [This study provides a evidence that there exists a vast untapped diversity of Actinomycete bacteria in the deep sea.]

Perez Baz, J., Canedo, L. M., Fernandez Puentes, J. L. & Silva Elipe, M. V. (1997). Thiocoraline, a novel depsipeptide with antitumor activity produced by a marine *Micromonospora*. II. Physico-chemical properties and structure determination. *Journal of Antibiotics* 50(9), 738-741. [This study describes the isolation and structure elucidation of thiocoraline.]

Pettit, G. R., Knight, J. C., Herald, D. L., Pettit, R. K., Hogan, F., Mukku, V. J., Hamblin, J. S., Dodson, M. J. & Chapuis, J. C. (2009). Antineoplastic agents. 570. Isolation and structure elucidation of bacillistatins 1 and 2 from a marine *Bacillus silvestris*. *Journal of Natural Products*. [This study describes the isolation, structure elucidation, and bioactivity of the bacillistatins.]

Pimentel-Elardo, S. M., Gulder, T. A. M., Hentschel, U. & Bringmann, G. (2008). Cebulactams A1 and A2 , new macrolactams isolated from *Saccharopolyspora cebuensis*, the first obligate marine strain of the genus *Saccharopolyspora*. *Tetrahedron Letters* 49(48), 6889-6892. [This study describes the isolation and structure elucidation of the cebulactams.]

Rainey, F. A., Ward-Rainey, N., Kroppenstedt, R. M. & Stackebrandt, E. (1996). The genus *Nocardiopsis* represents a phylogenetically coherent taxon and a distinct actinomycete lineage: Proposal of Nocardiopsaceae fam. Nov. *International Journal of Systematic Bacteriology* 46(4), 1088-1092. [This proposes a novel family to accommodate the genus *Nocardiopsis*.]

Renner, M. K., Shen, Y.-C., Cheng, X.-C., Jensen, P. R., Walter, F., Kauffman, C. A., Fenical, W., Lobkovsky, E. & Clardy, J. (1999). Cyclomarins A-C, new antiinflammatory cyclic peptides produced by a marine bacterium (S*treptomyces* sp.). *Journal of the American Chemical Society* 121(49), 11273-11276. [This study describes the isolation, structure elucidation, and antiinflammatory activity of the cyclomarins.]

Riedlinger, J., Reicke, A., Zahner, H., Krismer, B., Bull, A. T., Maldonado, L. A., Ward, A. C., Goodfellow, M., Bister, B., Bischoff, D., Sussmuth, R. D. & Fiedler, H. P. (2004). Abyssomicins, inhibitors of the para-aminobenzoic acid pathway produced by the marine *Verrucosispora* strain AB-18-032. *Journal of Antibiotics* 57(4), 271-279. [This study describes the isolation, structure elucidation, and bioactivity of the abyssomicins.]

Rychnovsky, S. D., Skalitzky, D. J., Pathirana, C., Jensen, P. R. & Fenical, W. (1992). Stereochemistry of the macrolactins. *Journal of the American Chemical Society* 114(2), 671-677. [This study describes the stereochemical determination of the chiral carbons in the macrolactins.]

Shin, H. J., Jeong, H. S., Lee, H. S., Park, S. K., Kim, H. M. & Kwon, H. J. (2007). Isolation and structure determination of streptochlorin, an antiproliferative agent from a marine-derived *Streptomyces* sp. 04DH110. *Journal of Microbiology and Biotechnology* 17(8), 1403-1406. [This study describes the isolation, structure elucidation, and antiproliferative activity of the streptochlorin.]

Schultz, A. W., Oh, D. C., Carney, J. R., Williamson, R. T., Udwary, D. W., Jensen, P. R., Gould, S. J., Fenical, W. & Moore, B. S. (2008). Biosynthesis and structures of cyclomarins and cyclomarazines, prenylated cyclic peptides of marine actinobacterial origin. *Journal of the American Chemical Society* 130(13), 4507-4516. [This study describes the detailed biosynthesis of the cyclomarins, exposing new biosynthetic pathways.]

Schumacher, R. W., Harrigan, B. L. & Davidson, B. S. (2001). Kahakamides A and B, new neosidomycin metabolites from a marine-derived actinomycete. *Tetrahedron Letters* 42(31), 5133-5135. [This study describes the isolation, structure elucidation, and antimicrobial activity of the kahakamides.]

Shin, J., Seo, Y., Lee, H. S., Rho, J. R. & Mo, S. J. (2003). A new cyclic peptide from a marine-derived bacterium of the genus *Nocardiopsis*. *Journal of Natural Products* 66(6), 883-884. [This study describes the isolation and structure elucidation of peptide MKN-349A.]

Sitachitta, N., Gadepalli, M. & Davidson, B. S. (1996). New α-pyrone-containing metabolites from a marine-derived actinomycete. *Tetrahedron* 52(24), 8073-8080. [This study describes the isolation, structure elucidation, and antimicrobial activity of the wailupemycins.]

Strangman, W. K., Kwon, H. C., Broide, D., Jensen, P. R. & Fenical, W. (2009). Potent inhibitors of pro-inflammatory cytokine production produced by a marine-derived bacterium. *Journal of Medicinal Chemistry* 52(8), 2317-2327. [This study describes the isolation, structure elucidation, and inhibition of cytokine production by the splenosins.]

Suzumura, K., Yokoi, T., Funatsu, M., Nagai, K., Tanaka, K., Zhang, H. & Suzuki, K. (2003). YM-266183 and YM-266184, novel thiopeptide antibiotics produced by *Bacillus cereus* isolated from a marine sponge II. Structure elucidation. *Journal of Antibiotics* 56(2), 129-134. [This study describes the isolation and structure elucidation of the thiopeptides.]

Takahashi, A., Ikeda, D., Nakamura, H., Naganawa, H., Kurasawa, S., Okami, Y., Takeuchi, T. & Iitakay (1989). Altemicidin, a new acaricidal and antitumor substance. II. Structure determination. *Journal of Antibiotics* 42(11), 1562-1566. [This study describes the isolation, structure elucidation, and bioactivity of altemicidin.]

Takahashi, C., Takada, T., Yamada, T., Minoura, K., Uchida, K. M., Eiko & Numata, A. (1994). Halichomycin, a new class of potent cytotoxic macrolides produced by an actinomycete from a marine fish. *Tetrahedron Letters* 35(28), 5013-5014. [This study describes the isolation, structure elucidation, and cytotoxicity of halichomycin.]

Teasdale, M. E., Liu, J., Wallace, J., Akhlaghi, F. & Rowley, D. C. (2009). Secondary metabolites produced by the marine bacterium *Halobacillus salinus* that inhibit quorum sensing-controlled phenotypes in gram-negative bacteria. *Applied and Environmental Microbiology* 75(3), 567-572. [This describes the identification of small molecules from *H. salinus* that inhibit quorum-sensing mechanisms in certain gram-negative bacteria.]

Trischman, J. A., Tapiolas, D. M., Jensen, P. R., Dwight, R., Fenical, W., Mckee, T. C., Ireland, C. M., Stout, T. J. & Clardy, J. (1994). Salinamides A and B: Anti-inflammatory depsipeptides from a marine streptomycete. *Journal of the American Chemical Society* 116, 757-758. [This study describes the isolation, structure elucidation, and antiinflammatory activity of the epibiont metabolites, the salinamides.]

Trischman, J. A., Jensen, P. R. & Fenical, W. (1994). Halobacillin: A cytotoxic cyclic acylpeptide of the iturin class produced by a marine *Bacillus*. 35(31), 5571-5574. [This study describes the isolation, structure elucidation, and moderate bioactivity of halobacillin.]

Udwary, D. W., Zeigler, L., Asolkar, R. N., Singan, V., Lapidus, A., Fenical, W., Jensen, P. R. & Moore, B. S. (2007). Genome sequencing reveals complex secondary metabolome in the marine actinomycete *Salinispora tropica*. *Proceedings of the National Academy of Sciences of the United States of America* 104(25), 10376-10381. [This study describes the natural product producing biosynthetic capacity of *S. tropica*, as well as the isolation and structure elucidation of salinilactam.]

Wang, G.-Y.-S., Kuramoto, M., Yamada, K., Yazawa, K. & Uemura, D. (1995). Homocereulide, an extremely potent cytotoxic depsipeptide from the marine bacterium *Bacillus cereus*. *Chemistry Letters* 9), 791-792. [This study describes the isolation, structure elucidation, and cytotoxicity of homocereulide.]

Williams, P. G., Asolkar, R. N., Kondratyuk, T., Pezzuto, J. M., Jensen, P. R. & Fenical, W. (2007). Saliniketals A and B, bicyclic polyketides from the marine actinomycete *Salinispora arenicola*. *Journal of Natural Products* 70(1), 83-88. [This study describes the isolation, structure elucidation, and chemopreventative properties of the saliniketals.]

Williams, P. G., Miller, E. D., Asolkar, R. N., Jensen, P. R. & Fenical, W. (2007). Arenicolides A-C, 26-membered ring macrolides from the marine actinomycete *Salinispora arenicola*. *Journal of Organic Chemistry* 72(14), 5025-5034. [This study describes the isolation, structure elucidation, and detailed stereochemical analysis of the arenicolides.]

Secondary Metabolites from Marine-derived Fungi (5.0.)

Abdel-Lateff, A., Konig, G. M., Fisch, K. M., Holler, U., Jones, P. G. & Wright, A. D. (2002). New antioxidant hydroquinone derivatives from the algicolous marine fungus *Acremonium* sp. *Journal of*

Natural Products 65(11), 1605-1611. [This study presents the isolation and structure elucidation of acremonin.]

Amagata, T., Amagata, A., Tenney, K., Valeriote, F. A., Lobkovsky, E., Clardy, J. & Crews, P. (2003). Unusual C25 steroids produced by a sponge-derived *Penicillium citrinum*. *Organic Letters* 5 (23), 4393-4396. [This study presents the isolation and structure elucidation of isocyclocitrinol A and the resulting revision of the structure of cyclocitrinol.]

Amagata, T., Doi, M., Ohta, T., Minoura, K. & Numata, A. (1998). Absolute stereostructures of novel cytotoxic metabolites, gymnastatins A-E, from a *Gymnascella* species separated from a *Halichondria* sponge. *Journal of the Chemical Society, Perkin Transactions 1*(21), 3585-3600. [This study presents the absolute stereochemical determination of gymnastatins A-E by NMR and chemical transformation.]

Amagata, T., Minoura, K. & Numata, A. (2006). Gymnastatins F-H, cytostatic metabolites from the sponge-derived fungus *Gymnascella dankaliensis*. *Journal of Natural Products* 69 (10), 1384-1388. [This study presents the isolation and structure elucidation of gymnastatins F-H.]

Bringmann, G., Lang, G., Gulder, T. A. M., Tsuruta, H., Muhlbacher, J., Maksimenka, K., Steffens, S., Schaumann, K., Stohr, R., Wiese, J., Imhoff, J. F., Perovic-Ottstadt, S., Boreiko, O. & Muller, W. E. G. (2005). The first sorbicillinoid alkaloids, the antileukemic sorbicillactones A and B, from a sponge-derived *Penicillium chrysogenum* strain. *Tetrahedron* 61 (30), 7252-7265. [This study presents the isolation and structure elucidation of sorbicillactones A and B, and anti-HIV activity.]

Bringmann, G., Lang, G., Michel, M. & Heubes, M. (2004a). Stereochemical assignment of the fungal metabolite xestodecalactone A by total synthesis. *Tetrahedron Letters* 45 (2829-2831). [This study presents the stereochemical assignment of xestadecalactone A by total synthesis of both enantiomers.]

Bringmann, G., Lang, G., Steffens, S. & Schaumann, K. (2004b). Petrosifungins A and B, novel cyclodepsipeptides from a sponge-derived strain of *Penicillium brevicompactum*. *Journal of Natural Products* 67 (3), 311-315. [This study presents the isolation and structure elucidation of the petrosifungins.]

Bugni, T. S., Bernan, V. S., Greenstein, M., Janso, J. E., Maiese, W. M., Mayne, C. L. & Ireland, C. M. (2003). Brocaenols A-C: Novel polyketides from a marine-derived *Penicillium brocae*. *Journal of Organic Chemistry* 68 (5), 2014-2017. [This study presents the isolation and structure elucidation of the brocaenols.]

Capon, R. J., Skene, C., Stewart, M., Ford, J., O'hair, R. A., Williams, L., Lacey, E., Gill, J. H., Heiland, K. & Friedel, T. (2003). Aspergillicins A-E: Five novel depsipeptides from the marine-derived fungus *Aspergillus carneus*. *Organic and Biomolecular Chemistry* 1 (11), 1856-1862. [This study presents the isolation and structure elucidation of the aspergillicins.]

Chen, G., Lin, Y., Wen, L., Vrijmoed, L. L. P. & Gareth Jones, E. B. (2003). Two new metabolites of a marine endophytic fungus (no. 1893) from an estuarine mangrove on the South China Sea coast. *Tetrahedron* 59 (26), 4907-4909. [This study presents the isolation and structure determination of lactones 1893A and 1893 B.]

Cueto, M., Jensen, P. R. & Fenical, W. (2002). Aspergilloxide, a novel sesterterpene epoxide from a marine-derived fungus of the genus *Aspergillus*. *Organic Letters* 4 (9), 1583-1585. [This study presents the isolation and structure elucidation of aspergilloxide.]

Cueto, M., Jensen, P. R., Kauffman, C., Fenical, W., Lobkovsky, E. & Clardy, J. (2001). Pestalone, a new antibiotic produced by a marine fungus in response to bacterial challenge. *Journal of Natural Products* 64 (11), 1444-1446. [This study presents the isolation, structure elucidation, and antibiotic activity of pestalone.]

Edrada, R. A., Heubes, M., Brauers, G., Wray, V., Berg, A., Grafe, U., Wohlfarth, M., Muhlbacher, J., Schaumann, K., Sudarsono, S., Bringmann, G. & Proksch, P. (2002). Online analysis of xestodecalactones A-C, novel bioactive metabolites from the fungus *Penicillium cf. montanense* and their subsequent isolation from the sponge *Xestospongia exigua*. *Journal of Natural Products* 65 (11), 1598-1604. [This study presents the isolation and structure elucidation of the xestodecalactones using online analysis.]

Garo, E., Starks, C. M., Jensen, P. R., Fenical, W., Lobkovsky, E. & Clardy, J. (2003). Trichodermamides A and B, cytotoxic modified dipeptides from the marine-derived fungus *Trichoderma virens*. *Journal of Natural Products* 66 (3), 423-426. [This study presents the isolation, structure elucidation, and cytotoxicity of trichodermamides A and B.]

Goldring, W. P. & Pattenden, G. (2006). The phomactins. A novel group of terpenoid platelet activating factor antagonists related biogenetically to the taxanes. *Accounts of Chemical Research* 39 (5), 354-361. [This study presents a nice review of studies exploring the phomactins' biological activity, biosynthesis, and total synthesis.]

Greve, H., Schupp, P. J., Eguereva, E., Kehraus, S., Kelter, G., Maier, A., Fiebig, H.-H. & Konig, G. M. (2008). Apralactone A and a new stereochemical class of curvularins from the marine fungus *Curvularia* sp. *European Journal of Organic Chemistry* 30, 5085-5092. [This study presents the isolation and structure elucidation of apralactone A.]

Guerriero, A., D'ambrosio, M., Cuomo, V., Vanzanella, F. & Pietra, F. (1988). Dendryphiellin A, the first fungal trinoreremophilane. *Helvetica Chimica Acta* 71 (1), 57-61. [This study presents the isolation and structure elucidation of dendryphiellin A.]

Hande, S. M. & Uenishi, J. I. (2009). Total synthesis of aspergillide B and structural discrepancy of aspergillide A. *Tetrahedron Letters* 50 (2), 189-192. [This study presents the total synthesis of aspergillide B and structural revision of aspergillide A.]

Hiort, J., Maksimenka, K., Reichert, M., Perovic-Ottstadt, S., Lin, W. H., Wray, V., Steube, K., Schaumann, K., Weber, H., Proksch, P., Ebel, R., Mueller, W. E. G. & Bringmann, G. (2005). New natural products from the sponge-derived fungus *Aspergillus niger*. *Journal of Natural Products* 68 (12), 1821. [This study presents the isolation and (incorrect) structure elucidation of the aspernigrins and pyranonigrins.]

Isaka, M., Suyarnsestakorn, C., Tanticharoen, M., Kongsaeree, P. & Thebtaranonth, Y. (2002). Aigialomycins A-E, new resorcylic macrolides from the marine mangrove fungus *Aigialus parvus*. *Journal of Organic Chemistry* 67 (5), 1561-1566. [This study presents the isolation and structure elucidation of the aigialomycins.]

Kito, K., Ookura, R., Yoshida, S., Namikoshi, M., Ooi, T. & Kusumi, T. (2008). New cytotoxic 14-membered macrolides from marine-derived fungus *Aspergillus ostianus*. *Organic Letters* 10 (2), 225-228. [This study presents the isolation and (incorrect) structure elucidation of the aspergillides.]

Lee, S. M., Li, X. F., Jiang, H., Cheng, J. G., Seong, S., Choi, H. D. & Son, B. W. (2003). Terreusinone, a novel UV-A protecting dipyrroloquinone from the marine algicolous fungus *Aspergillus terreus*. *Tetrahedron Letters* 44 (42), 7707-7710. [This study presents the isolation, structure elucidation, and UV-A protecting activity of terreusinone.]

Lin, Y., Wu, X., Feng, S., Jiang, G., Luo, J., Zhou, S., Vrijmoed, L. L. P., Jones, E. B. G., Krohn, K., Steingroever, K. & Zsila, F. (2001). Five unique compounds: Xyloketals from mangrove fungus *Xylaria* sp. from the South China Sea coast. *Journal of Organic Chemistry* 66 (19), 6252-6256. [This study presents the isolation and structure elucidation of xyloketals A-E and acetylcholine esterase inhibition activity of xyloketal A.]

Liu, W., Gu, Q., Zhu, W., Cui, C., Fan, G., Zhu, T., Liu, H. & Fang, Y. (2005). Penicillones A and B, two novel polyketides with tricyclo [5.3.1.03,8] undecane skeleton, from a marine-derived fungus *Penicillium terrestre*. *Tetrahedron Letters* 46 (30), 4993-4996. [This study presents the isolation and structure elucidation of the penicillones.]

Malmstrom, J. (1999). Unguisins A and B: New cyclic peptides from the marine-derived fungus *Emericella unguis*. *Journal of Natural Products* 62 (5), 787-789. [This study presents the isolation and structure elucidation of the unguisins.]

Mugishima, T., Tsuda, M., Kasai, Y., Ishiyama, H., Fukushi, E., Kawabata, J., Watanabe, M., Akao, K. & Kobayashi, J. (2005). Absolute stereochemistry of citrinadins A and B from a marine-derived fungus. *Journal of Organic Chemistry* 70 (23), 9430-9435. [This study presents the determination of the absolute stereochemistry of citrinadin A using circular dichroism.]

Numata, A., Amagata, T., Minoura, K. & Ito, T. (1997). Gymnastatins, novel cytotoxic metabolites produced by a fungal strain from a sponge. *Tetrahedron Letters* 38 (32), 5675-5678. [This study presents the isolation, structure elucidation (relative stereochemistry), and cytotoxicity of gymnastatins A-C.]

Numata, A., Takahashi, C., Ito, Y., Takada, T., Kawai, K., Usami, Y., Matsumura, E., Imachi, M., Ito, T. & Hasegawa, T. (1993). Communesins, cytotoxic metabolites of a fungus isolated from a marine alga. *Tetrahedron Letters* 34 (14), 2355-2358. [This study presents the original isolation and structure elucidation of the communesins.]

Oh, D. C., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2007). Induced production of emericellamides A and B from the marine-derived fungus *Emericella* sp. in competing co-culture. *Journal of Natural Products* 70 (4), 515-520. [This study presents the isolation, structure elucidation, and antibacterial activity of the emericellamides.]

Osterhage, C., Konig, G. M., Holler, U. & Wright, A. D. (2002). Rare sesquiterpenes from the algicolous fungus *Drechslera dematioidea*. *Journal of Natural Products* 65 (3), 306-313. [This study presents the isolation and structure elucidation of the drechslerines.]

Renner, M. K., Jensen, P. R. & Fenical, W. (1998). Neomangicols: Structures and absolute stereochemistries of unprecedented halogenated sesterterpenes from a marine fungus of the genus *Fusarium*. *Journal of Organic Chemistry* 63 (23), 8346-8354. [This study presents the isolation, structure elucidation, and biological activity of the neomangicols.]

Renner, M. K., Jensen, P. R. & Fenical, W. (2000). Mangicols: Structures and biosynthesis of a new class of sesterterpene polyols from a marine fungus of the genus *Fusarium*. *Journal of Organic Chemistry* 65 (16), 4843-4852. [This study presents the isolation, structure elucidation, anti-inflammatory activity and biosynthetic proposal of the mangicols.]

Rowley, D. C., Kelly, S., Kauffman, C. A., Jensen, P. R. & Fenical, W. (2003). Halovirs A-E, new antiviral agents from a marine-derived fungus of the genus *Scytalidium*. *Bioorganic Medicinal Chemistry* 11 (19), 4263-4274. [This study presents the isolation, structure elucidation, and antiviral activity of the halovirs.]

Sasaki, M., Tsuda, M., Sekiguchi, M., Mikami, Y. & Kobayashi, J. I. (2005). Perinadine A, a novel tetracyclic alkaloid from marine-derived fungus *Penicillium citrinum*. *Organic Letters* 7 (19), 4261-4264. [This study presents the isolation and structure elucidation of perinadine A.]

Schlingmann, G., Milne, L., Williams, D. R. & Carter, G. T. (1998). Cell wall active antifungal compounds produced by the marine fungus *Hypoxylon oceanicum* LL-15G256. II. Isolation and structure determination. *Journal of Antibiotics* 51 (3), 303-316. [This study presents the isolation and structure determination of lipodepsipeptides of *Hypoxylon oceanicum* (including 15G256γ).]

Schlingmann, G., Taniguchi, T., He, H., Bigelis, R., Yang, H. Y., Koehn, F. E., Carter, G. T. & Berova, N. (2007). Reassessing the structure of pyranonigrin. *Journal of Natural Products* 70 (7), 1180-1187. [This study presents the structural revision of pyranonigrin using NMR data.]

Seibert, S. F., Krick, A., Eguereva, E., Kehraus, S. & Koenig, G. M. (2007). Ascospiroketals A and B, unprecedented cycloethers from the marine-derived fungus *Ascochyta salicorniae*. *Organic Letters* 9 (2), 239-242. [This study presents the isolation and structure elucidation of ascospiroketals A and B.]

Siengalewicz, P., Gaich, T. & Mulzer, J. (2008). It all began with an error: The nomofungin/communesin story. *Angewandte Chemie International Edition* 47 8170-8176. [This study presents a nice review of the misidentification of nomofungin, and its identification as communesin B through total synthesis.]

Sugano, M., Sato, A., Iijima, Y., Oshima, T., Furuya, K., Kuwano, H., Hata, T. & Hanzawa, H. (1991). Phomactin A; a novel paf antagonist from a marine fungus *Phoma* sp. *Journal of the American Chemical Society* 113 (14), 5463-5464. [This study presents the isolation, structure elucidation, and platelet activating factor antagonistic activity of phomactin A.]

Takahashi, C., Numata, A., Ito, Y., Matsumura, E., Araki, H., Iwaki, H. & Kushida, K. (1994). Leptosins, antitumor metabolites of a fungus isolated from a marine alga. *Journal of the Chemical Society, Perkin Transactions 1* (13), 1859-1864. [This study presents the isolation, structure elucidation, and cytotoxicity of leptosins A-F.]

Tan, L. T., Cheng, X. C., Jensen, P. R. & Fenical, W. (2003). Scytalidamides A and B, new cytotoxic cyclic heptapeptides from a marine fungus of the genus *Scytalidium*. *Journal of Organic Chemistry* 68 (23), 8767-8773. [This study presents the isolation and structure elucidation of scytalidamides A and B.]

Tsuda, M., Kasai, Y., Komatsu, K., Sone, T., Tanaka, M., Mikami, Y. & Kobayashi, J. (2004). Citrinadin A, a novel pentacyclic alkaloid from marine-derived fungus *Penicillium citrinum*. *Organic Letters* 6 (18), 3087-3089. [This study presents the isolation and structure elucidation (relative stereochemistry) of citrinadin A.]

Tsukamoto, S., Hirota, H., Imachi, M., Fujimuro, M., Onuki, H., Ohta, T. & Yokosawa, H. (2005). Himeic acid A: A new ubiquitin-activating enzyme inhibitor isolated from a marine-derived fungus, *Aspergillus* sp. *Bioorganic and Medicinal Chemistry Letters* 15 (1), 191-194. [This study presents the isolation, structure elucidation, and ubiquitin-activating enzyme inhibitory activity of the himeic acids.]

Vongvilai, P., Isaka, M., Kittakoop, P., Srikitikulchai, P., Kongsaeree, P. & Thebtaranonth, Y. (2004). Ketene acetal and spiroacetal constituents of the marine fungus *Aigialus parvus* BCC 5311. *Journal of Natural Products* 67 (3), 457-460. [This study presents the isolation and structure elucidation of aigialospirol.]

Wei, H., Itoh, T., Kinoshita, M., Kotoku, N., Aoki, S. & Kobayashi, M. (2005). Shimalactone A, a novel polyketide, from marine-derived fungus *Emericella variecolor* GF10. *Tetrahedron* 61 (33), 8054-8058. [This study presents the isolation and structure elucidation of shimalactone A.]

Wu, X., Liu, X. H., Lin, Y., Luo, J., She, Z., Li, H., Chan, W., Antus, S., Kurtan, T. & Elsasser, B. (2005). Xyloketal F: A strong L-calcium channel blocker from the mangrove fungus *Xylaria* sp. (#2508) from the South China Sea coast. *European Journal of Organic Chemistry* 19 (4061-4064. [This study presents the isolation, structure elucidation, and calcium channel blocking activity of xyloketal F.]

Yanagihara, M., Sasaki-Takahashi, N., Sugahara, T., Yamamoto, S., Shinomi, M., Yamashita, I., Hayashida, M., Yamanoha, B., Numata, A., Yamori, T. & Andoh, T. (2005). Leptosins isolated from marine fungus *Leptoshaeria* species inhibit DNA topoisomerases I and/or II and induce apoptosis by inactivation of Akt/protein kinase B. *Cancer Science* 96 (11), 816-824. [This study presents the DNA topoisomerase inhibition activity of leptosins F and C.]

Ye, Y. H., Zhu, H. L., Song, Y. C., Liu, J. Y. & Tan, R. X. (2005). Structural revision of aspernigrin A, reisolated from *Cladosporium herbarum* IFB-E002. *Journal of Natural Products* 68 (7), 1106-1108. [This study presents the structural revision of aspernigrin A based on additional NMR data and X-ray crystallographic analysis.]

Discussion / Conclusion (7.0.)

Jensen, P. R., Williams, P. G., Oh, D. C., Zeigler, L. & Fenical, W. (2007). Species-specific secondary metabolite production in marine actinomycetes of the genus *Salinispora*. *Applied and Environmental Microbiology* 73(4), 1146-1152. [This study discusses the trends observed in secondary metabolite production within species of the same genus.]

Nicholls, H. (2007). Sorcerer II: The search for microbial diversity roils the waters. *PLoS Biol* 5(3), e74. [This article provides an overview, including planning the legal framework of the Sorcerer II expedition for microbial diversity.]

Penn, K., Jenkins, C., Nett, M., Udwary, D. W., Gontang, E. A., Mcglinchey, R. P., Foster, B., Lapidus, A., Podell, S., Allen, E. E., Moore, B. S. & Jensen, P. R. (2009). Genomic islands link secondary metabolism to functional adaptation in marine actinobacteria. *The ISME Journal*. [This study discusses the precence and evolutionary origin of biosynthetic gene clusters via genomic analyses of two marine actinobacterial strains, *S. arenicola* and *S. tropica*.]

Venter, J. C., Remington, K., Heidelberg, J. F., Halpern, A. L., Rusch, D., Eisen, J. A., Wu, D., Paulsen, I., Nelson, K. E., Nelson, W., Fouts, D. E., Levy, S., Knap, A. H., Lomas, M. W., Nealson, K., White, O., Peterson, J., Hoffman, J., Parsons, R., Baden-Tillson, H., Pfannkoch, C., Rogers, Y. H. & Smith, H. O. (2004). Environmental genome shotgun sequencing of the Sargasso Sea. *Science* 304(5667), 66-74. [This study attempts to analyze the extent of microbial diversity found in the ocean.]

Williamson, S. J., Rusch, D. B., Yooseph, S., Halpern, A. L., Heidelberg, K. B., Glass, J. I., Andrews-Pfannkoch, C., Fadrosh, D., Miller, C. S., Sutton, G., Frazier, M. & Venter, J. C. (2008). The Sorcerer II

global ocean sampling expedition: Metagenomic characterization of viruses within aquatic microbial samples. *PLoS One* 3(1), e1456. [This study analyzes the contribution of viruses to the global oceanic gene pool.]

Marine Microorganism Review Articles

Bhadury, P., Mohammad, B. T. & Wright, P. C. (2006). The current status of natural products from marine fungi and their potential as anti-infective agents. *Journal of Industrial Microbiology and Biotechnology* 33 (5), 325-337. [This review discusses the discovery and development of metabolites from marine-derived fungi, including approaches involving metabolic engineering.]

Blunt, J. W., Copp, B. R., Hu, W. P., Munro, M. H., Northcote, P. T. & Prinsep, M. R. (2008). Marine natural products. *Natural Products Reports* 25(1), 35-94. [This review provides a broad summary of natural products isolated from the marine environment and is organized based on source.]

Bugni, T. S. & Ireland, C. M. (2004). Marine-derived fungi: A chemically and biologically diverse group of microorganisms. *Natural Product Reports* 21 (1), 143-163. [This review covers 273 metabolites from marine-derived fungi and covers some basic principles of mycology.]

Bull, A. T., Stach, J. E., Ward, A. C. & Goodfellow, M. (2005). Marine actinobacteria: Perspectives, challenges, future directions. *Antonie Van Leeuwenhoek* 87(3), 65-79. [This review addresses biology and biotechnology-related issues of marine actinobacteria.]

Bull, A. T. & Stach, J. E. (2007). Marine actinobacteria: New opportunities for natural product search and discovery. *Trends in Microbiology* 15(11), 491-499. [This review discusses the possibilities of actinomycetes to produce novel therapeutic entities and the development of technologies that may help unearth new actinobacterial diversity.]

Burgess, J. G., Jordan, E. M., Bregu, M., Mearns-Spragg, A. & Boyd, K. G. (1999). Microbial antagonism: A neglected avenue of natural products research. *Journal of Biotechnology* 70(1-3), 27-32. [This review discusses the potential for production of antibiotics by marine epibiotic bacteria.]

Burja, A. M., Banaigs, B., Abou-Mansour, E., Grant Burgess, J. & Wright, P. C. (2001). Marine cyanobacteria: A prolific source of natural products. *Tetrahedron* 57 (46), 9347-9377. [This review discusses various properties of cyanobacteria, including ecology and secondary metabolite production.]

Butler, A. (2005). Marine siderophores and microbial iron mobilization. *Biometals* 18(4), 369-374. [This review provides a short summary of the structures of siderophores produced by marine bacteria and their role in iron mobilization.]

Butler, M. S. (2008). Natural products to drugs: Natural product-derived compounds in clinical trials. *Natural Product Reports* 25(3), 475-516. [This review summarizes the natural products involved in clinical trials between 2005 and 2007.]

Clardy, J. (2005). Using genomics to deliver natural products from symbiotic bacteria. *Genome Biology* 6(9), 232.1-232.4. [This review discusses using easily culturable bacteria and genomics to produce natural products that regularly derive from symbiotic bacteria.]

Cragg, G. M., Grothaus, P. G. & Newman, D. J. (2009). Impact of natural products on developing new anti-cancer agents. *Chemical Reviews* 109(7), 3012-3043. [This review summarizes the historical impact of natural products regarding the treatment cancer, and provides an update of the current status of anti-cancer natural products.]

Delong, E. F. (2007). Modern microbial seascapes. Forward. *Nature Reviews. Microbiology* 5(10), 755-757. [This forward summarizes a special series on marine microorganisms in the Journal *Nature Reviews. Microbiology*.]

Dobretsov, S., Teplitski, M. & Paul, V. (2009). Mini-review: Quorum sensing in the marine environment and its relationship to biofouling. *Biofouling* 25(5), 413-427. [This review summarizes the role of quorum sensing signaling and inhibition in marine bacteria by compounds derived from marine organisms.]

Ebel, R. (2006). Secondary metabolites from marine-derived fungi, in: P. Proksch & W. E. G. Mueller (Eds.) *Frontiers in Marine Biotechnology.* Wymondham: Horizon Bioscience, 73-143. [This chapter summarizes the discovery of natural products from marine-derived fungi.]

Fenical, W. & Jensen, P. R. (2006). Developing a new resource for drug discovery: Marine actinomycete bacteria. *Nature Chemical Biology* 2(12), 666-673. [This review discusses the prospects of marine actinobacteria to produce novel, biologically active, and clinically significant molecules.]

Fenical, W., Jensen, P. R., Palladino, M. A., Lam, K. S., Lloyd, G. K. & Potts, B. C. (2009). Discovery and development of the anticancer agent salinosporamide A (npi-0052). *Bioorganic & Medicinal Chemistry* 17(6), 2175-2180. [This summarizes the process of developing a small molecule such as salinosporamide A into a clinically viable anticancer agent.]

Fenical, W. (1993). Chemical studies of marine bacteria. *Chemical Reviews* 93(1673-1683. [This review describes the various environments that harbor marine bacteria.]

Gademann, K. & Portmann, C. (2008). Secondary metabolites from Cyanobacteria: Complex structures and powerful bioactivities. *Current Organic Chemistry* 12 (4), 326-341. [This review discusses metabolites from marine-derived fungi in the following categories: toxins, iron chelators, indole alkaloids, and protease inhibitors.]

Hay, M. E. (2009). Marine chemical ecology: Chemical signals and cues structure marine populations, communities, and ecosystems. *Annual Review of Marine Science* 1, 193-212. [This review highlights the roles and importance of chemical signaling in the marine environment.]

Jensen, P. R. & Fenical, W. (2002). Secondary metabolites from marine fungi, in: K. D. Hyde (Ed.) *Fungi in Marine Environments.* Hong Kong: Fungal Diversity Press, 293-315. [This chapter discusses natural products isolated from marine-derived fungi.]

Jones, A. C., Gu, L., Sorrels, C. M., Sherman, D. H. & Gerwick, W. H. (2009). New tricks from ancient algae: Natural products biosynthesis in marine cyanobacteria. *Current Opinion in Chemical Biology* 13 (2), 216-223. [This review discusses recent advances in understanding the biosynthesis of three cyanobacterial classes of natural product: mixed polyketide synthase/non ribosomal peptide synthetase (PKS/NRPS) metabolites, aromatic amino acid-derived alkaloids, and ribosomally encoded cyclic peptides.]

Jorgensen, B. B. & Boetius, A. (2007). Feast and famine - microbial life in the deep-sea bed. *Nature Reviews. Microbiology* 5(10), 770-781. [This review discusses the occurrence of microorganisms in the deep ocean and describes their living conditions.]

Karl, D. M. (2007). Microbial oceanography: Paradigms, processes and promise. *Nature Reviews. Microbiology* 5(10), 759-769. [This review covers a broad range of topics and generally addresses some ecological functions of microorganisms in the ocean.]

Konig, G. M., Kehraus, S., Seibert, S. F., Abdel-Lateff, A. & Muller, D. (2006). Natural products from marine organisms and their associated microbes. *Chembiochem: A European Journal of Chemical Biology* 7(2), 229-238. [This review discusses natural products from various types of interactions between marine microorganisms and their associated hosts (invertebrates, algae, etc).]

Laatsch, H. (2006) Marine bacterial metabolites. *Frontiers in Marine Biotechnology* (ed. P Proksch, WEG Müller), 225–288. Horizon Bioscience. [This chapter provides a comprehensive summary of natural products isolated from marine bacteria; it is organized by structural type.]

Lam, K. S. (2006). Discovery of novel metabolites from marine actinomycetes. *Current Opinion in Microbiology* 9(3), 245-251. [This mini-review provides a brief description of the occurrence of marine actinomycetes and their capability to produce bioactive secondary metabolites.]

Lebar, M. D., Heimbegner, J. L. & Baker, B. J. (2007). Cold-water marine natural products. *Natural Product Reports* 24(4), 774-797. [This review discusses the isolation of natural products from cold-water habitats; included within are sections on bacteria, fungi, and microalgae.]

Lu, X. L., Xu, Q. Z., Liu, X. Y., Cao, X., Ni, K. Y. & Jiao, B. H. (2008). Marine drugs--macrolactins. *Chemistry & Biodiversity* 5(9), 1669-1674. [This mini-review provides a short history of the isolation and bioactivity of the class of marine bacterial metabolites, the macrolactins.]

Miller, M. B. & Bassler, B. L. (2001). Quorum sensing in bacteria. *Annual Review of Microbiology* 55(165-199. [This review summarizes the general roles and processes of quorum sensing in bacteria.]

Molinski, T. F., Dalisay, D. S., Lievens, S. L. & Saludes, J. P. (2009). Drug development from marine natural products. *Nature Reviews. Drug Discovery* 8(1), 69-85. [This review provides a brief history of natural product drug discovery, but predominantly focuses on marine natural products, some from marine microbes, that are currently being investigated in clinical trials.]

Moore, B. S. (2005). Biosynthesis of marine natural products: Microorganisms (part A). *Natural Product Reports* 22(5), 580-593. [This review covers literature published of marine microbial natural products from 1999 to 2004, focusing on biosynthetic studies.]

Nett, M. & Konig, G. M. (2007). The chemistry of gliding bacteria. *Nat Prod Rep* 24(6), 1245-1261. [This review discusses the breadth of secondary metabolites from gliding bacteria, and provides brief taxonomic descriptions of these microorganisms.]

Olano, C., Mendez, C. & Salas, J. A. (2009). Antitumor compounds from marine actinomycetes. *Marine Drugs* 7(2), 210-248. [Broken down by structural type (polyketides, mixed polyketide-non ribosomal peptide, etc.), this review summarizes the molecules isolated from marine actinomycetes.]

Prudhomme, J., Mcdaniel, E., Ponts, N., Bertani, S., Fenical, W., Jensen, P. & Le Roch, K. (2008). Marine actinomycetes: A new source of compounds against the human malaria parasite. *PLoS One* 3(6), e2335. [This study evaluates the ability of salinosporamide A to inhibit malarial parasite *Plasmodium* spp.]

Saleem, M., Ali, M. S., Hussain, S., Jabbar, A., Ashraf, M. & Lee, Y. S. (2007). Marine natural products of fungal origin. *Natural Product Reports* 24 (5), 1142-1152. [This review discusses therapeutically significant molecules from marine-derived fungi and presents 103 fungal metabolites.]

Simmons, T. L., Andrianasolo, E., Mcphail, K., Flatt, P. & Gerwick, W. H. (2005). Marine natural products as anticancer drugs. *Molecular Cancer Therapeutics* 4(2), 333-342. [This review discusses the clinical status of select anticancer natural products isolated from marine sources.]

Singh, S., Kate, B. N. & Banerjee, U. C. (2005). Bioactive compounds from cyanobacteria and microalgae: An overview. *Critical Reviews in Biotechnology* 25 (3), 73-95. [This review discusses the use and genetic manipulation of cyanobacteria and microalgae, production processes and biosynthesis of pigments, as well as other bioactive compounds.]

Suttle, C. A. (2007). Marine viruses - major players in the global ecosystem. *Nature Reviews Microbiology* 5(10), 801-812. [This review discusses the ecological roles of marine viruses.]

Tan, L. T. (2007). Bioactive natural products from marine cyanobacteria for drug discovery. *Phytochemistry* 68 (7), 954-979. [This review summarizes 128 marine cyanobacterial alkaloids published in the literature between January 2001 and December 2006 and emphasizes their biosynthesis and biological activities.]

Ward, A. C. & Bora, N. (2006). Diversity and biogeography of marine actinobacteria. *Current Opinion in Microbiology* 9(3), 279-286. [This mini-review encompasses the presence of actinobacteria in the marine environment.]

Williams, P. G. (2009). Panning for chemical gold: Marine bacteria as a source of new therapeutics. *Trends in Biotechnology* 27(1), 45-52. [This review summarizes the advances in secondary metabolite discovery from marine bacteria as a source of new therapeutic molecules.]

Biographical Sketches

Brian T. Murphy obtained both BS and MS degrees in chemistry from the University of Massachusetts, Dartmouth under the direction of Professor Catherine C. Neto. He obtained his Ph D in chemistry from Virginia Polytechnic Institute and State University while studying under the direction of Professor David G. I. Kingston. There Brian focused on the isolation of anticancer molecules from plants and ascidians of Madagascar. Currently Brian holds a position as assistant professor of medicinal chemistry and pharmacognosy at the University of Illinois, Chicago (www.uic.edu/~btmurphy).

Katherine N. Maloney obtained her BS in chemistry at Pacific Lutheran University. Under the supervision of Professor Jon Clardy, Katherine earned her Ph D at Cornell University on the discovery

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William Fenical obtained his BS and MS degrees within the California State University system (California State Polytechnic University and San Jose State University). He obtained his Ph.D. in synthetic organic chemistry from the University of California, Riverside and did postdoctoral work with James Sims (UC-Riverside) in the field of marine natural products. Fenical has been a faculty member of the Scripps Institution of Oceanography (SIO, UC-San Diego) since 1973 and currently holds the title of distinguished professor of oceanography, pharmacy and pharmaceutical sciences at the University of California-San Diego. Professor Fenical is director of SIO's Center for Marine Biotechnology and Biomedicine.