Realizing the potential of marine biotechnology

CHALLENGES & OPPORTUNITIES

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> *"How inappropriate to call this planet Earth when it is quite clearly Ocean"*
>
> *—Arthur C. Clarke*

Introduction

The oceans are the Earth's largest biome and represent a unique environment characterized by high ionic concentrations, high pressures, and low as well as high temperatures. These conditions impose stringent selection criteria on organisms that inhabit the seas and have given rise to a plethora of phyletic diversity. Furthermore, since life began in the oceans around 3.8 billion years ago and terrestrial colonization by microbes only occurred over a billion years later, the oceans contain some of the most ancient life forms in existence.[1]

To place this into perspective, despite our human-centric obsession with land plant and land animal diversity, terrestrial colonization by plants is thought to have occurred only a half billion years ago.[2] As a direct consequence of this, a survey of the Kingdom Animalia shows that 21 of the 33 phyla are unique to the oceans, and only one is exclusively terrestrial.[3] Where both terrestrial and marine representatives exist, the number of marine species is greater in most cases. Of this biodiversity, only 12 marine animal phyla have been assessed for any biotechnological application, with the Porifera and Cnidaria representing 60% of the species accessed.[4] Given our human-centric view, it is inevitable that the study of animal diversity has turned first to life forms that are visible to the naked eye and which are relatively easy to study; hence 95% of marine species investigated for biotechnological applications are animals and plants, with the remaining 5% bacteria. To date, a heavy focus on terrestrial systems characterizes the detailed study of the microbial world. However, recent interest in the marine environment through the work of the Sorcerer II Global Ocean Survey, or GOS (among many others), has begun to address this imbalance.[5] A clear picture is beginning to emerge which shows that the oceans are a hotbed of microbial diversity. This diversity has rarely been exploited for biotechnological gain (so-called blue biotechnology). Whilst past work has focused primarily on the marine animal phyla, the vast majority of the microbial phyla have remained unexploited, despite preliminary work showing huge potential. Large-scale metagenomic surveys have revealed a diversity in metabolic function that has never been glimpsed previously. Upon analysis of their data, and despite being limited to sea surface microbes, the GOS team initially predicted twice as many novel proteins that were contained within public databases at the time.[6] New protein families are still being discovered at a linear rate with the addition of new sequences, implying that we are still far from discovering all of the novel protein families found in nature. Indeed, this novelty is typified by the virus-derived sequences that have been discovered in the marine environment.[7] Furthermore, the abundance of marine viruses (whose existence has only been known since the 1970s) is, quite simply, breathtaking: 10^{30} viruses inhabit the oceans (if lined up end-to-end, they would stretch approximately 10 million light years) and are responsible for 10^{23} infections every second.[8,9] Previously regarded as mere selfish bags of genes, the role of viruses in manipulating key metabolic processes (and hence their biotechnological potential) is now difficult to ignore.[9,10]

There is a growing recognition of the ocean's biotechnological potential, with the global market currently estimated at US$2.4 billion and with annual growth predicted at 10%. The European Commission describes it as "one of the most exciting technology sectors", and the Institute of Marine Engineering, Science, and Technology (IMarEST) describes the sea as a "biotechnological frontier waiting to be explored" with "potential for marine biotechnological products to be used as anticancer agents, for bulk chemicals such as adhesives, for feed additives for aquaculture, and for remediation of environmental damage".[11] Current applications for high-value marine-derived products exist in many markets including antifoulants, biofilm inhibitors, bioremediation, high- and low-temperature-tolerant enzymes with unique activities, human and animal tissue repair, nutraceuticals, and personal care products. As an example of a unique biomimetic product, the coupling of two natural adhesion structures, the gecko toe-pad and mussel byssus threads, has led to the water-resistant reversible adhesive "geckel".[12] In terms of bulk products, macroalgae are harvested for alginates and agar, and the potential of microalgae has now been investigated for large-scale production of polyunsaturated fatty acids (PUFAs) for food and feed additives and biofuels. Since primary productivity of microalgae is high and they do not compete for agricultural land, they are proposed as the most promising source of oils for biofuels. Questions that remain are which species to use to obtain the maximum growth rates and oil content (and, hence, maximum yield) and how to efficiently convert the biomass to liquid fuel.

Several other large-scale opportunities present themselves for marine biotechnological applications. The recent banning of antibiotics in animal feed in the EU has led to the investigation of algal extracts as prebiotics with promising results.[13] A worldwide ban on tin-based antifoulants for shipping is leading to the search for environment-friendly alternatives, from natural antifoulants derived from marine organisms incorporated in paints to the development of nanostructured materials mimicking mollusc shells with low adhesion properties.[14] An oral vaccine approach has been developed, based on a genetically modified microalga (*Chlamydomonas reinhardtii*), which might be used commercially for control of various bacterial and viral diseases of fish and shellfish in aquaculture.[15]

As a final example, there is a need for a sustainable supply of PUFAs for human nutrition and aquaculture feed, calling for further development of culture conditions for species rich in these essential nutrients. Current supply is met by growing the microalga *Cryptecodinium cohnii*, and docosahexaenoic acid and arachidonic acid from this source have been approved by the US Food and Drug Administration for use in infant formula (Enfamil®; Mead Johnson Nutritionals; Paramus, New Jersey, USA [subsidiary of Bristol Myers Squibb]; and Martek Biosciences; Columbia, Maryland, USA). Well-known but smaller-scale applications exist in the life sciences and include the use of green fluorescent protein from the jellyfish *Aequoria victoria* to visualize intracellular processes, and proteins from the horseshoe crab *Limulus polyphemus* for immunohistochemistry.

Barriers to exploitation

The marine environment can clearly offer a great deal to the industrial biotechnology community, yet there are a number of challenges which must be addressed if it is to realize its full potential. In brief these are: access (physical/legal); sustainable supply; greater understanding of marine species; molecular methods applicable to marine species; creation of integrated facilities; and policy initiatives to boost economic development based on the uptake of marine biotechnology by industry.

ACCESS: Physical

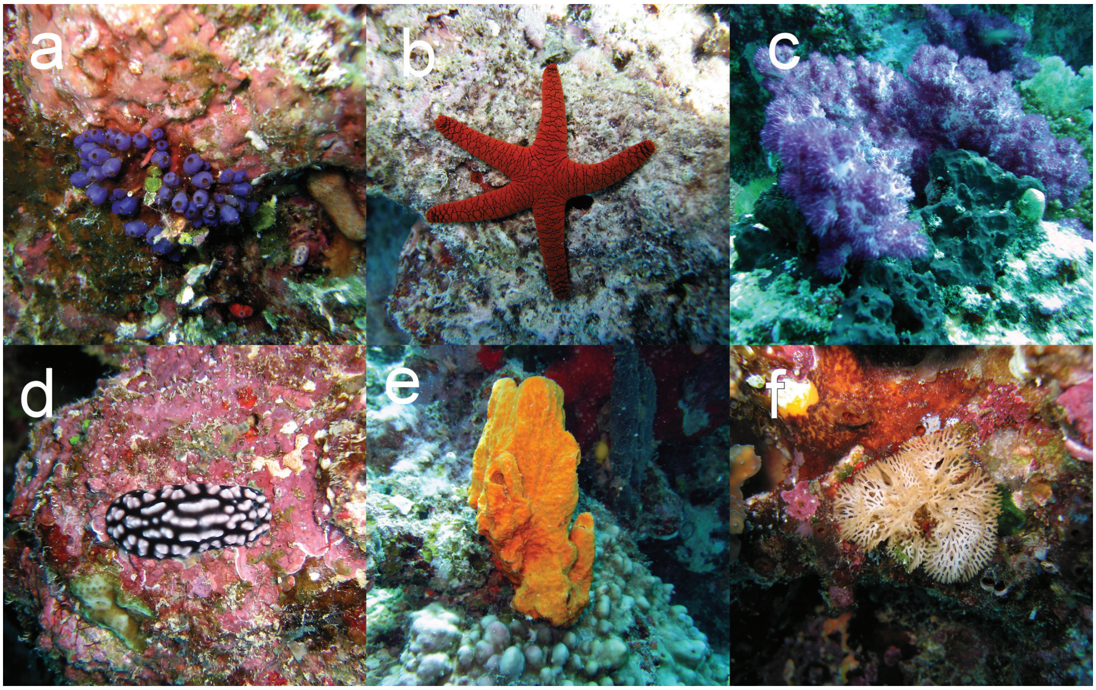
Very few facilities worldwide have the ability to access the deep ocean, whose average depth of 4000 m presents substantial engineering challenges. There is currently no submersible worldwide that can access the deepest point on the globe, Challenger Deep in the Mariana Trench (–10,911 m), after the loss in 2003 of the Japanese submersible Kaiko operated by Japan Agency for Marine-Earth Science and Technology, or JAMSTEC. The last exploration of Challenger Deep by Kaiko was in 1998, and no manned submersible has visited since Walsh and Piccard's expedition in the bathyscaphe Trieste in 1960. The recent news that Woods Hole Oceanographic Institution reached Challenger Deep using the US$8 million remotely operated, unmanned submersible, Nereus, in May 2009 is therefore to be applauded.

Access to deep sea hydrothermal vents with extreme temperatures or to the sea beneath polar ice presents even greater difficulties. Access to deep sediment cores is available via the International Ocean Drilling Program, using the Japanese vessel Chikyu,[16] most of whose time is dedicated to geological and oceanographic research; but a recent study using cores from this program show that microbial life exists deep under the ocean's floor.[17] The greatest "frontier challenge" for humankind is perhaps not the repeat of manned lunar missions, but exploration of the most inaccessible reaches of our own planet. Many oceanographic institutions worldwide have the ability to collect using submersibles, but the available time for these is oversubscribed, and these facilities may be difficult to access and/or prohibitively expensive for start-up biotechnology companies. Infrastructure and engineering development is therefore necessary to provide inexpensive and frequent access to the deep oceans, hydrothermal vents, and underneath polar ice for academic and applied purposes. Several initiatives worldwide are addressing this problem and to this end the UK's National Subsea Research Institute is being located in Aberdeen to meet both the oil industry's need for remotely operated underwater vehicle (ROV) development and research use by OceanLab, a facility for long-term monitoring of deep sea environments.

ACCESS: Legal

The second access issue concerns the legal status of samples obtained from seas outside of national jurisdiction. In territorial waters access to genetic resources is covered adequately by the Convention on Biodiversity, and it is in these waters that most bioprospecting and biodiscovery takes place. With increased access to the deep oceans, the issue of collections in international waters becomes a legal issue.

Access to seafloor samples for marine scientific research is governed by the International Seabed Authority under the United Nations Convention on Laws of the Sea (UNCLOS).[18] This convention predates the realization of the value of marine biodiscovery, and hence does not cover it adequately. The convention states that access to seafloor is for "peaceful uses of the seas and oceans, the equitable and efficient utilization of their resources, the conservation of their living resources, and the study, protection, and preservation of the marine environment". In effect the ocean's resources are the "common heritage of mankind": UNCLOS states that no state shall claim sovereignty over any part of the Area (the Area being defined as the international seabed and ocean floor) or its resources, but no specific reference is given to marine genetic resources. Exploiting these is indeed an arm's-length activity compared with the direct mining of minerals and metal ores from the seabed which the original drafters envisaged. Freedom to conduct marine scientific research requires sharing of results, which is not immediately compatible with intellectual property rights, yet the requirement



Marine invertebrate biodiversity: six different phyla: (a) Chordata (seasquirt); (b) Echinodermata (seastar); (c) Coelenterata (soft coral); (d) Mollusca (sea slug); (e) Porifera (sponge); (f) Bryozoa (sea moss)

for equitable sharing of financial and other economic benefits derived from this research suggests that someone has to "own", manage, and disburse the benefits. An increased interest in accessing marine genetic resources from the deep ocean for biotechnological application by industry requires a rapid resolution of these incompatibilities and is a fascinating challenge for international property rights and equitable management policies.

SUSTAINABLE SUPPLY

The main barrier to efficient exploitation of marine resources in situ for biotechnological applications is realizing a sustainable supply. Many routes can be chosen and each may be applicable under different circumstances. Natural harvest is most often used for bulk products such as alginates from macroalgae. Collection of marine invertebrates for high value products (e.g., enzymes and pharmaceuticals) is difficult due to low yields, seasonality, and variability and can only be achieved for small-scale trials. On the other hand, fishing and aquaculture wastes can offer an abundant source of high-value products. One such use arose from the extraction of cold alkaline phosphatase, used for dephosphorylation of DNA and proteins, from thawing shrimp waste (Biotec Pharmacon; Tromsø, Norway). Managed large-scale culture has been successful for the production of PUFAs (*Crypthecodinium cohnii*) and carotenoids (*Dunaliella salina*, *Haematococcus pluvialis*), but has been shown to be uneconomical for the production of potential pharmaceuticals from marine invertebrates. The cancer therapeutic trabectidin (now approved as Yondelis; Pharmamar; Madrid, Spain) was initially obtained from the ascidian (seasquirt) *Ecteinascidia turbinata*, initially by a US-based, now-defunct company Calbiomarine, and later transferred to the Mediterranean. This early stage production was estimated to cost $2,900–7,000 per gram of pharmaceutical material and hence an alternative was necessary for commercial production. In this case, which is perhaps a model for many marine-derived complex bioactives, a *Pseudomonas* strain was found which was easily grown in bioreactors and produced a precursor of trabectidin, which could then be chemically altered to generate the active product and analogues.[19] The culture of marine microorganisms can now be achieved, the main challenge being the corrosive nature of seawater on stainless steel culture vessels, but this can be addressed through the use of appropriate cleaning protocols. Nereus Pharmaceuticals (La Jolla, California) was able to obtain an initial batch of 1 kg of pharmaceutical-grade salinosporamide (NPI-0052) for use in clinical trials, through fermentation in saline media of the obligate halophile *Salinispora tropica* by its subcontractor IRL-Biopharm (Lower Hutt, New Zealand).

Sustainable supply is a particular challenge for production of promising bioactives from sponges and other invertebrates, where the molecules may actually be produced by microbial symbionts, many of which are in an obligate association with their hosts. The initial example of success in culturing sponge-derived bacteria to produce a high-value compound was the production of the antiparasitic manzamine alkaloids by a *Micromonospora* species isolated from an Indonesian *Petrosiidae* sponge, which was able to grow independent of its host.[20] In cases where the invertebrate is responsible for production of the compound of interest, tissue culture may offer an answer. Tissue culture of invertebrates is in its infancy due to our limited knowledge of marine invertebrate physiology, but is being developed at a number of institutes, with moderate success.[21] Potentially the most promising route is the use of recombinant DNA techniques to achieve expression of genes from difficult-to-grow or unculturable marine organisms in heterologous, easily cultured, microbial hosts. This, however, is easier said than done. Heterologous expression systems have been developed for a range of terrestrial organisms including *Escherichia coli* (bacteria), yeast (eukaryotic), *Arabidopsis* (plant), the fruit fly *Drosophila* (invertebrate), and the mouse (mammal) systems. A system has also been developed for the microalga *Chlamydomonas*. Put simply, the closer in origin the recombinant DNA is to the host expression system, the more likely it is to be productively and accurately processed, so that the desired protein is expressed (or even overexpressed), folded, and subjected to the correct posttranslational modifications necessary for activity. For example, for marine-derived genes, notable success has been obtained by the authors in expressing cyanobacterial genes in *E. coli*, and algal virus genes in *Saccharomyces cerevisiae*.[22,23] However, the sheer diversity of organisms from the marine environment, combined with their associated environments, has proven to be an enormous barrier to the heterologous expression of the majority of marine-derived genes. Despite the limited success to date, the vast majority of bacterial genes from the marine environment are unable to be expressed correctly in *E. coli*. Thus, perhaps the greatest barrier of all in marine biotechnology is the dearth of appropriate heterologous expression systems suitable for genomic material of marine origin.

UNDERSTANDING MARINE ORGANISMS & THE DEVELOPMENT OF MOLECULAR TOOLS

E. coli is the workhorse of modern molecular biology and the best-studied system on the planet.[24] Despite this intense study since its first isolation in 1885, almost 40% of its genes were classified as of unknown function when the genome was sequenced.[25,26] Few model systems can compete with *E. coli* with regard to the amount of biochemical understanding we have; yet, as *E. coli* shows, complete understanding is not necessary to turn an organism into a useful and versatile tool. With increased understanding of any model system comes the ability to develop and modify tools to manipulate it.

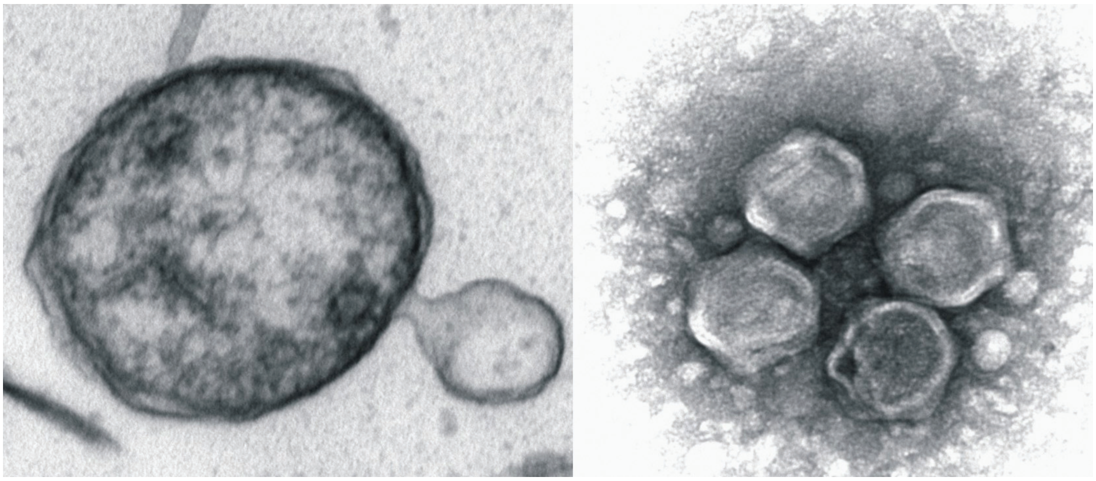
Compared with our perception of the vast diversity of marine species, our specific understanding of their genetics, physiology, and ecology is tiny. What is needed is a concerted approach to gather basic information (such as genome size, metabolic potential, growth conditions) on all marine animal, plant, and microbial phyla. At the very least, one or more candidates per phylum need to be identified for development as model heterologous expression vehicles for their respective phyla. We therefore urge the sequencing of the entire genomes of marine representatives of every animal, plant, and microbial phylum, as well as viruses. Again, this is easier said than done. The vast majority of marine microbes have resisted all efforts at culturing under laboratory conditions. Furthermore, many marine species live in essential symbiotic relationships, and all partners will need to be sequenced to understand the symbiosis and the factors that govern them (as well as the complementary or shared genetics). Viruses complicate things further since they require a suitable host for propagation.

Metagenomic approaches have circumvented the requirement for laboratory culture in order to obtain enough genomic material, but have their limitations.[27-29] By definition, metagenomic sequences are obtained from mixed populations, and the precise source of the genomic material is unknown unless suitable markers are associated with the sequences.[30] Material from common organisms will swamp sequences from much rarer ones. The larger the genomic fragment, the greater the chance of finding a suitable marker associated with the sequence, and originally this was quite common with the large insert BACs libraries that were used for the first metagenomic sequencing projects.[31]

The recent trend towards pyrosequencing fragmented genomic material directly (even with the increased sequencing read lengths of 450–500 bases) massively reduces the chance of finding markers and is heavily reliant upon the correct assembly of millions of small fragments. This is further complicated by viruses, which have no common marker and whose genomic material is among the most diverse on the planet.[27] Indeed, the sequences of many giant marine viruses contain regions with stretches of genes which have no similarity to any existing database entries.[32] This is by no means a rare occurrence in the field of marine genomics. Accurate annotation of marine-origin genes will require additional effort at the bench and in the development of bioinformatic tools. To achieve cloning, expression and functional characterization of marine genes and their associated products will require the development of the heterologous expression systems mentioned previously. The recently announced Genome Analysis Facility at the John Innes Centre in Norwich, UK, will provide sequencing capabilities for nonpathogenic species, including marine invertebrates, bacteria, and viruses and may make a significant impact in helping this situation.

INTEGRATED FACILITIES

There is a need for scientists from different disciplines to be co-located to achieve the most effective generation of new ideas for marine biotechnology. Many such centers exist in marine institutions and laboratories worldwide but there are few that truly embrace all aspects needed to be successful. In the USA, the Scripps Institution of Oceanography, Harbor Branch Oceanographic Institution, and the Centre of Marine Biotechnology at the University of Maryland offer good examples. An excellent example of academic, industry, and government interaction in Europe is MabCent in Tromsø, Norway, which aims to derive high-value small molecules and novel enzymes from cold-adapted invertebrates and microorganisms. A large government grant has been matched by the University of Tromsø and by local companies that have been successful in commercializing marine-derived biotechnology products such as the previously mentioned shrimp alkaline phosphatase. In the UK, the Centre of Excellence for Biocatalysis, Biotransformation, and Biocatalytic Manufacture (CoEBio3; University of Manchester) acts as an interface between academia and industry and uses Plymouth Marine Laboratory as a partner to access and exploit the marine environment. A more focused biodiscovery center is being created in Seoul, Korea (Center for Marine Drug Discovery), and a smaller facility is being built in Aberdeen, UK (Marine Biodiscovery Centre). From a commercial aspect, the European Centre for Marine Biotechnology in Oban, Scotland, provides an incubator unit for innovative marine biotechnology start-ups such as Aquapharm Biodiscovery and Glycomar.



Marine viruses can only been visualized by electron microscopy. Left, a large double-stranded DNA virus can be seen attached to the outer membrane of an *Ostreococcus* cell (the smallest living free eukaryote, with an average size of approximately 1 micron). Right, a group of similar-sized, uncharacterized *Micromonas* viruses.

Images by Karen Weynberg of Plymouth Marine Laboratory.

Core facilities available to a number of investigators and companies also speed up innovation in blue biotechnology. The Centre for Process Innovation (Wilton, UK) makes bioreactors available for saline and non-saline fermentations for process parametrization as well as the associated downstream processing. This type of facility and expertise is otherwise not available to start-ups and academic groups to take a process from bench-scale to production scale.

ACHIEVING THE RIGHT MIX

Making marine biotechnology effective for the generation of new ideas, processes, and products requires the bringing together of skills and equipment from a host of disciplines, including taxonomy (a dying art), marine invertebrate biology, marine microbiology, molecular biology, genetics, chemistry, biochemistry and biomedicine – in addition to which many other disciplines should be included as possible end users (biomaterials, nutrition, etc). The daily interaction among these scientists, when adequately resourced and focused on a common goal, will create novelty in many fields (such as the example of geckel referred to previously).

Achieving this implies researcher-researcher interactions as well as researcher-industry communication. Nevertheless, a great deal of mistrust exists, and researchers may refrain from interacting with others for a variety of reasons. Perhaps they hope to claim a "larger share of the pie" once exploitation is achieved. Maybe they have suffered as a result of "stolen" ideas, authorship issues, and anonymous peer review, which leave a bitter taste even if they arise independently of financial considerations. The thought of having ideas of commercial relevance stolen is often too hard to bear for many researchers, who hold on to the dream that this time next year they will be millionaires. Yet without the appropriate guidance, expertise, and industrial savvy it is common for even excellent ideas to end up going nowhere. Our view is that it is better to have a small percentage of something than 100% of nothing. The use of nondisclosure agreements and material transfer agreements with data-back provisions for protecting intellectual property at an early stage (thus allowing consultation with relevant industrial partners) can avoid many of these issues, but is quite often not considered.

In the UK, the development of networks, either virtual (such as the Bioscience Knowledge Transfer Network, or KTN) or based on a specific activity, such as CoEBIO3 in which Plymouth Marine Laboratory is involved, have allowed productive face-to-face interaction between academic and industrial partners that can help break down the barriers between applied and commercial scientists to promote the exploitation of ideas—but this needs boosting. The UK's Research Councils can have a role to play, as promoters and funders of the "sandpit" concept of developing grand-scale projects and programs of high-quality science with a specific goal. These activities are not frequent enough, and industry will benefit from taking more of a lead in promoting these interactions if they are to exploit marine bioresources effectively.

We can see the need for this most clearly in the pharmaceutical sector. Small molecules derived from terrestrial species are the origin of more than half of all currently used pharmaceuticals and of 75% of cancer therapeutics and anti-infective agents.[33] Similarly, most biotechnological products on the market today are derived from terrestrial species. The pharmaceutical industry now seems stuck, after a decade and a half of combinatorial chemistry based on structure-activity relationships, in a mind-set that too often sees the second, third, and following companies in a market "playing little tunes on the structures of the first company".

To understand why the astonishing biodiversity to be found in the seas has not been fully exploited, we have to look at how large pharmaceutical companies regard marine sources for novel products and processes. Some of the answer rests in the technical difficulties described earlier, but much is to do with attitude. Despite the obvious opportunities, the mainstream pharmaceutical industry ("Big Pharma") has little in-house experience in dealing with marine bioresources, and hence this work is driven by academic centers and start-up companies. In the pharmaceutical arena Pharmamar has been among the most successful, with a large pipeline of marine-derived cancer chemotherapeutics. The smaller US-based company Nereus

Pharmaceuticals (San Diego, California) has successfully and rapidly translated academic research on marine bacteria into clinical trials.

For non-pharmaceutical applications such as nutraceuticals, Martek leads the way, but smaller companies with broad portfolios such as Aquapharm Biodiscovery are also making a contribution in this area. Other companies have accepted marine bioresources as one of their routes to discovery of novel enzymes (Ingenza; Edinburgh, Scotland, UK) or cosmetic ingredients (Croda International; Goole, UK). Because of this, the risk for large companies can perhaps be mitigated by collaboration with, and, potentially, acquisition of, these higher-risk companies for their respective intellectual property portfolios. This model is already common for the pharmaceutical industry and is likely to become more common in the area of marine-based industrial biotechnology.

The next generation of marine scientists needs to be trained for the demands of the 21st century. In the current climate for academic research it is now rarely enough just to perform "blue skies" research; it is becoming increasingly common to have to justify end points and identify the potential exploitation opportunities associated with research projects. However, many marine scientists, attracted to the field for their love of the ocean, have not received appropriate training in biotechnological awareness. The movement of scientists from other research domains into the marine sector might aid the spread of this attitude, but the problem also needs to be addressed at the grassroots level. Those courses and modules in applied marine research that are available at many universities are often optional and certainly not viewed as essential requirements of marine science courses.

The need for appropriate training to derive maximum value from natural resources for small-molecule and biotechnological applications has been recognized, and forms the core of a report on this topic released in the UK in 2006.[34] This report notes that start-up companies in the UK struggle to recruit trained personnel; it also recommends that companies work with universities to address the skills gap and that funding be increased for interdisciplinary science to result in a new generation of scientists comfortable in applying techniques from various fields to solve complex problems. One way this has already been implemented in the UK is in the "discipline-hopping" fellowships, which allow postdoctoral scientists or academics to spend time learning another subject, to apply their knowledge in this new field as well as bring back the newly learned skills and techniques to their own research. One of the authors of this manuscript (Marcel Jaspars) is the recipient of such a fellowship, funded by the UK's Biotechnology and Biological Sciences Research Council, to learn molecular genetics techniques to apply to the field of marine natural product chemistry.

POLICY

Many of the challenges outlined above need a change in policy—economic, political or legal—to create a coherent drive to investigate the oceans and develop their biotechnological potential. It is likely, however, that opposition, even from within the marine sector, will greet any intention to shift policy significantly. It is nonetheless imperative that there be a shift away from the "buzz area" in current marine research, namely, climate change. It cannot be denied that climate change is of major concern in the present day, yet we need a balance with biotechnology as well as the other research areas referred to above.

This is being achieved in some countries, in different ways. Large-scale facility funding may be very effective; the largest initiative using this is the Centre for Marine Natural Products and Drug Discovery in Seoul, Korea, which represents a 10-year program and has an allocated budget of over US$70 million, to develop medicines for metabolic and immune disorders and infectious diseases. MabCent in Tromsø, Norway, brings together and builds on existing expertise in marine science and blue biotech SMEs and has funding assigned to it of $25M over 7 years. National programs exist in Ireland (Beaufort Programme) and Germany (Biomarin), and targeted platform or project funding for marine biotechnology research exists in a number of countries (Denmark and USA).

Making industry aware of new biotechniques and sources of innovation can be powerful, provided these are relevant to their products and processes and important for their future survival. In the UK, linkages between industry, academia, and government are fostered as a matter of policy through the Knowledge Transfer Networks, funded by the Technology Strategy Board. The main aim of these networks is to accelerate the rate of technology uptake by UK businesses to improve innovation performance. The Bioscience Knowledge Transfer Network brings to reality slogans such as "Nature's solutions to benefit Society" and "Use today's sunlight not yesterday's", by providing unique connections among white (industrial), green (plant-based), and blue sectors of industrial biotechnology. It acts as a conduit for biobased technology business to engage with government, other businesses, and the research community including major funders and trade organizations.

All early indicators suggest this is leading to an increased uptake of biotechnology of all "colors" by industry in the UK. The Bioscience KTN has had a particular impact in helping raise the profile of blue biotechnology in UK and Europe and is currently being assessed as a model for application in Canada.

Conclusions

To realize the potential that the oceans offer in terms of new products and processes requires the concerted effort of many parties. What is urgently needed is the coordination of marine sciences, including marine biotechnology, and the adequate funding of interdisciplinary initiatives. Effective academic–industrial collaboration is essential to bring any novel marine biotechnological outputs to the market. This will require the training of scientists in relevant disciplines and a new generation of interdisciplinary scientists who feel comfortable in applying tools from diverse fields to solve unique problems posed by the marine environment. We also need to increase our knowledge of the fundamental biology and ecology of marine species, which can only be gained by intensive research and the generation of marine-relevant tools together with integrated facilities.

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