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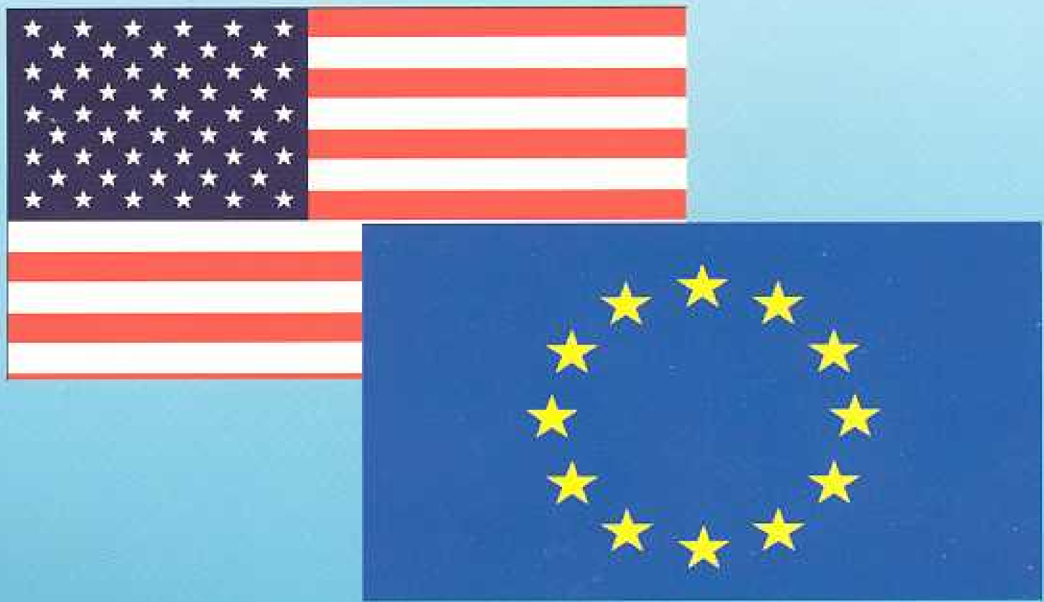
EC-US task force on biotechnology research

Marine microorganisms: Research issues for biotechnology



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European Commission

EC-US task force on biotechnology research

Marine microorganisms: Research issues for biotechnology

Proceedings from the US-EC workshop
on marine microorganisms
Brussels, Belgium
8 to 9 October 1996

Directorate-General
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Preface

The US-EC Task Force on Biotechnology Research was established on 7 September 1990 by an administrative arrangement between the European Commission and the United States Government, and was charged with increasing the mutual understanding between European Community activities and US programmes related to biotechnology research. The Task Force was designed to serve as a mechanism for the exchange of information regarding scientific aspects of biotechnology. In June 1996, the administrative arrangement between the Commission and the United States Government, which established the EC-US Task Force on Biotechnology Research, was renewed for a period of five years.

The discussions at the Plenary meetings of the Task Force have involved subjects deserving major international attention and collaboration. Within this framework, a workshop for invited scientists from Europe and the US was organised in October 1996 in Brussels on Marine Microorganisms: Research Issues for Biotechnology, the Proceedings of which are now the subject of this report.

The Workshop agenda was planned by an Organising Committee in Europe:

Dr. Chris Bowler, Naples, Italy
Dr. Joseph Hirschberg, Jerusalem, Israel
Professor Yves Le Gal, Concarneau, France
Professor Jan Olafsen, Tromsø, Norway
Professor John Sargent, Stirling, UK

working in cooperation with a US Steering Committee.

The Workshop was chaired by Professor Rita R. Colwell, President of the University of Maryland Biotechnology Institute and by Professor Jan A. Olafsen of the University of Tromsø who prepared the Report of the Workshop included in these Proceedings.

Thanks are due to all those who participated in the Workshop and who contributed to its organisation and success.

Dr. Bruno Hansen
EC co-chair

Dr. Mary Clutter
US co-chair

US-EC Workshop Report
Research Issues for Marine Biotechnology

Borschette Centre
36, rue Froissart, 1040 Brussels
October 8-9, 1996

Prepared
by
Rita R. Colwell
University of Maryland Biotechnology Institute
and
Jan A. Olafsen
University of Tromsø

A US-EC Workshop on Marine Microbiology/Biotechnology was held at the Borschette Centre, Brussels, October 8-9, 1996. The following report of the meeting is provided by the Co-chairs: Professor Rita R. Colwell and Professor Jan A. Olafsen.

Twenty scientists from Europe and 20 scientists from the U.S. met in Brussels to discuss research issues for marine biotechnology.

The achievements of marine biotechnology since 1983, when the field was first defined, include a number of important milestones. For example, several natural products associated with marine animals and plants have been shown to be produced by marine bacteria associated with those animals and plants. Thus, it is now possible to utilize marine microorganisms as a source of heretofore undescribed metabolites, some of which have potential as antibiotics, antimicrobials, antitumor agents, and related pharmaceuticals.

It has also been determined that there is an enormous biological diversity in the world's oceans. The Azoic theory, which held that the deepest parts of the oceans were devoid of life, has been disproved. The discovery of hydrothermal vents made it clear that there is, in fact, an enormous diversity of life in the deep sea.

The discovery of large populations of viruses, the influence of viruses in regulating algal populations, as well as the presence of indigenous viruses in hyperthermophiles from the deep sea, have been described. The numbers of viruses in estuaries have been shown to be greater than that of bacteria at certain times of the year, and seasonality in virus abundance and distribution has been noted.

The discovery of the Archaea, an ancient lineage of microorganisms more closely related to higher animals and plants than to the "true bacteria", has resulted in a new determination of the phylogeny of life on the planet.

Extremophiles, microorganisms living in extreme environments such as very high or very low pH, high hydrostatic pressure, extremely low temperatures (approximating freezing), and extremely high temperatures (above boiling), have been isolated, characterized, and proven a source of commercially important products.

The psychrophiles, bacteria able to grow at temperatures less than 10° C, had been isolated many years ago, but the potential of psychrophiles has been underestimated. It is now clear that enzymes functioning at very low temperatures do have valuable commercial applications and, thus, the psychrophiles have received more attention in recent years. It has also become clear that life at low temperatures is associated with production of biomolecules of commercial value.

Marine bacteria have been isolated and described that are unique, including a giant bacterium visible to the naked eye. Also described, but not yet isolated in pure culture, are bacteria occurring in abundance in some of the deeper regions of the Sargasso Sea in the Atlantic Ocean and also from areas of the Pacific Ocean. These taxa cannot yet be grown, but have been described by ribosomal RNA sequencing techniques. The use of molecular probes to discover new, as yet uncultured taxa has been widely applied and has provided exciting new information about the origin and diversity of life in the oceans.

It has been concluded from research done during the past decade that pure cultures are not necessarily the best means of understanding communities of bacteria in the natural environment. In fact, mixed cultures and biofilm cultures are proving to be effective in biodegradation and in carrying out complex metabolic processes in the natural environment.

Successful production of effective vaccines for aquaculture, starting in the 1970's, has advanced aquaculture of salmonids and a variety of other marine species significantly. We are also beginning to understand mechanisms of host colonization by bacteria, and how this may affect the spread of pathogenic bacteria in the environment.

The application of newly developed equipment, such as laser technology, confocal microscopy, nucleic acid sequencers, and synthesizers, etc., has opened up entirely new areas in marine microbiology and allowed rapid development of marine biotechnology.

Increased food production, new bioactive compounds, and improved materials are obvious targets for active research in marine biotechnology. To exploit the potential of marine biotechnology fully, it would be useful to pursue such industrial goals in parallel with fundamental research.

Finally, life in the marine environment offers excellent models for studies of reproduction, feeding, defense, adhesion, signaling, development and host-pathogen interactions. Basic research on biological mechanisms of marine organisms has yielded information instrumental to the understanding of the immune and nervous systems and molecular communication. The diversity of marine microorganisms and their abundance in various ecological niches in the sea carry the implication that there is still much to gain by attracting young scientists to this field.

Problems

There are certain problems that need to be addressed in marine biotechnology research, such as the following:

Public understanding of the potential of marine biotechnology and its applications needs to be improved. An example was given by one of the attendees at the workshop that a fish enzyme used in cheese production was not accepted because it was feared that the cheese might taste "fishy." Misinterpretations of marine biotechnology such as these result in denying the commercial application of the results of marine biotechnology research.

The production of transgenic fish and appreciation of their value in the marketplace also requires public understanding that there is a benefit in producing transgenic fish in closed systems. This technology provides a means of obtaining fish for human consumption that does not require wild harvest, i.e., capture fisheries, and improves the health and growth of fish as farmed animals.

The need to educate industry about the value of marine biotechnology is also important. A bacterial growth medium was developed, using fish peptones, which was much better for growing marine microorganisms than a traditional beef peptone-based medium. However, it was very difficult to break into the market because the industry feared that there were higher risks associated with utilizing fish peptones. These risks included a perceived lack of controlled sources and related reasons, which were, in fact, unfounded. Thus, not only is there public misunderstanding, but also lack of understanding and involvement by industry.

Even though there is much to be gained in improving marine food production and also in providing better methods for assessing production potential and health of the oceans, the traditional fishing industry has shown little interest in the use of biotechnology. The rapidly growing biotechnology industry has also been slow in exploiting the potential of marine biotechnology. This may partly be due to the perception that marine resources are available only by harvesting and that there is difficulty dealing with a large bureaucracy in place to oversee those activities. On the other hand, the aquaculture industry has been exploiting the benefits of improved feed and modern vaccines. However, the future of the aquaculture industry will be at risk without a basic understanding of bacterial colonization of eggs and larvae in intensive production units.

Perhaps some of the best examples of application of marine biotechnology lie in the many new, relatively small companies that are picking the fruits of the new scientific findings in molecular marine biotechnology. The chemistry of polysaccharides produced by marine algae has been studied for years, but only now is contributing to the rapid development of new drug-delivery systems. The emphasis is on utilizing the potential of microorganisms and the enzymes they produce in commercial production. Industry and the public must be made aware that rapid scientific developments require continuing investment in basic research and that this investment ultimately benefits industry.

Potential

Through the application of molecular biology tools to the marine sciences, the potential of the oceans are opened in a way not previously anticipated or even dreamed about. Furthermore, by taking a multidisciplinary approach to solving marine ecosystem problems, it is possible to address seemingly intractable problems of environmental pollution by application of basic scientific knowledge gained through interdisciplinary research.

Technology Transfer

The need to transfer technology developed in marine biotechnology to the industrial/private sector was discussed. Several issues were addressed, but the focus of the workshop was placed on basic research and the need to educate industry rather than problems of technology transfer, since marine biotechnology does not differ in this regard from other areas of biotechnology.

A major benefit of marine biotechnology is that the infrastructure is in place. We do not need to construct laboratories, research vessels, etc., but, instead, need to develop more fully the resources already in place to achieve new breakthroughs. Thus, aquaculture facilities not only benefit the aquaculture industry but also provide excellent laboratories for the study of marine animals under controlled conditions.

Communication

It was concluded by the workshop participants that high speed communication by e-mail, internet, and video teleconferencing, the latter exemplified by development of the "Virtual International University" presently underway in collaboration between several universities in Europe and the University of Maryland Biotechnology Institute in Baltimore, Maryland, provides the means by which scientific research and education can be accelerated. It is also recommended that an electronic newsletter and a home page on the World Wide Web be developed for information transfer and communication in marine biotechnology. The ability to communicate by video teleconferencing does not, however, negate the need to establish working groups of scientists, especially young scientists, in subject areas of mutually agreed focus.

An example of public education is the University of Maryland Center of Marine Biotechnology at the Columbus Center in Baltimore, which makes science, especially marine biotechnology, visible and understandable. National educational institutions, such as the Norwegian College of Fishery Science in Tromsø, and concerted developments in the marine sciences at the marine center in Brest, France, are examples of valuable, though more traditional, sites of public higher education.

Proposed Research Agenda

The research agenda addressed by the Workshop is as follows.

Marine Molecular Microbial Ecology

The need for basic research in marine molecular microbial ecology was underlined and emphasized, especially of coastal areas, and wetlands, where understanding community structure, eutrophication/productivity, and the ability to control production in marine ecosystems would benefit.

The applications of marine molecular microbial ecology to bioremediation, aquaculture, probiotics, and other critical areas were emphasized, particularly, since the future of the aquaculture industry worldwide relies on understanding molecular microbial ecology to improve fish farming methods and prevent disease, without over using antibiotics.

Marine Metabolites

It was pointed out that bioassays should be done, not just against bacteria that are not normally found in the sea, i.e., human pathogens, but also against those bacteria indigenous to the sea, such as fish pathogens, as well as other bacteria. This is important to understand better those interactions of bacteria that are modulated by chemicals, signaling pheromones, or other bioactive products that control or regulate growth, either by initiation, cessation, or metabolic maintenance in microorganisms, as well as signaling between microorganisms and macroorganisms.

Standardization of Methods

New programs are needed to develop methods for isolating and culturing those bacteria that are currently considered "nonculturable" and to improve methods for isolating those bacteria which are culturable, but for which optimal media are not yet available. This need to improve culture methods for microorganisms was emphasized emphatically by the workshop participants. Also, the need for modern culture collections for marine microorganisms was strongly emphasized. There is no longer an operating collection for marine microorganisms in Europe since the Torry Research Station in Aberdeen, Scotland has discontinued its culture collection of marine microorganisms. The inclusion of new isolates from the environment in a recognized collection will greatly facilitate searches for new metabolites or bioactive materials.

Adhesion/Attachment

The significance of biofilms has been cited above. Microbial adhesion to inert surfaces and biological systems needs to be better understood, both in terms of anti-fouling and pathogen colonization. The focus should be on a rational system for understanding attachment and the fouling process. An important research question raised was whether adhesion in the marine environment was different from that in the terrestrial environment. This area of study also includes biomaterials research. For example, marine organisms form very strong, flat, and hard structures in aquatic systems and attach to hard and soft surfaces. Understanding this kind of attachment would have applications in medicine, aquaculture, and use of materials such as paints and painted surfaces. It is important to emphasize that research involving interactions of physical chemistry, physics, and chemistry, along with microbiology, is important in this process, especially to understand better microbial adhesion to eggs and larvae in aquaculture. Research pertinent to the study of microbial adhesion and secondary metabolite production by adherent cells is also important.

Marine Model Systems

Development from the egg to larval and adult stages in the marine environment offers models for understanding biological development and evolution. Also, intensive production of fish and invertebrate larvae for aquaculture requires better understanding of the developmental process in order to improve health, growth, and quality of farmed marine animals.

Host-Pathogen Interactions

Understanding host-parasite and host-pathogen interactions in the marine environment would allow better comprehension of the disease process and especially the gradation from mutualism to commensalism, symbiosis, pathogenesis, and parasitism. The continuous system of an aquatic environment may provide an excellent model for studying such processes and interactions at different temperatures and under other conditions that prevail in marine ecosystems. Some marine animals carry, as part of their normal microflora, bacteria that are pathogenic for humans or fish. In order to understand such phenomena, and to prevent disease in aquaculture, the mechanisms governing establishment of a microflora on marine organisms must be better understood.

Basic Molecular Genetics of Marine Systems

It is clear there are new genes and a great deal of gene transfer taking place in the marine environment. Thus, different levels of gene expression exist in the marine environment that need to be understood. Marine microbial genetics and distribution of genetic systems in the ocean are very important research topics. In fact, the behavior of fish in schools and the fluctuating productivity that occurs in areas where aquaculture takes place, much like the phenomenon of farmed soil which becomes "tired," suggests that microbial replenishment and productivity fluctuation can be better analyzed. For example, the onset and termination of algal blooms are not yet fully understood. Thus, better management of the oceans would be possible by understanding basic genetics of the communities and the species indigenous to the world oceans.

Extremophiles, Thermophiles, Alkophiles, Acidophiles, Psychrophiles and Barophiles

Organisms found in the sea offer new perspectives on the capacity of microorganisms to colonize even the most extreme niches. New physiological understanding of microorganisms can be provided therefrom.

Genomics

It was concluded that cDNA sequencing would be very helpful in providing information about the genetic structure of marine microorganisms. Surveys and sampling of EST fragments would allow better understanding of the phylogenetic diversity in the oceans. A better genetic mapping of important marine microorganisms is needed, but may be somewhat hampered by their enormous diversity.

Marine Bioremediation

As noted earlier in this report, studies of basic marine molecular microbial ecology would be very important to bioremediation. In particular, it was noted that some potentially useful activities for bioremediation occur only in undisturbed consortia of microorganisms. Industry is demanding information on how these natural consortia work and at what rates. Therefore, using microorganisms to clean polluted sites, such as bays, estuaries, and fjords, is a high priority. Better insight into the impact of marine production systems, such as aquaculture, is needed. Some understanding of the role of microbes in cleaning up oil spills has been provided, but better methods are needed to apply this knowledge. A basic understanding of mechanisms of bioremediation in the marine environment will also provide better insight into general bacterial metabolism. Many chlorinated compounds are found in the ocean, and there are some very active dechlorinating bacteria in the sea that could be utilized for detoxifying such compounds, both in aquatic and terrestrial environments.

Screening For Bioactive Compounds

The relevance of bioactive compounds and the benefits of discovering new ones have been noted in this report. There is a need for more concerted action to screen for such compounds in the sea and in extreme environments, particularly since the infrastructure for such screening is largely in place.

Aquaculture/Mariculture

There are constraints on use of marine resources, namely sustainability. Aquaculture is the best mechanism for dealing with the shortage of food from the sea. Therefore, aquaculture must be a high priority, especially application of molecular biology to improve aquaculture production.

Benefits

The benefits of marine biotechnology are clearly demonstrated in the new discoveries of unusual forms of life that have been reported. The possible discovery and development of new antibiotics, biomaterials and antimicrobial treatments are among the benefits already noted in this report. Furthermore, the discovery of an abundance of viruses in the sea makes it highly likely that vital mechanisms for genetic transformations occur in the oceans, i.e. gene transfer. This phenomenon is less known in the marine environment and, therefore, can provide new information, perhaps even on the origin of viruses.

Challenges

Bringing young scientists into working collaborations with marine scientists and making known the possibilities of marine molecular biology to all scientists is an important challenge. It is an underdeveloped area of great promise for attention by all government agencies.

It is critical to educate the public and overcome the ignorance of the potential of marine biotechnology's contributions to society. Risk studies need to be done to alleviate the fear of the use of transgenic fish as food and to replenish exhausted fisheries of the world's oceans.

There is a lack of understanding of marine environments and marine systems by some components of industry. The marine environment holds more promise than harvestable resources currently indicate. Furthermore, marine fermentations do not corrode equipment if proper materials are used and adequate measures taken. Thus, education of industry is critical if full commercial benefits are to be realized.

Action

It may be appropriate to establish a working group (approximately six members including co-chairs) to focus the research agenda laid out in this report. It is important to initiate cooperation and collaboration to strengthen communication. The working group should establish a plan of action, with clear goals, that takes into account the complementary capabilities of the European nations and the United States.

Summary

Marine molecular biotechnology is an emerging discipline. Basic science is needed to realize its full potential; biotechnology will not flourish unless the basic science framework is in place. To help facilitate the development of marine molecular biotechnology, concerted actions need to be taken that would allow sharing of resources, including aquaria, ship facilities, and marine laboratories, would improve the mobility of scientists and sharing of scientific knowledge, and would provide access to a variety of experimental marine systems. To facilitate such actions, a working group should be formed. Communication amongst those working in molecular biology in the marine environment is critical to the development of this field and the working group should consider convening subsequent US-EC workshops to facilitate such communication. The United States and Europe will certainly continue to play an important role in the development of marine molecular biotechnology.