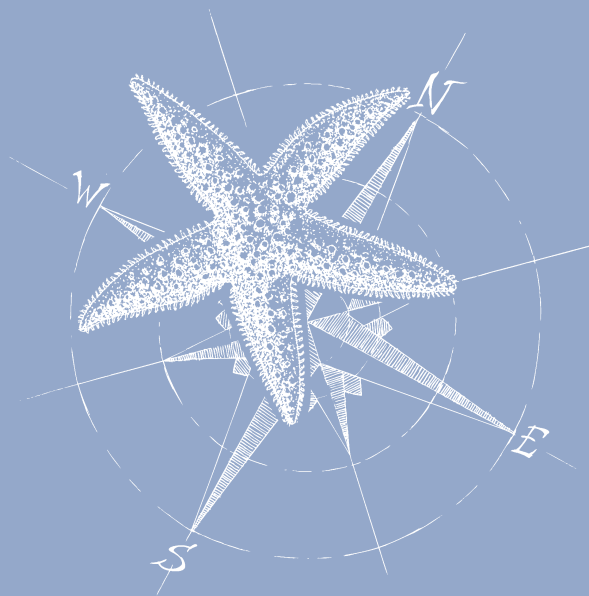


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New Partnerships for Blue Biotechnology Development



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Foreword

With this first issue, the Mediterranean Science Commission is proud to launch its new *CIESM Marine Policy Series*, a collection that will address questions which we consider of major importance at the sensitive interface between marine science and policy.

Recent years have brought major advances on the front of Mediterranean marine research, amply demonstrating that gaps in knowledge are no longer an obstacle for scientific excellence or for sound maritime governance in our region. It is rather the persistent dysfunctionings of the communication between research, industry and policy levels which prevent optimal harnessing of the innovations that are flowing out of the marine science and technology sector.

CIESM is determined to facilitate dialogue and collaborations between marine research and all concerned maritime stakeholders and policy makers. We hope that this Series will play a useful role in this endeavour.

This report, focused on the fast-growing marine biotechnology sector, and carefully edited by Drs Laura Giuliano and Michèle Barbier, is the outcome of a very fruitful brainstorming exercise which our Commission organized in 2011. Some thirty experts were invited to Monaco on this occasion (see list of participants at end of volume) for in-depth discussions that took place in both parallel and plenary sessions. As the reader will remark, the topics covered were dense, including inter alia blue nano- and bio-technology applications for enhancing performance and eco-compatibility in maritime transport, biosensors, bioremediations, anti-biofouling, production of pharma- and neutra-ceuticals. Given the vulnerability and sensitivity of Mediterranean countries in this regard, particular attention was paid to the much needed international cooperation in strengthening access, benefit sharing and intellectual property rights.

Prof Frédéric Briand
Editor, *Marine Policy Series*
Director General, CIESM





Blue Biotechnology and Nanotechnology in Maritime Transport

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1. Key issues

1.1 What are the key problems facing the shipping industry?

- o Today's Problems
 - Ballast water treatment
 - Biofouling and biocorrosion
 - Viscuous drag and its effects on vessel speed
 - Sanitation of ventilation and conditioning pipelines
- o Designing ships for the future
 - *"Bioinspired materials"*
 - Alternatives to steel
 - Biodegradability
 - Protection from corrosion and biofouling
- o How to "bury" a dead ship? How deal with the enormous waste disposal problem?
- o Contamination of ships, ports, and other facilities?

1.2 Nanotechnology and blue biotechnological applications in areas

- o New materials
- o Processes
- o Integrating blue biotech into design principles for the future

1.3 Research and technological issues

- o Suitable funding
- o Scale-up of production of new materials
 - From the nanoscale – to the scale of hundreds of tons
 - Field trials and results' evaluating

1.4 Partnering

- o Modes of collaboration
 - Goals
 - Scope
 - Who brings what to the partnership?
 - How much does a scientist know about application-based research?
The scientist should be part of the project from its inception.
- o The regional cluster model
 - Common interests without fixed geographical borders
 - Advantages and disadvantages of the cluster model
 - What form does R&D take in a cluster?

1.5 Intellectual property

- o Who owns it? Who profits from it? Rights and responsibilities
- o Patents and legal restrictions.
 - Are they always necessary?
 - The role of secrecy vs. the need to *publish or perish*
 - The role of the academic – Are there models for this kind of industry? Is the academic a partner, or a sub-contractor?

2. Projected directions for basic research

2.1 Nanotechnology

Life as we know, which occurs within a continuum of size dimensions, rests on the way molecules are efficiently assembled so as to allow highly sophisticated biological processes in response to signals. In fact, differences in nanoscale molecular assembly of the same compound may lead to significant changes in its physical and chemical properties. Due to the need to expand the knowledge base in this area, nano- science and technology will probably have a stronger impact on the design and construction of ships for the future.

The following questions represent a sampling of typical scientific questions and challenges that could impact ship design and construction in the future.

1. What are the principles driving the self-assembly of molecules to form structures with unique mechanical and architectural properties?
2. Can the design principles be used to develop new materials and even nanomachines, whose size can be exploited to penetrate tiny pores and in normally impermeable surfaces?
3. Can new materials be generated which exhibit unusual properties of hardness, resilience, versatility and compatibility with other materials?
4. Can a biological process be mimicked (a process termed biomimetics) using chemical reagents and appropriate templates for assembly of molecular structures (such as nanotubes, nanowires, nanoparticles, etc) ?

2.3 Blue biotechnology

The development of modern genomics and the emergence of high-throughput gene sequencing technology have led to the emergence of a new concept in microbiology - the microbiome. The term microbiome refers to the entire microbial population within a specific environmental niche. Microbiomes in different environments have been shown to change in population diversity and density as a function of changes in environmental conditions. Within the human body for example, shifts in dietary habits, ingestion of even slightly polluted foods and water supply, age, etc. can affect the microbiome in the gut which can in turn lead to dramatic emergence of pathogenic organisms, toxin production, establishment of persistent infections, etc. Microbiomes described in pipelines, for example, indicate that specific populations appear to be preferentially located at centers of corrosion.

1. What are the characteristics of specific microbiomes in ships (i.e. tanks, outer surfaces, bilges, etc.)?
2. How stable are microbiomes and how do they change with the age of a ship, its cargo and specific trade routes?

Answers to these questions, also under investigation in modern disease control



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(i.e. dentistry), will lead to the development of “ship microbiology” with various applications. Here follow two examples:

- New monitoring systems to check the emergence of novel, often damaging organisms on board.
- Microbial bioremediation to degrade organic pollutants in ballast water (i.e. using ballast tanks as floating bioreactors). Since the largest bioremediation application involves the use of microbes to degrade organic waste in water purification systems in all parts of the globe, such problems that face the shipping industry today may be addressed using applications from other industries. For example, biodegrading organisms, once identified in the ballast water, could be incorporated into biofiltration systems for continuous bioremediation as developed by G.E. Corp. for treatment of highly toxic PCBs that were accumulating in New York rivers. It is tempting to envision a “biopipe” constructed modules of biofilters carrying such microbes, through which ballast water could be pumped in a eco-friendly disposal system.

3. Provisional recommendations

The participants emphasized the enormous potential of nanoscience and nanotechnology to impact many of the issues listed above.

Specific recommendations include:

- a. **Evaluate properties of surfaces** to enable development of more suitable paints and coatings.
- b. **Use the properties of bioactive small and polymeric molecules** for incorporation into a program in development of new materials through the implementation of biomimetics.
- c. **Study the strength and robustness in the development of new ship construction materials** – *e.g.* new fibers, composites etc.
- d. **Develop “bioinspired” materials** to enhance ship performance, stability and recycling. Nanobiotechnology will be clearly a pillar of programs designing ships for the future.
- e. Biotechnology solutions may already be at hand for development in current problems such as **biofouling** (antiadhesion of fouling organisms), **corrosion**, etc.
- f. **Biodegradation and remediation** in sludge disposal, filtercleaning, bilge water treatment etc.

3.1 Ships for the future

New principles of nanotechnology and biotechnology must be incorporated into new projects aiming at designing “ships for the future”.



3.2 Partnering

It was recommended to focus concretely on a particular project that would incorporate the cooperative efforts of a multidisciplinary consortium from its initial stages on. In fact it is clear that the success of the program will depend on proper management and coordination between scientists, engineers, business people and legal advisers. This will enable appropriate lines of communication, and establishment of common goals based on realistic appraisals of project magnitude. The only model for cooperation discussed in this session was based on the recent experience of European clusters like Pôle Mer PACA and Liguria DLTM, represented at the meeting; these appeared to offer a number of advantages including significant partial funding, regional cooperation, and a well established infrastructure for coordination.

3.3 Intellectual Property

Since the project is likely to involve a variety of stakeholders from universities and research institutes, shipping companies, engineering groups, and government agencies from various countries, it is recommended that legal advisors actively participate in the design and structuring of the cooperation. Who owns resulting technology, who has the right to market the technology and where, and who shares in the profits accruing from the results of the project all need to be made explicit before strong commitments are made.

3.4 Project flexibility

Scale-up of the magnitude envisioned here brings its own problems and difficulties. It is likely that future development of an initial discovery will require additional expertise in a number of disciplines including biochemical engineering, scale-up of production, incorporating new principles of biology (i.e. novel organisms, combinatorial technology, bioinformatics, synthetic biology, high-throughput screening, etc.). Structuring the project design stage by stage will allow for the gradual addition of suitable experts.





Blue Biotechnology for biomedical sectors

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with inputs received during and after the workshop from

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1. Rationale

The participants noted that four important stages of development in Blue Biotechnology should be taken into account:

- 1. Exploratory stage:** Identification of problems and goals, securing funds.
- 2. Fundamental stage:** Basic scientific research in biodiversity/ bioprospecting, identification of compounds and enzymes, biochemical and chemical research, and bioinformatics.
- 3. Applied stage:** Testing and application of compounds, enzymes and processes.
- 4. Industrial stage:** Scale-up, production and utilization of the end products of biotechnological research.

They identified important opportunities and perspectives in this particular blue biotech sector, as well as drivers and barriers (including those related to the legacy framework) enabling blue biotechnology to become a profitable, highly competitive sector, and discussed their vision. Here follows a synthesis of their main conclusions.

2. Opportunities

Exploration of the sea and of its biota is still far from completed (1). Although the oceans contain much greater biodiversity than is found on land, efforts to exploit this biodiversity by identifying new chemical compounds have hardly begun: at present, there are some 20,000 marine-derived natural products compared with more than 155,000 natural, terrestrial products.

The main targets identified are the following:

2.1 Enzymes for industrial purposes

Industrial enzymes with new and emerging applications (technical enzymes, food enzymes and animal feed enzymes) represent the heart of biotechnology processes. - Proteases figure amongst the most valuable (technical) commercial enzymes. They have applications in detergent, pulp and paper manufacturing. A great challenge shall be to identify and isolate proteases from various marine biological sources.

Oxydizing enzymes (*i.e.* laccases) have much biotechnological potential in diverse fields of industrial application including effluent detoxification, kraft pulp and dye bleaching, polymer synthesis, cosmetics, bakery, wine and beverage stabilization, manufacture of anticancer drugs, and as part of biosensor for immunoassays. These enzymes have frequently been isolated from extremophiles. Extreme marine environments clearly represent a source for new enzymes.

CHALLENGES:

- New methodological tools to characterize enzymes more efficiently.
- Bioactive molecules to “light up” in different parts of the body (based on the success of recent tests using viruses to detect circulating tumour cells)^{1,2}.
- Better cultivation methods to overcome the limits of cloning into heterologous hosts.

2.2 Secondary metabolites for fine chemistry and pharma

Despite the growing demand (mainly due to increasing bacterial resistance to existing drugs), the sector of antibiotic development is facing a crisis in wealthy nations. This problem adds up to a long-standing one – the scarcity of antibiotics to treat diseases prevalent in poorer regions. The crisis results from various factors: economic, regulatory and scientific (loss of expertise in antibiotic development). These problems are especially acute for small firms that would require a set of supportive measures to mount a world-class effort at medicinal chemistry and pharmacology.

In parallel with high-throughput technologies (such as combinatorial chemistry aiming to provide the pharmaceutical industry with the chemical diversity necessary to significantly increase the therapeutic ratio and potency of active principles), natural products continue to play a highly significant role in the drug discovery and development process of new leads (2, 3). The isolation of a constantly increasing array of novel bioactive secondary metabolites suggests that “we have barely scratched the surface of nature’s vast chemical library” (3) and especially of the less explored marine environment (4, 5). In cancer therapy there is an FDA-approved marine drug in the US Pharmacopeia, namely cytarabine (Cytosar-U®, Depocyt®), while another marine metabolite, trabectedin (Yondelis®), has been approved by EMEA, and approval is pending for the US market. Ziconotide, derived from the toxic peptides of marine gastropods, is on the market with the commercial name of Prialt from 2004 for the treatment of chronic pain. Furthermore, a number of other compounds of marine origin is currently in Phase I-III trials, or investigated preclinically as potential clinical candidates (6).

Even though there are undoubtedly many unique and biologically active marine natural products waiting to be discovered, new sophisticated strategies are evolving to fully explore the pharmacological potential of previously isolated natural products. These include target-oriented bioassays, “in silico” target fishing (7), combinatorial derivatization and the synthesis of analogues related to pharmacologically active natural products (8).

Among other novel leads these can be derived from the sustainable exploitation of the huge “biomass” of invasive species in the Mediterranean, as well as from the exploration of neglected culturable organisms (i.e. marine protists). A well-balanced

1 Circulating tumour cells detected by a novel adenovirus-mediated system may be a potent therapeutic marker in gynaecological cancers. *Br J Cancer*. 2012 Jul 24;107(3):448-54.

2 A simple biological imaging system for detecting viable human circulating tumor cells. *J Clin Invest*. 2009 Oct;119(10):3172-81.

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and strategic network of expertises would increase the potential for new discoveries targeting high added-value products such as drugs, nutraceuticals, fertilizers, plant hormones, insect repellents, cosmetics, antifoulants, etc..

CHALLENGES:

- New down-stream processing methods to lower cost production
- Better cultivation methods. Most microbes are yet unculturable, which makes the identification and the production of metabolites (and antibiotics in particular) difficult.
- Cross-sector screening programs for the identification of metabolites of pharmaceutical interest targeting large microbial collections, and enrichment cultures of academic institutions.
- New classes of antibacterial agents against new microbial targets (f.ex.: enzymes of pathogen's core metabolism i.e: topoisomerase, a conformationally flexible enzyme; enzymes enabling the pathogen to resist hosts's defences etc.).
- Drug analogs
- Select novel drug candidates from marine sources
- Rediscover (re-evaluate) known metabolites
- Exploit waste/hazardous biomass from invasive pests
- New target-oriented bioassays
- Realistic solution to the supply issue
- Definition of biosynthetic pathways committed to bioactive molecules in eukaryotes
- Cultures of symbiotic bacteria and associated to invertebrates.

Box 1.

Some successful stories from the sea

- *The isolation of C-nucleosides from the Caribbean sponge, *Cryptotheca crypta*, four decades ago, provided the basis for the synthesis of cytarabine, the first marine-derived anticancer agent to be developed for clinical use.*
- *Trabectedin (also known as ecteinascidin 743) is an anti-tumor drug. It is marketed by under the brand name Yondelis. It is approved for use in Europe, Russia and South Korea for the treatment of advanced soft tissue sarcoma. It is also undergoing clinical trials for the treatment of breast, prostate, and pediatric sarcomas. Trabectedin is a metabolite of the sea squirt *Ecteinascidia turbinata*.*
- *Ziconotide is the active ingredient of the commercial pain killer Prialt. Ziconotide is a synthetic derivative of ω -conotoxin, a peptide toxin produced by *Conus magus*, a species of cone snail. Prialt is used to alleviate severe chronic pain but is neither an opioid nor a NSAID, these being the two main classes of analgesics (painkillers). Unlike opioids prialt does not appear to be addictive or cause respiratory depression.*

2.3. Cosmetics

From its very beginning, the cosmetic industry has developed a firm relationship with biotechnology - most of cosmetics and beauty aids being composed of natural extracts from plants or animals. Today, one can find cosmetics having fish extracts, fruit acids and even products derived (ingredients sourced) from bacteria (*i.e.* ectoine, a moisturizer from *Halomonas elongata*). Marine algae contain anti-oxidants, pigments and vitamins that are being increasingly used in cosmetic products. They are also a source of natural, non toxic colours (*i.e.* orange pigments from Chlorophyta, blue and red pigments from Rhodophyta). Modern biotechnology has immensely contributed to the advancement of cosmetic preparation.

CHALLENGES:

- Micro-encapsulation, stabilizers (*i.e.* liposomes, cyclo-dextrines, compatible solutes)
- Anti-aging (hydrating)
- Pigments (colours), sun (UV) screen products
- Whitening (compounds that block melanin synthesis)
- Treatment of baldness, stopping hair loss/augmenting hair growth (control of the level of collagen and elastin in the skin)
- Bio-surfactants (cleansers, foaming agents, solubilizers)
- Emulsifiers (exopolysaccharides produced by marine microorganisms)

2.4. Flavours and fragrances

Biological progress is rapid and now companies are able to produce a variety of smells and flavors once impossible to make in the lab. The future of flavor production lies in new metabolic pathways or fermentation methods that might be isolated from the sea. Several enzymes from marine organisms are certainly responsible for producing tastes and smell that might be the missing links for food, beverages or perfumers. This source has not been explored enough to date.

CHALLENGES:

-Identify marine organisms to produce flavors and fragrances quickly and cheaply.

2.5. Adjuvants and stabilizers for vaccines

Prevention of morbidity and mortality by vaccination is considered one of the most successful achievements in the history of medicine. Nevertheless, even though vaccines have become safer and more effective in recent years, public anxiety regarding possible side effects of vaccination has increased. This trend is supported by often unfounded fears of a link between vaccination and the development of certain diseases - perpetuated in some cases by misleading media reports. Consequently, risk benefit decisions need to be well informed and based on scientific evidence.

New generation vaccines are mainly constituted by highly purified pathogen

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subunits, like proteins purified from recombinant microorganisms. Despite being greatly advantageous in terms of safety, purified antigens are often poorly immunogenic. Therefore, adjuvants are required to trigger higher and more persistent immune responses. Very few adjuvants are approved for human use, due to safety concerns and also because many potent adjuvants in pre-clinical models have failed in clinical trials. Hence the need to identify novel safe molecules displaying good antigen delivery and immune potentiator properties.

Although there are positive steps in the direction of sustainable development of pharmaceutical industries, multinational pharmaceutical companies are still investing much more in development in order to keep ahead of the competition than in new policies aimed to treat infections endemic in poor regions. Thus, only the more developed countries may use new vaccines, yet. New options should be provided so as to help pharmaceutical industries anticipating worldwide society's medical needs.

CHALLENGES:

- Newer assays to better predict vaccine efficacy and adverse event; development of better tools to evaluate individual immune responses
- Development of vaccines mediating broad coverage against highly variable pathogens (for instance headless conserved regions of hemmagglutinin against flu) (9)
- New methods to enhance immunological responses.

BOX 2.

Some successful stories from the sea

- *Glycolipid and glycoprotein antigens using carriers such as keyhole limpet haemocyanin (KLH) together with a saponin adjuvant, QS-21.*
- *Adjuvants containing squalene (MF59).*
- *Using Archaeal gas vesicles for vaccines: Genetically manipulated halophilic Archaea may be induced to produce vesicles with any protein on their surface. The theory is that injecting such gas vesicles into humans would elicit the production of antibodies to attack the virus antigens. This would open the possibility of vaccine creation for almost any disease, even an emerging one. Gas vesicle delivery system would be unlike anything currently in use and far more versatile.*

2.6 Polymers for industrial and biomedical activities

Worldwide attention has been focused on the critical importance of materials in the creation of new devices and systems. It is now recognized that organic, inorganic,

multiphase and composite polymers are often the limiting factor in bringing a new technical concept to fruition and that polymers are often the materials of choice in these demanding applications. Particularly, the use of new polymers for biosystems may lead to solution of complex, interdisciplinary problems, including environmentally-compatible manufacturing options as well as innovative highly performing pharmaceutical systems (*i.e.* diagnostics, therapeutics).

CHALLENGES:

- Polymers for biosensors and affinity chromatography
- Polymers for drug release and drug carrier systems
- Biocompatible polymers and polymer surfaces
- Bioabsorbable and biodegradable polymers
- Microfabrication and novel processing
- Polymers in biotechnology
- Biologically engineered polymers
- Composites, adhesives, interphases and interfaces
- New elastomers, coatings and sealants
- Flammability, flame retardants and flame resistants
- Polymeric membranes, thin films and nanofilms
- Polymeric catalysts

2.7 Phage therapy

Phage cycles in marine environments (*i.e.* the adsorption phase), can bring new insights to specific therapies.

2.8 Bioinformatics, gene and enzyme databases

Due to recent advances in the understanding of the structural biology of drug action, bioinformatics promises to revolutionize the process of drug discovery and development. One of the main challenges in genomics is to identify the role of genes and proteins in regulation networks and metabolism.

Furthermore, bioinformatics allows the identification of genes for the potential synthesis of new chemicals (as well as enzymes) of interest. This allows the identification of the right samples where to look in for the isolation of genes (and if possible of microorganisms) for the production of metabolites/ enzymes of interest. These “academic” samples could be conveniently shared with industry in screening programs.

Unfortunately, most of the knowledge in functional genomics is not directly and easily retrievable from databases.

CHALLENGES:

- New analytical methods to enable an optimized use of the existing data sets



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- (*i.e.* virtual screening³)
- Better insights into protein functions (*i.e.* exploiting structural data to improve recognition of domains, and to detect evolutionary relationships between domains)
- New tools, *i.e.* learning algorithms, to extract useful knowledge (texts on gene interaction, protein localization, and function discovery) from existing literature
- Chemical genomics

2.9. Biology of “robustness” (*i.e.* biochemistry of age-related diseases)

A great challenge is being provided by the study of the biology and the biochemistry of rare robust (bacterium *Deinococcus radiodurans* and small aquatic animals Bdelloid rotifera and Tardigrades) and immortal (medusa *Turritopsis nutricula*) organisms in order to understand the limits of life and – eventually – to learn if and how humans could acquire robustness (resilience and longevity).

Researchers involved in this sector have been solving key questions of great importance for medicine *i.e.*: the mechanism of repair of DNA pulverized by excessive radiation doses (10, 11); the “chemistry of cell death”, which appeared to be related to protein damages rather than DNA damages. The most recent results show that biological robustness is achieved by the presence of a protein protection system against reactive oxygen species (ROS) consisting of small molecular weight metabolites (12). This research line is based on the assumption that germ line is practically immortal and soma is usually mortal. It aims towards the exploration of mechanisms and development of methods for the measurement of the “biological quality” (fitness) of the soma that, in fine, is the underlying basis of health and longevity.

CHALLENGES:

- Biology of robustness – search for the molecular basis of resilience in diverse robust organisms including robust human cells (stem and tumor cells)
- Biogerontology – quantitative measures (by quantification of proteome oxidation) of real biological age of each individual, *i.e.*, his life expectancy.
- Biology of human destiny – biological “profiling” of proteins susceptibility to oxidative changes (carbonylation) allowing for a targeted individualized preventive medicine.
- Gerontology–applying personalized proteome-protective antioxidants in relation to individual hereditary predisposition to disease.

³ Producing a plethora of simulated data upon which one may build and demonstrate different approaches.

3. Improving the collaborative frame

- Facilitate transfer of knowledge (from research to industry)
- Provide (researchers with) access to (industrial) technological facilities and services
- Durable funding instruments for fundamental research (not immediately considered applicable, *i.e.* bioprospecting)
- Regulatory requirements and patent incentives to encourage steps forward (*i.e.* IP vs. non-exclusive license to practice marketable solutions; IP vs. right to publish)
- Favorable (cost effective) policy from the EPO (*i.e.* reduce to cost of patent maintenance)

4. Innovative (policy) solutions

- New 'players on the scene', *i.e.*: *Not-for-profit* firms which could pursue research differently, protecting their intellectual property by filing patents, but also advertising their work openly, with the goal of licensing the intellectual property gratis to any company or agency that commits to produce and distribute the resulting drugs on a basis that would serve the needs of patients and society (for example, distribution in low-income markets could be on a for-cost basis whereas distribution in wealthy markets could remain for-profit). The profit sector could provide leadership. Encouraged by tax incentives, the industry could give sabbaticals to its scientists and executives to work at a not-for-profit firm in rotation. The majority of the funding for a non-profit firm would probably have to come from government and foundations.

Tax incentives could encourage the for-profit sector to furnish services in kind or at cost, including equipment, supplies, chemicals, clinical development, and regulatory and legal services. Manufacturing could be contracted to factories in low- and middle-income countries.

- Optimized strategies to help SMEs weather the economic storm by bringing them together with national biotech industry associations, venture capitalists, financing bodies, and other stakeholders to help tackle the financial challenges and constraints facing them.
- (National) product-oriented development and innovation projects shall help poor countries achieve autonomy in the development and production of relevant vaccines. This can be carried out by technology transfer agreements for the local production of new vaccines. Capability of national manufacturers (aimed at achieving domestic production of new vaccines within the lowest time frame and at the lowest cost possible), the size of the public market, and the thrust and energy of the National Immunization Programs can make Third Countries attractive and become promising markets, and so attract the attention of multinational vaccine producers.





Marketing opportunities for Jellyfish

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with inputs received during and after the workshop from

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1. Commercialization of jellyfish

1.1 Harvesting and aquaculture alternatives

The experience of Valentina Basilevich who leads a technological laboratory processing jellyfish in Vladivostok, Russia, provided a very concrete, most useful start. This laboratory specifically manages the last step of seafood treatment for human consumption: jellyfish, fish, squids and octopus are processed in a semi-dried way (as a preservation technique) and used in juices, soup, etc. The average catch of jellyfish by fishermen is 200,000T/year, which occurs during a very short period of time (a few months every year). Half of this fishery is processed for human food, the other half is used as food additive for chicken meal.

The potential of jellyfish process and commercialization naturally raises the possibility to grow them in aquaculture. Jellyfish are difficult to cultivate as they present a complex life cycle with a polyp stage that transforms into swimming jellies under favorable conditions. Their cultivation is under study; in China, the polyp stage is maintained in aquaculture.

Jellyfish, an important ecosystem component, are proliferating/blooming at a higher and higher frequency worldwide, which represents a real risk of an ecosystem shift from a fish to a gelatinous sea (13). Fishing nets and boats are not well adapted for catching blooms of large jellies. In fact, jellyfish are already caught along the coast or pushed away, during spring or summer time in many regions and the harvested jellyfish are thrown away. This biomass should be exploited.

1.2 Challenges in different marketing sectors

The potential of marketing jellyfish in different sectors presents interesting challenges.

AgroFood sector – Jellyfish are already exploited for human food (in Russia, China, Southeast Asia, Japan, Pakistan, etc.), and in some regions as food additive for animals (14, 15). As an example, the presence of various carbohydrate and polyunsaturated fatty acids in jellyfish reflect/could answer a real need in aqua and agriculture feeding.

For successful jellyfish applications in this sector, many problems have to be addressed (see Table 1 below) and a roadmap should be drawn up.

Materials sector - Various studies demonstrate that, due to the presence of both microelements and biopolymers (fibrillin, mucin, collagen, etc) in their bodies, jellyfish present desirable “plasticity” features. In Russia, these characteristics were studied for cement fabrication in replacement of costly biological (albumin) and chemical additives. The inclusion of jellies increases the mechanic strength of normal cement by 50%. These properties, which could be transferred to the road asphaltting process, add plasticity and resistance to the cement, which is of importance in regions exposed to seismic risks.

Table 1: Summary of challenges facing potential jellyfish applications

Applications	Challenges
<p>Application 1: Food / Food additives Classical use in Chinese cuisine. Recent development as Sushi stuff in Okinawa in Japan. However, it depends on low labor costs of poor fishermen in Vietnam or Thailand. Edible species are restricted.</p> <p>Application 2: Feed (Domestic Animal / Fish Culture) Additives A Secret (?) Spermatozoon of <i>N.Nomurai</i> Attracts Fish (Not Ovum) Fish feed does not demand dialysis.</p> <p>Application 3: Fertilizer. Dialysis is needed before fertilizing. Putting raw jellies cause weeding.</p>	<p>Challenge 1: How to take out water (95-97 wt%) Heat Drying Cost Freeze Drying = high cost Preservation in salts is employed for food application but useful contents may be lost as well</p> <p>Challenge 2: How to take out salts (A half of the rest) Dialysis = high cost</p> <p>Challenge 3: Cost & Energy for Transportation</p> <p>Problems in Species Assignment (not easy even by the experts) <i>e.g. Rhopilema/ Rhizostoma/ Neopilema</i> Similar Species are not similar in the nature of materials <i>e.g.</i> Edible or Not Edible Degradative and water soluble, collagens or not A DNA assignment kit maybe useful.</p> <p>Problems in storage Most of the species are self degradable within one day in ambient temperatures. Both microbes and enzymes of their own seem to affect. The latter is not suppressed even at low temperatures <i>e.g.</i> -80 °C. Storage under frozen condition is difficult. Preservation of high amount of jellies may generate other problems, <i>e.g.</i> odor smell, sanitation.</p>
<p>Application 4: Cement Additives</p>	<p>No problem with salt No problem with drying system - costs – possibility to apply crude, homogenised jellyfish</p>
<p>Application 5: Extraction of a High-Lank Innovative Materials. (Qniumucin Cost 1g ~ 1 – 5 euros, collagens 1g ~ 0.1-0.5 euros)</p>	<p>Challenge 5: Balance with the cost for waste treatment. (Minus cost for application) Depends on the law in each country. (ex: London Dumping Convention)</p>

1.3 IP issues:

Intellectual property rights represent a crucial component of commercialization. Participants agreed that a first important step is to assess the need to patent or not a technology and the commercial benefit or lack thereof. There are cases in which knowhow provides better protection of time lead in the market, further enhanced by continuous R&D.

The market segment to which the products are aimed often determines the need to develop strong IPs. Such markets are nutraceuticals, food additives and pharma products. When development time and regulatory processes are long, there is a strong need to protect the market position for the long term; then patents are a good start.

In some cases where regulatory processes can be costly and long, as for example the use of jellyfish as additive to cement, these processes provide protection and significant time lead over the competition.

There is a critical need to harmonize EU regulations with those of the USA on the subject of publication vs. patenting. In the EU any publication before application for IP will nullify the IP, while in the USA there is a period of up to 12 months between publication of an innovation and the application for IP.

As many IP licensing agreements between universities or research institutes and commercial companies are already in place, lessons from existing successful agreements should be learned. This will enable the creation of some agreement models offering various options for different cases.

Box 3.

Recommendations on jellyfish marketing

In case of successful commercialization of jellyfish the harvest of jellies for processing should be facilitated in coastal waters, particularly before, during and after the summer season, where increasing jellyfish blooms cause havoc to the tourism industry. The benefit of their catch should be evaluated considering both their role and threat in the ecosystem; adapted modus operandi should be proposed to fishermen.

Short, medium and long-term marketing possibilities for jellyfish should be explored, and a roadmap designed, for each potential application/ sector of relevance.

2. Benefits expected from innovative partnerships

During the discussion, the current lack of basic research funding was highlighted. Within the current (European, national, etc.) R&D funding system, new mechanisms of funding should be explored so as to avoid bureaucratic process (such as IP management, lab management, funding report management, etc.). In Europe, the time now spent by a researcher to manage reports, IP issues, or communication prevents innovative work and slows down cutting-edge research advances.

2.1 Research Funding – Public and private sectors collaboration for funding

Within a new partnership structure/ concept, IP agreements between universities and companies should include a part of funding for basic research. It was also suggested that the concept of doing basic research to obtain potential data for application could be considered the way around. If possible, new partnership would start from ongoing/ past successful application funding to be injected into research on the same topic (on a larger scale) – so as to deepen and strengthen related basic knowledge.

Another suggestion for innovative funding concerned the concept of an auction system by which research institutes would present short summaries of their IP in various areas, and commercial companies would review those and propose terms for using the IP commercially. With such a system much of the red tape associated with commercializing IP would be bypassed.

To favor effective exchange among private and public researchers, more business/ management skills should be developed in academia as successfully implemented by the Magnet program in the USA. Magnet schools are public schools with specialized courses or curricula. Another approach is to add staff with both scientific background and strong business development skills to university research labs so as to help commercialize the resulting IP and focus some of the research on market needs.

2.2 Pilot incubators in Mediterranean Countries

The purpose of technology incubators is to foster innovation and entrepreneurship by providing funding and business development along with company building skills. It was suggested that CIESM could encourage an incubation program for Blue Biotechnology projects in the Mediterranean Basin. The evaluation process would be done by independent specialists in each scientific discipline and by people from the relevant market. The findings would be submitted to an investment committee for a final decision. Such examples exist in Japan, USA or Israel. In the latter case, the system involves an investment of \$500k per project, where the State provides 85% of the funding and the incubator 15%. The funding is aimed at converting an idea or concept into a working prototype addressing a true need in the relevant market.

2.3 Communication strategy

Communication, just like business, requires full expertise and skills that are not usually expected from scientists. It is essential first to define the target so as to develop the adequate strategy. Scientific basic research data or semi- end-product presenting an opportunity for application, require the identification of relevant partners to develop the product/ idea, relevant end-users, who both need adapted vocabulary.

A joint communication strategy should be designed between the university and the industry for those axes emerging from a partnership.

Box 4. **New partnerships between private and public sectors**

Some expectations

To bridge the gap between basic research and business for pre and/or pro competitive research, future partnerships should not reinvent the wheel, but benefit from existing successful agreements. A set of different model agreements (see Note on IPs in this CIESM Report) used successfully in other regions would be helpful for future development between academia and industry, EU and non EU countries, pre and pro competitive research.

New partnerships between private and public sectors would benefit from these existing successful IP agreement, which should include inter alia: basic research funding, management strategy communication strategy.

A way forward could be the development of Blue Biotech incubation programs involving co-funding by EU and concerned entrepreneurs.

Collective intellectual property strategies for access and benefit sharing over marine genetic resources in the Mediterranean

Tom Dedeurwaerdere (Univ. Leuven, Belgium)

1. Rationale

New methods for culturing marine microbial organisms, molecular biology, and computational methods for large scale genomic, metagenomic and environmental data mining hold immense potential for the development of new commercial applications from marine biodiversity and for understanding basic biochemical and ecological processes in the marine world. To realize the full potential of large scale collaborative marine research, rapid and continued access to collected research materials and to the wealth of related data is needed. However, in the current situation, many developing and transition countries implement increasingly restrictive access and benefit sharing legislation, without special exceptions for pre-competitive access to valuable research resources. On the other hand, in the developed economies, examples of patenting of upstream and general purpose research materials and methods continue to generate concerns from developing and transition countries, who ask to benefit in a fair and equitable manner from the progress of scientific innovations with marine genetic resources collected under their jurisdiction or to adopt a common heritage approach for genetic resources from international waters (16).

In the current legal environment, the range of obstacles to the full realization of the new opportunities offered by research and innovation with marine resources presents a formidable challenge. This shows the need for appropriate organizational forms, legal arrangements and social practices, which can help to better secure the marine community's need to address issues of common concern, such as sustainable use of marine resources, biodiversity conservation and climate change mitigation.

The discussions at the workshop followed a previous exercise lead by CIESM in 2008 (17). They focused on a set of innovative collective intellectual property strategies between the various public, private and non-profit partners involved in basic research, and research and development, with marine genetic resources. Such strategies could promote innovation, while at the same time contributing to benefit sharing with source states in mutually agreed manner, through measures such as sharing in research results or build in research exemptions for source countries (whether only for non-commercial research, or also for commercial research) in the case of intellectual property on downstream applications.

Two sets of propositions were presented in the overview of intellectual property strategies for access and benefit sharing by the author of this note, and discussed at the workshop:

- (1) strategies dealing with pre-competitive access to genetic resources for use in research and screening of interesting isolates

- (2) strategies dealing with collaborative arrangements for commercial applications

2. Strategies dealing with pre-competitive access to genetic resources for use in research and screening of interesting isolates

Genetic resources collected in the Mediterranean can be claimed as falling under the national jurisdiction of the coastal states. Increasingly, coastal states are claiming their rights to share in the benefits of research with these resources under the Convention of Biological Diversity. On the other hand, many measures for equitable benefit sharing are quite straightforward, especially in the case of pre-competitive access to research resources, such as participation of scientists of source countries in the collecting missions, sharing of research results and capacity building. However, a case by case approach of such access and benefit sharing agreements in the Mediterranean is likely to lead to high transaction (negotiation and administrative) costs both for public and private research, slowing down the research process. As a result, the promise of biodiversity-based innovation, and new research results that can be used in blue biotechnology in particular, might fail to be realized.

Important steps in the direction of a more coordinated approach for pre-competitive access to marine genetic resources could be made by the systematic adoption in marine Mediterranean research of measures that:

For access: introduce standard material transfer agreements (MTAs) for access to genetic resources within the Mediterranean science community for the purpose of basic research and screening of isolates and chemical compounds at the pre-competitive stage of research. The major benefit of such standard agreements would be to prevent a race to the bottom, by either providers (who might impose ad hoc restrictions for access) or users (who might end up blocking access to research results even for the members of the Mediterranean research community). Such a framework agreement could learn some lessons from the experience with the standard MTA adopted for plant genetic resources in the International Treaty for Plant Genetic Resources for Food and Agriculture, which builds a pool of resources that can all be accessed under the same terms and conditions for research, breeding and training ;

For use: explicitly give the permission to researchers and collections, for all uses of genetic resources at the pre-competitive stage of the innovation process, to redistribute resources to collaborating scientists and farmers, or to other collections that operate under the same framework agreement (as is for example the case in the standard MTA adopted by the European Culture Collection Organisation - ECCO).



3. Strategies dealing with collaborative arrangements for commercial applications

Many agreements for collective intellectual property management in collaborative research between public and private entities or between private entities exist that provide for appropriate sharing of benefits or research among the parties to the agreement and under mutually agreed terms, in the case of the development of commercial applications from the utilization of genetic resources that are pooled by these parties. These collective approaches are often neglected in the current discussions, in spite of extensive experience with these agreements and their potential contribution both to speeding up innovation and providing tangible benefits for source countries that would take part in these agreements.

At the workshop, Tom Dedeurwaerdere detailed two such types of arrangements:

- (1) Agreements amongst private entities for collective IP management, such as cross-licence agreements, patent pools, or patent clearing houses ;
- (2) Open innovation models for partnerships amongst private and public / non-profit entities, where each party keeps its own IP, but clear agreements exist for publication rights and continued access to the research resources for public/ non-profit scientists policies

Two examples of open innovation models were especially discussed and well received at the workshop: the University of California at Berkeley – INTEL research collaboration, and the model agreements used at Universities in Israel.

Further reading

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Annex 1

Profiles of seminar's participants

Patrick Baraona is General Manager of the pole of competitiveness "Mer PACA" in France. Today the pole gathers 300 members (70% of companies and 30% research centres) involved in the development of the maritime economy in various fields as: safety and security, naval and yachting, marine energy resources, marine biology resources, environment and coastal engineering.

Before becoming managing director of the pole, Patrick Baraona was, from 2001 to 2004, the Chairman and CEO of the Cybernetix group specialised in development and manufacturing of automatic and robotics systems. Among the founders of this company, created in 1985, he took successively the position of R&D manager, technical director, engineering director, deputy general manager then between 1994 and 2001 general Manager. During this last period in 1997 he contributed to the inscription of the company on the Paris Stock Exchange. Prior to that from 1983 to 1985, he was submarine robotic project manager for the Comex Group in Marseille.

Patrick Baraona holds a PhD in Automatic and Robotic from the LAAS of CNRS at the Toulouse University (1981) and was hired by INRIA for one year as researcher in robotic and artificial vision, at the University of Rhodes Island, of Kingston, USA (1982).

Michèle Barbier Dechraoui is scientific officer at CIESM. She received her Ph.D. in Marine Molecular Biology from the University Pierre and Marie Curie, France, 1996. She worked on the biology (molecular and cellular) of Dinoflagellates in the Pacific, Gulf of Mexico (at NOAA), Atlantic (at IFREMER) to understand Harmful Algal Blooms. Thereafter she decided to move on scientific management (inter alia, in Roscoff (CNRS) she managed the EU-FP6 Network of Excellence 'Marine Genomics Europe'. At CIESM Headquarters, she focuses on the application of marine sciences to the fast-growing Mediterranean Biotechnology sector, including the Intellectual Property Rights

Valentina Bazilevich is Head of the Laboratory Biology of Marine Invertebrates, Institute of High Technologies and Economic Studies, Pacific State, University of Economy at Khabarovsk, Russia. Her interest is in technologies of processing the same Far-Eastern-scifoid jellyfishes just like Mediterranean jellyfishes. Foodstuff from scifoid jellyfish correspond to tastes of European consumers. Perspective directions concern the technologies for processing jellyfish taking into account their unique features.

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Her lab offers the experience of processing of jellyfishes to businessmen, being guided, first of all, by results of the genetic researches, from jellyfish consumption to the person. Safe technologies of jellyfish processing are offered.

Fabrizio Beltrametti is Chief executive officer of Actygea Srl. Actygea activity bridges the gap between commercially interesting research at Universities/Research Centres and industrial activities in biotechnology. Focus is in particular on the application areas, which require know-how of bioprocess technology, microbiology and biochemistry. Contract research and specialty fermentation/downstream services are offered on fee-for-service or equal base. Actygea's founders have a long lasting and documented record of success in the field of metabolites of microbial origin. Actygea can offer a reliable service in the field of: microbial fermentation, strain improvement and purification, mutagenesis and selection, gene manipulation, genome shuffling (proprietary technology ActyGenShuff), fermentation medium development (proprietary database ActyMedDat), downstream processing of metabolites of microbial origin, research in the field of microbiology of uncommon actinomycetes, strain maintainance, biocatalysis.

Actygea owns pre-GMP fermentation/downstream facilities in a very flexible pilot plant (from shake-flask to pre-industrial scale). With more than fifteen years of hands-on experience in pharmaceutical and biotech industry, our scientists and technical staff are highly qualified and bring together competencies ranging from gene expression and genome shuffling to microbial fermentation and process scale up.

Actygea was a partner in several projects involving the exploitation of microorganisms isolated from marine environments, as producers of metabolites for the pharmaceutical industry (in particular antibacterial and antifungals). As a general consideration, Actygea is interested in developing every microbial-based process using organisms of marine origin, per se or as source of genetic information.

Frédéric Briand, is Director General of the Mediterranean Science Commission (CIESM).

Early career in Canada as University Professor, with field studies of marine and lake communities of north and central America, and pioneering theoretical research on the rules governing the architecture of both aquatic and terrestrial foodwebs. Followed by positions at IUCN in Europe (Head of Conservation Science), and UNESCO in North Africa (Director of pilot Program on environment and demography). Author / editor of a number of scientific books, and of noted papers (Nature, Science, PNAS, ...) on food webs, ecosystem resilience, the cybernetics of complex systems and Mediterranean issues. Founder and Editor of the CIESM Monograph Series on Marine Sciences (now reaching 40 volumes). Oversees the international development and science strategy of the Mediterranean Science Commission, with particular attention to the design of multi-lateral initiatives and cross-sectors cooperation with business and industry. Sits on the Board of various international bodies and programs (IWC, GESAMP, PTMB, EC projects).

Giancarlo Coletta is purchasing Director at the Grimaldi Group in Naples, a completely family owned, multinational company operating in the logistics industry, specializing in the operations of roll-on/roll-off vessels, car carriers and ferries. It has specific expertise within the scope of maritime transport, port terminal operations, land transport companies, shipping agencies. The Group is committed to excellence, social responsibility and transportation solutions that promote environmentally sustainable mobility. The expansion of the Grimaldi Group Naples outside the Mediterranean market began in 1969, with the start of a scheduled service between Italy and UK. Today the range of services offered has expanded well beyond the original boundaries and vessels operated by the “Grimaldi Lines” cover the entire Mediterranean, Northern Europe, Scandinavia and the British Islands, even many ports in West Africa and South America. Today the Group transports by sea about 1,800,000 vehicles/year with a fleet of over 100 vessels owned and 40 on charter. The Grimaldi Group also manages some terminals in the port of Antwerp, Cork, Esbjerg, Lagos, and Monfalcone. Palermo, Salerno and Valencia, and is the owner of the port of Wallam (Sweden).

Conscious of the importance of environmental protection, the Grimaldi Group has given way to a program to expand its fleet by providing numerous Ro-Ro technologically advanced multipurpose vessels. Regarding its experience in the innovation processes, Grimaldi has participated in several research projects including SAFENVSHIP, STARSHIP now concluded and participates to project SISPRECODE for environmental friendly marine paints and participate as a consultant to the research project SISTEMA (System Integrated Secure Land Sea) financed 22.9 million euro for an integrated ‘land / sea’ for passengers and goods to remove the bottleneck between the last mile to the sea and the first mile to the ground”. Moreover, the Grimaldi also participates in the EU project Handling the Waves, whose object is a decision support system for the management of the ship in adverse weather conditions. The Grimaldi Group interests in environmental friendly technologies and/or Biotechnologies are relevant to limitation of Ship Emission and pollution. In particular Air emission (SO_x, NO_x, CO, CO₂, particulate), Water emission (Black water, grey water, ballast water, antifouling paints), Waste (garbage, packaging, incineration).

Milton Simões da Costa is full professor at the Department of Life Sciences University of Coimbra, and chair of the Committee Marine Microbiology and Biotechnology at CIESM. He was President of the Portuguese Society of Microbiology (SPM) from 1996 to 2002 and Vice-President of the Federation of European Microbiological Societies (FEMS) from 2004 to 2007. He is currently President of the Federation of European Microbiological Societies (FEMS).

Milton da Costa has been active in teaching at the undergraduate and graduate levels. Supervised undergraduate research projects, 21 M.S. theses, 13 Ph.D. dissertations as well as postdoctoral research work. His primary research has been devoted to the study of thermophilic and halophilic bacteria ranging from taxonomy and systematics, biodiversity, biochemistry of polar lipids of extremophiles, the discovery of new compatible solutes from hyperthermophiles and thermophiles and their biosynthetic pathways. His lab also works on the molecular ecology of *Legionella*

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spp. in natural environments and the evolution of pathogenesis genes in several species of legionellae. Their work on compatible solute synthesis led to the finding of several essential genes and gene products in *Mycobacterium tuberculosis*. Deep borehole microbiology associated with mineral water sources.

Their research has led to the submission of four patents and the publication of 141 original research papers and seventeen chapters in English language books. His lab has received ten European Commission Grants and 22 Portuguese Research Grants. Mineral water companies have funded research in lab from 1983 to the present. Set up an ISO accredited lab for the microbiological quality control of water and food at the BIOCANT Technological Park. For two years this lab has been performing quality control of umbilical cord stem cells for bacteria, viruses and antibiotic sensitivity tests on the bacterial isolates.

Angelo Fontana is Leader of the Bioprospecting Lab, Institute of Biomolecular Chemistry, Consiglio Nazionale delle Ricerche, Pozzuoli – Naples. His research activity is focused on isolation, structure characterization and function elucidation of bioactive secondary metabolites from marine eukaryotes, with a major emphasis on invertebrates and microalgae. The research activity involves functional studies (ecophysiological role) and potential application for human wellbeing. Since 1993, major emphasis is on the biosynthesis of marine secondary metabolites by use of labeled precursors, purification of key enzymatic activities and molecular techniques. In the last years, the interest of the research group has been broadened to include the study of the metabolic pathways related to production of biofuels – mainly bio-oil and biohydrogen - from marine microalgae and bacteria.

Laura Giuliano is scientific advisor at CIESM. In 1996, she obtained her Ph. D. on "Distribution and functional characterization of marine bacteria in relation to the hydrological characteristics of the water bodies ». After a post-doc at the National Centre for Biotechnology (GBF, Germany) she worked at the National Research Council (CNR) in Italy, with various commitments including research and supervision. She has published 40 scientific articles on peer-reviewed international journals and several national and international articles (including press articles) for promoting science across a larger public. She participated to national (EOCUMM, PNRA, CLUSTER-SAM, PON-SABIE) and international projects (BIODEEP, COMMODE, EUROCEANS) mainly with leading responsibilities. She has been member of different evaluation panels for selecting research proposals to be funded by both national (CNR-It, MIUR-It, PNEC-Fr) and intergovernmental Commissions (EU FP5, FP6). Between 2003 and 2007, she has been the Italian Ambassador of the International Society for Microbial Ecology (ISME).

Frank Oliver Glöckner is Head of the Microbial Genomics and Bioinformatics Group at the Max Planck Institute for Marine Microbiology, Bremen and he is Professor at

the Jacobs University Bremen GmbH.

Recent developments in 'omics' technologies as well as improvements in sampling and laboratory equipment have opened a new dimension in research of marine biodiversity, ecosystem functioning and blue biotechnology. Reflecting the size, heterogeneity and complexity of the marine ecosystem, an unprecedented amount of environmental data, biodiversity data, as well as functional and organism-specific data are already produced or envisaged. This ever growing deluge of electronically available data needs to be processed, integrated and visualized for in depth analysis by domain experts with respect to a better understanding of evolution, niche adaptations and ecosystems functioning. Furthermore, these data harbour a wealth of new metabolic processes and functions, with ample potential for biotechnological applications. It is the focus of the Microbial Genomics and Bioinformatics Research Group at the Max Planck Institute for Marine Microbiology in Bremen to develop enabling technologies to transform the wealth of sequence and environmental data into ecosystem knowledge and new targets for biotechnology. Techniques used are bioinformatic whole genome and metagenome analysis, binning of sequence fragments, phylogenetic inference, expression profiling as well as software and database development for integrated data analysis.

His personal interest in attending the workshop "Innovative Partnerships for Blue Biotechnology development" is to learn more about current developments and strategies in the field of marine bio- and nanotechnology with a special focus on the intellectual property issues. The knowledge gained will stimulate further discussions on the exploitation of marine microbial diversity with respect to better ecosystems understanding and biotechnology applications.

David Gutnick is Professor Emeritus in Microbiology, Biotechnology at the Tel-Aviv University. His laboratory activity is concentrated on linking environmental microbial processes such as bioremediation of pollutants such as crude oil and other petroleum products to the production of novel products such as bioemulsifiers and biosurfactants. The first such product has been the polymeric bioemulsifier emulsan. Their approach is multidisciplinary incorporating genetics and molecular biology to modify and improve both the producing strain and the efficacy of the product itself. In addition, modifications have been introduced to enable the design of efficient and inexpensive formulations for various applications. The activity of the biopolymer emulsan depends on the presence of a specific protein which is required for optimal activity. This emulsification enhancing pep[tide (*EEP*) is unique in its ability to interact with a variety of water soluble polysaccharides, thereby converting these into emulsifying biopolymers termed "*EEPOSANS*". Eeposans represent a new class of such products and provide a vehicle for recycling waste polysaccharides such as cellulose, pectins, etc. The laboratory is now actively involved in defining and exploiting the essential features of this new *EEPOSAN TECHNOLOGY*.

In the past his lab showed that polymeric bioemulsifiers can be applied in a variety of oil field applications such as viscosity reduction of heavy fuels and oils for pipelining, cleaning storage containers, and combustion of stable oil-in-water emulsions, generation of non-toxic degreasing formulations etc. Currently, these appli-

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cations are being evaluated in large scale field trials in China. In addition, emulsan is being used by the U.S. Navy in a formulation for the desludging of filters on many of its ships.

William Helbert is the leader of the group "Structure des Polysaccharides marins", Station Biologique de Roscoff, CNRS. Doctor in chemistry (Joseph Fourier University, Grenoble, France), he spent two years at the Wood Research Institute, Kyoto University, Japan. He was supported by the Japan Society for the Promotion of Science (JSPS) to work on Structural diversity of native cellulose microfibrils. He worked with NOVO-NORDISK, Bagsvaerd (Danemark) and with ALSTHOM PAPER Co., on cellulose solvents potentials for paper industry. He published 55 publications in international peer-reviewed journal and owns 6 patents.

His interest consists in studying the chemical and three-dimensional structure of marine polysaccharides in order to understand and "manipulate" their physico-chemical and biological properties. His investigations are currently focussed on carrageenans and ulvans which are the main component of red and green algal cell wall respectively. His research is articulated around two main axes:

1) Analysis of the chemical structure of carrageenans and ulvans using enzymes in order to decipher complexity and structural diversity of these macromolecules. Enzymes are well-known to represent very useful tools to solve the chemical structure of complex polysaccharides (e.g. glycosaminoglucons, pectins or starch). He takes advantage of the availability of enzymes discovered in the laboratory to develop strategies aiming at determining the composition and, more especially, the distribution of repetition units along the polysaccharides chain.

2) Despite the exponential increase of number of gene sequences by the sequencing of genomes, the discovery of new family and/or catalytic function remains constant. In this context, he is developing strategies of screening for new polysaccharides degrading enzymes (glycoside hydrolases and polysaccharide lyases) and polysaccharides modifying enzymes (sulfatases, sulfurylases).

Margarita Kambourova is Head of the Department of Extremophilic Bacteria, Institute of Microbiology (IMikB), Bulgarian Academy of Sciences. Her research fields are:

- Biodiversity of extremophilic bacteria. The application of the molecular approach for characterization of the bacterial and archaeal diversity in hot springs.
- Novel microorganisms from extreme habitats. Isolation, morphological, physiological and phylogenetic characterization of novel bacteria.
- Biosynthetic capacity of extremophilic microorganisms to synthesise biotechnologically valuable enzymes. Production of different hydrolases by thermophilic microorganisms: α - and β -amylases, glucosidase, pullulanase, inulinase, pectinase, xylanase, lipase, protease, gellan-lyase et al.
- Purification and characterization of thermostable enzymes.
- Immobilization of synthesized enzymes and of cell-producers for their more ef-

fective application as industrial biocatalysts by entrapment in different gels or attachment to membranes.

- Investigation on Black sea coastal zone are initiated together with colleagues from the Central Ecological Laboratory. Structure and function of microbial communities in coastal marine ecosystems under anthropogenic impact. Effect of oil pollution on bacterial community structure “shift”. Identification of key catabolic genes in oil-degrading bacterial pathways – potential biomarkers for oil pollution.

Adolf (Adi) Kellermann is the Head of Science Programme in the Secretariat of the International Council for the Exploration of the Sea (ICES) since 2004. He is a biological oceanographer and zoologist by education with diverse research interests. He started his career after his PhD earned from the Kiel University 1985 as a researcher in Antarctic Waters, working on the early life history of Antarctic Fishes. He took part in the 1981-91 BIOMASS programme. During a 3-year NSF grant at the University of Hawai’i at Manoa (1989-91) he extended his research into growth dependent processes in Antarctic fish early life stages, yielded by daily increments of embryo and larval otoliths. In 1992, he changed sides and moved into research management from a position of being coordinator of a research endeavour “Ecosystem Research Schleswig-Holstein Wadden Sea” which was an ambitious 7-year venture with more than 40 individual projects. The main objective was to transfer research into advice for decision and policy-making in Germany’s largest marine National Park. During that period, he developed the concept for the “Trilateral Monitoring and Assessment Programme TMAP” in the European Wadden Sea and coordinated its implementation until 2004 as a Senior Scientist. He has written more than 50 scientific publications including books or book chapters, articles in peer-reviewed journals as well as articles for the public.

His current activities involve preparing the ICES Annual Science Conference, scientific symposia, cooperation with other IGO’s and overseeing ICES publications and the about 90 Working Groups under the ICES Science Programme. Since 2010, he is the coordinator of MARCOM+ (“Towards an Integrated Marine and Maritime Science and Technology Community”).

Willem P.J. Laros is Policy adviser at the Community of European Shipyard’s Associations (CESA) and leads the European Technology Platform WATERBORNE Support Group Secretary..

After graduating as a naval architect from Delft Technical University (1973) he spent 35 years in several technical and commercial management positions in the Dutch (naval) Shipbuilding Industry. Still active as senior advisor to the Board of the Damen Shipyards Group – one of the bigger European Shipbuilding Companies with more than 30 yards worldwide – he is Chairman of the R&D working group of the Community of European Shipyard’s associations (CESA) and Secretary of the European Technology Platform WATERBORNE, the R&D coordination body of the col-

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lective European Maritime Industry and as such involved in EMAR2RES and MARCOM+ initiatives to further cooperation between the Marine and Maritime Research and Science Communities.

At numerous occasions he has been instrumental to initiate and kick start R&D projects with the aim to improve shipdesign, -performance and -operation. In our quest to improve the carbon footprint of maritime transport as well as other forms of emissions many technologies are already available to lower our dependence on fossil fuels by better use of fuel both in terms of efficiency and cleaner operations. But more is needed. Here nano technology and bio-mimics can play a ground breaking role in decreasing viscous resistance, one of the three elements of the ships resistance while it moves through the water and thus in decreasing the required trust generated by the propulsion plant. Viscous resistance of the ship's hull surface has long been considered as very difficult to influence but by smoothing and anti fouling paints.

Alenka Malej is a program director at the Marine Biology Station Piran, National Institute of Biology and full professor of ecology at University of Ljubljana, Slovenia. She has broad experience in the coordination of national/international research projects and was head of the Marine Biology Station in Piran for more than two decades. A. Malej is a member of the Bureau Central de la Commission Internationale pour l'Exploration Scientifique de la Mer Méditerranée (CIESM), chairperson of the National Committee for the Intergovernmental Oceanographic Commission (IOC) and national MED POL co-ordinator of the UNEP MAP (United Nations Environmental Programme, Mediterranean Action Plan). In 2010 she was nominated as expert to serve on the Group of experts established pursuant to paragraph 180 of UN General Assembly resolution 64/71 on Oceans and the Law of the Sea. She acted as a consultant/expert for UNEP/MAP, was visiting scientist/professor at many renown marine institutions and taught Coastal Zone Management at UNIDO and UN-ESCO international courses, International MBA Degree Programme, ICPE Ljubljana, and Joint Study of the universities of Trieste, Italy and Koper, Slovenia.

Her main research interest is marine plankton with focus on the ecology and biology of gelatinous zooplankton. Current research activities are related to the trophic ecology of gelatinous zooplankton, biogeography of jellyfish (Scyphozoa, Ctenophora), recurrence of jellyfish blooms and their impacts on marine ecosystem and human activities.

Ernesto Mollo is researcher at the CNR -Consiglio Nazionale delle Ricerche-, "Istituto di Chimica Biomolecolare" in Italy. His expertise includes biomolecular chemistry, marine chemical ecology, and invasion biology. A primary focus of my work has been the study of bioactive natural products from marine organisms. However, in addition to the biomedical interest of the metabolites, in which both structures and organisms often lose their own importance, my researches also aimed at bet-

ter understanding the ecological roles of the compounds, and their phyletic and geographic distribution in nature. Another important part of his activity has been dedicated in the conduction of diving campaigns for the exploration of the marine chemical diversity on a global scale. The researches, carried out in the frame of International Research Agreements along the coasts of Spain, Greece, Venezuela, Mexico, Cuba, Costa Rica, Egypt, Tunisia, Portugal, India, Russia, Australia, Antarctica, and China, led to the selection of several sources of novel bioactive metabolites.

His current research interests include the development of chemistry based methods and protocols for the assessment of factors affecting marine biological invasions in the Mediterranean Sea. They also deal with the evaluation of possible uses in biotechnology of undesired biomaterials from invasive pests, to both reduce their impact on ecosystems and to produce socio-economic outcomes for the coastal productive community. Moving in this perspective, he is trying to define an articulated research strategy to study the biotechnological potential of exotic species in many different applicative fields, such as, health, food, agriculture, environment and fisheries, by crossing the traditional boundaries between academic disciplines. More recently, he focused his attention on the incorporation of computational methods in blue biotechnology to increase the pharmacological screening efficiency, to design targeted modifications of specific structures to create new therapeutic agents, and to prevent the negative effects produced by randomly-guided sampling activities on the marine environment.

Aziza Mouradi is professor at the « Laboratoire de Biochimie, Biotechnologies et Environnement », Faculté des Sciences, Université Ibn Tofail, Kenitra, Morocco. Since its independence, Morocco has dedicated lot of energy to the development of its agriculture. Since 20 years the efforts for marine natural resources valorisation has been increased.

In 2009, the Halieutis plan for sea products valorisation was published. It plans to reach an aquaculture production of 200 000 tons in 2020. What could be the contribution of marine biotechnology in this project? In parallel, Morocco is engaged in a development plan for renewable energy with several wind and solar farms.

The Moroccan Atlantic coast of Sahara is characterized by favourable cultivation conditions for microalgae:

- ⇒ one of the highest levels of sun irradiation in the world,
 - ⇒ Temperatures below 30°C for most of the year.
 - ⇒ Marine waters rich in nutrients due to the presence of a coastal upwelling system.
 - ⇒ Desert lands along the coast easily convertible to aquaculture.
- The development of cultures of microalgae for fuel, biomass, food or feed productions is an opportunity for Morocco.
- Although micro algae growth rate is higher than terrestrial plant, there is still a lot of scientific and technical improvement to be do done to compete with terrestrial crops.

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Her lab works on: selection of more suitable species, improvement of culture conditions, development of new culture systems, improvement of harvest methods, new valorisation of the production.

Gokdeniz Neser is assistant professor at the Institute of Marine Sciences and Technology, Dokuz Eylul University in Turkey.

Turkey with its 8333 km of coastline along four different seas (the Black Sea, the Marmara Sea, the Aegean Sea and the Mediterranean) where very rich biodiversity can be seen has a great potential to provide a significant contribution to research on blue biotechnological products and service. In order to benefit from this magnificent potential, **BIUe Biotechnological L Products and Service Cluster of Izmir (BULPS)** has been formed. The cluster has been focused on technical or/and engineering use of marine organisms and processes to improve the living standards of the people and sustainable use of the marine resources. The activities carrying on by the cluster are:

- Exploring marine resources at the four different seas of Turkey and R&D activities on their usage in biotechnological production and services.
- Medical, chemistry (marine paints in particular), food and aquaculture industries and waste treatment plants are the main interest of the cluster.
- Biofuel production from living marine resources (algae in particular) is also covered by cluster's interest.

The current research in the cluster are as follow:

- Isolation and characterization of secondary metabolites from seaweeds
- Inhibition/activation of medicinally important enzymes via bioactive metabolites from marine living things
- Development of biosorbents by using marine wastes
- Isolation of bioactive metabolites from dead leaves of sea grasses
- Plant growth stimulating agents from seaweeds
- Biofouling and antifouling processes
- Biodiversity
- Microbial community analysis by cultural and molecular techniques in marines samples (Community analysis on the black sea sediments)
- Biofilm microorganisms and studies on biofilm removal (especially enzymatically and with quorum quenching mechanisms)

Miroslav Radman is currently exceptional class professor of cell biology at the Medical School of the Rene Descartes University – Paris-5. Founder and Director of the Mediterranean Institute of Life Sciences (MedILS (www.medils.hr) in Split, Croatia. Science adviser to the Prime Minister of Croatia, Member of the French « Academie des Sciences », Croatian Academy of Sciences and Arts, Academia Europaea, World Academy of Arts and Sciences and the European Molecular Biology Organization (EMBO).

Recipient of over a dozen major international and national science awards, frequent keynote or plenary speaker. Over 600 lectures and seminars worldwide. Published

about 200 research and review articles in the areas of DNA repair, DNA replication, mutagenesis, genetic recombination, evolution, microbiology and cancer research. Average impact factor of research papers in last 5 years is 16.2. Three discoveries (SOS system, mismatch repair and molecular basis of the genetic barriers between related species) are present in the basic genetics and molecular biology textbooks worldwide.

One of his research interests is the biology of robust species. Classical studies of gene mutations causing functional defects teach nothing about the possibilities of improving the performances of the “wild type”. Only mutants outperforming the wild type can teach about possibilities of life’s reinforcement. Bacterium *Deinococcus radiodurans* is *par excellence* such natural “mutant” capable of surviving treatments that kill most uni- and multi-cellular organisms hundred times over: for instance extreme exposures to radiation, toxic chemicals and radical dehydration (desiccation). The marine medusa *Turritopsis nutricula* is another kind of robust organism because of its apparent immortality.

Recent work of his research group on *D. radiodurans* and robust Bdelloid rotifers shows that the extraordinary efficiency for repairing over a thousand DNA double-strand breaks (DSBs) per cell is not due to evolution of special repair proteins but results from the evolved general protection of standard DNA repair systems, as well as all other proteins, against their inactivation by radiation-induced (and other) reactive oxygen species (ROS). Entire proteome is protected, apparently by a cocktail of ROS-neutralizing metabolites, and acts equally efficiently on *E. coli* proteome and human proteins. We have shown that the chemistry of cell death is protein damage, rather than DNA damage. The impact of these discoveries on the research of aging, biotechnology, bioremediation, and on public health, will be discussed.

Vassilios Roussis is Director of the Laboratory of Pharmacognosy and Chemistry of Natural Products, at the University of Athens. The Mediterranean algae biodiversity comprises endemic species as well as recently colonized species, originating from the Atlantic Ocean and the Red Sea. Economics determine the direction of all industries today and the algal products industry is no exception. The algal product industry of today focuses on the farming of edible seaweeds and the production of fine chemicals and polysaccharide phycocolloids. Macroalgae constitute a promising and easily exploitable source of biomass. Macroalgae can be easily cultivated without significant cost and without impact on the environment. The cultivation of the algae can also contribute in the bioremediation of the areas where cultivation will take place. Algal biomass can be derived from invasive species that have already been introduced in the environment as their eradication is unrealistic.

Processing of the algae biomass includes (1) non polar secondary metabolites for use in the pharmaceutical industry, food supplements, growth hormones for agriculture, biodiesel and new agents against biofouling; and (2) the remaining biomass can be used for the production of polysaccharides new chemicals and production of bio ethanol. There is a pressing need to

- develop new antifouling agents. Invasive algae contain such chemicals that can replace the toxic and persistent heavy metal complexes that were used for the

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- control of biofouling;
- develop technology for the efficient incorporation of such biodegradable metabolites in nano spheres of copper dioxide that would increase their efficiency and life span;
- develop new methods for the processing of remaining algal biomass for the production of fine chemicals, bioethanol, biobutanol or other compounds that would provide new eco friendly energy sources.

Lucio Sabbadini is Manager R&S at the Ligurian regional Marine and Maritime Cluster (DLTM) in Italy. This organization has the scope to support research activities, to boost the transfer of research results into innovations, to address the educational path to future technologies.

The blue biotech, on their understanding, have a great potential to give an answer to some research topics:

- prevention of disease of fish in seawater farming, which affect wild species
- development of natural antifouling
- identification of new/advanced bio-indicators to monitor the environmental condition on critical areas

Following what above, they are considering to be more proactive in the blue biotech field - e.g. supporting research-industry matching events and applied research projects, etc.

Candan Tamerler is Professor and Chair in the Molecular Biology and Genetics Department and the director of Molecular Biology-Biotechnology and Genetics Research Center in Istanbul Technical University.. She also works at the Genetically Engineered Materials Science and Engineering Center (NSF-MRSEC), and holds a long term visiting professor position at the Department of Materials Science and Engineering, University of Washington, Seattle, USA. She has been one of the first researchers in Molecular Biomimetics, adapting biocombinatorial approaches for the selection of solid binding peptides, and their implementations in materials science and biotechnology. Candan focuses her research in protein/peptide biotechnology, in recent years; her focus is more on the fundamental understanding of the bio/nano interface and the practical implementation of the engineered hybrid materials systems using engineered polypeptides as the major building blocks for the bio-nanotechnological applications. She continues to serve her expertise in the post selection engineering of peptides to tailor their structure and function for the desired materials interactions, and use them as the utility in materials assembly and bionanofabrication.

Nature provides inspiration for engineering structural and processing design criteria for the fabrication of the practical materials to perform life's functions. During the last two decades, the realization that nanoscale materials have interesting physical characteristics based on their nanometer scale size driven the potentials

and expectation in both engineering and medical systems. The high organization observed at the molecular-, nano-, micro and macro scales in biological materials ultimately result in myriad of different soft and hard tissues. Right now, there is an increasing awareness on rather than mimicking these structures, towards producing them using biological routes. Brick and mortar architecture with layered segmented aragonite tiles of nacre; complex architecture of calcite single crystals in sea urchin; lens shaped tips of the spicules of sponges with excellent light collection properties; diatoms-microscopic algae with symmetric patterns of micrometric and nanometric pores from light guiding to immobilization/separation processes, surface adhesion of mussels, barnacles, sea stars, toxins as pharmacological agents are among the attractive examples with technological relevance. In the recent years, bold novel approaches with transformative character started to appear in marine science, and these may revolutionize the use of marine resources. Undiscovered diversity addressed with a wide range of opportunities possibly will launch new platforms where the new genes, new biological components, new hybrid systems will forefront the need of biobased approaches applicable to bio- and nanotechnologies. The complexity, and largely unexplored aspect of this area require fully integrated interdisciplinary teams to work together to face the challenges and make opportunities achievable.

Kiminori Ushida is Senior Research Scientist at the Supramolecular Science Laboratory, RIKEN (The Institute of Physical and Chemical Research) in Japan.

His lab recently founds a novel mucin which is common in various species of jellyfish and structural analysis has been almost completed. This mucin, different from conventional ones taken from mammals, has exceptionally simple structure and low glycoforms and therefore can be utilized as well-defined mucin source in an industrial scale. Mucins are entirely important for every animal including human but have not been provided as single material suitable for general application. His lab would like to open up "mucin chemistry" where they can get designer mucins as our own will from this jellyfish mucin. Now he is very interested in the extraction of extracellular substance from jellyfishes some of which may very useful as substitution of our own extracellular substance.

He provided an interesting movie showing a fight of set-net fishermen with mass occurrence (>5000) of giant jellyfish (>100kg) that happens everyday for small fishing company in autumn giving high social, economical, and emotional damage to fishermen and their community.

Maria (Maro) Varvate is co-founder and Managing Director of OceanFinance-Marine Intelligence Consultants. She holds a Diploma and Master of Engineering (2002) in Naval Architecture and Marine Engineering from the National Technical University of Athens, a Master in Corporate Finance (2004) from the SDA Bocconi, Milano and a Master in Business Administration (2007) from the Athens University of Economics and Business.

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In 2006, the R&D oriented consulting company OceanFinance was established with the aim to provide the shipping market with advanced methodologies of financial engineering and consulting in green transportation solutions. Her main responsibilities in the company are the implementation of feasibility studies for new-technology projects as well as the application of key performance indicators methodologies for corporate performance measurement in shipping.

OceanFinance is the exclusive R&D provider of a number of leading shipping and trading companies on a worldwide basis. In this capacity, it has collaborated extensively with the Laboratory for Maritime Transport of the NTUA in a number of cooperative European projects providing market knowledge and end-user feedback on the application of the respective research methodologies (i.e. SuperGreen, Envishipping et al). Finally, the company invested - through a Joint Venture - in the project Adriatic Lines (Marco Polo II awarded) aiming to shift over the first 3 years, 1.111,6 million tons km from EU road and reduce the transit time of freight for the East European (mostly Greece, Turkey, Bulgaria, Balkans) with West European Markets.

Wojciech Wawrzynski is Professional Secretary for scientific cooperation at the International Council for the Exploration of the Sea (ICES), Copenhagen, Denmark. His background is in economics and science management and his major fields of research are efficiency of various financial mechanisms for the European Research Area and science communication. Formerly Head of the Coordination and Promotion of Research Unit at the Sea Fisheries Institute in Gdynia, Poland, he is currently manager of the MARCOM+ EU Project.

Roland Wohlgemuth is researcher at Sigma-Aldrich. Marine microbes in seawater and their complex metabolic processes are involved in global carbon, nitrogen, oxygen and phosphorus cycles and essential for the maintenance of ocean life. It is therefore of fundamental interest to understand primary bio-mass production in the oceans, light harvesting and carbon fixation, primary recycling of waste/nutrients. Only 0.1% of the microbes in seawater have been estimated to be cultivable. Metagenome approaches have proven extremely useful for the exploration of microbial biodiversity in marine environments. Functional approaches for the exploration of C 1-chemistry is both of fundamental, applied and practical interest.

Once the feasibility of a biocatalytic reaction or a sequence of multistep biocatalytic reactions have been proven, up- and downscaling experiments have been useful for engineering the most adequate process design. Spatial and temporal organisation of biocatalysts, reactands or products is another interesting engineering option for biocatalytic process design. Communication across scientific and technological disciplines including the value creation perspective is important for the development of the final marine product-in-the-bottle. Whether the successful problem solution will come from marine sciences, biology, chemistry or engineering, progress in the understanding of the molecular mechanisms of enzyme action will be key for the further development of the science of synthesis, marine metabolic pathways and

life on our planet in the 21st century.

Michail M. Yakimov is Head of Laboratory of Marine Molecular Microbiology and Biotechnology at the Institute for Coastal Marine Environment (IAMC-CNR, Messina, Italy) and more than 15 years is working in the field of marine petroleum microbiology. He is pioneering the isolation and study of obligate marine hydrocarbonoclastic bacteria and discovered several new genera: *Alcanivorax*, *Oleiphilus*, *Oleispira*, *Thalassolituus*. In the frame of past and ongoing EC Projects, Yakimov's Lab characterised the petroleum-degrading microbial communities, performed the sequencing and functional analysis of their genomes, studied their proteome response to the number of environmental stimuli, and characterised the crude-oil induced proteins and enzymes in a number of marine environments including deep-sea. Importantly, together with University of Bangor Yakimov's Lab have completed the genome sequencing and functional analysis on the psychrophilic oil degrader *Oleispira antarctica* which appears to be an important member in the deep-sea oil degrading microbial community in the Gulf of Mexico (Science, 2010, 330 (6001): 204-208. During the Workshop, Dr. Michail M. Yakimov will present the recent achievements in the field of marine petroleum microbiology including the data on *in situ* bioremediation experiments oriented to cleanup the sediments heavily contaminated with aliphatic and polyaromatic hydrocarbons.





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