

## A new network for the advancement of marine biotechnology in Europe and beyond

Rotter, Ana; Bacu, Ariola; Barbier, Michèle; Bertoni, Francesco; Bones, Atle; Cancela, Leonor; Carlsson, Jens; Carvalho, Maria; Ceglowska, Marta; Dalay, Meltem; Dailianis, Thanos; Deniz, Irem; Drakulovic, Dragana; Dubnika, Arita; Einarsson, Hjörleifur; Erdogan, Aysegül; Erolodogan, Tufan; Ezra, David; Fazi, Stefano; FitzGerald, Richard; Gargan, Laura; Gaudencio, Susana; DeNardis, Nadica; Joksimovic, Danijela; Katarzyte, Marija; Kotta, Jonne; Mandalakis, Manolis; Matijosyte, Inga; Mazur-Marzec, Hanna; Massa-Gallucci, Alexia; Mehiri, Mohamed; Nielsen, Søren Laurentius; Novoveská, Lucie; Overlinge, Donata; Portman, Michelle; Pyrc, Krzysztof; Rebours, Céline; Reinsck, Thorsten; Reyes, Fernando; Rinkevich, Baruch; Robbins, Johan; Rudovica, Vita; Sabotic, Jerica; Safarik, Ivo; Talve, Siret; Tasdemir, Deniz; Schneider, Xenia; Thomas, Olivier; Torunska-Sitarz, Anna; Varese, Giovanna; Vasquez, Marlen

*Published in:*  
Frontiers in Marine Science

*DOI:*  
[10.3389/fmars.2020.00278](https://doi.org/10.3389/fmars.2020.00278)

*Publication date:*  
2020

*Document Version*  
Publisher's PDF, also known as Version of record

*Citation for published version (APA):*  
Rotter, A., Bacu, A., Barbier, M., Bertoni, F., Bones, A., Cancela, L., Carlsson, J., Carvalho, M., Ceglowska, M., Dalay, M., Dailianis, T., Deniz, I., Drakulovic, D., Dubnika, A., Einarsson, H., Erdogan, A., Erolodogan, T., Ezra, D., Fazi, S., ... Vasquez, M. (2020). A new network for the advancement of marine biotechnology in Europe and beyond. *Frontiers in Marine Science*, 7(7), Article 278. <https://doi.org/10.3389/fmars.2020.00278>

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain.
- You may freely distribute the URL identifying the publication in the public portal.

### Take down policy

If you believe that this document breaches copyright please contact [rucforsk@kb.dk](mailto:rucforsk@kb.dk) providing details, and we will remove access to the work immediately and investigate your claim.



# A New Network for the Advancement of Marine Biotechnology in Europe and Beyond

## OPEN ACCESS

### Edited by:

Sachin Kumar,  
Sardar Swaran Singh National  
Institute of Renewable Energy, India

### Reviewed by:

Paula Branquinho Andrade,  
University of Porto, Portugal  
Aldo Nicosia,  
Institute for Biomedical Research  
and Innovation, Italian National  
Research Council, Italy  
Angela Cuttitta,  
Italian National Research Council, Italy

### \*Correspondence:

Ana Rotter  
ana.rotter@nib.si

### Specialty section:

This article was submitted to  
Marine Biotechnology,  
a section of the journal  
Frontiers in Marine Science

**Received:** 05 January 2020

**Accepted:** 07 April 2020

**Published:** 12 May 2020

### Citation:

Rotter A, Bacu A, Barbier M,  
Bertoni F, Bones AM, Canela ML,  
Carlsson J, Carvalho MF,  
Ceglowska M, Dalay MC, Dailianis T,  
Deniz I, Drakulovic D, Dubnika A,  
Einarsson H, Erdoğan A,  
Eroldoğan OT, Ezra D, Fazi S,  
FitzGerald RJ, Gargan LM,  
Gaudêncio SP, Ivošević DeNardis N,  
Joksimovic D, Kataržytė M, Kotta J,  
Mandalakis M, Matijošytė I,  
Mazur-Marzec H, Massa-Gallucci A,  
Mehiri M, Nielsen SL, Novoveská L,  
Overlingé D, Portman ME, Pyrc K,  
Rebours C, Reinsch T, Reyes F,  
Rinkevich B, Robbins J, Rudovica V,  
Sabotić J, Safarik I, Talve S,  
Tasdemir D, Schneider XT,  
Thomas OP, Toruńska-Sitarz A,  
Varese GC and Vasquez MI (2020) A  
New Network for the Advancement  
of Marine Biotechnology in Europe  
and Beyond. *Front. Mar. Sci.* 7:278.  
doi: 10.3389/fmars.2020.00278

Ana Rotter<sup>1\*</sup>, Ariola Bacu<sup>2</sup>, Michèle Barbier<sup>3</sup>, Francesco Bertoni<sup>4</sup>, Atle M. Bones<sup>5</sup>,  
M. Leonor Canela<sup>6</sup>, Jens Carlsson<sup>7</sup>, Maria F. Carvalho<sup>8</sup>, Marta Ceglowska<sup>9</sup>,  
Meltem Conk Dalay<sup>10</sup>, Thanos Dailianis<sup>11</sup>, Irem Deniz<sup>12</sup>, Dragana Drakulovic<sup>13</sup>,  
Arita Dubnika<sup>14</sup>, Hjörleifur Einarsson<sup>15</sup>, Aysegül Erdoğan<sup>16</sup>, Orhan Tufan Eroldoğan<sup>17</sup>,  
David Ezra<sup>18</sup>, Stefano Fazi<sup>19</sup>, Richard J. FitzGerald<sup>20</sup>, Laura M. Gargan<sup>7</sup>,  
Susana P. Gaudêncio<sup>21</sup>, Nadica Ivošević DeNardis<sup>22</sup>, Danijela Joksimovic<sup>13</sup>,  
Marija Kataržytė<sup>23</sup>, Jonne Kotta<sup>24</sup>, Manolis Mandalakis<sup>11</sup>, Inga Matijošytė<sup>25</sup>,  
Hanna Mazur-Marzec<sup>26</sup>, Alexia Massa-Gallucci<sup>27</sup>, Mohamed Mehiri<sup>28</sup>,  
Søren Laurentius Nielsen<sup>29</sup>, Lucie Novoveská<sup>30</sup>, Donata Overlingé<sup>23</sup>,  
Michelle E. Portman<sup>31</sup>, Krzysztof Pyrc<sup>32</sup>, Céline Rebours<sup>33</sup>, Thorsten Reinsch<sup>34</sup>,  
Fernando Reyes<sup>35</sup>, Baruch Rinkevich<sup>36</sup>, Johan Robbins<sup>37</sup>, Vita Rudovica<sup>38</sup>,  
Jerica Sabotić<sup>39</sup>, Ivo Safarik<sup>40,41</sup>, Siret Talve<sup>42</sup>, Deniz Tasdemir<sup>43,44</sup>,  
Xenia Theodotou Schneider<sup>45</sup>, Olivier P. Thomas<sup>46</sup>, Anna Toruńska-Sitarz<sup>26</sup>,  
Giovanna Cristina Varese<sup>47</sup> and Marlen I. Vasquez<sup>48</sup>

<sup>1</sup> Marine Biology Station Piran, National Institute of Biology, Piran, Slovenia, <sup>2</sup> Department of Biotechnology, Faculty of Natural Sciences, University of Tirana, Tirana, Albania, <sup>3</sup> Institute for Science and Ethics, Nice, France, <sup>4</sup> Institute of Oncology Research, Faculty of Biomedical Sciences, USI, and Oncology Institute of Southern Switzerland (IOSI), Bellinzona, Switzerland, <sup>5</sup> Cell, Molecular Biology and Genomics Group, Department of Biology, Norwegian University of Science and Technology, Trondheim, Norway, <sup>6</sup> Department of Biomedical Sciences and Medicine, CCMAR, CBMR/ABC, University of Algarve, Faro, Portugal, <sup>7</sup> Area 52 Research Group, School of Biology and Environmental Science/Earth Institute, University College Dublin, Dublin, Ireland, <sup>8</sup> Interdisciplinary Centre of Marine and Environmental Research, University of Porto, Porto, Portugal, <sup>9</sup> Marine Biochemistry Laboratory, Institute of Oceanology, Polish Academy of Sciences, Sopot, Poland, <sup>10</sup> Department of Bioengineering, Faculty of Engineering, Ege University, İzmir, Turkey, <sup>11</sup> Institute of Marine Biology, Biotechnology and Aquaculture, Hellenic Centre for Marine Research, Heraklion, Greece, <sup>12</sup> Department of Bioengineering, Faculty of Engineering, Manisa Celal Bayar University, Manisa, Turkey, <sup>13</sup> Institute of Marine Biology, University of Montenegro, Kotor, Montenegro, <sup>14</sup> Rudolfs Cimdins Riga Biomaterials Innovations and Development Centre, Institute of General Chemical Engineering, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga, Latvia, <sup>15</sup> Department of Natural Resource Sciences, University of Akureyri, Akureyri, Iceland, <sup>16</sup> Application and Research Center for Testing and Analysis, Ege University, İzmir, Turkey, <sup>17</sup> Department of Aquaculture, Faculty of Fisheries, Cukurova University, Adana, Turkey, <sup>18</sup> Department of Plant Pathology and Weed Research, ARO The Volcani Center, Rishon LeZion, Israel, <sup>19</sup> Water Research Institute, IRSA-CNR, Rome, Italy, <sup>20</sup> Department of Biological Sciences, University of Limerick, Limerick, Ireland, <sup>21</sup> UCIBIO-Applied Molecular Biosciences Unit, Department of Chemistry, Blue Biotechnology and Biomedicine Lab, Faculty for Sciences and Technology, NOVA University of Lisbon, Caparica, Portugal, <sup>22</sup> Ruđer Bošković Institute, Zagreb, Croatia, <sup>23</sup> Marine Research Institute, Klaipėda University, Klaipėda, Lithuania, <sup>24</sup> Estonian Marine Institute, University of Tartu, Tallinn, Estonia, <sup>25</sup> Institute of Biotechnology, Life Sciences Center, Vilnius University, Vilnius, Lithuania, <sup>26</sup> Division of Marine Biotechnology, Faculty of Oceanography and Geography, University of Gdańsk, Gdynia, Poland, <sup>27</sup> AquaBioTech Group, Mosta, Malta, <sup>28</sup> Marine Natural Products Team, Institute of Chemistry of Nice, CNRS, UMR 7272, University Nice Côte d'Azur, Nice, France, <sup>29</sup> Department of Science and Environment, Roskilde University, Roskilde, Denmark, <sup>30</sup> Scottish Association for Marine Science, Scottish Marine Institute, Oban, United Kingdom, <sup>31</sup> MarCoast Ecosystems Integration Lab, Technion Israel Institute of Technology, Haifa, Israel, <sup>32</sup> Virogenetics Laboratory of Virology, Malopolska Centre of Biotechnology, Jagiellonian University, Krakow, Poland, <sup>33</sup> Moreforskning Ålesund AS, Ålesund, Norway, <sup>34</sup> Institute of Crop Science and Plant Breeding, Christian-Albrechts-Universität zu Kiel, Kiel, Germany, <sup>35</sup> Fundación MEDINA, Granada, Spain, <sup>36</sup> Israel Oceanographic and Limnological Research, National Institute of Oceanography, Haifa, Israel, <sup>37</sup> Flanders Research Institute for Agriculture, Fisheries and Food, Ostend, Belgium, <sup>38</sup> Department of Analytical Chemistry, University of Latvia, Riga, Latvia, <sup>39</sup> Department of Biotechnology, Jožef Stefan Institute, Ljubljana, Slovenia, <sup>40</sup> Department of Nanobiotechnology, Biology Centre, ISB, CAS, České Budějovice, Czechia, <sup>41</sup> Regional Centre of Advanced Technologies and Materials, Palacký University, Olomouc, Czechia, <sup>42</sup> Research and Development Department, Ministry of Rural Affairs, Tallinn, Estonia, <sup>43</sup> GEOMAR Centre for Marine Biotechnology (GEOMAR-Biotech), Research Unit Marine Natural Products

Chemistry, GEOMAR Helmholtz Centre for Ocean Research, Kiel, Germany, <sup>44</sup> Faculty of Mathematics and Natural Sciences, Kiel University, Kiel, Germany, <sup>45</sup> XPRO Consulting Limited, Nicosia, Cyprus, <sup>46</sup> Marine Biodiscovery, School of Chemistry and Ryan Institute, National University of Ireland, Galway, Galway, Ireland, <sup>47</sup> Department of Life Sciences and Systems Biology – Mycotheca Universitatis Taurinensis, University of Turin, Turin, Italy, <sup>48</sup> Department of Chemical Engineering, Cyprus University of Technology, Limassol, Cyprus

Marine organisms produce a vast diversity of metabolites with biological activities useful for humans, e.g., cytotoxic, antioxidant, anti-microbial, insecticidal, herbicidal, anticancer, pro-osteogenic and pro-regenerative, analgesic, anti-inflammatory, anti-coagulant, cholesterol-lowering, nutritional, photoprotective, horticultural or other beneficial properties. These metabolites could help satisfy the increasing demand for alternative sources of nutraceuticals, pharmaceuticals, cosmeceuticals, food, feed, and novel bio-based products. In addition, marine biomass itself can serve as the source material for the production of various bulk commodities (e.g., biofuels, bioplastics, biomaterials). The sustainable exploitation of marine bio-resources and the development of biomolecules and polymers are also known as the growing field of marine biotechnology. Up to now, over 35,000 natural products have been characterized from marine organisms, but many more are yet to be uncovered, as the vast diversity of biota in the marine systems remains largely unexplored. Since marine biotechnology is still in its infancy, there is a need to create effective, operational, inclusive, sustainable, transnational and transdisciplinary networks with a serious and ambitious commitment for knowledge transfer, training provision, dissemination of best practices and identification of the emerging technological trends through science communication activities. A collaborative (net)work is today compelling to provide innovative solutions and products that can be commercialized to contribute to the circular bioeconomy. This perspective article highlights the importance of establishing such collaborative frameworks using the example of Ocean4Biotech, an Action within the European Cooperation in Science and Technology (COST) that connects all and any stakeholders with an interest in marine biotechnology in Europe and beyond.

**Keywords:** marine biotechnology, marine natural products, blue growth, marine biodiversity and chemodiversity, responsible research and innovation, stakeholder engagement, science communication, sustainability

## INTRODUCTION

During four billion years of evolution in the ocean, marine organisms have evolved in their environment to biosynthesize a plethora of biopolymers and biomolecules. These include the unique secondary metabolites that are produced in response to environmental stimuli. They play important biological roles in improving competitiveness, providing chemical defense against predators or competitors and facilitating reproductive processes. These biomolecules are not always essential for the growth and development of the organism, but they are important for the survival and well-being in its environment. Furthermore, some compounds such as marine enzymes have properties essential for industrial applications like thermostability or tolerance to a diverse range of pH and salinity conditions. These properties are being utilized in various industries such as in the food, animal feed, leather, textile and horticulture industries, and in bioconversion and bioremediation processes (Rao et al., 2017). Marine biotechnology appeared in the 1960s and 1970s

when scientists realized the potential of living organisms and their natural products for industrial exploitation (Dias et al., 2012). Initially, the investigation of marine ecosystems relied on the easily accessible organisms like corals and sponges as well as macroalgae that have high biomass levels and were representative of targeted ecosystems (Greco and Cinquegrani, 2016). Therefore, most of the known natural products deriving from the marine environment were initially isolated from macro-organisms. On realizing that marine microbial biodiversity is vast, largely underexplored and unexploited, the application of marine microbial biotechnology aiming to valorize marine resources is a natural step forward in the development of the biotechnology sector.

For a long time, it has been considered that only around 1% of the whole marine microbial population could be cultured under laboratory conditions (Vartoukian et al., 2010). However, recent findings suggest the percentage of culturable microbial population is higher; an estimated 13–78% of genera are cultured, depending on the environment (Lloyd et al., 2018). For example,

environments with high human engagement and disease-driven research benefit from greater culturing effort (Lloyd et al., 2018; Steen et al., 2019). Since many cells in non-human environments belong to novel phyla, new culturing approaches and innovations will increase the percentage of uncultured microbes (Steen et al., 2019). Culture-independent methods using omics approaches are nowadays used to detect microorganisms that are yet uncultured. These methods include high-throughput sequencing, metagenomics, transcriptomics, proteomics, metabolomics, and bioinformatics resources for the identification of organisms and elucidation of metabolic pathways responsible for production of chemical compounds, as well as DNA-based or heterologous expression systems. Microbial identification is only an initial step and additional research is essential to develop cultivation techniques to obtain the necessary biomass in a sustainable manner. Next, biochemical and genetic engineering methods are required for the production of high quantities and quality of proteins, marine oils and other secondary metabolites of interest. **Figure 1** provides a schematic representation of parameters that should be considered for the whole bioprospecting process, starting from the selection of marine organisms, for their cultivation prior to their utilization for the biosynthesis of high-value bio-components and for investigation of their biological potential in various industries.

Natural products are currently the most common source of therapeutic agents. The World Health Organization estimates that approximately 80% of the world's population uses remedies based on natural products to treat their basic health problems. Over 35,000 bioactive compounds have been isolated and chemically characterized from marine organisms since the 1960s (Lindequist, 2016). While before 1985 less than 100 natural products were discovered annually, in the late 1990s, this number rose to over 500 new products discovered yearly up to over 1,000 since 2008, mainly due to the advances in analytical methods (Lindequist, 2016; Carroll et al., 2019). The application of new dereplication strategies using mass spectrometry (MS) and the use of high-resolution Nuclear Magnetic Resonance (NMR) spectrometers with cryoprobes have enabled the discovery of new natural products even at the nanomole scale (Klitgaard et al., 2014). The most common approach used for the discovery of new marine bioactive chemical entities involves the screening of crude extracts or partially purified fractions of similar polarities against selected test organisms or therapeutic targets, followed by the purification and the structure elucidation of the active ingredients. The purification of metabolites is usually performed by means of chromatographic separation techniques combined with high-resolution MS based approaches that allow a rapid and accurate identification of the molecular mass and formulae of bioactive compounds. These methods are becoming a gold standard for the rapid and reliable dereplication of natural product extracts or fractions (Gaudêncio and Pereira, 2015).

The unique structural architecture and broad range of activities exhibited by marine metabolites have caught the attention of the scientific community. This has resulted in the development of research programs promoting innovation

and industrial uptake along with the creation of new jobs and of a competitive environment for biotechnology-oriented enterprises as stated in the Blue Growth Strategy of the European Union (EU). This orientation is in line with the strategy for “A sustainable bioeconomy for Europe: strengthening the connection between economy, society and environment” which is a 2018 update from the original 2012 Bioeconomy Strategy by the European Commission (EC). The strategy aims to create a more innovative, resource-efficient and competitive society that will reconcile drug discovery and food security with the sustainable and economically viable use of renewable resources for industrial purposes while ensuring environmental protection.

## PREREQUISITES FOR MARINE BIOTECHNOLOGY

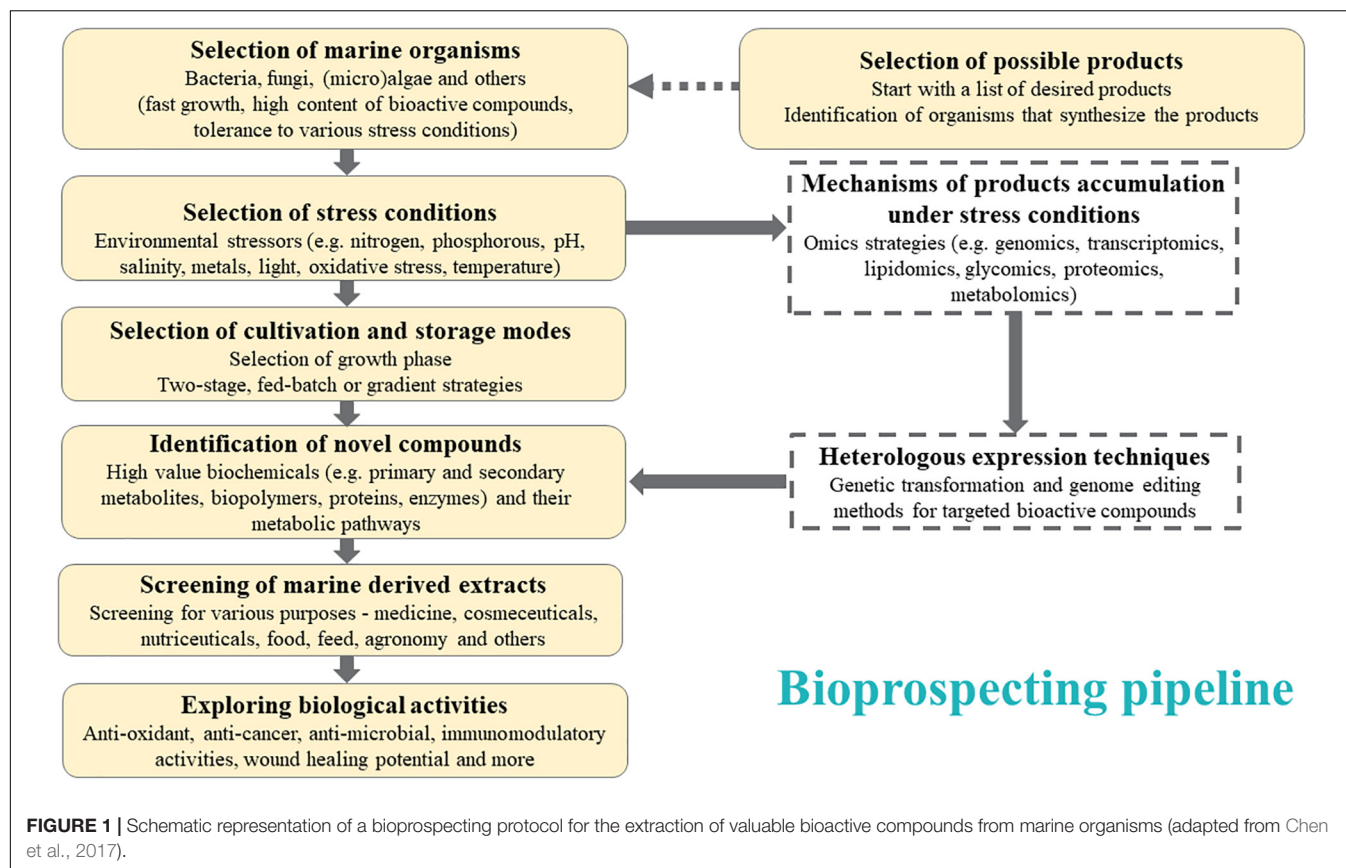
### Sustainability

There are two sustainability levels that must be considered to effectively implement marine biotechnology in practice: (i) environmental and (ii) supply sustainability. (i) Environmental sustainability tackles the main sources of marine biomass which come either from species harvested in nature or from those that can be cultivated. It is especially relevant when wild stocks are the only source of supply and they are over-harvested, or where targeted marine species are rare, in the deep, or difficult to re-sample. The harvesting/sourcing of any target species should thus not threaten marine biodiversity and the future availability of target species. To minimize the environmental impact, the biotechnology community should consider valorizing side and waste streams and co-products, target sustainably cultured marine organisms and those that are sufficiently productive to supply specific high added-value biomolecules. (ii) Sustainable supply of biomolecules represents key bottlenecks, as they are usually present in trace amounts. To guarantee a sustainable sourcing and production of target compounds, biologically active molecules or whole organisms should therefore be considered in a life cycle assessment and a multi-risk environmental analysis context. This will attain a global evaluation including environmental, health and economic aspects for both the biological (sourcing) and technical (supplying) cycle. Industrial symbiosis and circular economy approaches must therefore be applied to find sustainable ways for utilization of marine bioresources (blue growth) using green production techniques that economize on exhaustible resources (green growth, Rodrik, 2014).

### Industry

Marine biotechnology generates various products and services, from the production of biofuels, food, feedstuffs and products for use in agriculture (high-volume, low-value, and low-risk products), to the discovery of new biomaterials, cosmetics, nutraceuticals and pharmaceuticals (low-volume, high-value and high-risk products). Research and development investments for





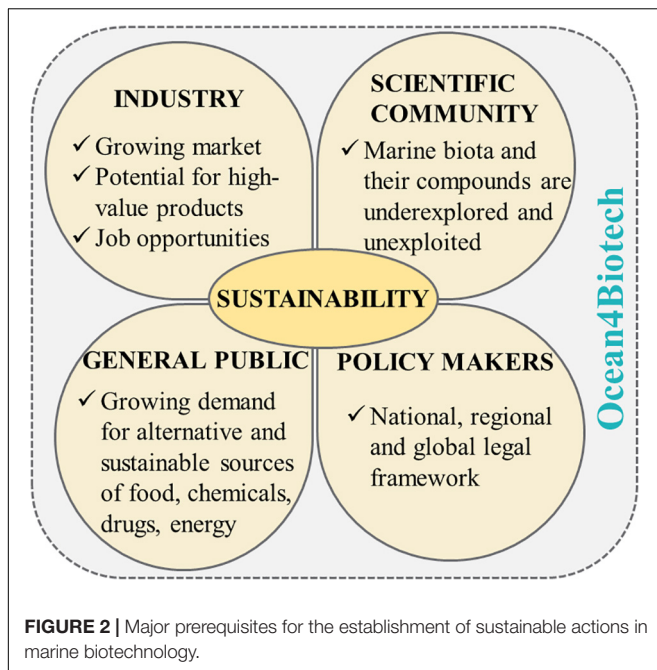
the discovery of marine-derived drugs entail high levels of capital expenditure and risk tolerance, as they require the use of state-of-the-art infrastructures and many years of basic and applied research (Figure 2). Despite some limitations, there are successful examples, as to date there are ten approved drugs, one example being trabectedin (ET-743), a product isolated from a Caribbean sea squirt *Ecteinascidia turbinata*, which is used for the treatment of advanced soft tissue sarcoma. This product first reached the market in 2007, after 20 years of research (Cuevas and Francesch, 2009). In practice, out of every 2,500 analogs from the marine environment that enter preclinical testing, only one may be safe and effective enough to reach clinical use (Gerwick and Fenner, 2013). There is a collaboration and communication gap between raw ideas and materials and their potential laboratory innovation and commercialization (Datta et al., 2014). This is being tackled by adopting three different strategies. (i) Firstly, by stimulating public-private partnerships in consortia that apply for research and innovation funding (such as Horizon 2020 and Horizon Europe, Europe's biggest research and innovation funding resource). (ii) Another alternative are the business incubators (such as Rocket57 in Northern Europe), think tanks or stakeholder events that are often regionally financed to answer strategic regional developmental priorities and present a contact point for joining researchers, small and medium enterprises, industrial representatives and investors. (iii) Financial stimulation of networking activities (the example of

COST Action Ocean4Biotech is presented in the next chapter of this article). The global marine biotechnology market is expected to reach ~\$6.4 billion by 2025<sup>1</sup> and it currently represents only ~1% of the whole biotechnology market. Noteworthy, the oceans cover over 70% of the Earth's surface and contain an estimated 25% of the world's species (Mora et al., 2011), of which most are unknown and undervalorized. Hence, the marine biotechnology market is expected to expand at a much higher pace (Figure 2) when high-throughput techniques and the collaboration between industry, science, general public and policy makers will be routinely used. The predominant players in the European marine biotechnology consist of some 140 micro SMEs (estimated by Ecorys, 2014) and academia that lack the financial stability necessary for sustained and long-term cutting-edge research.

## Scientific Community

To fully explore the ocean and its biota, the current screening and/or cultivation approaches of marine organisms of interest for biotechnological applications need to be optimized (Figure 2). High-throughput techniques produce vast amounts of data and can uncover the biodiversity and the metabolic potential of marine organisms. Hence, knowledge on data management, processing and data analysis to maximize the quality and quantity

<sup>1</sup><https://www.smithers.com/resources/2015/oct/global-market-for-marine-biotechnology>



of resulting information needs to be advanced. Experts from the field of statistics, bioinformatics and chemometrics are essential in biotechnology research groups nowadays and their pipelines and databases should be integrated, harmonized and publicly available to prevent duplication of efforts, reduce the overall costs and support the discovery process.

## General Public

While the world population is rising and is expected to reach over 8.5 billion by 2030, bioresources and available areas for cultivation and manufacture are declining. Hence, there is a growing demand for additional sources of food, drugs, and chemicals (Figure 2). Marine biotechnology has the potential to mitigate these needs both by increasing the current production and by introducing new products in the food, feed, pharmaceutical, nutraceutical, healthcare, welfare, biomaterials, and energy sectors. Nowadays, consumers expect innovative, efficient, safe, sustainable, ethical, financially, and environmentally friendly solutions. We need to raise public awareness and improve communication to a broad audience regarding the benefits of marine biotechnology products to gain consumers' interest in eco-friendly products that meet high standards of sustainability.

## Policy Makers

Some national, regional and global strategies and guidelines are already in place to recommend investment into marine biotechnology and stimulate networking and transdisciplinary collaboration at the international level (Figure 2). These include the United Nations (UN) sustainable development

goals<sup>2</sup>, national and EU legislation that must be developed and harmonized. The UN Convention on the Law of the Sea<sup>3</sup> sets the rules for the exploitation, conservation and management of living marine resources. The Nagoya Protocol on Access to Genetic Resources and Benefit Sharing provides a legal framework aimed at creating transparency for those interested in the production and exploitation of genetic materials. Marine biotechnology development needs also to comply with the Habitats Directive (92/43/EEC) on the conservation of natural habitats and of wild fauna and flora, the Marine Strategy Framework Directive (MSFD) (2008/56/EC, CD 2017/848) establishing a framework for community action in the field of marine environmental policy, the EU Water Framework Directive – WFD (Directive 2000/60/EC), and the Maritime Spatial Planning Directive (2014/89/EU) for the planning of multiple uses of the maritime and coastal areas. Biomolecules and their production processes must also comply with specific regulations related to the targeted application (e.g., EU 2015/2283 Novel Foods and Ingredients, EC No 1223/2009 Cosmetic Regulation, EC No 1924/2006 Nutrition and Health Claims, EC No 1907/2006 REACH Regulation, among others). The widespread acceptance and certification of these novel compounds is a rigorous and time-consuming process where legislative documentation might need updating as novel compounds are being identified. It is thus necessary to encourage collaboration among scientists and policy makers, as outlined during the UNESCO High-Level Conference on the Ocean Decade (2018). Moreover, intellectual property strategies need to be established and agreed upon to conduct research in accordance with ethical recommendations for bioprospecting in the open ocean and beyond the national jurisdictions covered by the Nagoya protocol.

## THE ESTABLISHMENT OF A COLLABORATIVE NETWORK AS A SOLUTION FOR ADVANCING MARINE BIOTECHNOLOGY: COST ACTION Ocean4Biotech

Efficient and sustainable exploitation of the ocean's potential is possible only if industrial actors, researchers, the general public, policy makers and environmental experts work together. This direct interaction among different stakeholders across different countries is not always possible and limited programs have been supported until today that allow a minimal direct transdisciplinary interaction (see more in **Supplementary Table S1**).

From this viewpoint, the EU COST program that was established in 1971 represents an excellent opportunity for the creation of research networks on diverse topics, called COST Actions. These networks offer an open space for collaboration among stakeholders across Europe (and beyond),

<sup>2</sup><https://sustainabledevelopment.un.org/>

<sup>3</sup>[https://www.un.org/depts/los/convention\\_agreements/texts/unclos/unclos\\_e.pdf](https://www.un.org/depts/los/convention_agreements/texts/unclos/unclos_e.pdf)

thereby catalyzing research advancement and innovation<sup>4</sup>. One of the recently approved Actions is CA18238 – European transdisciplinary networking platform for marine biotechnology (Ocean4Biotech)<sup>5</sup>. The motivation behind creation of this network is included in the SWOT analysis (see **Supplementary Table S2** and the discussion therein). Ocean4Biotech is an international, unique and inclusive network that gathers experts from transdisciplinary fields of exact and natural sciences, social sciences and humanities, giving the Action participants the opportunity to work together and share their experiences creating a spill-over effect to foster marine biotechnology and bioeconomy in a sustainable way. Ocean4Biotech will apply the Responsible Research and Innovation Roadmap (Theodotou Schneider, 2019) involving scientists, citizens, policy makers and industry in the co-creation of knowledge and in the establishment of sustainable collaborative networks.

Notably, Ocean4Biotech builds upon existing knowledge from current and past projects and initiatives (see **Supplementary Table S1**). It aims to establish strong collaborations to avoid the duplication of efforts. The difference between Ocean4Biotech and the current and past efforts is this Action is envisaged as a “connecting-the-dots” funnel initiative that will gather scientists and professionals from all areas related to the marine biotechnology field. This enables a wider approach aiming to facilitate the circular economy in the marine biotechnology sector. Researchers from all fields and levels of expertise relevant to marine biotechnology will have the opportunity to participate in the Action and will be included in knowledge exchange activities (between the scientific fields as well as within, e.g., senior-to-junior knowledge transfer), establishing new collaborations and having an opportunity for career advancement. The developments from this COST Action can impact the industrial sector, and in turn will most likely influence governance boards. However, the efforts of Ocean4Biotech to establish connections between its members and linkages with other initiatives will not be possible without proactive science communication, extensive dissemination along with active engagement and outreach activities. Efficient communication will enable informing on the activities and objectives of the Action and will attract researchers to prepare and initiate new collaborations that will span beyond the lifetime of Ocean4Biotech.

## HOW WILL Ocean4Biotech FOSTER ADVANCES IN THE FIELD OF MARINE BIOTECHNOLOGY?

There are five general objectives within the Ocean4Biotech COST Action:

(1) **Description of marine biodiversity.** Knowledge of marine biodiversity is still limited. Moreover, there is a large interregional variability in species distribution and in their taxonomic knowledge. The lack of experts in marine species

taxonomy, duplicates/redundancies/inconsistencies in the primary nucleotide databases, lack of type species and polyphyly of traditionally established taxa result in many misidentified or unidentified species/strains (many of which hold great potential for biotechnological applications). These are also important challenges to marine natural product programs. Hence, human resources, research effort, time and cost-efficient methods are needed to overcome the current gap in knowledge on biological and chemical diversity in marine ecosystems. These may be addressed by high-throughput methods that facilitate the discovery, classification and supply of organisms. However, high-throughput methods for biodiversity monitoring have not been routinely adopted and the methodology for biodiscovery is often not standardized. In fact, bioinformatics pipelines and big data analyses are changing the landscape for marine biotechnology, as around 18,000 new species are uncovered yearly<sup>6</sup>. Ocean4Biotech will propose operating procedures for uncovering the biodiversity using high-throughput methods, such as DNA barcoding approaches (Leese et al., 2016). These methods can then be combined with a more quantitative assessment by *in situ* hybridization techniques that allow the quantification and localization of specific microbial clusters within the environmental matrices. Such biodiversity assessment provides crucial information for subsequent monitoring and exploitation of marine organisms. The environmental impacts of such biological prospecting are considered minimal at the early stages of sampling, where the size of samples collected is small. Moreover, the standardization of the biodiscovery process is necessary as chemodiversity, even in the same taxa, greatly varies along geographical and environmental gradients, as well as seasonally and timely along the life cycle of organisms.

(2) **Natural product discovery** is a process involving separation techniques in parallel with biological screening, followed by structure elucidation of the pure bioactive metabolites. If the target compound from a given species shows biotechnological potential, scale-up production and supply will certainly increase the environmental impact. However, the organic synthesis of the compound (although time-consuming and expensive) and/or production of the compound of interest using biological synthesis generally overcome the need for repeated collection and over-exploitation of the natural ecosystem. Therefore, Ocean4Biotech will build a compendium of pipelines, i.e., methods and procedures, detailed on a case study basis, starting from the creation of marine biorepositories, the identification of the collected species using integrative systematics, screening for specific bioactivities for selected industries, identification of the bioactive metabolites and their sustainable production, business plan development, marketing strategy, where legal and ethical aspects to be considered along with adherence to strict guidelines for protection of the environment and sustainability. These pipelines will serve as guidelines and tutorials for future product development and will

<sup>4</sup><https://www.cost.eu/who-we-are/about-cost/>

<sup>5</sup><https://www.ocean4biotech.eu/>

<sup>6</sup>[https://www.eurekalert.org/pub\\_releases/2018-05/scoe-elt051718.php](https://www.eurekalert.org/pub_releases/2018-05/scoe-elt051718.php)



enable the transfer of knowledge between disciplines. These pipelines will highlight the complementary transdisciplinary aspect of marine biotechnology and as a link with other sectors of biotechnology. According to the principles sustainability the supply chain decision-making will require the inclusion of social and economic aspects together with environmental aspects. Thus, the Action will apply an integrated framework for Life Cycle Sustainability Assessment (LCSA). Wherever possible, it will combine physical LCA considering different environmental impact categories (e.g., climate change, eutrophication or acidification) at different life-cycle levels (partial LCA) with social LCA (SLCA) and Life Cycle Costing (LCC), based on UNEP/SETAC guidelines. The approach used in this Action will build on existing models (Perez-Lopez et al., 2018). It will also follow the methodological framework for conducting LCA as outlined by the International Standards Authority (ISO) 14040 series.

(3) **Sharing infrastructure.** There is an increasing need to create a bridge between research and innovation capabilities from the academia and business sectors. This includes the availability of the research infrastructure, thereby providing access to a range of new tools and facilities to allow marine biotechnology to thrive. Many of the tools and techniques used in marine biotechnology are widely used in other areas of science and technology. Engaging in collaborative research projects is one way of providing access to these facilities and encouraging multidisciplinary research. Ocean4Biotech will enable the diverse actors to share their expertise and infrastructure, mostly through short-term scientific missions and new collaborative activities. Preference will be given to users from the less research-intensive countries<sup>7</sup> or early career investigators that need access to state-of-the-art analytical equipment, microbial cultures or screening facilities.

(4) **Responsible Research and Innovation.** The ocean should be monitored, valorized and governed in a sustainable manner to generate the maximum benefit to science and society but limiting the negative footprints on the marine environment. This will be addressed within the Action by adopting the Responsible Research and Innovation (RRI) concept, which is based on six pillars.

(i) **Ethics.** We are all responsible for the stability and resilience of the Earth systems (Barbier et al., 2018). Accordingly, ethical issues and challenges will be identified, addressed and used to advocate for protection of marine ecosystems and promote responsible resource management and environmental policies together with societal awareness.

(ii) **Open access.** To efficiently co-create knowledge and capitalize from previous research, it is vital to consider transparency, efficiency, traceability, access to data, reciprocal relations, biosafety, nature conservation and transfer of knowledge to third countries.

(iii) **Gender equality** will be promoted throughout the Action by empowering especially early career and female colleagues to

apply for managerial roles and in the future establish and lead consortia for valorization of marine biotechnology products.

(iv) **Governance.** Although the marine biodiversity has no borders, access to natural resources is framed under the Convention of Biological Diversity, promoting the conservation of biodiversity, the sustainable use of biological entities and their fair and equitable sharing. The latter is also covered in the Nagoya Protocol, which provides a legal framework for the fair and equitable sharing of benefits arising from the use of genetic resources which may sometimes delay or block certain research activities.

(v) **Public engagement.** Action participants will employ communication tools and different activities to further inform legislative authorities, researchers and industry with the aim of facilitating the regulatory requirements that are sometimes a bottleneck to transnational collaboration.

(vi) **Science education.** We will focus many of our activities into education of the next generation of researchers (i.e., early career investigators), with a special focus on the countries that are less research intensive, i.e., the so-called inclusiveness target countries<sup>8</sup>. These countries have developed their national strategic priorities in the frame of the EU Smart Specialization Strategy (S3), aiming to ensure a balanced development between regions<sup>8</sup>. Since marine biotechnology, including its products and applications, is well represented in all national S3 priorities, the timing is perfect to develop capacity-building educational opportunities that span beyond the traditional academic curricula. We will enable closing the educational gaps in three ways. (i) By short term scientific missions, which are mobility activities that involve a direct hands-on interaction and experience abroad. (ii) By offering financial opportunities for active participation in conferences that target any of the marine biotechnology related topics. (iii) Importantly, our trainings and workshops, that will be publicly promoted, will cover topics that integrate academy, technological centers and industry (as also promoted by the EuroMarine Working Group, 2019). By offering multidisciplinary skills, this strategy will avoid the risk of training a marine-related workforce that the market may not absorb (EuroMarine Working Group, 2019).

(5) **Knowledge co-creation and integration.** (i) The Action will be geographically inclusive as it will produce an open-access database of exploitable species for marine biotechnology in the Ocean4Biotech participating countries. In addition to the World Register of Marine Species (WoRMS<sup>9</sup>), this Action participants will focus on those species with putative biotechnological potential. (ii) The Action will be inclusive in the biological sense and include species regardless of the kingdom (from bacteria and algae to zooplankton and other species that are suitable for exploitation). (iii) Methodologically, the participants will integrate all levels of the biotechnological pipeline; from bioprospecting to cultivation, biological screening, compound isolation

<sup>7</sup><https://www.cost.eu/who-we-are/cost-strategy/excellence-and-inclusiveness/>

<sup>8</sup><https://ec.europa.eu/jrc/en/research-topic/smart-specialisation>

<sup>9</sup><http://www.marinespecies.org/>



and optimization of the isolation process, and structure elucidation. (iv) This is a truly transdisciplinary Action, integrating expertise and including experts from various fields: marine (micro)biology, chemistry, food science, agriculture, pharmacology, medicine, environmental protection, engineering, energy, data science, omics techniques, statistics, law, policy making, economy, business planning, and more. The network will transfer knowledge from traditional academic institutions to exploitation industries leading to the elaboration of ecosystem services linked to policy makers' priorities, citizens, industry and SMEs.

## CONCLUSION

This Ocean4Biotech COST Action will contribute to the implementation of the Bioeconomy Strategy and the European Green Deal<sup>10</sup>. It will also mainstream the responsible research and innovation principles among the scientific and industry communities to foster the interaction between marine scientists and other marine biotechnology stakeholders, including the general public. Such interaction will be multidirectional rather than top-down and co-creative instead of just being introduced by the authorities and/or knowledge holders. Outreach and communication activities will provide information to the broad community and improve their capacity to understand the challenges and opportunities to make appropriate decisions in the field of marine biotechnology. An inclusive, integrative approach is essential to catalyze the expansion of marine biotechnology in Europe and worldwide and to finally harvest the products of this promising field of research. Finally, the establishment of interdisciplinary connections and collaborations during Ocean4Biotech's lifetime will not only lead to future research collaborations that include industrial representatives as well, but also provide establishment of communication channels with policymakers, governments, and other stakeholders, including the public. This will eventually enable beneficial social and environmental impacts that will ultimately contribute to a more efficient and sustainable use of marine bioresources.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

## AUTHOR CONTRIBUTIONS

AR designed the manuscript concept and drafted the manuscript. All authors read, commented, improved, and approved of the final version of the manuscript.

<sup>10</sup>[https://ec.europa.eu/info/sites/info/files/european-green-deal-communication\\_en.pdf](https://ec.europa.eu/info/sites/info/files/european-green-deal-communication_en.pdf)

## FUNDING

AR and TR: the publication is part of a project that has received funding from the European Union Horizon 2020 Research and Innovation Programme under grant agreement no. 774499 – GoJelly project. AMB: research supported by grant 267474 from Research Council of Norway. MFC: wishes to acknowledge the funding from CEEC program supported by FCT/MCTES (CEECIND/02968/2017); ACTINODEEPSEA project (POCI-01-0145-FEDER-031045) co-financed by COMPETE 2020, Portugal 2020, ERDF and FCT; Strategic Funding UIDB/04423/2020 and UIDP/04423/2020 through national funds provided by FCT and ERDF. AD: supported by the ERDF Activity 1.1.1.2 “Post-doctoral Research Aid” of the Specific Aid Objective 1.1.1, Operational Programme “Growth and Employment” (No. 1.1.1.2/VIAA/1/16/048). MLC: acknowledges funding from Portuguese FCT/UID/Multi/04326/2019, MAR2020 projects/OSTEOMAR/16.02.01-FMP-0057 and ALGASOLE/16.02.01-FMP-0058, INTERREG/ALGARED+ and Atlantic Area/BUEHUMAN/EAPA/151/2016. RF: gratefully acknowledges support from the Marine Institute under the Marine Research Programme by the Irish Government (Grant-Aid Agreement No. PBA/MB/16/01). SG: this work was supported by the Applied Molecular Biosciences Unit-UCIBIO which is financed by national funds from FCT/MCTES (UID/Multi/04378/2019). SG thanks financial support provided by FCT/MCTES through grant IF/00700/2014. AM-G: acknowledges the financial contribution of the project BYTHOS funded by the European Union's Interreg V-A Italia-Malta Programme under project code CI-1.1-9. CR: gratefully acknowledge the Research Council of Norway for their financial contributions through the PROMAC (244244) and the Norwegian Seaweed Biorefinery Platform (294946) projects. XS: acknowledges the funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement no. 710566 for the project MARINA. HM-M, AT-S, and MC: National Science Centre in Poland (project number NCN 2016/21/B/NZ9/02304) and The Statutory Programme of the Institute of Oceanology, PAS (grant no. II.3). MMA and TD: acknowledge the funding from the General Secretariat for Research and Technology (GSRT) and the Hellenic Foundation for Research and Innovation (HRFI) under grant no. 239 (SPINAQUA project). AR: this research was funded by the Slovenian Research Agency (research core funding P1-0245).

## ACKNOWLEDGMENTS

This publication is based upon work from COST Action CA18238 (Ocean4Biotech, <https://www.ocean4biotech.eu/>), supported by COST (European Cooperation in Science and Technology) programme.

## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fmars.2020.00278/full#supplementary-material>

## REFERENCES

- Barbier, M., Reitz, A., Pabortsava, K., Wölfl, A. C., Hahn, T., and Whoriskey, F. (2018). Ethical recommendations for ocean observation. *Adv. Geosci.* 45, 343–361. doi: 10.5194/adgeo-45-343-2018
- Carroll, A. R., Copp, B. R., Davis, R. A., Keyzers, R. A., and Prinsep, M. R. (2019). Marine natural products. *Nat. Prod. Rep.* 36, 122–173. doi: 10.1039/c8np00092a
- Chen, B., Wan, C., Mehmood, M. A., Chang, J.-S., Bai, F., and Zhao, X. (2017). Manipulating environmental stresses and stress tolerance of microalgae for enhanced production of lipids and value-added products—a review. *Bioresour. Technol.* 244, 1198–1206. doi: 10.1016/j.biortech.2017.05.170
- Cuevas, C., and Francesch, A. (2009). Development of Yondelis (trabectedin, ET-743). A semisynthetic process solves the supply problem. *Nat. Prod. Rep.* 26, 322–337. doi: 10.1039/b808331m
- Datta, A., Mukherjee, D., and Jessup, L. (2014). Understanding commercialization of technological innovation: taking stock and moving forward. *R D Manag.* 45, 215–249. doi: 10.1111/radm.12068
- Dias, D. A., Urban, S., and Roessner, U. (2012). A historical overview of natural products in drug discovery. *Metabolites* 2, 303–336. doi: 10.3390/metabo2020303
- Ecorys (2014). Study in support of Impact Assessment work on Blue Biotechnology, Revised Final Report FWC MARE/2012/06 – SC C1/2013/03. Available online at: <https://webgate.ec.europa.eu/maritimeforum/system/files/Blue%20Biotech%20-%20Final%20Report%20final.pdf> (accessed November 23, 2019).
- EuroMarine Working Group (2019). *Strategic Agenda on Enhancement of Human Resources to Support Blue Growth Sectors*. Italy: National Research Council.
- Gaudêncio, S. P., and Pereira, F. (2015). Dereplication: racing to speed up the natural products discovery process. *Nat. Prod. Rep.* 32, 779–810. doi: 10.1039/c4np00134f
- Gerwick, W. H., and Fenner, A. M. (2013). Drug discovery from marine microbes. *Microb. Ecol.* 65, 800–806. doi: 10.1007/s00248-012-0169-9
- Greco, G. R., and Cinquegrani, M. (2016). Firms plunge into the sea. Marine biotechnology industry, a first investigation. *Front. Mar. Sci.* 2:124. doi: 10.3389/fmars.2015.00124
- Klitgaard, A., Iversen, A., Andersen, M. R., Larsen, T. O., Frisvad, J. C., and Nielsen, K. F. (2014). Aggressive dereplication using UHPLC–DAD–QTOF: screening extracts for up to 3000 fungal secondary metabolites. *Anal. Bioanal. Chem.* 406, 1933–1943. doi: 10.1007/s00216-013-7582-x
- Leese, F., Altermatt, F., Bouchez, A., Ekrem, T., Hering, D., Meissner, K., et al. (2016). DNAqua-Net: developing new genetic tools for bioassessment and monitoring of aquatic ecosystems in Europe. *RIO* 2:e11321. doi: 10.3897/rio.2.e11321
- Lindequist, U. (2016). Marine-derived pharmaceuticals – challenges and opportunities. *Biomol. Ther.* 24, 561–571. doi: 10.4062/biomolther.2016.181
- Lloyd, K. G., Steen, A. D., Ladau, J., Yin, J., and Crosby, L. (2018). Phylogenetically novel uncultured microbial cells dominate earth microbiomes. *mSystems* 3:e00055-18. doi: 10.1128/mSystems.00055-18
- Mora, C., Tittensor, D. P., Adl, S., Simpson, A. G. B., and Worm, B. (2011). How many species are there on earth and in the ocean? *PLoS Biol.* 9:e1001127. doi: 10.1371/journal.pbio.1001127
- Perez-Lopez, P., Feijoo, G., and Moreira, M. (2018). “Sustainability assessment of blue biotechnology processes: addressing environmental, social and economic dimensions,” in *Designing Sustainable Technologies, Products and Policies*, eds E. Benetto, K. Gericke, and M. Guiton (Cham: Springer), 475–486. doi: 10.1007/978-3-319-66981-6\_53
- Rao, T. E., Imchen, M., and Kumavath, R. (2017). Marine enzymes: production and applications for human health. *Adv. Food Nutr. Res.* 80, 149–163.
- Rodrik, D. (2014). Green industrial policy. *Oxf. Rev. Econ. Policy* 30, 469–491.
- Steen, A. D., Crits-Christoph, A., Carini, P., DeAngelis, K. M., Fierer, N., Lloyd, K. G., et al. (2019). High proportions of bacteria and archaea across most biomes remain uncultured. *ISME J.* 13, 3126–3130. doi: 10.1038/s41396-019-0484-y
- Theodotou Schneider, X. (2019). *Responsible Research and Innovation Roadmap*. RRI Tool from the MARINA Horizon 2020 project. Available online at: [https://www.researchgate.net/publication/339630196\\_The\\_Responsible\\_Research\\_and\\_Innovation\\_RRI\\_Roadmap#fullTextFileContent](https://www.researchgate.net/publication/339630196_The_Responsible_Research_and_Innovation_RRI_Roadmap#fullTextFileContent) (accessed October 21, 2019).
- Vartoukian, S. R., Palmer, R. M., and Wade, W. G. (2010). Strategies for culture of ‘unculturable’ bacteria. *FEMS Microbiol. Lett.* 309, 1–7.

**Conflict of Interest:** FB: institutional research funds from Acerta, ADC Therapeutics, Bayer AG, Cellectia, CTI Life Sciences, EMD Serono, Helsinn, ImmunoGen, Menarini Ricerche, NEOMED Therapeutics 1, Oncology Therapeutic Development, PIQUR Therapeutics AG; consultancy fee from Helsinn, Menarini; expert statements provided to HTG; travel grants from Amgen, Astra Zeneca, Janssen-Cilag AG, Jazz Pharmaceuticals, PIQUR Therapeutics AG.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The reviewer PA declared a shared affiliation, with no collaboration, with one of the authors, MFC, to the handling Editor at the time of review.

Copyright © 2020 Rotter, Bacu, Barbier, Bertoni, Bones, Cancela, Carlsson, Carvalho, Ceglowska, Dalay, Dailianis, Deniz, Drakulovic, Dubnika, Einarsson, Erdoğan, Eroldogan, Ezra, Fazi, FitzGerald, Gargan, Gaudêncio, Ivošević DeNardis, Joksimovic, Kataržytė, Kotta, Mandalakis, Matijošytė, Mazur-Marzec, Massa-Gallucci, Mehiri, Nielsen, Novoveská, Overling, Portman, Pyrc, Rebours, Reinsch, Reyes, Rinkevich, Robbens, Rudovica, Sabotič, Safarik, Talve, Tasdemir, Schneider, Thomas, Toruńska-Sitarz, Varese and Vasquez. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.