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Bioprospection of marine microorganisms: potential and challenges for Argentina

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ABSTRACT

The marine environments of Argentina have a remarkable extension, as well as high biological productivity and biodiversity of both macro- and microorganisms. Despite having a great potential for biotechnological applications, the microorganisms inhabiting these ecosystems remain mostly unexplored and unexploited. In this review, we study the research topics and the interactions among Argentinean laboratories, by analyzing current articles published on biotechnology-related marine microbiology by researchers of this country. In addition, we identify the challenges and opportunities for Argentina to take advantage of the genetic potential of its marine microorganisms. Finally, we suggest possible actions that could improve the development of this research field, as well as the utilization of this knowledge to solve societal needs.

Key words: bioprospection, marine microorganisms, challenges, Argentina

RESUMEN

Bioprospección de microorganismos marinos: potencialidades y desafíos para Argentina. El medio ambiente marino de la Argentina tiene una notable extensión, como así también una alta productividad biológica y biodiversidad de macro y microorganismos. A pesar de presentar un gran potencial para aplicaciones biotecnológicas, los microorganismos que habitan estos ecosistemas permanecen mayormente inexplorados y sus propiedades aún no explotadas. En este trabajo de revisión, estudiamos los temas de investigación y las interacciones entre grupos de investigación argentinos, por medio del análisis de los artículos publicados hasta el momento en temáticas relacionadas con la aplicación biotecnológica de microorganismos marinos. Además, identificamos los desafíos y las oportunidades para que la Argentina tome ventaja del potencial genético de sus microorganismos marinos. Por último, sugerimos posibles acciones que podrían mejorar el desarrollo de este campo de estudio, como así también la utilización de este conocimiento para resolver las necesidades de la sociedad.

Palabras clave: bioprospección, microorganismos marinos, desafíos, Argentina

INTRODUCTION

Marine microorganisms remain comparatively untapped in relation to those from terrestrial and freshwater environments. As the extent of marine microbial biodiversity, and consequently natural product potential, seems to be limitless (31), marine ecosystems constitute invaluable sources for bioprospection (33). The partnership between biotechnology and the conceptual framework of microbial ecology (41, 69) provides a golden opportunity for bioprospection of these unexplored environments. The use of molecular techniques for further improvement of these natural capabilities, poses few conceptual limits to the services that these communities might provide. In Argentina, microbial communities inhabiting marine environments remain mostly unexplored and unexploited. In the second part of this review we will recount potential environments for bioprospection in this country, describe the current research lines in this field as well as identify the challenges and opportunities for Argentina to take advantage of its genetic potential.

MARINE ENVIRONMENTS OF ARGENTINA

On the South Western Atlantic Ocean, Argentina has the most extensive continental margin of South America, with an area of approximately 2,000,000 km^2 (60). The continental shelf, located between the shoreline and the continental brake, accounts for approximately half of this area (37). It widens progressively to the south, reaching a maximum width of 860 km at 51^o S (39). The continental shelf terminates to the east in a sharp break, located between 110 and 165 m water depth (73). The continental slope is intersected by approximately 50 canyons of variable widths and depths (60, 73). The continental rise presents a gentle slope crossed by

various submarine canyons and valleys, located between 3,200 and 5,000 m water depth (60). To the east, the continental rise is connected with the abyssal plain, which reaches a maximum water depth of 6,212 m (32).

Water circulation in the Argentine Sea is driven by strong tides, large freshwater discharges such as the La Plata River plume, high wind speeds and, most importantly, by the influence of two boundary currents: Brazil and Malvinas (39, 59). The Malvinas current is part of the northern branch of the Antarctic Circumpolar Current flowing northward along the continental shelf break. These high latitude waters are not as stratified as tropical waters, and thus they are rich in nutrients due to more efficient upward mixing. Warm, nutrient-poor and salty waters of the Brazil current collide with cold, nutrient-rich and relatively fresh waters of the Malvinas current at the Brazil/Malvinas Confluence (25). The location of the collision of these two currents varies seasonally between 30 and 46° S over Buenos Aires province, Argentina. This confluence creates a region of high variability of water mass properties, at a scale of 100-200 km (39). A highly complex vertical stratification structure is formed as a result of the mixing of Subtropical and Subantarctic waters, creating one of the most energetic regions of the world's oceans (74). Intense intrusions of Malvinas current waters into the northern Patagonia continental shelf occur near 41° S (63). The most obvious evidence of the entry of these nutrient-rich waters is the high level of biological activity found in the Patagonia region, which is considered a Class I marine ecosystem with a productivity rate larger than 300 grC/m^2 yr^{-1} (39). This high productivity has consequences on higher trophic levels as well. For example, fish catch in the Patagonian shelf is one order of magnitude higher than in Southern Brazilian waters (39).

The extension of the continental shelf of Argentina allows for the development of a great diversity of marine fronts covering several scales of space and time, in particular from 32° southward (1). Fronts can be defined as a narrow zone with enhanced horizontal gradients of water properties (temperature, salinity, nutrients, etc.) that separates broader areas with different water masses or a different vertical structure (6). Fronts play a paramount role in ecological processes allowing for an exceptionally large primary production, and in many cases enhanced biological activity at higher trophic levels as well (1, 8). In addition, they offer adequate feeding and/or reproductive habitats for nektonic species and they act as retention areas for larvae of benthic species promoting the establishment of adult beds (1). Their main forcing are current convergence, tides, continental run-off, wind, solar heating, bathymetry, among others (1).

With more than a century of presence in Antarctica, Argentina maintains a territorial claim in an area located from south of the 60° S latitude to the South Pole, and from 25° to 74° W, which includes the Antarctic Peninsula. Argentina maintains 13 stations in this area, six of them year-round. The productivity of the marine ecosystem surrounding the Antarctic Peninsula is limited by the extreme weather conditions and low light penetration that characterize this area (www.lme.noaa.gov). The Antarctic Peninsula is one of the most rapidly warming regions on Earth, having experienced a 2 °C increase in the annual mean temperature and a 6 °C rise in the mean winter temperature since 1950 (23). The glacially sculpted coastline along the west coast of the Antarctic Peninsula is highly convoluted and characterized by deep embayments that are often interconnected by channels, facilitating the transport of heat and nutrients (23). During the ice-free season, a nearshore southward flow circulation is observed along this coast. This current, called the Antarctic Peninsula Coastal Current, might be critical for providing a favorable environment for biological production in this marine ecosystem (47). The circulation at the Weddell Sea, located east of the Antarctic Peninsula, is dominated by the Weddell Gyre. During this clockwise circulation the water loses a significant amount of heat as it travels from the eastern Weddell to the northern tip of the Antarctic Peninsula (72). South of the Weddell Sea, the Filchner-Ronne Ice Shelf is floating over the continental shelf (50). In these structures, ice fragments are usually calved off as icebergs from the ice front, or the ice is melted from the shelf base (50). Interestingly, free-drifting icebergs of the Weddell Sea have been suggested to be hot spots of continual micronutrient release that could serve as areas of increased production and sequestration of organic carbon (77).

The Argentinean marine environments, with their notable extension, complex topography and water circulation patterns, as well as high biological productivity and biodiversity, hold numerous niches extremely valuable for the bioprospection of microorganisms with biotechnological potential. In particular, Subantarctic and Antarctic marine regions, remote and mostly pristine, contain microbial communities adapted to extreme climates that are remarkably suitable for bioprospection. In addition, marine fronts offer an exceptional concentration of microbiological life with strong annual cycle (71). In the next sections, research performed by Argentinean

researchers on marine microorganisms with biotechnological potential, as well as challenges and opportunities in this field, will be reviewed.

CURRENT RESEARCH LINES

In Argentina, scientific research is contributing to the knowledge of marine microorganisms with biotechnological potential in areas such as food and pharmaceutical industries, as well as environmental protection. Table 1 shows, to the best of our knowledge, the studies published in periodic journals or books during the last two decades in biotechnology-related marine microbiology. Out of a total of 42 articles, 11 characterized marine microorganisms isolated from Subantarctic and Antarctic regions, and/or their enzymes (Table 1). The characterized enzymes from marine isolates include hydrolases of wide industrial use such as glycosidases (15, 17) and proteases (16, 24, 54, 80-84). Cold-adapted enzymes characteristically show high catalytic efficiency at low temperatures and the possibility of heat inactivation, which make them suitable candidates for many biotechnological purposes, including food and feed industry, textile and cleaning industries, biofuel production, fine chemical synthesis, among others (13).

Table 1. Published research articles in biotechnology-related marine microbiology

Biotechnological interest	Microorganisms	Source	Research topic/Application	References
Industrial Biotechnology	Lactic acid bacteria	Fresh anchovies (*Eugraulis anchoita*)	Characterization of *Leuconostoc* and *Lactobacillus* strains for the development of anchovy-based products	(5)
	Psychrotolerant bacteria (*Shewanella* sp. G5)	*Munida subrrugosa* intestinal content, Beagle Channel, Tierra del Fuego, Argentina	Cold-active ß-glucosidases for use as food additives	(15, 17)
	Psychrotolerant bacteria	Seawater and alimentary tracts of various benthonic organisms, Ushuaia coast, Tierra del Fuego, Argentina	Cold-active α-L-rhamnosidases for use as food additives	(28)
	Psychrotolerant and psychrophilic bacteria	Seawater and the intestines of benthonic organisms collected from the Beagle Channel, Argentina	Cold-active proteases with industrial applications	(16)
	Psychrotolerant bacteria (*Pseudoalteromonas* sp.)	Subantarctic sea	Intracellular α-L-rhamnosidase as debittering agents for fruit juices	(40)
	Subantarctic bacteria	Intertidal sediments, Isla de los Estados, Argentina	Cold active proteases (diverse industrial applications)	(54)
	Psychrotrophic (*Pseudoalteromonas* sp.)	Intestinal tract of hake (*Merluccius hubbsi*), San Jorge Gulf, Chubut, Argentina	Cold active proteases (diverse industrial applications)	(24)
	Antarctic bacteria	Seawater, sediments and dead marine animals, Antarctica	Cold active proteases (diverse industrial applications)	(80-84)
	Microalgae	Native species	Lipid extraction and characterization for biodiesel production.	(64)
Pharmaceutical Biotechnology	Fungi *(Acremonium furcatum)*	Intertidal sediments, Buenos Aires coast, Argentina	Amides of D-*allo*- and L-isoleucine derivatives with antifungal activity for plant biocontrol	(26)
	Fungi (*Cladosporium* sp.)	Intertidal marine sediment, San Antonio Oeste, Rio Negro, Argentina	Long-chain and α,β-unsaturated aldehydes with antibacterial activity	(27)
	Fungi (*Paecilomyces marquandii*)	Marine sediments	Ureido sorbicillinol derivative (antimicrobial)	(9)
	Lactic acid bacteria (*Lactococcus lactis* TW34)	*Odontesthes platensis* intestinal tract, northeast coast of Chubut, Argentina	Lactococcal bacteriocin (aquaculture antimicrobial)	(75)

Table 1. Published research articles in biotechnology-related marine microbiology *(continued)*

Biotechnological interest	Microorganisms	Source	Research topic/Application	References
Pharmaceutical Biotechnology	Lactic acid bacteria	Intestinal tract, tegument and gills of marine fish, Chubut coast, Argentina	Antilisterial activity	(79)
	Lactic acid bacteria	Intestinal tract, tegument and gills of fish, sediments and water, Bahía Blanca estuary, Argentina	Antimicrobial activity against fish pathogens	(76)
	Microalgae (*Phaeodactylum tricornutum*)	-	Optimization of methods to increase eicosapentaenoic acid (EPA, 20:5n-3) recovery (various medical applications)	(12)
Environmental Biotechnology Bioremediation	Psychrotrophic and psychrophilic oil-degrading bacteria	Superficial seawater, San Jorge Gulf coast, Chubut, Argentina	Analysis of lipid storage compounds (biofuels and other applications)	(2)
	Bacteria	Seawater and sediments, Comodoro Rivadavia coast, Argentina	Hydrocarbon-degradation potential and microbial community composition (bioremediation)	(66, 67)
	Bacteria	Polluted and pristine intertidal sediments, Chubut, Argentina	Alkane biodegradation (bioremediation)	(57)
	Bacteria (*Bacillus subtilis* 09)	Intertidal sediments, San Antonio Oeste, Rio Negro, Argentina	Lipopeptide biosurfactant (bioremediation)	(20, 48, 55, 56)
	Bacteria	Intertidal sediments, Aristizábal and Gravina Peninsulas, Chubut, Argentina	Alkane biodegradation and biosurfactants (bioremediation)	(58)
	Bacteria	Sediments, Bahía Blanca estuary, Argentina	Hydrocarbon biodegradation (bioremediation)	(18, 19)
	Bacteria	Oily bilge waste, Chubut, Argentina	Hydrocarbon biodegradation (bioremediation)	(51, 52, 53)
	Bacteria (*Aeromonas, Pseudomonas, Vibrio*)	Water, Rio de la Plata estuary, Argentina	Linear alkylbenzene sulfonate biodegradation (bioremediation)	(62)
	Uncultured environmental bacteria	Marine sediments from Chubut and Tierra del Fuego provinces, Argentina	Characterization and quantification of PAH biodegradation genes (bioremediation)	(22, 36, 38)
	Bacteria *Pseudomonas* sp. J26	Intertidal sediments from Patagonia, Argentina	Naphthalene dioxygenase activity (bioremediation)	(70)
	Halomonas spp.	Salt brine samples from Bahía Blanca Estuary and seawater from Mar del Plata, Argentina	Chemotactic response to gas oil (bioremediation)	(21)
Various technological applications	Microalgae (*Phaeodactylum tricornutum*)	Strain LFF Pt 01, Lab. Fermentaciones, FBCB, UNL	Carbon metabolism with applications in aquaculture, polyunsaturated fatty acids, pharmaceutical industry	(3)

The extensive campaigns carried out by Argentinean researchers at remote, high-latitude marine environments were fundamental to the success of bioprospection in these cases.

A major subject of study is the role of marine microbiota in pollutant biodegradation in coastal environments of Argentina. Research studies have involved the analysis of hydrocarbon degradation by isolates, consortia and microbial communities (18, 19, 21, 57, 58, 66, 67), production of lipid storage compounds by hydrocarbon-degrading bacteria (2) as well as production of microbial surfactants to facilitate biodegradation (20, 48, 56, 58). In addition, bioremediation of bilge waste has been achieved in reactor systems (51-53). More recently, culture-independent techniques, including metagenomics, have been used for an assessment of the diversity of hydrocarbon-degrading bacterial populations and their catabolic pathways, as well as the estimation of biodegradation potential in Patagonian marine sediments (22, 35, 36, 38). The

biodegradation of other water pollutants such as linear alkylbenzene sulfonates by marine and estuarine isolates from the Rio de la Plata has also been described (61, 62). Studies in this area led to the identification or isolation of indigenous microorganisms which are particularly valuable for *in-situ* bioremediation strategies, avoiding environmental safety concerns of using allochthonous inocula.

Another important topic addressed by Argentinean researchers is the study of novel antimicrobial compounds produced by marine microorganisms such as fungi (9, 26, 27) or lactic acid bacteria (75, 76, 79). For instance, the latter produce antimicrobial compounds (*e.g.* bacteriocins) which can be used as biological control agents or food bio-preservatives (10, 29). Another research line developed in Argentina revealed the potential of lactic acid bacteria as functional starter cultures for the development of anchovy-based products (5). Lastly, an issue that presents great potential is the cultivation and study of marine microalgae. These microorganisms have various commercial uses such as animal feedstock, as source of fatty acids for biodiesel and nutraceuticals, and as a source of other high-value biomolecules [(3, 64), Leonardo Curatti, personal communication]. Despite the lack of formal bioprospecting programs in Argentina, in contrast with other countries (42, 68), national research groups have discovered many valuable macromolecules and activities with potential biotechnological applications based on individual-based efforts during the last 20 years.

CHALLENGES AND OPPORTUNITIES

Bioprospecting, in its modern form, involves the use of advanced technologies to develop different products exploiting biodiversity (4). In particular, some key technologies, such as omics-driven approaches and novel cultivation strategies, have the potential to generate major breakthroughs in the field, as they allow the access to the yet-to-be-cultured microbial majority. These techniques are usually costly, and for marine bioprospection there are additional high costs associated with the field work. In developing countries, the resources needed to make use of their biodiversity are not always readily available (43). Building and strengthening research capacities in these countries in disciplines such as -omics, systems biology and bioinformatics is essential to allow them to actively participate in the development and commercialization of new products from their often vast microbial biodiversity (78). Besides investments, the implementation of national and regional collaborative research networks optimizes the use of the often scattered available resources, and encourages the utilization of multidisciplinary approaches, essential to this field. Finally, partnerships between research institutions and the local biotech industry as well as research conducted by the private sector constitute an essential gear in this machinery.

Argentina belongs to the group of developing countries with an established scientific capacity (30). In particular, science and technology investments in Argentina have significantly increased over the last years. From 2004 to 2008, the proportion of the country gross domestic product (GDP) assigned to science and technology-related activities increased from 0.49 to 0.61 % (46). Although still far from the proportion allocated by developed nations, only Brazil and Chile exceed this level of investment among South American countries. Unlike developed countries, funding of research and development in Argentina mainly comes from the public sector. Government research funding is mainly provided by the National Agency for the Promotion of Science and Technology (ANPCyT) and the National Research Council (CONICET), dependent on the recently created Ministry of Science, Technology and Productive Innovation (MINCyT). Industry only funds 26.5 % of the total investment, representing 0.14 % of the country GDP, while in countries with high-income economies it funds an average close to 65 %, 1.5 % of their GDP (46). Of an equivalent of approximately 57,000 full-time trained human resources, including researchers, PhD students and technicians working in R&D in Argentina in 2008, only 15 % corresponded to private companies (46).

In the National Strategic Plan on Science, Technology and Innovation 2006-2010, biotechnology was defined as a priority area, and under this frame the ANPCyT funded 117 biotechnology-related projects during the 2006-2008 period (45). Furthermore, in 2007 a law was promulgated in Argentina to promote the development of biotechnology innovation and production processes (LEY 26270, (65)). Argentina´s most developed biotechnological field is agricultural biotechnology due to its export-oriented agricultural sector, key for the economy of the country (30). As a consequence, public and private investments in the biotechnological field have been mostly allocated in relation to these interests. One example is the creation of INDEAR (Instituto de Agrobiotecnología de Rosario, www.indear.com) an Argentina-based agricultural biotechnology company originated in a private-public partnership. This company recently acquired a second-generation sequencer (Roche 454 GS-FLX Titanium) to address questions

about soil biodiversity and agricultural sustainability. This acquisition positioned Argentina as the second country in South America, after Brazil, having this technology available. Although originally obtained through an agricultural biotechnology research project, this instrument is available as a sequencing service for both the Argentinean scientific community and private companies, and could potentially benefit the field of marine biotechnology. Similarly, an Illumina MiSeq system will be available in 2012 at the sequencing service of the Biotechnology Institute, National Institute of Agropecuary Technology (INTA). Another investment that is relevant for applied marine microbiology, in this case covered by public funds, is the recent relaunching of oceanographic campaigns to the Argentine Sea and Antarctica aboard the Puerto Deseado Oceanographic vessel (www.conicet.gov.ar). This is an excellent opportunity for the bioprospection of marine microorganisms from yet-to-be explored habitats such as benthic environments.

Considering the extension of the marine environments in Argentina and the diversity of niches available for bioprospection, there are relatively few research articles published in this field (Table 1). Microbiologists have historically focused mainly on basic and biomedical issues, being research in environmental microbiology much less developed. Within this field, the majority of the research work has focused on microorganisms from terrestrial environments. As an example, in three Argentinean scientific meetings held from October 2010 to May 2011 [46th Annual Meeting, Argentinean Society for Biochemistry and Molecular Biology Research (SAIB) Microbiology Section, XII Argentinean Congress of Microbiology - I Congress of Agricultural and Environmental Microbiology (AAM), and VII General Microbiology Argentinean Congress (SAMIGE)] there were approximately 8 times more abstracts of soil-related environmental microbiology studies than those focused on marine microorganisms, being the former mostly related to agricultural issues. Nonetheless, there has been an important increase in the number of publications in biotechnology-related marine microbiology in the last years, as more than 50 % of the articles were published after 2008 (Figure 1). The increase in the number of presentations at local scientific meetings also evidences this trend. Although in Argentina the research activity is highly centralized in major cities, such as Buenos Aires (46), 34 out of 42 articles have researchers outside Buenos Aires city as corresponding authors (Table 2). The Patagonian National Research Center (CENPAT-CONICET) located in Puerto Madryn, Province of Chubut, leads the field, followed by PROIMI-CONICET from San Miguel de Tucumán city, Province of Tucumán (Figure 2). Furthermore, an active collaboration among Argentinean institutions is evidenced by coauthorship (Figure 2). Interestingly, the only two articles with a corresponding author from a foreign institution were published before the year 2000 (Table 1). In subsequent years, although coauthorship with foreign groups has been frequent, the corresponding authors were Argentinean, evidencing the consolidation of research groups in the field. The private sector, in contrast, is a partner in only one full-length publication, in which the corresponding author is from Spain, and the private partner is a Spanish company (Table 2). However, the products of these partnerships are not always reflected in publications, due to confidentiality issues.

Published articles in applied marine microbiology show a concentration of research interests, with the majority of the publications focusing on the study of cold-active enzymes, antibacterial compounds or hydrocarbon biodegradation from coastal environments. The existence of few subjects of study in a rather small scientific community has the advantage of allowing the development of productive collaborations within the country, as can be seen in Figure 2. However, this will certainly leave a great number of unexplored issues, and as a consequence, unmet societal needs, for example the development of pharmaceutical products, nutraceuticals or enzymes applicable in green chemical synthesis. It is important to notice that most of the research lines are still early in their exploration, studying applied issues but not

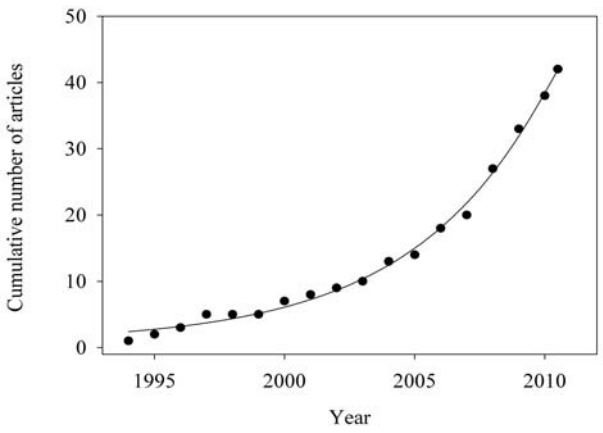

Figure 1. Productivity of Argentinean researchers in applied marine microbiology. The cumulative number of articles published in scientific journals was plotted as a function of time, considering January 1994 to July 2011 time frame.

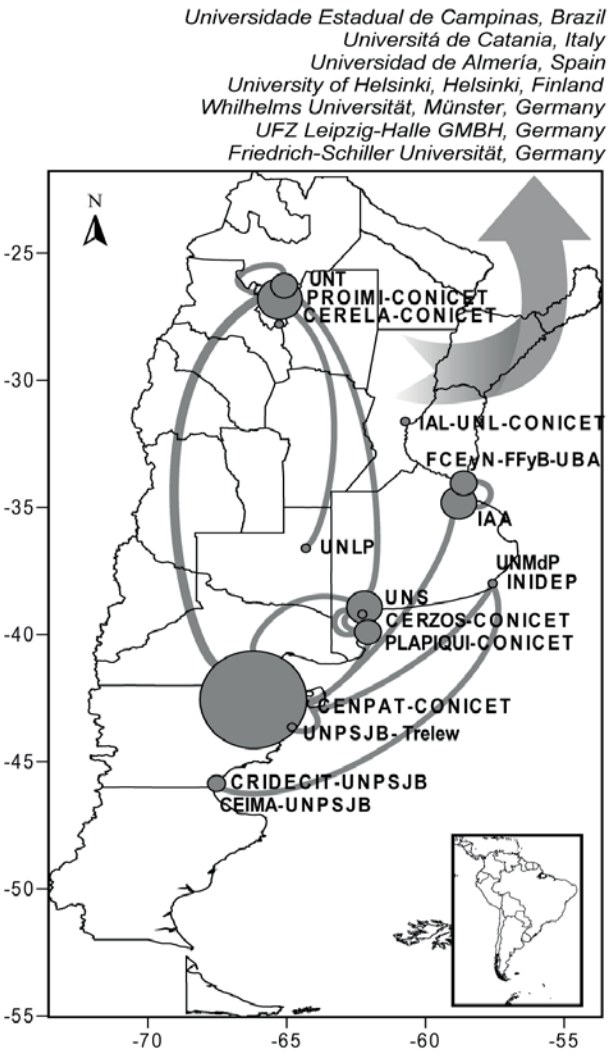

Figure 2. Productivity and collaboration among Argentinean research institutions and with foreign institutions. Research institutions, in alphabetical order: CEIMA-UNPSJB: Centro de Estudios e Investigación en Microbiología Aplicada - Universidad Nacional de la Patagonia San Juan Bosco. CENPAT-CONICET, Centro Nacional Patagónico-CONICET; CERELA-CONICET, Centro de Referencia para Lactobacilos – CONICET; CERZOS-CONICET-UNS, Centro de Recursos Naturales Renovables de la Zona Semiárida – CONICET – UNS; CRIDECIT-UNPSJB, Centro Regional de Investigación y Desarrollo Científico Tecnológico - Universidad Nacional de la Patagonia San Juan Bosco sede Comodoro Rivadavia; FCEyN-UBA, Facultad de Ciencias Exactas y Naturales-Universidad de Buenos Aires; FFyB-UBA, Facultad de Farmacia y Bioquímica-Universidad de Buenos Aires; IAA, Instituto Antártico Argentino; IAL-UNL-CONICET, Instituto de Agrobiotecnología del Litoral- Universidad Nacional del Litoral-CONICET; INIDEP, Instituto Nacional de Investigación y Desarrollo Pesquero; PLAPIQUI-CONICET-UNS, Planta Piloto de Ingeniería Química-CONICET-UNS; PROIMI-CONICET, Planta Piloto de Procesos Industriales y Microbiológicos-CONICET; UNLP, Universidad Nacional de La Pampa; UNMdP: Universidad Nacional de Mar del Plata. UNPSJB Trelew, Universidad Nacional de la Patagonia San Juan Bosco sede Trelew; UNS, Universidad Nacional del Sur; UNT, Universidad Nacional de Tucumán.

close to producing patents or products. In Argentina, biotechnological patents are still mostly held by foreign individuals and entities. The dependence index (number of patents solicited by non residents/number of patents solicited by residents) for biotechnological patents was 17.7 in 2007-2008 (45). This value is significantly higher than the index for the total of patents in the country, which is 5.5 for the same period (46). As research is an essential prerequisite for the further development of biotechnology (68), it is therefore crucial to stimulate basic and applied research. Product development through private-public partnerships is also fundamental in order to decrease the level of dependence in this field. One example of such collaboration is the one between the Argentinean Antarctic Institute and Bio Sidus S.A. This collaboration aims at isolating bacteria from Antarctica, sequencing their genomes and investigating their cold adapted enzymes useful for industrial purposes (www.biosidus.com.ar/biodiversidad.php). So far, this has resulted in the isolation of a new Antarctic marine bacterial species, *Bizionia argentinensis* JUB59 (EU021217) and the complete sequence of its genome (GenBank accession number AFXZ01000000) (7, 34). Large scale initiatives for the bioprospection of marine microorganisms including research groups from various fields, government institutions, non-government organizations as well as industry would have an even larger impact, driving marine microbial biotechnology research beyond individual-based efforts.

CONCLUSIONS AND POSSIBLE ACTIONS

The extreme diversity of the microbial life inhabiting Argentinean marine environments represents a unique source of genetic information that could provide key biotechnological products and processes, if their potential is unveiled. In Argentina, the bioprospection of marine microorganisms is gaining momentum, as demonstrated by the increase in the number of published articles in this field over the last years. Recent increases in funding and research capabilities such as the availability of oceanographic vessels will be fundamental for the exploitation of yet-to-be explored habitats. Active policies tending to strengthen existing scientific capacities, to favor their connections with the private sector and to encourage the creation and development of start-up companies are essential for moving beyond this point, and as a consequence for the development of marine

Table 2. Research productivity (measured as number of publications) of Argentinean institutions in biotechnology-related marine microbiology. Articles are described and cited in Supplementary Table 1. The main institution was inferred from the corresponding author´s affiliation. Secondary institutions are listed in order of importance taking into account number of joint publications with the main institution (between parentheses). Country of origin is Argentina unless otherwise noted

Main Institution	Other collaborating Institutions	Number of publications
CENPAT-CONICET, Pto. Madryn, Chubut	PLAPIQUI-CONICET, Bahía Blanca, Bs. As. (3) Universidad Nacional de Luján, Luján, Bs. As. (2) PROIMI-CONICET, S.M. de Tucumán, Tucumán (2) UNPSJB, Trelew, Chubut (2)	12
PROIMI-CONICET, S.M. de Tucumán, Tucumán	Universidad Nacional de Tucumán, S.M. de Tucumán, Tucumán (3) Universidad Nacional de la Pampa, Santa Rosa, La Pampa (3) CENPAT-CONICET, Pto. Madryn, Chubut (1) Friedrich-Schiller-Universität, Germany (2) Universitá di Catania, Italy (1)	6
Instituto Antártico Argentino, Cdad. de Buenos Aires	FFyB-UBA, Cdad. de Buenos Aires (5)	5
UNS, Bahía Blanca, Bs. As.	CENPAT-CONICET, Pto. Madryn, Chubut (2) PROIMI-CONICET, S.M. de Tucumán, Tucumán (1)	4
FCEyN-UBA, Cdad. de Buenos Aires	Universidade Estadual de Campinas, Sao Paulo, Brazil (2)	3
CRIDECIT-UNPSJB, C. Rivadavia, Chubut	UFZ Leipzig-Halle GMBH, Germany (1)	2
INIDEP, M. Del Plata, Bs. As.	CRIDECIT-UNPSJB, Comodoro Rivadavia, Chubut CENPAT-CONICET , Puerto Madryn, ChubutComisión Nacional de Energía Atómica, Cdad. de Buenos Aires	1
CEIMA-UNPSJB, C. Rivadavia, Chubut		1
Universidad Nacional de Mar del Plata, Argentina		1
Universidad Nacional de la Pampa, La Pampa, Argentina	PROIMI-CONICET, S.M. de Tucumán, Tucumán	1
CERELA-CONICET, S.M. de Tucumán, Tucumán	University of Helsinki, Finland	1
Instituto de Agrobiotecnología del Litoral- UNL-CONICET, Santa Fe, Santa Fe		1
UNPSJB, Trelew, Chubut	CENPAT-CONICET, Puerto Madryn, Chubut	1
CERZOS-CONICET, Bahía Blanca, Bs. As.	UNS, Bahía Blanca, Bs. As. PLAPIQUI-CONICET, Bahía Blanca, Bs. As.	1
Universidad de Almería, Almería, Spain	UNPSJB, Comodoro Rivadavia, Chubut Derivados del Etilo S.A., Almería, Spain	1
Wilhelms-Universität Münster, Münster, Germany	UNPSJB, Comodoro Rivadavia, Chubut	1
Total articles		42

biotechnology in the country. It is acknowledged that both a top-down innovation environment (where governments provide large investments required for facilities and capabilities), and a bottom-up innovation environment (led by individuals and organizations engaged in innovation and production) are needed in order for a country to be successful in innovation (14). In fact, bottom-up innovation can also be stimulated by government policies, such as efficient intellectual property policies, transparent and consistent regulations, and tax laws favorable to R&D investment (14).

In many countries, the development of marine biotechnology is considered a key strategy for solving significant environmental and societal challenges. Assessments of the situation as well as recommendations for the development of marine biotechnology are periodically released (11, 42, 44, 49, 68). Optimally, the current Argentinean situation should be analyzed by a committee integrated by experts of various sectors, in order to elaborate specific recommendations for Argentina. However, some of the actions suggested in other countries that we feel could apply to Argentina include: (a) to conduct surveys in the private sector in order to detect current industry needs and opportunities, to better concentrate research efforts; (b) to promote mutually beneficial interaction and collaboration between academic research and industry, and create technology transfer pathways; (c) to enhance the development of new biotech companies by creating marine biotechnological institutes or biotech poles co-located with marine laboratories and/or universities; (d) to include

biotechnology training in undergraduate and graduate programs with emphasis in building an interdisciplinary expertise, (e) to implement awareness programs in middle-level education, for students to explore biotechnology-related career options, and (f) to develop a legal framework aiming to regulate the exploitation of marine genetic resources as well as to define rights and intellectual property issues derived from bioprospection of marine microorganisms. The implementation of a national strategy for the development of marine biotechnology with emphasis in microbiology has the potential of contributing to the creation of highly qualified jobs through the further development of the biotech industry. This development has the added value of being able to respond to societal needs by exploiting the country's readily available marine resources in a sustainable way.

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