DOCTORAL INPHINIT FELLOWSHIPS PROGRAMME – INCOMING FRAME INFORMATION CALL 2021

The doctoral fellowship programme INPhINIT ”la Caixa” is devoted to attracting talented Early-Stage Researchers—of any nationality—who wish to pursue doctoral studies in Spanish or Portuguese territory. Sponsored by ”la Caixa” Foundation, it is aimed at supporting the best scientific talent and fostering innovative and high-quality research in Spain and Portugal by recruiting outstanding international students and offering them an attractive and competitive environment for conducting research of excellence.

Doctorate INPhINIT Incoming offers 35 PhD fellowships for early-stage researchers of any nationality to pursue their PhD studies in research centres accredited with the Spanish Seal of Excellence Severo Ochoa, María de Maeztu or Health Institute Carlos III and Portuguese units accredited as “excellent” or “exceptional” according to the evaluation of the Fundação de Ciência e Tecnologia. This frame is addressed exclusively to PhD research projects on STEM disciplines: life sciences and health, experimental sciences, physics, chemistry and mathematics.

To know more about the call please visit:

https://fundacionlacaixa.org/en/educacion-becas/becas-la-caixa/doctorado-inphinit/

CIIMAR is one of the host organizations of INPhINIT Incoming and will offer **up to 10 research projects** to be carried out in a multidisciplinary and international research team. The offers are described as follows:

DESCRIPTION OF PhD POSITION OFFERS AT CIIMAR

"UNRAVELLING THE ECOLOGICAL DRIVERS OF DEEP-SEA VULNERABLE MARINE ECOSYSTEMS BIODIVERSITY AND STRUCTURE IN THE TEMPERATE NORTHEAST ATLANTIC"

Research project:

Sponges and corals form a variety of highly-structured habitats, known as sponge/coral gardens, aggregations and reefs. They are particularly prevalent in the deeper areas of the continental shelves and slopes, and play key roles in ecosystem function, from recycling of major nutrients to provision of habitat, nursery and feeding grounds for many other invertebrate and fish species. Their sensitivity to the impacts of anthropogenic activities (fisheries, oil gas exploitation, climate change) is increasingly recognized, which led to their classification as Vulnerable Marine Ecosystems (VMEs). Yet, baseline knowledge into VMEs biology and ecology is scarce and dispersed, hampering the development and implementation of area-based tools for their conservation and sustainable management.

The main goal of this project is to investigate the community composition, structure and environmental drivers of distribution of deep-sea VMEs along the Portuguese continental shelf and slope using video annotation of underwater imagery and a combination of multivariate statistics and advanced ecological modelling techniques.

The PhD student will integrate the DEEPbaseline project, an awardee of the Ocean Conservation Fund supported by Oceano Azul Foundation and Oceanário de Lisboa, that will bring together scientists, local fishing communities and associations, fisheries managers, and the wider society to foster awareness and advance conservation actions towards VMEs sustainability.

Research Team: Deep-Sea Biodiversity and Conservation (CIIMAR)

Our research focuses on the understanding of basin to global scale diversity, distribution and connectivity patterns of deep-sea vulnerable marine species and ecosystems, and how ecological and evolutionary processes, as well as anthropogenic pressures underpinning such patterns. We combine various disciplines (taxonomy, systematics, biogeography, and ecology) and integrate various methods from advanced microscopy to genomics, and statistical modelling. Our focal areas comprise the deep temperate and (sub-)tropical Atlantic, although some studies have a global scope.

We are also committed to advance the science-policy-society interface and transfer generated knowledge and developed tools to support the implementation of major agreements and instruments established to ensure sustainable management and conservation of marine biodiversity, from national through to global levels.

Job position description:

We are looking for motivated candidates with a MSc in Marine/Biological Sciences and good ecological statistics skills. Experience in participating in projects and fieldwork related to deep-sea benthic ecosystems, skills on taxonomy of VME-indicator groups (e.g. sponges, corals) and video annotation analyses are highly desirable.

The student will: i) participate in research cruises aimed at collecting imagery, environmental data and samples; ii) perform video annotation; and iii) undertake multiple ecological statistics and modelling analyses. It will also have the opportunity to communicate and disseminate project results in various platforms, from publications in scientific journals and participation in conferences, to engagement with stakeholders and the development of outreach activities and social media contents.

The grantee will be based at CIIMAR (www.ciimar.up.pt), a leading marine and environmental research and advanced training institution in Portugal, working at the frontier of knowledge and innovation. CIIMAR has a vibrant and international environment, and provides excellent support to incoming students and researchers, namely through a PhD students' committee which organizes various scientific and social events. The student will also have the opportunity to make research and training stays at other research institutes, in Portugal and abroad, and ample international networking.

Deep-Sea Biodiversity and Conservation research focuses on the understanding of basin to global scale diversity, distribution and connectivity patterns of deep-sea vulnerable marine species and ecosystems, and how ecological and evolutionary processes, as well as anthropogenic pressures underpinning such patterns. We are also committed to advance the science-policy-society interface and transfer generated knowledge and developed tools to support the implementation of major agreements and instruments to ensure sustainable management and conservation of marine biodiversity.

Group Leader:

Assistant Researcher
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"USING PHENOTYPIC PLASTICITY FOR IMPROVING FISH AQUACULTURE PRODUCTION AND WELFARE IN A CHANGING ENVIRONMENT"

Research project/ Research Group description:

Phenotypic plasticity involves adjustments in both fish physiology and behaviour required to survive in adverse or unpredictable conditions during the early stages. Such plasticity can be induced by environmental changes, resulting in long-lasting effects on animal performance and fitness at a later stage. In particular, marine fish species exhibiting a high growth rate and rapid development may be susceptible to such effects. Therefore, environmental conditions may have an important effect on developmental plasticity when applied in the early life stages of fish. However, the information on how these conditions when applied in early life stages may impact the physiology and behaviour of cultured fish species at later stages is scarce. Previous studies in European seabass and common sole have shown that temperature and low dissolved oxygen levels applied during early life induced long-lasting effects. These results may have important outcomes in fish aquaculture as phenotypic plasticity could be used to optimize production, along with genetic selection programs.

The Ph.D. thesis proposal will investigate whether exposing aquaculture fish in early life to different environmental factors may result in changes in physiological and behavioural responses in later life, as an effect of phenotypic plasticity. Based on relevance in the regional aquaculture production and the previous experience of this group, the current Ph.D. study will investigate the physiological and behavioural outcomes of climate changes in two marine aquaculture fish species: Gilthead seabream (*Sparus aurata*), and meagre (*Argyrosomus regius*).

LANUCE research group is mainly focused on the optimization of sustainable practices for aquaculture using smart and precision farming and also improvement of quality, safety, and welfare of aquatic animals under a market-oriented approach.

Two of LANUCE´S senior researchers will supervise (Leonardo Magnoni) and co-supervise (Rodrigo Ozorio) the Ph.D. study. LM has 20 years of expertise in fish physiology, in special on cross effects of aquafeed formulation in fish subjected to environmental oscillations. LM is also devoted to behavioural responses of aquaculture fish to environmental changes. RO has more than 20 years of scientific experience in Aquaculture Research, with special emphasis on the nutritional dynamics of fish, dietary effects associated with health, and quality traits of foodfish for human consumption.

Job position description:

The Ph.D. study will investigate how fish subjected to different environmental factors during the early life stages may result in both the physiology (stress responsiveness, biochemical parameters, and enzymatic activities, metabolic rate, and transcriptional response) and behaviour changes (feeding and copying style) during its later life stages (juvenile/adult). The

factors selected for the current Ph.D. project are of particular relevance since fish will eventually experience variations in environmental conditions under intensive aquaculture (changes in dissolved O_2 levels, temperature, salinity, and water currents). During the fish trials, the different environmental factors will be set to adequate levels, without affecting survival.

The candidate for this Ph.D. proposal should have previous scientific experience in fish physiology, behaviour, and/or aquaculture research.

The current study will in-depth the knowledge on the effect of environmental conditions in early life stages may have on fish welfare by investigating physiological and behavioural effects in individual fish in later life stages. The potential outcome of this research related to changes in both physiological and behavioural responses in individual fish upon conditions experienced during early life has profound significance for this cultured species as may provide important knowledge of potential applicability. The proposal contains an innovative approach to further develop precision farming in fish species.

Group Leader:

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"UNRAVELLING DEEP SEA MICROBIAL DIVERSITY FOR BIOREMEDIATION OF POLLUTED ENVIRONMENTS"

Research project/ Research Group description:

The candidate will integrate ECOBIOTEC (Bioremediation and Ecosystems Functioning), a research group that aims to contribute to the advance of marine and environmental science from a multidisciplinary point of view. We couple fundamental ecology and ecosystems function research with bioprospecting and biotechnology tools for ecosystems recovery. Studies on fundamental microbial ecology and biogeochemistry of key elements in highly diverse environments (from estuarine to deep sea ecosystems), and research on biological degradation/transformation of contaminants generate essential knowledge to develop biotechnological tools for innovative bioremediation approaches. We are also interested in the diverse services and societal benefits that marine and estuarine ecosystems provide, namely in unravelling the potential of oceans as a natural resource of microorganisms capable of providing bioactive molecules with multiple benefits to the society and in exploring native microorganisms for environmental cleaning/recovery through nature-based solutions.
The supervising team (Ana Paula Mucha, Fátima Carvalho and Catarina Magalhães) has been involved in several national and international projects in the field of bioremediation, and the development of present PhD proposal will be supported by the projects BIOREM (Bioremediation of hydrocarbon pollutants by autochthonous microorganisms in aquatic environment - PTDC/BTAGES/32186/2017), ACTINODEEPSEA (Bioprospecting actinobacteria from portuguese deep-sea waters for the production of novel secondary metabolites with pharmaceutical and biotechnological applications - PTDC/BIA-MIC/31045/2017), EMSO-PT (European multidisciplinary sea floor and water column observatory – Portugal PINFRA/22157/2016) and ATLANTIDA (ATLANTIDA - Platform for the monitoring of the North Atlantic ocean and tools for the sustainable exploitation of the marine resources 03/SAICT/2019).

Job position description:

The rationale of this proposal considers that a huge diversity of microbial consortia, with different ecological relationships and a large range of metabolic processes, inhabits a multitude of extreme environmental niches at deep-sea that are naturally or accidentally exposed to several contaminants such as petroleum hydrocarbons or metals. Such consortia and their single species microbial components can be directly used as inoculants or as source of biological products, like catabolic enzymes or biosurfactants that can be exploited in pollutant- and site-specific bioremediation approaches. Characterizing and recovering this diversity, by microorganisms' cultivation and gene mining will be of key importance to understand the exploitation relevance of these microorganisms and their components in novel biotechnological processes. This project intent to provide the proof of concept that it is possible to exploit the

metabolic capacities of natural deep sea communities, site-specific collections of microbial strains or mixed microbial cultures, for bioremediation purposes. Hence, this project aims to unravel, exploit and manage the microbial diversity available in a series of extreme sites located in deep sea and sub-sea floors environments. The project aims to manage such resources for developing novel processes based on microbial biotechnology that can address bioremediation of polluted environments.

Group Leader:

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“THE YIN AND YANG OF METAZOAN ENDOCRINE SYSTEMS IN THE ANTHROPOCENE EPOCH”

Research project/ Research Group description:

Why some animal species are more sensitive than others to man-made chemicals is a major issue of the Anthropocene. To address such a question, we must consider a Systems Toxicology approach: from genomic diversity to physiological and functional integration. Animals exhibit conserved and divergent sensitivities to external stimuli. Yet, the extent of genetic variation underlying such dissimilar responses is far from fully assessed. Thus, taking this physiological range in consideration a simple, yet intrinsically complex question, arises: how do man-made chemicals “exploit” genetic/physiological a biodiversity? A flurry of studies has disclosed the harmful effects of exposure to Endocrine Disrupting Chemicals (EDCs). EDCs act in many cases as high-affinity ligands of transcription factors, the Nuclear Receptors (NRs). Yet, a variable NR gene repertoire has been appointed to different Metazoan lineages. Decisively also, is whether orthologous receptors remained functionally stable over evolutionary time scales. Our knowledge remains extremely sparse. The central topic of this proposal is to address the Metazoan taxonomic scope of NR-mediated disruption. Acting at the frontier of Evolutionary Biology and Toxicology, we will: 1) investigate and provide a fine-scale mapping of NRs in multiple Metazoan lineages combining extensive database mining with transcriptomic approaches of multiple species; 2) determine the binding profile of NRs to a vast collection of EDCs in evolutionary and ecosystem representative species,; and finally 3) determine the physiological and molecular signatures of in vivo EDC exposure through next gen sequencing tools at evolutionary informative phyla. This approach puts into context the role of NRs, sculpted by eons of evolution, in endocrine disruption processes, which would be impossible to reveal with model species.

Job position description:

The applicant is expected to attain a general and solid background in Biological Sciences. Given the scope of the proposal, a keen interest in bioinformatics, big data, and comparative genomics is expected.

Group Leader:

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"ECO-TECHNOLOGIES FOR TREATMENT OF RAW WATERS CONTAMINATED WITH HARMFUL ALGAL BLOOMS (HABS)"

Research project/ Research Group description:

TOXICROP is a EU research project (MSCA-RISE nr 823860), which the main focus is the risk assessment of the use of eutrophic waters in agriculture. This project also seeks the development of environmental friendly technologies applied to water treatment and removal of toxic cyanobacteria and cyanotoxins from eutrophic waters.

Within the water treatment technologies investigated in this project are the Constructed Wetlands (CWs) and Multi-soil Layering (MSL). CWs and MSLs are amongst the most well succeeded nature-based solutions. The technologies have been used to clean different types of wastewaters, including tertiary treatments of municipal wastewaters. The principles of CWs operation rely on its complex ecosystem structure and function. The action of microorganisms and plants, and the sedimentation, precipitation and adsorption capabilities of CWs enable this technology to remove organic compounds and several persisting water pollutants.

The efficiency of these technologies for cleaning 1) biomasses of different cyanobacteria and 2) different cyanotoxins in contaminated waters are investigated in TOXICROP project by combining different functions of vegetation, soil, and organisms, in aerobic and anaerobic conditions.

Job position description:

The candidate will be involved in the research of Constructed wetlands (CWs) for removal of toxic cyanobacteria and cyanotoxins in eutrophic raw waters.

The candidate will learn to operate with microcosm models and will investigate the processes related with contaminant adsorption, assimilation by microbial and plant biomasses and biotransformation/biodegradation.

To carry out the investigation, the candidate will employ state-of-the art analytical techniques based on LC-MS to identify and quantify cyanotoxins and assess the water quality before and after treatment.

The candidate will also employ high-throughput sequencing (NGS) methods of 16S rRNA genes to investigate microbial activity and the dynamics of microbial communities in CWs during experimental operation, as well as groups of bacteria associated to the elimination/degradation of cyanobacterial toxins.

Finally, the candidate will have the opportunity to interact and work with a multidisciplinary team from CIIMAR, Aarhus University and University of Marrakesh, with a long experience in toxicology of cyanobacteria, chemistry and applied ecology, and thereby to explore complementary research methodologies.

Group Leader:

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“TARGETING AMYLOIDS WITH BLUE BIOTECHNOLOGY AND BIOSENSING SOLUTIONS: FROM NEURODEGENERATION TO BIOFOULING”

Research project/ Research Group:

Three big concerns of Humanity – protein misfolding and oligomerization diseases, bacterial production of biofilms, and biofouling – have amyloid proteins in common. It is aimed to develop high/medium-throughput screening tools to detect and identify cyanobacteria-derived bioactive compounds, to address these concerns, having amyloid proteins as target.

The remarkable biodiversity of Cyanobacteria increases the degree of structural array of the different families of compounds produced, including some with therapeutical applications. BBE group keeps a collection of more than 1000 different cyanobacteria and other photosynthetic microorganisms – LEGE-CC, to be screened during the project, to discover new drugs with anti-amyloid properties, using techniques and methodologies developed through out.

Amyloid proteins are characterized by a distinct β-sheet-rich fold – the cross- -sheet, associated with amyloid diseases (Alzheimer’s, Parkinson’s, and prion diseases), forming elongated unbranched fibrils. Reporter assays will be used to screen the LEGECC for anti-amyloid active compounds and guide drug discovery.

Curli fibers are produced by many Enterobacteria, mediating host cell adhesion and invasion, scaffolding the communities into biofilms, where they are the major component. It is aimed to search for new antimicrobial agents, effective against bacteria in their biofilm stage, targeting amyloid proteins production and aggregation. Amyloid fold is now recognized as a ubiquitous part of normal cellular biology, and functional amyloids have been identified in all kingdoms of life, playing a role in many biologic processes such as on barnacles’ and other species adhesives, responsible for their attachment to immersed surfaces making them efficient macrofoulers. There is a need for environmental-friendly anti-fouling nontoxic agents on maritime industries to mitigate enormous economic and environmental impacts. It is intended to seek them within the cyanobacterial world.

Job position description:

The candidate will integrate the Blue Biotechnology and Ecotoxicology (BBE) research team at the Interdisciplinary Centre of Marine and Environmental Research (CIIMAR). The team has a vast experience in many of the skills needed to conduct this

project, apart from hosting the BBE Culture Collection – LEGE-CC. BBE research lines include isolation and structure elucidation of antimicrobial and anti-fouling substances from microorganisms, evaluating their mode of action.
Two different types of high/medium-throughput cell-based sensor methodologies will be developed and validated to identify bioactive compounds. Sensor-based reporter assays will be used to screen LEGE-CC for anti-amyloid activity and guide drug discovery: (1) based on nuclear receptors (NR), less explored therapeutic targets of neurodegenerative diseases, using human cells as chassis for engineered vectors to detect NR ligands acting on amyloid production and aggregation; (2) to detect the activity of curli proteins promoter in *E. coli*, as a proxy for curli genes expression in a dose response manner, in the presence of bioactive compounds, in combination with appropriate amyloid stains. Identified compounds will have their structure and mode of action elucidated using advanced chemistry, NGS transcriptomic and proteomic methodologies.
Applicants shall prove a good preparation in molecular biology, biochemistry, and microbiology. Familiarity with microalgae and cyanobacteria culture techniques are advantages but not fundamental at the time of the application. Hired fellow must dedicate to laboratory work with precision and organization and will be responsible for the preparation of cyanobacteria cultures, extracts, idealization, assembling and testing of reporter sensors and other molecular tools to be used.
It is expected that the candidate will apply for national, and transnational funds for training periods abroad in high-level academic or industrial secondments, and for participation in congresses.

Group Leader:

Researcher Isabel Cristina Oliveira González Cunha

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"BIO-BASED SUSTAINABLE STRATEGIES TO IMPROVE HEALTH AND DISEASE RESISTANCE IN FARMED ANIMALS"

Research project/ Research Group description:

Unsuitable farming conditions can lead to antibiotic overuse as prophylactic and therapeutic treatments, being a major cause for the emergence and widespread of antimicrobial resistance. Therefore, alternative and sustainable infection management strategies are urgently needed.

Nutrition can have significant health implications for animals and, particularly in fish, best practices on diet formulation are of major importance, as feeds probably represent the leading expenditure to the aquaculture industry. The term functional or fortified feed is used to describe feeds with added benefits beyond the animal's essential nutritional requirements, being both health status and growth expected to be improved. Therefore, a shift away from chemotherapeutic and antibiotic treatments would be possible.

An activated immune system has specific nutrient requirements and in this context, research in physiology and nutrition of functional ingredients/additives in health and disease of humans and other animals increased in recent years. In particular, functional AA could be an advantage to fine-tune dietary formulations in order to develop sustainable nutritional strategies to increase disease resistance in farmed animals.

The present research project intends to contribute to this endeavour with innovative and sustainable strategies to improve fish immunity and resistance to pathogens. A multidisciplinary approach, using up to date methodologies, will be used to investigate further valorization of algae and halophyte fractions by upgrading to pure high value bioactive compounds and formulation of bioactive products (i.e. functional feeds).

This proposal will join projects AQUACOMBINE and ATLANTIDA, which were conceived to develop novel dietary formulations able to avoid the colonization and spread of pathogenic microorganisms, including multi-resistant microorganisms, among farmed animals and the subsequent spread to human beings through the food chain.

Job position description:

The main objective of this research project is to develop sustainable functional feeds to improve fish immunity (i.e. systemic and mucosal defence mechanisms) and resistance to pathogens, as well as the synergistic effects of nutrition and vaccination in a way to improve vaccine efficiency against bacterial and viral pathogens. In particular, it is intended to:

i) develop in vitro methodologies and assays to evaluate the suitability of bioactive compounds as health promoting additives;
ii) study the effects of diets supplemented with functional additives on mucosal (i.e. skin, gills, gut) and systemic (i.e. blood, head-kidney, spleen) immunity and resistance to pathogen infection;
iii) explore the potential of functional additives to improve vaccine efficiency. In this case, only bioactive compounds with some potential effect on enhancing both neutrophils and macrophages trafficking and proliferation will be studied. Therefore, it is hypothesized that bioactive compounds could act similarly to adjuvants categorised as signal 1 facilitators by influencing the fate of the vaccine antigen in time, place, and concentration, ultimately improving its immune-availability, which are required for activation of specific T and B lymphocytes.

During the course of the project, the PhD candidate will acquire technical skills on cell culture, flow cytometry, proteomics, transcriptomics, microbiology and in vivo animal experimentation. There will be room to participate in advanced courses whenever needed.

The PhD candidate will join a multidisciplinary team (i.e. biologists, biochemists, vets) of young motivated researchers in the field of nutritional immunology. The team has an extended network of collaborations including both academic and industrial sectors. Besides Portugal, most important collaborations are settled in Spain, Norway and France. Therefore, the PhD candidate will benefit from project secondments.

Group Leader:

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"NEW MARINE DIVERSITY SCENARIOS IN THE ANTHROPOCEAN"

Research project/ Research Group description:

In the face of climate change, accurate predictions of future biodiversity scenarios require moving forward from simple correlative approaches and developing new process-based models. One way to increase the robustness of projections is to improve our knowledge of the multiple aspects of species' biology that in combination promote their persistence under rapid environmental change and increase the probability for evolutionary rescue. Defining species physical tolerance, i.e. environmental niche breath, its plasticity and adaptive capacity across their distribution ranges is essential for anticipating the ecosystem-wide implications of species shifts under future ocean climate change. The aim of this project is to identify and compare ***species environmental sensitivity*** across their distributional range. To assess marine species vulnerability to climate change we require a greater understanding about ***differential sensitivity*** to stress (e.g., warming) of populations across species distributional range. Additionally, this work will provide very relevant management tools by identifying populations that could act as **climate rescuers** and be used in restauration programs. As target species we will use habitat founders or keystone species such as marine forest seaweeds.

Job position description:

The candidate will be joining a very active research team involved in research the impact of climate change on marine ecosystems. The team is involved in several national and European funded projects (Seeingshore, FutureMARES, etc), which will allow the candidate to move and interact with other research institutions. The candidate will participate in sampling surveys to assess biodiversity patterns across the Iberian Peninsula rocky-shores. He/she will design and implement experiments to test organismal level responses of species to environmental drivers, incorporating several drivers and molecular to fitness-linked responses. Experimental outcomes will allow refining projections on future biodiversity scenarios. Mechanistic and multispecies modelling tools will be developed in collaboration with members of the CIIMAR team.
The candidate will acquire skills in the ecophysiology of marine organisms, ecology of marine communities, statistics and other modelling tools and spatial distribution modelling among others.

Group Leader:

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"EMERGING CONCERNS: TOXIC EFFECTS OF PERFLUOROALKYL SUBSTANCES ON BEES"

Research project/ Research Group description:

Plant-pollinator interactions are vital relationships involving mutual gains; pollinators collect food resources and their activities facilitate plant reproduction. About 90% of flowering plants require pollination to reproduce, and 75% of food crops show increased production due to pollination. Bees have a key role in the pollination process. The importance of bees in ecosystem services and the maintenance of life on the planet is counterbalanced by the increasing worldwide decline of these pollinators. In the past years, declines in bee diversity have been documented in various regions, in relation to habitat destruction and fragmentation, insufficient floral resources and pesticide use. As serious as interfering with the survival and longevity of bees is the contamination by pesticides and perfluoroalkyl substances (PAFSs) in bee products of human use, e.g. honey. In fact, PAFSs are widespread environmental contaminants that were detected in honey and can cause acute toxicity to honeybees. There is, however, a lack of information on their chronic toxicity and adverse outcome pathways, hampering the risk assessment of PAFSs and their potential impact on pollination. Moreover, the incipient data available impeds the establishment of effective management and conservation actions, preventing bee and crop yield decline. The research proposed will use a combination of ecotoxicological and ecotoxicogenomic tools to investigate the effects and risk of PAFSs to bee pollinators. The work will be developed within the scope of the BEESNESS project (CIRCNA/BRB/0293/2019 funded by programme "SR&TD Projects on the Occasion of the V Centenary of the Circumnavigation Voyage" (Portuguese Foundation for the Science and Technology). BEESNESS is a multidisciplinary collaborative project involving CIIMAR, Cardiff University (UK) and Brazilian universities UNICAMP and UNIOESTE.

Job position description:

Laura Guimarães is the head of the Coastal and Marine Environmental Toxicology team at CIIMAR and Invited Assistant Professor at the Faculty of Sciences of the University of Porto. She is a Biologist and PhD in Biomedical Sciences by the University of Porto. Over her career, she worked in seven different research (national and international) and/or university institutions as researcher or teaching staff. She has over 90 international peer-reviewed publications (including 55 full articles in international journals and four book chapters). Over 80% of her scientific production was made independently of her PhD supervisor with self-gathered

funding and encompassing national and international collaborations. She participated in 35 national or international R&D projects (five as coordinator). Currently, she is running two international projects. She supervised five postdoctoral researchers, two PhD theses and ten MSc theses. At the moment, she is supervising/cosupervising four PhD students and two MSc students. LG is also a member of the Portuguese Ocean Teacher Global Academy Regional Training Centre. Main research interests of METOX are in: i) new technologies and methods to diagnose environmental quality and health; ii) metabolism and modes-of-action of priority and emerging contaminants (e.g. pharmaceuticals, metal nanoparticles, hazardous and noxious substances); iii) integrated chemical and effects-based monitoring; iv) effects-based evaluations for reuse of reclaimed water and cleaning of oil spills; vi) approaches and tools to increase scientific and ocean literacy. Considering that main water and ocean contamination events come from land activities, the research takes an integrated approach from terrestrial to aquatic animals and systems. The research addresses targets of UNESCO Sustainable Development Goals (SDG) 1 (no poverty), 2 (Zero Hunger), 4 (Quality education), 6 (Clean water and sanitation), 14 (Life below water), and 15 (Life on land).

Group Leader:

Dr. Laura Guimarães

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“TROJAN HORSES FOR HEAVY METAL CONTAMINATION AND DRUG RESISTANCE – AN INGENIOUS HERO FOR AN INGENIOUS ENEMY”

Research project/ Research Group description:

THE PROBLEMS: Heavy metal contaminations and aquatic ecosystems bacterial transport-mediated resistance

THE QUESTION: Can these problems be addressed with efflux pump inhibitors (EPIs) and siderophores?

WORKING HYPOTHESES: Aquatic bacteria rely on their transport system to secrete toxic metals and antibiotics. Several EPIs are promising drugs for reverting efflux-mediated resistance. In an ongoing project, new compounds revealed synergic activity with known antibiotics and others exhibited potent Gram-positive antibacterial activity. Siderophores are small, high-affinity iron-chelating compounds that coupled with antibiotics act as prodrugs Trojan horses reaching Gram-negative bacterial that could manage heavy metal contamination and drug resistance in environmental relevant bacteria.

AIMS: Design and synthesis of antibacterial adjuvant compounds based on a prodrug Trojan horse approach.

APPROACHES: Hybridization of promising in-house EPIs/antibacterials with established siderophores. Screening for antibacterial activity and capacity to modulate microbial efflux transporters.

EXPECTED RESULTS: Discovery of new Trojan horses of antibiotics/EPIs with potential environmental use and economic valorization.

GROUP DESCRIPTION: The objectives of Natural Products and Medicinal Chemistry Group at CIIMAR are the search for new compounds with potential biological and pharmacological properties from marine biodiversity, design and synthesis of novel compounds based on marine natural products scaffolds, determination of biophysicochemical parameters and study of their mechanisms of action on cellular and molecular targets and particularly related to antimicrobial activity, as well as efficient methodologies for isolation, synthesis and analysis of chiral compounds. Extensive knowledge and expertise in the synthesis and discovery of new bioactive substances, including antimicrobials and efflux pump inhibitors, is guaranteed by supervisor E Sousa.

Job position description:

A multidisciplinary strategy in Medicinal Chemistry and Microbiology, combining synthesis and biological assays, will be followed to discover new Trojan horses based on a siderophore-prodrug approach that could mitigate toxic heavy metal contamination and/or antibiotic resistance of bacteria. The best antibacterial small molecules and/or with higher synergic activity with known antibiotics, obtained in-house within project PTDC/SAUPUB/28736/2017, are being characterized for in vitro studies. In this position, these hits will be conjugated with known siderophores to overcome toxic metals contamination and drug resistance. This approach will follow TWO TASKS in an iterative way to allow compounds optimization:

1. Synthesis of hybrids of siderophores with new compounds with potential antibacterial/EPI activity – 1st year and 1st semester of 3rd year
The candidate will gain competences in synthesis and purification of small molecules, as well as spectroscopic analysis and stability studies.
Environmentally friendly approaches using microwave-assisted multicomponent one-pot one-step polycondensations will furnish the desired antimicrobials. Known siderophores will be conjugated to antimicrobial/EPI small molecules. The stability of the conjugates will be investigated at different pH, times, temperatures and medium assays.
2. Screening of conjugates for antibacterial activity and modulation of efflux pumps: 2nd year and 2nd semester of the 3rd year
These studies will be performed in collaborative work with several participant groups:
- The antibacterial activity will be investigated in multidrug resistant (MDR) strains important for human health and aquatic ecosystems and possible synergistic effects when in combination with antibiotics.
- Potential interactions in the presence of metals will be explored by analyzing time-depending metal complexation with the conjugates.
- The activity of prodrugs on strains expressing the AcrAB-TolC pump will be assessed.

Group Leader:

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