



Viewpoint

New challenges of marine ecotoxicology in a global change context

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ABSTRACT

Currently, research agenda in marine ecotoxicology is facing new challenges with the emergence of newly and complex synthesized chemicals. The study of the fate and adverse effects of toxicants remains increasingly complicated with global change events. Ecotoxicology had provided for a decades, precious scientific data and knowledge but also technical and management tools for the environmental community. Regarding those, it is necessary to update methodologies dealing with these issues such as combined effect of conventional and emergent stressors and global changes. In this point of view article, we discuss one hand the new challenges of ecotoxicology in this context, and in the other hand, the need of updating agenda and methodologies currently used in monitoring programs and finally recommendations and future research needs. Among recommendations, it could be cited the necessity to perform long-term experiments, the standardization of sentinel species and taking benefit from baseline studies and omics technologies.

1. Introduction: marine ecotoxicology in a global climate change context

As the majority of scientific disciplines, ecotoxicology had gone through several stages and is considered as a multi-disciplinary, multi-threaded and dynamic research axis dealing with complementary scientific and technical aspects. Ecotoxicology focuses on the study of the exposure, the accumulation and the effects of environmental stressors at different scales, ranging from the molecules, cell, organ, system, whole organism, population, community, to ecosystem and biosphere levels (Cairns, 2005; Zhou et al., 2013). Historically, ecotoxicology as an academic discipline and research interest, “was born as a combination of ecology and toxicology and, loyal to its multidisciplinary origins, has rapidly advanced integrating many disciplines including biochemistry, physiology, systems biology, bioinformatics, biostatistics, ‘omics’ technologies or mechanistic modeling among others” (Campana and Wlodkovic, 2018). According to Cairns (2005), “challenge to ecotoxicologists is to carry out, during a period of unprecedented ecological change, the four major activities of hazard evaluation: (1) screening or range-finding toxicity tests, (2) predictive toxicity tests, (3) validating or confirming tests, and (4) monitoring.” So, the main objective of ecotoxicology still remains to understand and ultimately predict effects of contaminant stress on ecological systems (Walker, 2006). As well as new chemicals are elaborated and performed (e.g. nanoparticles, new synthesized pesticides, complex drug molecules, etc.), ecotoxicology expanded

towards new and cutting-edge branches such as nanoecotoxicology or highly relevant techniques such as ecotoxicogenomics. Despite chemical contamination, five major stressors are changing marine environments including climate changes, natural habitats changes, natural stock over-exploitation and eutrophication (Chapman et al., 2017). Climate change is one of the major global issues, threatening the planet at different levels (Brierley and Kingsford, 2009; IPCC, 2014). Conceptually, global changes could be defined as “changes in the global environment (including alterations in climate, land productivity, oceans or other water resources, atmospheric chemistry, and ecological systems) that may alter the capacity of the Earth to sustain life” (GCRA, 1990). Global climate change is characterized by an increase of mean global temperature and consequently changing precipitation patterns, coupled with an increasing frequency of extreme temperature and precipitation events (Coutmou and Rahmstorf, 2012; IPCC, 2014). The National Aeronautics and Space Administration (NASA) recent reports reported that the whole global temperature has increased about 1.1 °C from 1884 to 2017 (NASA Global Climate changes, 2018). Recent climate projections scenarios predict significant increases in air and ocean temperature and changes in ocean chemistry by 2100 (IPCC, 2014). In the same context, ocean acidification has increased about 30% from the beginning of the Industrial Revolution (mid 1800) until now (US National oceanic and Atmospheric Administration, 2018). Ocean acidification as the result of the increase of atmospheric carbon dioxide level will modify carbon dioxide-carbonate equilibrium in water into acidic (Nikinmaa, 2013).

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Living organisms had always lived and evolved in changing environment, and thus from the life appearance on earth (Silvestre et al., 2012). Consequently, changes in global temperature, pH of the ocean, chemical composition of the atmosphere, and radiation are part of the major events organisms have to deal with during the course of evolution (Silvestre et al., 2012).

The combined occurrence of ocean increasing temperature and ocean acidification imposes eco-physiological challenges to marine organisms, eliciting interactive negative effects on survival, growth and overall physiological fitness (Pörtner, 2001; Harley et al., 2006; Kroeker et al., 2010; Silvestre et al., 2012; Harvey et al., 2013; Nikinmaa, 2013; Romero-Lankao et al., 2014; Pimentel et al., 2015). Recent years, some researchers highlighted the need of considering the effect of global changes in marine organism as well as marine habitats components (Fabry et al., 2008; DeLorenzo, 2015). For example, recently Allemand and Osborn (2019), reported that coral reefs ecosystems are among the most endangered because of global changes (ocean acidification, global warming, chronic pollution) and overexploitation of natural resources.

Effects of global changes may induce a wide range of effects on marine ecosystems, including increased water temperature, water current alteration, increased salinity, increased erosion, and alteration in freshwater runoff patterns in the case of estuarine habitats (Grabemann et al., 2001; Knowles and Cayan, 2002; DeLorenzo, 2015; McKinney et al., 2015). Currently, research in marine ecotoxicology should take in account, global changes effects in organisms for a better environmental monitoring significance (Noyes and Lema, 2015; Cabral et al., 2019; Tlili and Mouneyrac, 2019). Some reports focused on the existence of potential interactions between toxicants availability/effects and natural environmental responses pertaining to global change symptoms (Hooper et al., 2013; Nikinmaa, 2013; DeLorenzo, 2015; McKinney et al., 2015; Sampaio et al., 2018). Knowledge about the potential interactions between contaminants, toxicity assessment methods and global changes effects, still remains not sufficient (Nikinmaa, 2013; McKinney et al., 2015; Noyes and Lema, 2015; Cabral et al., 2019; Tlili and Mouneyrac, 2019). According to available data and simulation scenario, it's well established that a warmer climate and greater acidic and eutrophic marine ecosystems will potentially contribute to increase combined stress leading to be organisms more sensitive to even slight perturbations caused by chemical stressors, since organisms are pushed to the limits of their physiological tolerance range (Hooper et al., 2013; Kalenborn et al., 2011). Currently, another missing gap in marine ecotoxicological studies is the scarcity and the absence of long-term experiments studying the potential effects of emergent problematic issues such as contamination by plastics (micro and nano), drug residues, nanomaterials, new synthesized pesticides, or other emergent contaminants (Tlili and Mouneyrac, 2019).

In this context, researchers in ecotoxicology are concerned by this necessity of developing new research agenda dealing with urgent priorities and as consequence update methodologies dealing with those new aspects of challenges (Artigas et al., 2012; Hooper et al., 2013; Nikinmaa, 2013; Vigh and Villa, 2013; Dahms, 2014; DeLorenzo, 2015; Hartl, 2015; Noyes and Lema, 2015). In this point of view article, we discuss first the new challenges of ecotoxicology in a global change context and secondly the need of updating agenda and methodologies currently used and finally some recommendations and proposal for the future global change ecotoxicology.

2. Current methodologies in marine ecotoxicology

2.1. Environmental monitoring of marine habitats

Environmental monitoring is a complementary integrated approach associating ecological, chemical and biological characteristics of natural habitats and largely used from decades to assess the environmental health status of those ecosystems. For marine ecosystems, the implementation of biomonitoring strategies has been proposed since long time

(Amiard and Amiard-Triquet, 2008). Biomonitoring has been defined as "the systematic use of living organisms or their responses to determine the condition or changes of the environment" (Rosenberg, 1998).

Due to the limitations associated with the chemistry-based surveillance (e.g. bioavailability, spatial-temporal variability, analytical detection limits, high cost of contaminant analysis), biomonitoring, based on the use of living organisms to provide information on the quality of aquatic environments has been proposed, and now is a widely accepted approach for assessing contaminant bioavailability (Oehlmann and Schulte-Oehlmann, 2003; Zhou et al., 2008; Waykar and Deshmukh, 2012). Historically, the US EPA (United States Environmental Protection Agency) Mussel Watch program was a pioneer program for marine monitoring using mussels as bioindicators of water quality (Farrington et al., 2016). In 2000, the European Parliament and Union (EPU), established the Water Framework Directive (WFD) with the inclusion of comprehensive Environmental Risk Assessment (ERA) for the monitoring of aquatic environments (Varea et al., 2020). Later, in 2008, the European Union (EU) further established the Marine Strategy Framework Directive (MSFD) with the application of Environmental Monitoring (EM) for an integrative ERA in oceanic and coastal waters (European Parliament and Union, 2008; Varea et al., 2020). This important step was completed in 2014 by the integration of biomonitoring programs in the MSFD (Varea et al., 2020).

2.2. The determinant role of sentinel species selection

From the beginning of marine monitoring programs, different species have been investigated to determine their potential use as sentinel organisms. Marine biomonitoring studies were mainly based on the use of sentinel species representative of the water column, such as bivalves widely used for the assessment of environmental levels of contaminants (e.g. Mussel Watch program) as well as for examining biological effects of contaminants (WGBEC, 2006; Amiard and Amiard-Triquet, 2008) but also organism able to reflect sediment quality, the compartment considered as the final sink of different kind of both conventional and emergent pollutants. Sentinel species are defined as "any species providing a warning of a dysfunction or an imbalance to the environment, or, more restrictedly, a warning of the dangers of substances to human health" (Berthet, 2013). Therefore, a sentinel species may be different regarding to the information given, when used in environmental monitoring: *i*) a bioindicator species providing information by its presence, absence and/or of abundance of individuals, *ii*) a bio-accumulative species; the capacity of which to accumulate contaminants at levels much higher than those in the environment designates it as the material of choice for the monitoring of the degree of contamination of the environment, *iii*) a species for which modifications of biological parameters at one or various levels of organization (molecular, cellular, physiological, organism or behavioral) are used to estimate the risks associated with the presence of contaminants (Berthet, 2013). According to criteria cited above, a relatively large list of species from different levels of ecological organization (principally crustaceans, mollusks and fish), could be proposed for the biomonitoring of marine ecosystems (Waykar and Deshmukh, 2012; Zuykov et al., 2013; Tlili and Mouneyrac, 2019). Indeed, most bivalves usually have a broad geographical distribution, are sessile or exhibiting an extremely limited mobility, and thus reflecting the local conditions of their habitat, have a relative long lifespan allowing for time integration and accumulation rate calculations in contamination studies, easily handling in both laboratory and field conditions and both for active and passive biomonitoring (Oehlmann and Schulte-Oehlmann, 2003; Coelho et al., 2006; Waykar and Deshmukh, 2012). Regarding the global effects of climate change on marine organism, it seems evident that global climate change could affect the natural responses of sentinel species as well as wildlife complements. In this context, climate change may increase the vulnerability, the stress level of marine organisms and ecosystems, that will cause the interactions between marine pollution effects and climates changes a

serious needing specific attention (Lelieveld et al., 2001; Dahms, 2014). In comparison with terrestrial ecosystems, the impacts of climate change on the aquatic organism are likely to be more perilous, since many invertebrates and fish are ectotherms and depend on water temperature (Sunday et al., 2011., Ben-Hasan and Christensen, 2019). Considering the population level, global climate change may select more tolerant individuals, since future populations could gradually adapt to longer durations of elevated temperatures, higher or lower salinities, hypoxia and acidification (DeLorenzo, 2015). Those changes will consequently effect species interactions, biodiversity and ecological equilibrium. In the actual statue of knowledge, large-scale ecological consequences of global changes are principally studied with predictive models and simulations. For marine ecosystems, recognized predictions regarding climate-induced changes on the composition and distribution of the marine organisms include shifts in the species distribution from lower to higher latitudes, shifts from near-surface to deeper waters, variation in annual phenology, declines in calcifying species, and increases in the abundance of warm-water species (IPCC, 2014; Poloczanska et al., 2016). For example, in Mediterranean Sea, a surface temperature water increase (0.3–0.6°C) recorded from 1950 to 2009 was associated to an increase of the abundance of warm water species, specially originated from the Red Sea (PNUE-PAM-CAR/ASP, 2011).

3. Biomarkers as tools for environmental assessment in a global change ecotoxicology

The methodology of measuring biomarkers in sentinel species has been extensively developed since the last 30 years, as consequence to the need for early-sensitive environmental tools able to reveal sublethal effects in organisms, and responding precociously, well before measurable effects on individual performance and population/community changes occur (Amiard and Amiard-Triquet, 2008; Amiard-Triquet and Rainbow, 2009). By definition a biomarker is “a bio-chemical, cellular, physiological or behavioral variation that can be measured in tissue or body fluid samples or at the level of whole organisms that provides evidence of exposure to and/or effects of, one or more chemical contaminants (and/or radiations)” (Depledge and Fossi, 1994). By the mid-1980s a wide range of biomarkers that constitute an early warning system have been developed in environmental assessment but the methodology of biomarkers use and interpretation is a continuous process of revisiting and evolution and some core biomarkers are selected for further standard biomonitoring tools (Adams, 2005; Forbes et al., 2006; Amiard and Amiard-Triquet, 2008; Mouneyrac and Amiard-Triquet, 2013; Dahms, 2014). One of the reasons of this revisiting process, is that despite the useful of biomarkers in identifying potential stressors in the marine ecosystem before environmental change occurs, it is difficult to attribute cellular responses to ecologically relevant impacts. So, it will be necessary to use individual biomarkers that have a strong relationship to ecological measurements, namely ecological biomarkers (Amiard Triquet et al., 2013; Biagianni-Risbourg et al., 2013). In order to cover different biological endpoints and for more ecologically relevance, biomarkers are almost used in a multi-biomarker approach to reveal potential stress due to different classes of contaminants (Tlili et al., 2013). Well, despite the large literature on biomarkers and their use in biomonitoring studies, their incorporation in regulatory legislation for environmental risk assessment is still limited and criticized. Many reasons could explain this, among which is the influence of confounding factors (e.g. size, sex of organisms, reproductive status, season, temperature and salinity) that may interfere with responses of biomarkers strictly attributable to differences in chemical stress (Hagger et al., 2006; Kalman et al., 2010; Fossi Tankoua et al., 2011; Mouneyrac and Amiard-Triquet, 2013; Amiard-Triquet and Berthet, 2015; Barrick et al., 2016; Milinkovitch et al., 2019). Another important biotic interaction that could be considered as confounding factor is parasitism, since host-parasite interactions are ubiquitous in aquatic habitats (Minguez et al., 2009; Minguez and Giambérini, 2019). In fact, parasites

could induce different host physiological changes in their favor such as an energetic reallocation for their own development; or a weakening of the host immune system (Plaistow et al., 2001; Rigaud and Moret, 2003). Those interactions lead to some serious implications for environmental risk assessment, including results misinterpretation (Minguez et al., 2009). From another side, many authors had reported the potential interactions of associated microbial communities in the survival and/or the modulation of biological responses of host organisms in polluted ecosystems (Claus et al., 2016). For example, some reports discussed the important role of gut microorganisms in many marine species used in ecotoxicology such as fish and mollusks (Evariste et al., 2019; Li et al., 2020). In fact, gut microbial communities play an important role in the regulation of homeostasis of multiple host physiological functions as well as in resistance towards environmental contaminants (Rowland et al., 2017; Evariste et al., 2019). Associated microorganisms could modulate biological responses to pollutant exposure and consequently could be considered as a confounding factor for biomarkers measurement in species. In this sense, Evariste et al. (2019) reported that biotransformation capacities of gut bacteria were demonstrated to be efficient in the neutralization/metabolization/degradation of several pollutants such as trace metals (Diaz-Bone and Van de Wiele, 2010), biocides (Velmurugan et al., 2017; Yim et al., 2008), polycyclic aromatic hydrocarbons (PAHs) (Van de Wiele et al., 2005), pharmaceuticals (Sousa et al., 2008) and recently microplastics (Li et al., 2020). In a recent report, Redfern et al. (2021), had demonstrated the main role of gut microbial community associated to the Atlantic killifish (*Fundulus heteroclitus*) in the adaptive resistance to PAHs.

Now, it's seems to be an evidence, that the biomarkers approach is a useful tool to evaluate environmental assessment of impacted sites, if only there are used correctly taking account natural fluctuation and confounding factors (Milinkovitch et al., 2019). However, what we are trying to elucidate in the current paper, is the suitability of the biomarkers use in a global change context. This will help scientific community to clarify the need of updating biomarkers methodology and propose suitable tools.

4. New challenges of marine ecotoxicology in a global change context

4.1. Why current practices should be up-to-date?

Last years, many researchers highlighted the urgent need to deeply study of the interaction between both global change forcing factors and chemical stressors on marine ecosystems to encompass the complex climate modifications anticipated (Dahms, 2014; DeLorenzo, 2015).

In this sense, a more understanding of how climate change alters chemical contaminant distribution, fate and effects will be critical to achieving valid environmental risk assessments (DeLorenzo, 2015; Noyes and Lema, 2015). Global change effects are expected to influence the distribution and toxicity of chemical stressors that may trigger and worsen declines in some species and population health (Noyes et al., 2009; Hooper et al., 2013; Moe et al., 2013; DeLorenzo, 2015; Noyes and Lema, 2015). On this part, we will discuss some examples illustrating possible interactions of global change stressors on pollutants availability, bioaccumulation process and responses of conventional biomarkers. Due to the diversity of cases and the complexity of the action mechanisms of global change forcing factors, we will only focus on global warming effects.

4.2. Interaction between pollutants availability, biomarkers responses and global warming

Metallic pollution in marine ecosystems is still a serious environmental precaution due to metals distribution, fate, the diversity of entrance ways and their high toxicity at sub-individual level. Global

change factors could interact with their toxicity in marine organism since metal solubility and speciation state in seawater varies with abiotic parameters including salinity, temperature, oxygen, and pH (DeLorenzo, 2015). As temperature tends to increase metal uptake and subsequent metal toxicity (Fritioff et al., 2005), ambient temperature increasing could interact with pollutant toxicity, herein the case of metals. For example, the toxicity of Cd, Cu, Zn, and Pb to the juvenile crayfish *Orconectes immunis* was significantly increased under elevated temperature (Khan et al., 2006). A 3–4 degree increase in temperature caused three-fold increases in metal-induced oxygen consumption (Khan et al., 2006). In another example, increasing temperature from 15 °C to 20 °C increased metal uptake in the Mediterranean fish *Solea senegalensis* and altered metallothionein levels and metal partitioning into liver and kidney (Siscar et al., 2014). As a crucial physical element, temperature is involved on all biological organization levels, from molecular diffusion and biochemical reactions, to membrane permeability, to cellular, tissue and organ function, and to their integration in the whole organism (Byrne, 2011). So, at least from conceptual point of view, modification on global temperature will affect the entire biological cascade from molecular to behavioral and consequently population levels (Guderley and St-Pierre, 2002; Byrne, 2011). In this sense, Lannig et al. (2006, 2008) demonstrated that increasing temperature from 20 °C to 28 °C significantly increased cadmium toxicity by increased oyster mortality, rapid hypoxemia lipid peroxidation, and decreased condition index. Other research showed that metal detoxification mechanisms (e.g. glutathione levels, rate of protein synthesis and metalloproteins expression) decreased at the higher temperature, reducing capacity for metal metabolism (Lannig et al., 2006; Banni et al., 2014; Boukadida et al., 2016). For other conventional persistent pollutants, such as PAHs, studies demonstrated that the increasing temperature induced a decrease in detoxification enzyme activities and an increase in Benzo(a) pyrene (BaP) accumulation and toxicity in mussels *Mytilus Galloprovincialis* (Kamel et al., 2012). The differences in temperature effects are thought to be driven by biotransformation activity that can yield either more toxic or less toxic degradation products, depending on the pesticide (Harwood et al., 2009). In the case of biocides (e.g. the largely used pesticide chlorpyrifos) for example, increased biotransformation rates at higher temperatures have been shown to increased production of the more toxic oxon-analog (Harwood et al., 2009).

5. Limits of conventional methodologies: what baseline studies will provide?

The successful use of conventional biomarkers into marine monitoring programs requires the development of effective strategies taking in account the role of confounding factors (Barrick et al., 2016). Confounding factors have been well documented for both core biomarkers and ecological biomarkers (Amiard Triquet et al., 2013). The most studied confounding factors on biomarker response and interpretation in aquatic organisms are abiotic factors, precisely temperature, salinity and the influence of size/weight/age (Amiard-Triquet and Berthet, 2015). So, if biomarkers responses in marine organism are naturally influenced/modulated by abiotic factors such as temperature, their use for global change ecotoxicology seems relevant in condition to taking in account responses modulation. Ideally, the distinction between chemical stress responses and natural/induced effect of physical stressors should be well characterized, at the laboratory level, before the recommendation of the use of those tools in combined stressors context.

The idea to avoid the effects of confounding factors on the biomarker approach in marine ecotoxicology is not new. Many research efforts focused on the standardization and control for genetic and individual variability (e.g. same size range, sex) and physic-chemical factors (especially temperature, salinity and pH changes) in a purpose to have equivalent data between comparable studied groups (Durou and Mouneyrac, 2007; Kalman et al., 2010; Amiard-Triquet and Berthet, 2015; Barrick et al., 2016). Thus, the standardization of the measurement of

the confounding factors influence on biomarkers responses could allow to the development of predictive models able to define the baseline representative of reference conditions (Artigas et al., 2012; Amiard Triquet et al., 2015; Vethaak et al., 2015; Barrick et al., 2016). As result, the establishment of baseline assessment criteria (BAC) and environmental assessment criteria (EAC) to define environmental quality (OSPAR Commission, 2013) could be used. Those described methods operate by defining the range of values expected in a reference site as the BAC and values outside this range as the EAC (Barrick et al., 2016). In addition, it's important to note that the establishment of BAC or/and EAC for a sentinel species required the respect of strict precautions such as the collection of organisms from a reference site for at least two seasonal cycles in order to establish the influence of confounding factors when measuring chemical/physical biomarkers in order to facilitate the identification of contaminated sites from a part and to study the natural responses to physical stressors (OSPAR Commission, 2013; Amiard Triquet et al., 2015; Barrick et al., 2016).

6. Omics as promising tools for global changes ecotoxicology?

If biomarkers have been proposed as reliable indicators of the toxic exposure of many sentinel species to a wide range of pollutants, omics-based diagnostic tools will soon revolutionize the routine assessment of the health status of sentinel organisms (Gouveia et al., 2018). During the last twenty years, genomics-based, proteomics, transcriptomics and metabolomics approaches provided insights into the mechanisms underlying the biological responses in natural biota following exposures to environmental contaminants particularly in the case of chronic exposure at low dose/concentrations (Tanguy et al., 2008; Lockwood et al., 2010; Banni et al., 2011, 2014; Canesi et al., 2011; Negri et al., 2013). The accessibility of new genomic resources, the development of high-throughput molecular technologies such as microarray, pyrosequencing and next generation sequencing have provided information and helped to identify molecular targets of conventional and emergent contaminants (e.g. nanoparticles, micro and nano-plastics, pharmaceuticals products, newly synthesized biocides) that contribute to stress in natural marine organisms (Dahms, 2014; Barrick et al., 2019). Studies dealing with the characterization of global change effect at the molecular level on marine organism still scarce and are limited to laboratory experiments. Otherwise, some of those studies focused on the widely used sentinel species, the mussel *M. galloprovincialis*. Negri et al. (2013) showed that heat stress (at 24 °C) associated to copper exposure in mussels lead to the up-regulation of genes involved in cytoskeletal protection and down-regulation of chitin related metabolism genes under Cu- and heat-stress. Boukadida et al. (2016) reported that the mRNA expression of antioxidants enzymes and Metallothioneins (MTs) isoforms was relevant in *M. galloprovincialis* exposed to both heat stress and a mixture of metals (Ag and Cu), despite the absence of clear responses of biomarkers (SOD, Catalase, GSTs and lipid peroxydation). Recently, Mlouka et al. (2019) demonstrated the suitability of the use of microarray analysis to study the changes in gene expression patterns in response to increasing water temperature in *M. galloprovincialis* and *M. edulis* larvae. Thus, it's now well establishing that under environmental stress (even natural or induced); marine organisms can develop compensatory mechanisms that help them adapt to new conditions. However, it's still tricky to interpret complex data issuing from genomics and transcriptional tools in terms of adaptive value, increased fitness, or organismal evolution, especially that available proteomic and genomic available data in marine organism are still insufficient (Silvestre et al., 2012).

7. Conclusion: recommendations for a future research agenda in global change ecotoxicology

Considered as co-founding factors, physical parameters were largely studied in marine ecotoxicology studies and it does will be interesting to

explore data issuing to clearly characterize the effects of global change factors in marine organism. In this sense, baseline studies may to have an important impact on the future to reinforce the largely use and the interpretation of biomonitoring tools. It's now necessary that research in marine ecotoxicology concentrate their effort on a short-list of sentinel species, especially fully studied from genomic and proteomic point of view. Among this species, figure the zebra fish (*Danio rerio*), a fully sequenced fresh water fish, largely used in chemical screening, toxicity assessment and biomonitoring (Tanguay, 2018) and the marine blue mussel *M. edulis* (Beyer et al., 2017). Well, despite research effort, the task is not easy and critics about the use of those sentinel species, are still topical. Despite advantages, Scientifics aware about the ecological significance of their sub-individual response. Regrading to marine bivalves as suitable sentinel organisms for the monitoring of both climate change and pollution, the development of biosensors approach (by measuring valvometry and/or other behavioral markers) could be benefic for global change ecotoxicology studies (Guterres et al., 2020).

In other hand, long-term experiments combining chronic chemical exposure and changing physical parameters (e.g. Temperature and pH variation) should be performed on model organism and/or in mesocosms. Those long-term experiments could improve the state of knowledge concerning the effected of combined stressors on the biological and ecological traits of marine habitats. Consequently, this could contribute the study of acclimation and adaptive process, until now, based on scenari performing and modeling.

Climate change variables may influence the fate of toxicants in marine ecosystems accelerating ocean acidification at local scale and complicating adverse effects on marine organisms. If those aspects are currently well studied in conventional toxicants (e.g. trace metals, PAHs, PCBs, biocides, ect.), it's still a missing gap concerning the influence of climate change on the fate and potential interaction of emergent toxicants such as micro and nanoplastics, drugs and health/care products residues, nanoparticles and new synthesized pesticides.

We think that the future of global change ecotoxicology could take benefit from baseline studies and omics technologies to provide easy, universal, robust and interpretable tools for the study of combined pollution and global change effects in aquatic ecosystems.

CRediT authorship contribution statement

Sofiene Tlili: Conceptualization, Methodology, Writing – review & editing. **Catherine Mouneyrac:** Conceptualization, Methodology, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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