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TORPP - Turtles, One Health Research & Plastic Pollution: A multidisciplinary consortium to evaluate the environmental and health impact of Micro/NanoPlastics (MNPs) pollution

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ABSTRACT

Although the World Health Organization characterizes a One Health concern as one in which there is the capability to incorporate numerous disciplines to tackle health challenges threatening humans, animals and ecosystems, scientific efforts frequently remain compartmentalized. Here we report an original consortium, TORPP, spanning 16 disciplines, focused on Micro/NanoPlastics (MNPs) pollution as a One Health concern. Whereas the MNP topic has been largely studied in marine ecology, research effort remains scarce in human medicine. Equally, while marine ecology is highly skilled in MNP sampling and characterization, human medicine has developed pathophysiological concepts and tools that can be used more broadly to evaluate the health impact of MNPs. TORPP consortium propose that these strengths and knowledges must be transferred across fields of study to advance our understanding of MNP toxicity to organisms, by uniting integrative approaches (ecological, experimental and clinical) under a common conceptual and analytical framework.

1. Plastic pollution scale, environmental and human health issues

Plastic pollution represents one of the greatest environmental and health challenge of our time [1,2]. In 2010, between 4.8 and 12.7 million metric tons of land-based plastic waste entered the marine environment, contributing to the 5 trillion of plastic debris already polluting the world's oceans [3]. Despite an increasing research effort globally, the true extent and bioaccumulation of Micro/NanoPlastics (MNP) pollution, as well as its impact on the health of living organisms, remains largely unknown [4]. The most robust and extensive data on

MNP toxicity come from marine ecosystems and suggest a wide array of adverse effects, including alteration of gene expression, dysbiosis, and neurotoxicity [5–7]. Charlton-Howard et al. [8] defined “plasticosis” pathology in seabirds as MNP-induced digestive fibrosis, which shares many similarities to human IBD (inflammatory bowel disease). Today, surprisingly, a human health risk assessment for plastic particle pollution is currently not feasible due to the lack of data on both toxicological hazards and human exposure. Before 2024, human cohorts were rare, samples sizes small [9,10], and research effort appeared marginal. Recently, Marfella et al. [11] found that patients with carotid artery plaque, in which MNPs were detected, had a higher risk of myocardial

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¹ TORPP Association (Turtles, One-health Research & Plastic Pollution) – <https://torpp.net/>

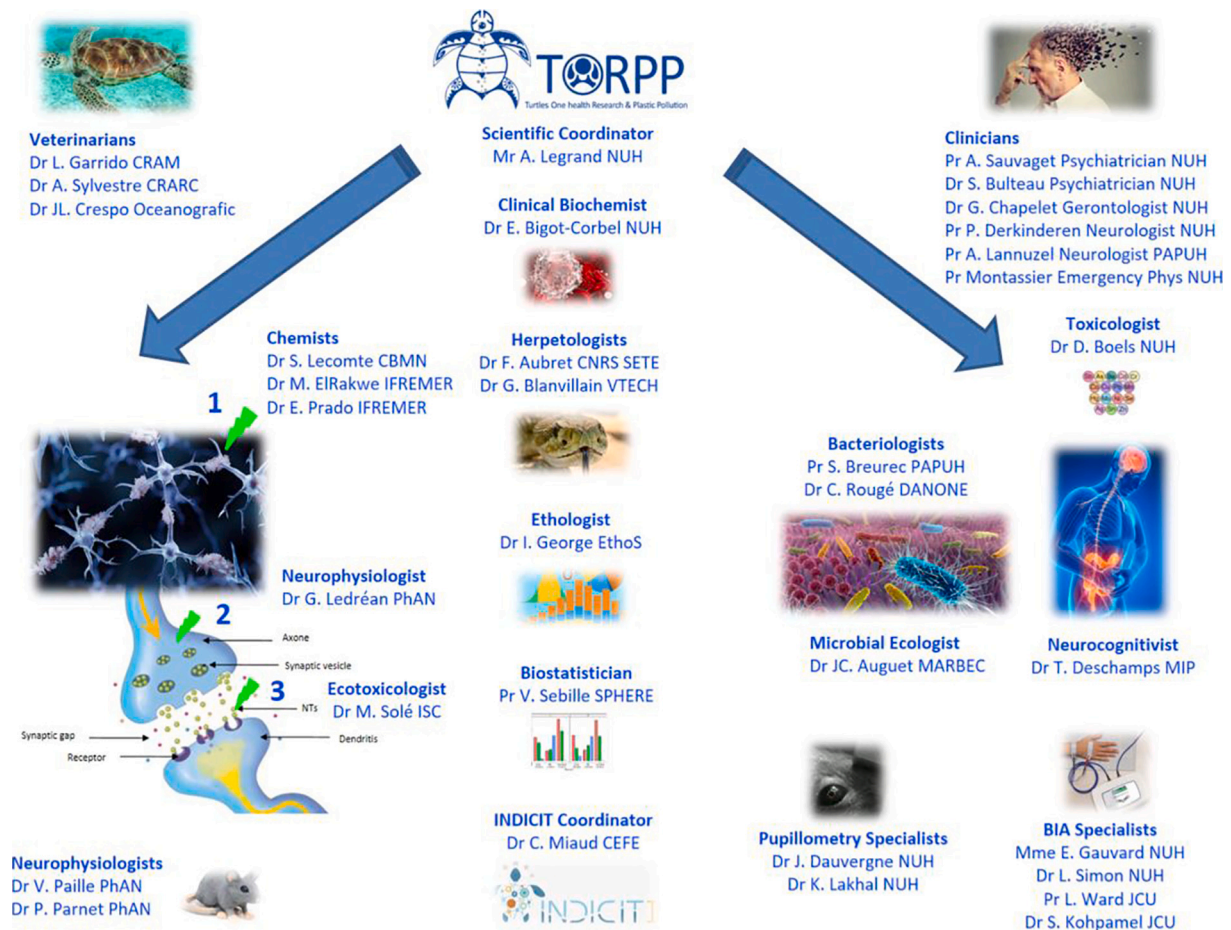


Fig. 1. TORPP Consortium Composition (<https://torpp.net/>).

infarction, stroke or death from any cause 34 months after follow-up. Considering the complexity of this issue and a clear contribution of MNPs to the exposome [12], a multidisciplinary approach seems necessary.

2. Marine turtles and humans, pragmatic bioindicators species for MNPs

The abundance of MNPs (plastic particles measuring <5 mm) in both the terrestrial and marine environments poses an emerging threat to the global health of ecosystems and organisms throughout the globe. Given their microscopic sizes and ubiquity, MNPs are typically absorbed by a large array of organisms, disseminating and bioaccumulating in all tissues and interfering with all biological functions [2]. Bio-indicator monitoring is invaluable because it makes up for the impossibility of exhaustive counting of plastic waste in the environment, given its wide distribution and high environmental and seasonal variability.

Due to their life history-traits and diet, marine turtles are heavily and chronically exposed to MNPs, which they bioaccumulate throughout their lives. Levels of contamination are thus usually much higher than in any other oceanic *meso*/apex predators [13]. Since 2013, loggerhead sea turtles are used as a bio-indicator to monitor the impact of plastics for the DCMM (Marine Strategy Framework Directive for European Marine Waters) and in areas covered by the OSPAR (Northeast Atlantic region) and Barcelona conventions. Around 100 institutions, including research and veterinary laboratories, care centers, and stranding networks, have been trained to apply standardized data collection on the presence, dry mass, characteristics, size and color of plastics in the digestive system of turtles found dead.

On the other hand, humans are increasingly becoming aware that they are being exposed to chronic levels of MNPs absorption due to many industrial processes (i.e. food and goods packaging) as well as via direct inhalation. Few studies have quantified the levels of chronic MNP contamination in humans, however, a study from Cox et al. [14] suggests that people who meet their recommended water intake through bottled sources only, ingest an average of 90,000 plastic particles annually. In addition, the average annual consumption of MNPs for a standard adult male has been estimated at 114,000 particles [14].

From a strong One Health perspective, humans and marine turtles are thus intuitive models to monitor health impacts from MNPs pollution, as both organisms share chronic/multiple-exposure routes and similar longevity. Moreover, by studying these two ecological models in real life conditions rather than in controlled experimental settings, TORPP aims to assess MNP toxicity by specifically investigating the impacts of MNPs' typology, size and exposition duration on comorbidities.

3. TORPP origins: the need for a multidisciplinary approach to better address MNP threat

Despite convergent interests on MNP hot topic, disciplines largely work in a compartmentalized way [15]. One of the key objectives of the TORPP consortium is thus to foster discussions and facilitate the transfer of knowledge, expertise, and technologies between scientific specialties.

To illustrate this, with respect to the characterization and quantification of MNPs, very few studies have been undertaken on humans compared to marine ecology. The biomedical world lags behind the ecological field in terms of pre-analytical methodology and analytical

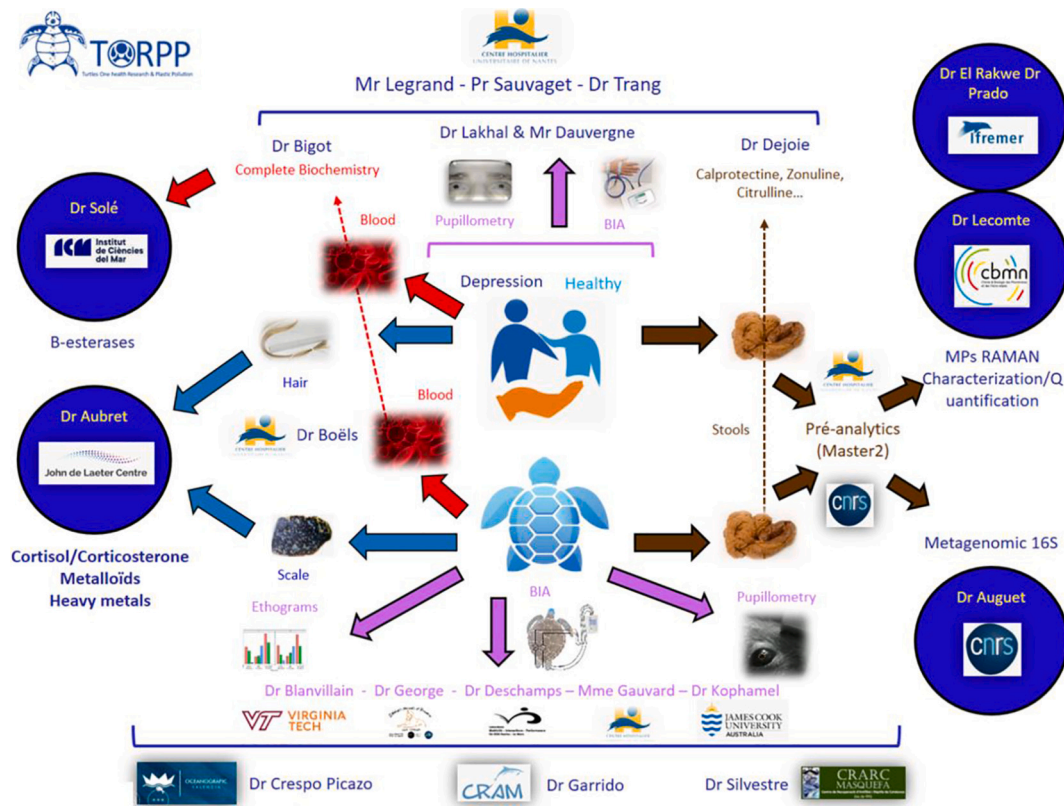


Fig. 2. MIGUD One Health Research, designed by TORPP Consortium.

strategies. Therefore, the TORPP group was created to design MNPs research on humans and turtles, using standardized sampling and pre-analytic and analytic treatments by marine specialists with the goal to maximize data robustness and species comparisons.

Regarding microbiome research, pre-analytical and analytical frameworks (e.g., stool sampling, metagenomics flows, biostatistics) also fluctuate between disciplines. Rectal swabbing has long been validated as a robust proxy of human stools, but not in ecology, despite obvious practical advantages. Thus, we tested this technique for the first time in marine turtles during the CAOUA study (<https://biodivoc.edu.umontpellier.fr/recherche/projets-pilotes/projet-caoua/>). This study also tested several immuno-inflammatory human biomarkers (e.g., calprotectine, cytokines) to try to reinforce our mechanistic understanding of MNPs dysbiogenic effect in marine turtles. Inversely, there is a growing body of evidence in marine ecology that plasmatic B-esterases are adequate candidate biomarkers of xenobiotic exposure associated to plastics in marine life [16]; so TORPP clinicians plan to measure it for the first time in an upcoming clinical research.

Finally, the nutritional effects due to MNP-induced dysbiosis is also an important outcome to investigate. In medicine, Bioelectrical Impedance Analysis (BIA) have long ago replaced standard biometry measures to accurately monitor changes in body composition. Medical and veterinary clinicians from TORPP tested BIA on marine turtles for the first time in 2019, and hope to make the use of BIA systematic in rehabilitation centers in the coming years.

4. Neurotoxicity: the most alarming one health issue of MicroPlastics?

Beyond its immuno-inflammatory and nutritional effects, neurocognitive impact of MNPs is now recognized as a serious health issue based on two non-exclusive mechanisms. First, MNPs can generate direct neurotoxicity. MNPs can directly disrupt the central nervous system via percolation through the blood-brain barrier [6], which

generates neuronal lesions, inhibits synaptic esterases [16], and provokes amyloidopathy and proteinopathy [17]. Second, MNPs can generate indirect neurotoxicity, through dysbiogenic effects [5], which likely disrupts the microbiota-Gut-Brain Axis (mGBA) [18]. Largely studied in humans, mGBA is a key mediator of bidirectional communication between mesenteric and central nervous systems, which shapes host cognition and behaviors, but this has never been studied in ecology.

A cross-disciplinary analysis of the literature reveals dysbiogenic effects of MNPs and neurocognitive impairment, such as working memory, non-spatial memory and visual recognition in murine models exposed to MNPs. Neurocognitive disorders have also been described in shrimp, zebrafish and hermit crabs, with severe alterations of anti-predatory behavior for example [7]. In humans, cognitive disorders related to microbiota dysbiosis and mGBA disruptions have also been largely described in neurodegenerative and mental health pathologies such as Parkinson's and Alzheimer's diseases, autism spectrum disorder, schizophrenia, or depression [19]. Yet, ecotoxicological aetiology related to MNPs has never been explored in any of these neuropathologies.

5. TORPP, innovative multidisciplinary group to tackle plastic pollution issue

Since 2020, the TORPP consortium has designed integrative ecological, experimental and clinical trials to study the toxicity and neurocognitive risk associated with MNPs exposure in turtles and humans. This unique One Health consortium intends to maximize multidisciplinary and cross-referenced views to better tackle the challenge of MNPs pollution (Fig. 1). Pilot project CAOUA was the first TORPP funded project in 2021, focusing on microbiota and health impact of MNPs in Mediterranean loggerhead turtles (*Caretta caretta*). One hundred and fourteen stranded loggerhead turtles from the Gulf of Lion were sampled, and the association between MNP fecal contamination and health parameters (e.g., microbiota composition,

biochemical and hematological variables) were investigated. MIGUD research (Microplastics Gut-brain-axis and Depression – Fig. 2) is a pilot matched case-control clinical study on 62 patients to test MNPs contribution to the physiopathology of depression. In a One Health approach, it addresses complementary ecological study on marine turtles to detect neurocognitive disorders in highly contaminated marine turtles. We plan to test pupillometry in marine turtles for the first time by measuring pupillary dilatation velocity from flashlight stimulations, with the goal to detect sub-clinical neurological effects induced by MNPs. Finally, exploratory approaches on “swimming signature” of marine turtles (kinematic and/or kinetic features of movements) transposed from gerontological medicine will investigate possible movement anomalies associated with cognitive interference.

6. Conclusion

In the last 4 years, and thanks to sustained transdisciplinary interactions (TORPP association <https://torpp.net>), the TORPP consortium has gradually grown to involve 16 specialties, 12 research institutes and 4 countries. Medical specialties from Nantes and Poitiers-Pitre university hospitals (France) have started to test the aetiological contribution of MNPs to multiple physiopathologies on both humans and marine turtles. We propose that MNPs could be involved in arterial stiffness, valvular aortic calcifications, or may play a role in neurodegeneration and proteinopathy. Finally, given the abundant data on mGBA disturbances and related cognitive troubles in human, TORPP group aims to advance the study of MNPs dysbiosis, particularly on magnetotactic bacterial communities, which may be linked to geomagnetic sensitivity necessary for marine turtle's orientation during their migration [20]. A One Health framework is gradually taking over as a new paradigm for powerful research which should be highly beneficial for all disciplines.

Ethics statement

No ethical approval was required for this study.

Funding statement

There is no funding to declare.

CRediT authorship contribution statement

A. Legrand: Conceptualization, Supervision, Validation, Writing – original draft. **G. Blanvillain:** Conceptualization, Supervision, Validation, Writing – review & editing. **T. Deschamps:** Conceptualization, Supervision, Validation, Writing – review & editing. **G. Chapelet:** Supervision, Validation, Writing – review & editing. **F. Aubret:** Supervision, Validation, Writing – review & editing. **L. Garrido:** Supervision. **A. Martinez-Silvestre:** Validation. **J.C. Auguet:** Supervision, Validation, Writing – original draft, Writing – review & editing. **A. Sauvaget:** Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare no competing interests.

Data availability

No data was used for the research described in the article.

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