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Microbiota analysis for risk assessment of xenobiotics: toxicomicrobiomics, incorporating the gut microbiome in the risk assessment of xenobiotics and identifying beneficial components for One Health

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Abstract

This work explores three areas of relevance to the gut microbiome in the context of One Health; the incorporation of the microbiome in food safety risk assessment of xenobiotics; the identification and application of beneficial microbial components to various areas under One Health, and specifically, in the context of antimicrobial resistance. We conclude that, although challenging, focusing on the microbiota resilience, function and active components, are critical for advancing the incorporation of the gut microbiome in the risk assessment of xenobiotics. Moreover, research technologies, such as toxicomicrobiomics, culturomics and genomics, especially in combination, have revealed that the human microbiota may be a promising source of beneficial taxa or other components, with the potential to metabolise and biodegrade xenobiotics. These may have possible applications in several health areas, including in animals or plants for detoxification or in the environment for bioremediation. This approach would be of particular interest for antimicrobials, with the potential to ameliorate antimicrobial resistance development. Finally, we propose that the concept of resistance to xenobiotics in the context of the gut microbiome may deserve further investigation in the pursuit of holistically elucidating their involvement in the balance between health and disease.

Keywords: One Health, gut microbiome, xenobiotics, microbiota-disrupting chemicals, next-generation risk assessment, antimicrobial resistance, next-generation probiotics

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1. Introduction

1.1. Microbiome and One Health

The human microbiome, a characteristic microbial community occupying a complex, but reasonably well-defined habitat with distinct physio-chemical properties, encompasses the microorganisms involved (microbiota), as well as their structural and molecular elements (e.g. nucleic acids), metabolites and surrounding environmental conditions (Berg et al., 2020). One Health (OH) is the holistic methodology of transdisciplinary cooperation to improve human, animal, plant and environmental health simultaneously, and its adoption is continuously expanding (CDC, 2020; Bronzwaer et al., 2021). Due to their functionalities and physiological potential and considering their known associations with a range of diseases, microbiomes are key elements in the OH framework (CNBBSV, 2019; Merten et al., 2020). Their significance is partly due to pathogenic and commensal microbial transfer between humans, animals and the environment, and the human microbiome stands out with regard to its interactions with environmental and dietary chemicals that affect human health outcomes (Trinh et al., 2018). Of particular interest are the contact and mutual influence between the human gut microbiome (GM) and exogenous toxic chemicals, xenobiotics, focusing on their fate, metabolism and toxicity (NASEM, 2018; Abdelsalam et al., 2020).

1.2. Microbiota-disrupting chemicals and the gut microbiome

Among xenobiotics, endocrine-disrupting chemicals (EDCs) are especially important and they have been associated with metabolic disorders, such as obesity, as well as with changes in the GM (Gálvez-Ontiveros et al., 2020; Aguilera et al., 2021). Recently the concept of microbiota-disrupting chemicals (MDCs) has been proposed, which comprise EDCs and other xenobiotics with potential to alter the gut microbiota's composition and metabolism (Aguilera et al., 2020) via dietary exposure, e.g. bisphenols, parabens (Andújar et al., 2019; Monteagudo et al., 2021; Robles-Aguilera et al., 2021).

The interactions between MDCs and the GM are complex. This is partly because multiple general mechanisms are involved, including; direct effects of the MDC on the microbiome; altered epithelial-barrier functions (affecting uptake or excretion of MDCs); direct chemical transformations of MDCs; secondary transformation of host-generated metabolites (e.g. deconjugation by β-glucuronidases); and altered expression of host-tissue metabolic enzymes and pathways (e.g. in the liver via microbial signalling molecules) (Ulluwishewa et al., 2011; Patterson and Turnbaugh, 2014; Peterson and Artis, 2014; Kelly et al., 2015; Selwyn et al., 2015, 2016; Claus et al., 2016; Spanogiannopoulos et al., 2016; NASEM, 2018). Although these interactions can decrease MDC exposure and toxicity effects, they can also increase them. For example, several bacterial phyla in the human GM can produce azoreductases, which have been shown to reduce azo dyes that are common in foods into mutagenic and carcinogenic aromatic amines (Rafii et al., 1990; Xu et al., 2007). Overall, the role of these complex interactions in modifying human susceptibility to MDCs is beginning to be elucidated.

1.3. Risk assessment of xenobiotics and the gut microbiome

Risk assessment (RA) is the science-based component of the food safety risk analysis framework, alongside risk management and risk communication. RA comprising; hazard identification; hazard characterisation; exposure assessment; and risk characterisation (CAC, 1999; European Commission, 2002). Traditionally, xenobiotic RA relies on data from animal experiments, human trials and/or human observational/epidemiological studies. Importantly, the extrapolation of this data across species or studied populations is not without challenge, partially due to GM variability (e.g. in homogeneous populations, such as healthy adults) and variation (e.g. between species or life stages) and the complexity of MDC/GM interactions (NASEM, 2018). Thus, the need for the incorporation of the GM in food safety RA of xenobiotics is well-justified (Merten et al., 2020) and by extension to MDCs.

1.4. Seeking beneficial taxa/components in the gut microbiome

Another area of relevance to the GM in the context of OH is the identification of beneficial taxa and derived components (e.g. enzymes and biocompounds) in the GM and their potential application. In this context, toxicomicrobiomics, which study the aforementioned microbiome-xenobiotic/MDC interactions, along with culturomics, which aim to cultivate components of the human GM through the use of optimised selective and/or enrichment culture conditions coupled with metagenomic taxa

identification, can shed light on the microbiome's capacity to metabolise xenobiotics (Aziz, 2018; Lagier et al., 2018; CNBBSV, 2019; Abdelsalam et al., 2020; López-Moreno et al., 2022) and by extension MDCs. Thus, these approaches can help identify GM components with beneficial effects under OH, for example detoxification activity (López-Moreno et al., 2021b) or next-generation probiotics (NGPs) (López-Moreno et al., 2021a).

1.5. Antimicrobial resistance and the gut microbiome

A third area of relevance is antimicrobial resistance (AMR). Undoubtedly, AMR is an important OH issue, with the major contributor being the misuse of antibiotics (WHO, 2015, 2021; O'Neill, 2016). Moreover, the GM has previously been considered as a reservoir for antibiotic resistance genes (Gibson et al., 2015; Anthony et al., 2021). Moreover, non-antibiotic antimicrobials, including MDCs triclosan and parabens, commonly used as preservatives in foods, food contact materials (FCMs) and personal care products (Soni et al., 2001, 2002, 2005; CIR, 2008; Halden et al., 2017), may also contribute to AMR (SCCS, 2010). This is because some resistance mechanisms are common to both biocidal MDCs and antibiotics, for example, the former may; exert selective stress leading to the expression of bacterial resistance mechanisms and their dissemination; and/or maintain mobile genetic elements carrying genes involved in antibiotic cross-resistance (SCENIHR, 2009). Therefore, detoxification potential from specific GM taxa become of particular interest in the context of such antimicrobials.

2. Work programme

2.1. Aims

This work builds upon a previous EU-FORA project (Cerk and Aguilera-Gomez, 2022) and aims to explore three areas of relevance to the microbiome in the context of OH. Firstly, the incorporation of the GM in RA of xenobiotics was explored. Secondly, the potential application of beneficial GM taxa (or their bioactive compounds), identified via toxicomicrobiomics and culturomics approaches was considered. Finally, a specific aspect of this application was further investigated in the context of AMR, and xenobiotic resistance was also considered.

2.2. Additional activities

Additional activities and training opportunities were identified during this EU-FORA fellowship project, based on the fellow's background and professional interests. These are listed in Appendix A.

2.3. Outputs

The three focal areas of this work and their links to each-other, OH and the GM are summarised in Figure 1. The first area, i.e. the incorporation of the GM in RA of xenobiotics, relates primarily to human health. However, depending on the output of the RA and the antimicrobial or not nature of the xenobiotic, the other two areas, i.e. the application of beneficial GM taxa/compounds generally or specifically in the context of AMR, could be highly relevant to holistic xenobiotic risk management.

The following sections present the outputs for each of these three areas. These have been previously published in a scientific journal (Ampatzoglou et al., 2022) and presented at scientific conferences, during the fellowship programme. Further detail is available in Annex A.

2.3.1. Moving towards the gut microbiome's incorporation in risk assessment of xenobiotics

2.3.1.1. The need – current challenges to address

GM variation and variability adds layers of complexity to the already intricate interactions between MDCs and health. The observed differences in the composition, gene content and function of the GM has been attributed to multiple factors including age (Yatsunenko et al., 2012), antibiotic use (Dethlefsen and Relman, 2011), diet (Yatsunenko et al., 2012), disease state (Mar et al., 2016), environmental exposures (NASEM, 2018), exercise (O'Sullivan et al., 2015), genetics (Goodrich et al., 2014), geography (Yatsunenko et al., 2012), pregnancy status (Koren et al., 2012), sex (Markle et al., 2013), socioeconomic status (Levin et al., 2016) and surgical interventions (Tremaroli et al., 2015). Moreover, these factors may only explain a small fraction of the total GM variation

(Falony et al., 2016; CNBBSV, 2019). Importantly, due to this variability, observations of microbiome-influenced toxicities in a studied population might have little relevance to other populations with substantially different GM composition and function (Rodricks et al., 2019).

In addition, there is considerable variation between the GMs of humans and animals, due to anatomical, physiological, functional, immunological and compositional differences. Some of these have been partially overcome via the use of 'humanised' animals in toxicological studies (Sonnenburg and Bäckhed, 2016). Nevertheless, extrapolation from such studies to humans still carries considerable uncertainty (Rodricks et al., 2019) and, along with the intraspecies variability, necessitates the use of uncertainty/safety factors, frequently reaching two orders of magnitude (Dorne and Renwick, 2005; Benford et al., 2018). Based on these factors, traditional RAs may overestimate or underestimate the risk associated with exposure to an MDC, partially because they do not account for its interactions with the microbiome (NASEM, 2018; Merten et al., 2020). Consequent risk management decisions may place considerable pressure on the industry. For example, EFSA's recent proposal to considerably reduce the tolerable daily intake for bisphenol A (BPA) (EFSA, 2021), may further increase the use of bisphenol analogues in FCMs, which may also trigger dysbiosis and obesogenic phenotypes (Andújar et al., 2019; Monteagudo et al., 2021).

Although the need is clear to incorporate the GM in the RA of xenobiotics, there are additional hurdles, i.e. the fundamental requirements to; establish causation and molecular mechanisms linking phenotypes, e.g. obesity, with microbiota profiles (Fischbach, 2018); and define what constitutes a healthy GM, which still remains elusive (Merten et al., 2020). Considering that these tasks require significant resources, it might be a useful first step to establish principles on how to evaluate the potential of xenobiotics to alter the GM.

2.3.1.2. Assessing the potential of xenobiotics to alter the gut microbiome

Interestingly, a three-tier framework has recently been proposed by the Unilever Safety and Environmental Assurance Centre for assessing the potential of personal care formulations to perturb the skin and oral microbiomes (Métris et al., 2021). The following sections briefly present this framework and suggest amendments which could make it suitable for application to the GM in the context of xenobiotic RA.

First tier – xenobiotic cross-reference

The first tier benchmarks new formulations against ones regarded as safe because of a long 'history of safe use' (HoSU). However, this approach cannot apply directly to xenobiotics, for reasons such as their nature as contaminants or that they may not be intended to be ingested (e.g., if used in FCMs). Moreover, it is challenging to establish robust links between GM, cumulative exposure and resulting adverse effects (Gruszecka-Kosowska et al., 2022; Ortiz et al., 2022). Nevertheless, evidence has been compiling in recent years on the impact of several contaminants and groups of xenobiotics, including pesticides, bisphenols, phthalates, metals, triclosan, parabens and polybrominated diphenyl ethers, on human and animal gut microbiomes (Aguilera et al., 2020). As it expands, this evidence could potentially serve as an early cross-reference tier which would raise initial concerns, depending on the nature and chemical structure of a xenobiotic under RA.

Second tier – microbiome resilience

The second tier focuses on microbiome resilience. Other authors highlighted resilience, along with resistance to perturbation, as a key feature of healthy microbiomes, attributed to their rich and diverse metabolic pathways (Lloyd-Price et al., 2016; McBain et al., 2019; Cheng et al., 2022). Importantly, this tier assesses risk in relative terms. Thus, it circumvents the need to define the healthy microbiome, since it is only concerned about the return to its baseline state, independently of whether healthy or desirable. Of course, the length of exposure of the microbiome to the potential perturbator would be a critical consideration. Overall, however, this tier could be a reasonable approach to screen MDCs based on the resilience of the GM under various experimental approaches, extending from 'humanised' animals (NASEM, 2018) to *ex vivo* and *in vitro* models, such as simulator of the human intestinal microbial ecosystem (SHIME) (Van den Abbeele et al., 2012), minibioreactor arrays (Auchtung et al., 2015) and multi-compartment microfluidic-based gut-on-chip systems (De Gregorio et al., 2020; Signore et al., 2021).

Third tier – elucidating links between changes in the gut microbiome and health status

Finally, the third tier makes use of next-generation sequencing microbiome data in relation to host health status. This requires further development, is the most challenging tier and is, certainly, relevant to the RA of xenobiotics in the context of the GM. Métris et al. (2021) highlighted the requirement to focus not only on the microbiome's composition (including both relative and absolute abundances), but more importantly on its function. This is not surprising, given that microbiome variability between relatively homogeneous groups of people (e.g. healthy individuals of same sex and similar age) is less prominent at the functional level (Tian et al., 2020) and that compositional variation, more generally, might not necessarily impart key functional differences due to functional redundancy (NASEM, 2018). Regarding research methodology, metatranscriptomics, is an established approach to focus on the functional taxa in the microbiome. More recent methodologies, however, have combined flow cytometry with omics technologies to characterise active microbial fractions in the GM, revealing a number of taxa underrepresented by traditional 16S rRNA metagenomics (Peris-Bondia et al., 2011; Maurice et al., 2013). These approaches are likely to offer valuable insights in the extrapolation of this tier's approach to the GM, especially in the pursuit for key species or other types of biomarkers associated with host health or disease, which will be crucial for the incorporation of the GM in the RA of MDCs.

2.3.2. Identifying beneficial gut microbiome taxa/components for application under One Health

Taxa culturing strategies, in the context of the interactional triangle between EDCs (obesogens)-gut microbiota (dysbiosis vs eubiosis)-human health (obesity vs leanness), are key in obtaining and selecting strains (associated with pro-obesity and antiobesity phenotypes) with potential use as NGPs (López-Moreno et al., 2021a). The latter, unlike traditional probiotics, do not have a defined HoSU, and are thus subjected to more stringent regulatory requirements (O'Toole et al., 2017; Cerk and Aguilera-Gomez, 2022). Nevertheless, strains isolated from the human gut could more readily be used under OH, e.g. as probiotics for animals, plants and environmental protection and bioremediation.

Recent work has demonstrated that toxicomicrobiomics and culturomics are promising in exploring the potential of human GM taxa to metabolise obesogenic MDCs and selecting species able to tolerate or biodegrade BPA (López-Moreno et al., 2021b; López-Moreno et al., 2022). Moreover, whole-genome sequence (WGS) analysis of a relevant *Bacillus* species derived from the human gut microbiota shed light on the encoded metabolic pathways and key enzymes involved in BPA breakdown (Figure 2).

Thus, similar approaches, involving toxicomicrobiomics, culturomics and genomics, could be used going forward to explore the human GM as a source of beneficial microbes (NGPs), enzymes and bioactive compounds linked to MDC detoxification or biodegradation, with various potential applications under OH (Figures 1 and 3).

2.3.3. Gut microbiome and antimicrobial resistance under One Health

MDCs, such as triclosan and parabens, contribute to the AMR issue, primarily through resistance development against themselves (self-resistance), but also potentially through development of cross-resistance against antibiotics (Ribado et al., 2017). Although the evidence supporting cross-resistance development in situ is not conclusive (SCCS, 2010), the potential contribution of MDCs to AMR and their mechanisms merit further data compilation (Valkova et al., 2002; Hughes et al., 2020; Rozman et al., 2021). Moreover, given that antimicrobial MDCs would likely have higher potential to alter and perturb microbiomes (compared to non-antimicrobial xenobiotics), they have been proposed as candidate chemicals in investigations that would built our understanding around the xenobiotic-microbiome interactions in the context of xenobiotic RA (NASEM, 2018).

Nevertheless, even non-antimicrobial xenobiotics may pose resistance development issues in the context of the GM, as exposure to them may apply a selective pressure in favour of microbial taxa with specific enzymatic arsenals and metabolic pathways. For example, López-Moreno et al. (2022), associated BPA exposure and the obese phenotype in children to higher BPA biodegradation potential in their GM. Moreover, they reported that BPA-resistant strains isolated from human gut microbiota exhibited xenobiotic biodegradation and antimicrobial effects linked to polyketide biosynthesis (Torres-Sánchez et al., 2021). Therefore, in the presence of BPA, these strains may further modulate the composition and function of the human gut microbiota, potentially reducing GM diversity and inducing dysbiosis and adverse metabolic effects (Aguilera et al., 2020). The mechanisms, via which gut

microbiome taxa may be affected by non-antibacterial MDCs, potentially leading to dysbiosis, could include growth inhibition or promotion and metabolism modulation (Lindell et al., 2022). For example, several artificial sweeteners, spice extracts and food dyes have been shown to inhibit the growth of specific bacterial strains *in vivo*, while certain natural xenobiotics and food additives appear to promote the growth of other strains under similar conditions, likely acting as nutrient sources (Pan et al., 2012; de Bello González et al., 2016; Lu et al., 2017; Wang et al., 2018; Ruiz-Ojeda et al., 2019; Frame et al., 2020). Additionally, an alkaloid found naturally in coffee, trigonelline, has shown potential to alter the metabolism of a common human gut commensal in vivo (Anwar et al., 2018). Although limited, this evidence suggests that the potential for xenobiotic resistance development, in the context of the GM, may warrant further consideration and research, beyond antimicrobial resistance.

Overall, applying GM taxa and biocompounds able to metabolise antimicrobial MDCs to crosscutting areas under OH could potentially ameliorate AMR pressure (Figure 1).

3. Conclusions

The explored three areas of relevance to the GM in the context of OH open new avenues of research; the incorporation of the GM in RA of xenobiotics; the identification and application of beneficial GM components to various areas under OH, and specifically, in the context of AMR. This work took a first step with this combined approach and reached the following conclusions:

- Focusing on the GM's resilience circumvents some of the challenges. Moreover, looking at function, rather than composition, and exploring the active components of the GM can help establish biomarkers of health and disease, which is necessary for the incorporation of the GM in the RA of xenobiotics.
- The human GM may be a promising source of beneficial microbes (i.e. probiotics and NGPs), enzymes and bioactive compounds, with the potential to metabolise xenobiotics. These can be explored with toxicomicrobiomics and culturomics and may have potential applications in various areas under OH, e.g., as probiotics in animals or plants for xenobiotic detoxification or as xenobiotic biodegraders in environmental protection and bioremediation.
- This approach would be of particular interest for antimicrobials (such as triclosan or parabens), because applying relevant components isolated from the human GM to similar areas under OH could help ameliorate the risk of AMR development.
- Finally, the concept of resistance in the context of the GM could theoretically be extended from antimicrobials to xenobiotics, and the notion of xenobiotic resistance may warrant further consideration.

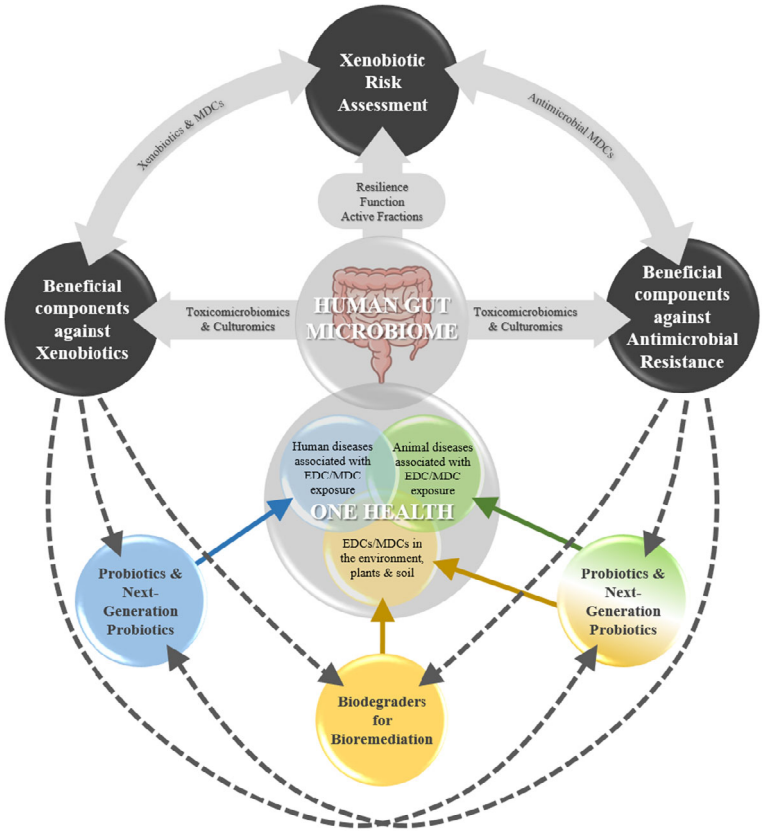

Figure 1: Three interlinked areas of relevance to the human gut microbiome (GM) in the context of One Health (OH); incorporation of the GM in food safety risk assessment of xenobiotics; identification and application of beneficial GM taxa and components (e.g., enzymes and bioactive compounds) to various areas under OH, and; specifically, in the context of antimicrobial resistance. EDC: endocrine disrupting chemicals, MDC(s): microbiota disrupting chemicals (Ampatzoglou et al., 2022)

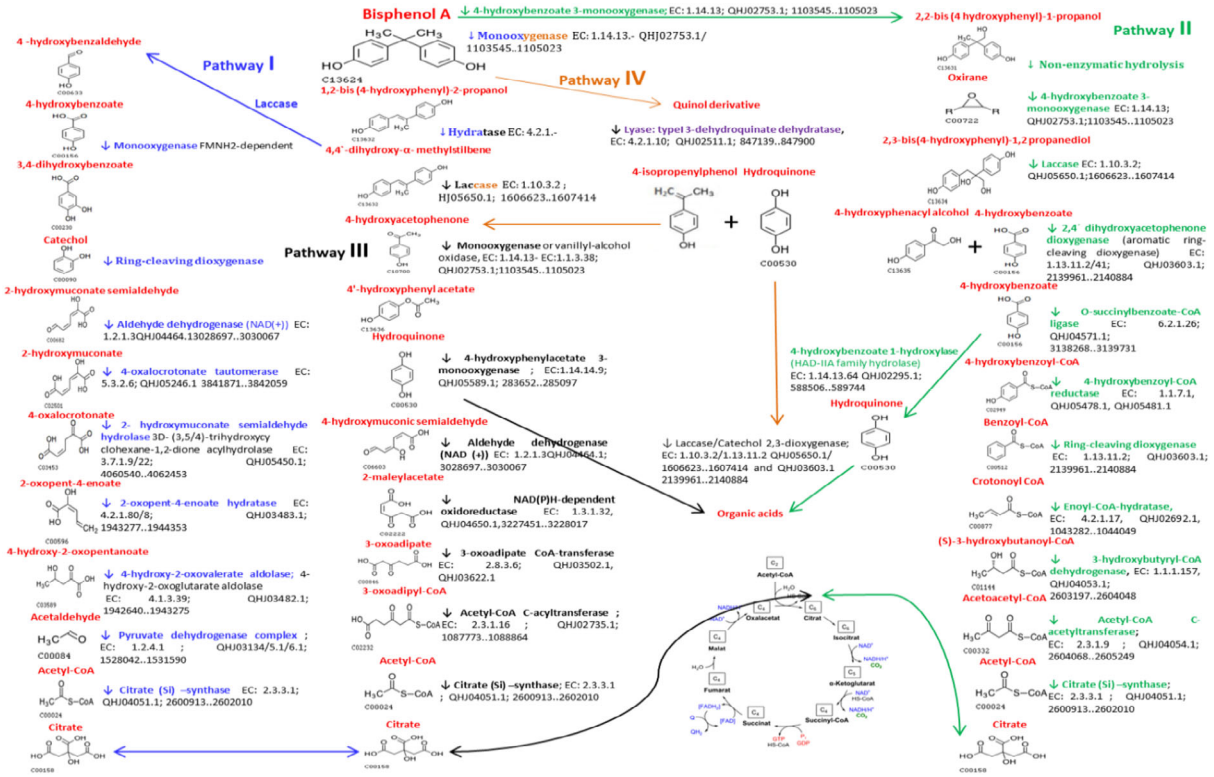

Figure 2: Proposed biodegradation pathways of bis-phenol A based on the whole-genome sequence analysis of *Bacillus* species AM1: reaction steps, enzymes, EC number, protein ID, and specific genes loci (with permission from López-Moreno et al., 2021b)

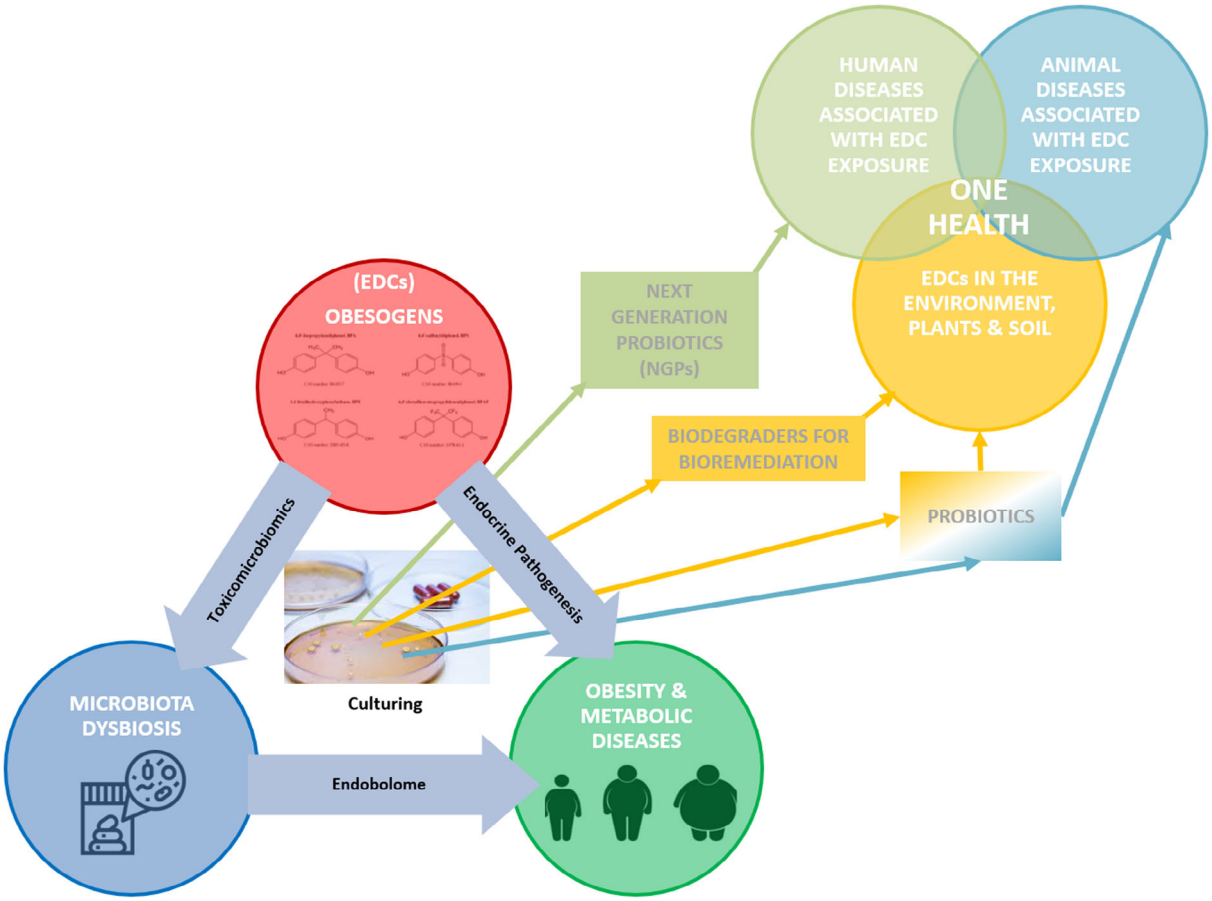

Figure 3: Next Generation Probiotics (NGPs), probiotics and biodegraders derived via culturing from the gut microbiota in the context of the triad micro-biome (dysbiosis vs eubiosis) – endocrine disrupting chemicals (EDCs)/xenobiotics/obesogens – human health (obesity vs normal weight) and their envisaged application in three areas under One Health (presented to the International e-Symposium on Probiotics, Prebiotics & Gut Microbiome: Key Regulators for Human & Animal Health, November 11, 2021, Ludhiana, India)

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Abbreviations

AMR	antimicrobial RESISTANCE
BPA	Bisphenol A
CAC	Codex Alimentarius Commission
CDC	Centers for Disease Control and Prevention
CIR	Cosmetic Ingredient Review Expert Panel
CNBBSV	Comitato Nazionale per la Biosicurezza, le Biotecnologie e le Scienze della Vita
EDCs	endocrine-disrupting chemicals
FCMs	food contact materials

GM	(human) gut microbiome
HoSU	History of Safe Use
INYTA	"José Mataix Verdú" Institute of Nutrition and Food Technology
MDCs	microbiota-disrupting chemicals
NASEM	National Academies of Sciences, Engineering, and Medicine
OH	One Health
RA	risk assessment
SCCS	Scientific Committee on Consumer Safety
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SHIME	Simulator of the Human Intestinal Microbial Ecosystem
UGR	University of Granada
WGS	whole-genome sequence
WHO	World Health Organization

Appendix A – Additional activities undertaken by A. Ampatzoglou

The fellow joined the Biology and Biotechnology Group (BIO190, Halophilic Microorganisms and Environmental Bioremediation Research Group) at the hosting site (UGR), successfully applied to the UK Science Council for the Chartered Scientist (CSci) award, via his professional body, the Institute of Food Science and Technology (IFST) and attended the EU-FORA training modules and additional training opportunities. Salient examples are listed below.

- EU-FORA training modules by EFSA, the Austrian Agency for Health and Food Safety (AGES), the German Federal Institute for Risk Assessment (BfR) & the Hellenic Food Authority (EFET) on the following topics:
    - Data collection and reporting, 22–25 August 2022, online.
    - Emerging Risks, Nanomaterials, Omics in Risk Assessment & Risk Ranking, 6–10 Jun 2022, Athens, Greece.
    - Risk Perception, Risk Communication, Crisis Response & Media Training, 21–25 March 2022, Berlin, Germany and online.
    - Genetically Modified Organisms, Animal Health, Animal Welfare, Plant Health, Pesticides, Nutritional & Environmental Risk Assessment, 22–26 November 2021, Vienna, Austria and online.
    - EU Food Safety System & Legislation & a comprehensive overview of Microbiological & Chemical Risk Assessment (induction training), 30 August–17 September 2021, Parma, Italy and online.
- US Food and Drug Administration (FDA) and Alliance to Stop Foodborne Illness, Collaborating on Culture in the New Era of Smarter Food Safety, Food Safety Culture webinar series, including:
    - Building a coalition of food safety culture champions in your organisation, 18 May 2022
    - Making Leaders Risk Aware and Push to Reduce Risk, 16 February 2022.
    - Kick Off Meeting, 4 November 2021.
- BfR and Federal Office of Consumer Protection and Food Safety (BVL), Super(?)foods and Supplements – Risky or Healthy? 30 June–1 July 2022, online conference.
- EFSA, European Centre for Disease Prevention and Control (ECDC), European Chemicals Agency (ECHA), European Environment Agency (EEA), European Medicines Agency (EMA) & Joint Research Centre (JRC), ONE – Health, Environment, Society – Conference 2022, 21–24 June 2022, Brussels and online conference.
- Microbiome Virtual International Forum online webinar series, including:
    - Toward the development of defined microbial therapeutics, 16 June 2022.
    - Topic models for interpretable multidomain microbiome data, 9 February 2022.
- US FDA Grand Rounds online webinar, including:
    - One Health at FDA: From Concept to Application, 14 June 2022.
    - MinION Sequencing of Foodborne Pathogens, 14 April 2022.
- FoodSafety4EU EU Green Week Partner Event, How can we communicate food safety in the context of sustainable food systems? 1 June 2022, online event.
- The institute of Food Science and Technology (IFST), Spring Conference (SC22) – Minding the Gap; Communication, Skills and Technologies, 4–6 May 2022, online conference.
- The Frontiers Forum, The CRISPR health revolution, 31 March 2022, online webinar.
- EU-FORA training visit to the Spanish Agency for Food Safety & Nutrition (AESAN), covering Risk Assessment & the AESAN Scientific Committee, Risk Communication & Risk Management of Biological & Chemical Hazards, Nutritional Safety, Food Official Control & Alerts, 23–24 February 2022, Madrid.
- EU-FORA training visit to the Spanish National Centre for Food (CNA), covering Food Contact Materials, Food Processing Contaminants, Veterinary Drug Residues, Biotechnology, Microbiology & Antimicrobial Resistance, 25 February 2022, Majadahonda, Spain.
- University of Granada, Machine Learning and Big Data for Bioinformatics, 7 February–1 April 2022, massive open online course (MOOC).

- European Institute of Innovation and Technology (EIT) Food, The Human Microbiome, 24 January–11 February 2022, MOOC.
- EIT Food, The Future of Food Conference 2021, 30 November–1 December 2021, virtual event.
- Introduction to BioCyc for New Life Sciences Graduate Students and Post Docs, covering; Introduction to BioCyc; Smart tables and Comparative Analysis, and; Transcriptomics and Metabolomics Data Analysis, 3, 10 and 17 November 2021, online webinar series.
- Workshop OBEMIRISK-Knowledge platform for assessing the risk of Bisphenols on gut microbiota and its role in obesogenic phenotype: looking for biomarkers, 14–15 October 2021, Granada.

Annex A – Scientific output dissemination of EU-FORA fellowship project

The following outputs of this EU-FORA fellowship project have been published in scientific journals or communicated in scientific conferences.

A.1. Scientific papers

Torres-Sánchez A, López-Moreno A, Moreno A, Ortiz P, **Ampatzoglou A**, **Gruszecka-Kosowska A**, Ruiz-Rodríguez A, Monteoliva-Sánchez M, **Aguilera M**, 2022. Microbiome taxa and metabolite profiles altered in endocrine disorders or by xenobiotics and the counteraction with Next Generation Probiotics, International Journal of Molecular Sciences, review submitted for publication.

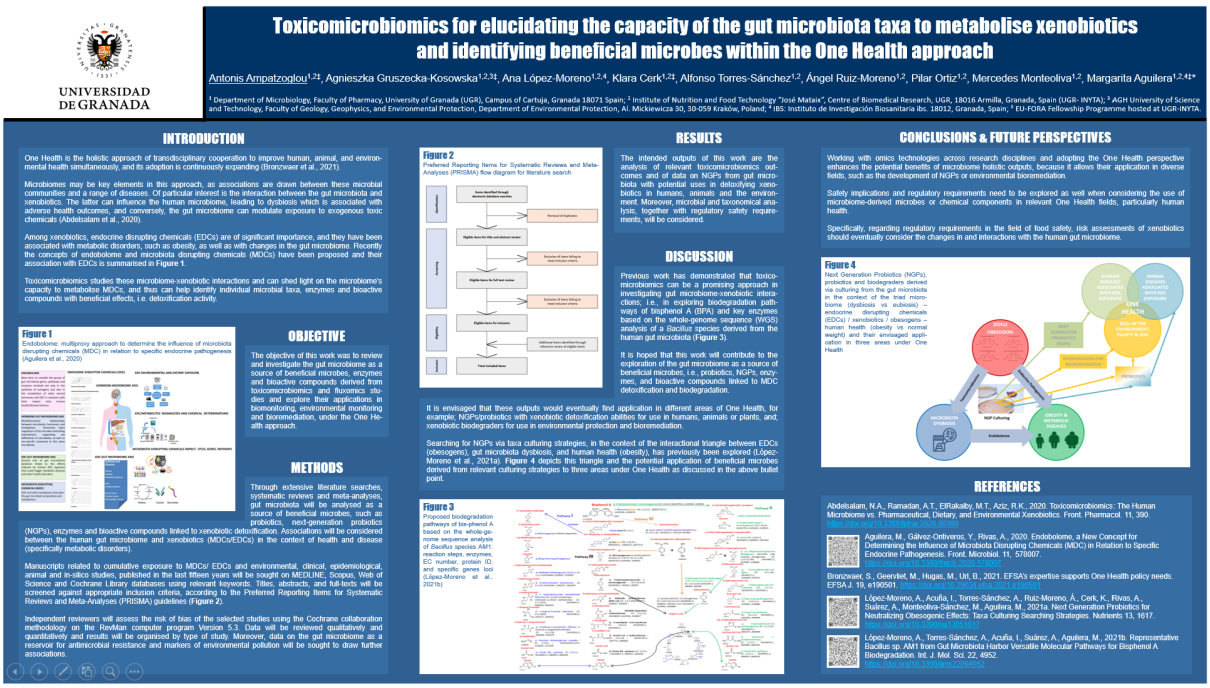
Gruszecka-Kosowska A, **Ampatzoglou A**, **Aguilera M**, 2022. Integration of Omics approaches enhances the impact of scientific research in environmental applications. International Journal of Environmental Research and Public Health, 19(14), 8,758. doi: 10.3390/ijerph19148758.

Ampatzoglou A, **Gruszecka-Kosowska A**, Torres-Sánchez A, López-Moreno A, Cerk K, Ortiz P, Monteoliva-Sánchez M, **Aguilera M**, 2022. Incorporating the gut microbiome in the risk assessment of xenobiotics & identifying beneficial components for One Health. Frontiers in Microbiology, 13, 872,583. doi: 10.3389/fmicb.2022.872583.

Ortiz P, Torres-Sánchez A, López-Moreno A, Cerk K, Ruiz-Moreno Á, Monteoliva-Sánchez M, **Ampatzoglou A**, **Aguilera M**, **Gruszecka-Kosowska A**, 2022. Impact of cumulative environmental & dietary xenobiotics on human microbiota: risk assessment for one health. Journal of Xenobiotics, 12(1), 56–63. doi: 10.3390/jox12010006.

A.2. Poster communications at scientific conferences

Moreno A, Ortiz P, López-Moreno A, Torres-Sánchez A, **Ampatzoglou A**, **Gruszecka-Kosowska A**, Ruiz-Rodríguez A, Monteoliva-Sánchez M, **Aguilera M**, 2022. Representación de taxones microbianos cultivables inducidos por exposición a xenobióticos en microbiota de niños. XIX Taxon, Reunión del Grupo de Taxonomía, Filogenia y Biodiversidad, October 13–15, 2022, Mallorca, Spain (abstract accepted).**Ampatzoglou A**, **Gruszecka-Kosowska A**, López-Moreno A, Cerk K, Torres-Sánchez A, Ruiz-Moreno A, Ortiz P, Monteoliva M, **Aguilera M**, 2021. Toxicomicrobiomics for elucidating the capacity of the gut microbiota taxa to metabolise xenobiotics and identifying beneficial microbes within the One Health approach. International e-Symposium on Probiotics, Prebiotics & Gut Microbiome: Key Regulators for Human & Animal Health, November 11, 2021, Ludhiana, India (**Best poster award received-presented by A. Ampatzoglou**).



A.3. Oral communication at scientific conference

Ampatzoglou A, **Gruszecka-Kosowska A**, Torres-Sánchez A, López-Moreno A, Cerk K, Ortiz P, Monteoliva-Sánchez M, **Aguilera M**, 2022. Exploring the incorporation of gut microbiome omics data in next-generation risk assessment of xenobiotics in foods. Next Generation Challenges in Food Microbiology, FoodMicro 2022, August 28–31, 2022, Athens, Greece (abstract accepted).