UNIVERSITÀ POLITECNICA DELLE MARCHE

PROBIOTICS AS AN EMERGING STRATEGY TO COUNTERACT ENDOCRINE DISRUPTOR CHEMICALS (EDCs) TOXICTY

Oliana Carnevali

Department of Life and Environmental Sciences, DiSVA

March, 2025

UNIVERSITÀ POLITECNICA DELLE MARCHE

Project: PROBIOTICS AS AN EMERGING STRATEGY TO COUNTERACT EDCs TOXICITY

Supervisor: Prof. Oliana Carnevali

The Supervisor

Full Professor in Developmental Biology, **President** of "Master course in Molecular and Applied Biology"

Member of the Committee of Experts for Research Policy - (CEPR) MIUR, **Member** of GEV 05 Committee, Coordinator of subGEV "Integrated Biology" for National Evaluation of Research Quality, **Delegate** of International Relations UNIVPM; **Vice President** of the International Society Fish Endocrinology (ISFE)

She's an expert on the assessment of gamete quality, spanning from zebrafish to humans. In recent years, her attention has shifted towards Reproductive Toxicology, specifically investigating reproductive disorders induced by environmental pollutants with hormone-like activities (EDCs). This scientific endeavor has been complemented by research efforts aimed to understanding the concomitant metabolic disorders in response to contaminants in aquatic organisms. She is particularly focused on elucidating the molecular basis of such dysfunctions and the role of the endocannabinoid system. Additionally, she has undertaken studies on the role of intestinal microflora in: reproduction, metabolism, ossification processes, and the overall well-being of aquatic organisms. Recently, she has also ventured into exploring the potential of probiotics to mitigate the metabolic toxicity induced by EDCs, offering promising avenues for intervention and remediation.

Author of more than **280 peer-reviewed publications** in international journals, with an ***h* index= 59**, FWCI 2.022 and more than 16,000 citations (from Scopus)
Scopus ID: 55861380700,
https://www.scopus.com/authid/detail.uri?authorId=55861380700
ORCID ID: 0000-0001-5994-0572, https://orcid.org/0000-0001-5994-0572

Most recent Research Projects

International Projects

2021-2022 National research Council of Thailand*: Manipulation of the endocannabinoid system for cancer treatment: Zebrafish as a model-***Co PI**

2019-2024 EU-*ICCAT* Swordfish conservation program

GFI 2014-2018 (Grant for Fertility Innovation) *IR Microspectroscopy on GCs: a new non-invasive oocyte assessment-Funded by Merk Serono* ***Co-PI***

PI2018 H2020-MSCA-ITN-2017 Type of action: MSCA-ITN-ETN Proposal number: 766347 acronym: BioMedaqu. **Participant**

National projects

2018 Programma Operativo FEAMP Italia 2014-2020 Obiettivo specifico 4.1. Priorità 4 del PO FEAMP. Interventi a sostegno dello sviluppo locale di tipo partecipativo (CLLD).

2018 Ministero delle Politiche Agricole Alimentari e Forestali (MIPAAF) 2018 development of a national monitoring program of blue fin tuna (*Thunnus thynnus*) and swordfish (*Xiphias gladius*) and evaluation of the current state of their reproductive capacity.

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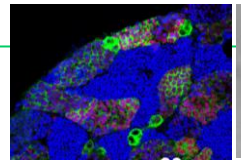
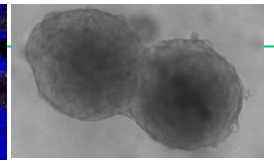
LAB_CARNEVALI

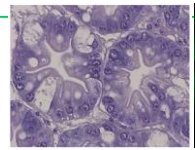
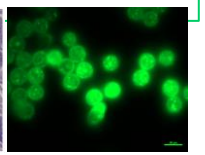
The research group: Development and Reproductive Biology

The research of the group intertwined 3 research pillars.
The first one, led by Prof. Oliana Carnevali, concerns the **Reproductive Biology,** from zebrafish to humans; an activity that has been developed within the framework of European projects or in collaboration with assisted fertilization centers. In the last years, major interest has been focused on the **reproductive, metabolic, and bone-related disorders induced by environmental pollutants with hormones-like activities** (EDCs). The molecular basis of such dysfunctions and the alterations of endocannabinoid system were investigated. To achieve our goals, we are conducting experiments *in vivo* (using zebrafish) and *in vitro* both in 2D (human fetal osteoblast) and 3D (human gut organoids and bone spheroids) cell models. Moreover, we are investigating the role of gut microbiota in the well-being of organisms and, very recently, we started to explore the use of probiotics as a mitigating strategy against EDCs toxicity using multidisciplinary approaches that encompass confocal microscopy, molecular biology, and OMICs studies.

During the last few years, part of the research (led by Prof. Giorgia Gioacchini) investigate **the effects of environmental pollutants and climate change on the reproductive biology, embryonic development and health status of some important key species inhabiting different areas of the Mediterranean Sea**. At present, we are involved in different research projects which focus on different species such as the European sardine (*Sardina pilchardus*), bluefin tuna (*Thunnus thynnus*), swordfish (*Xiphias gladius*), common cuttlefish (*Sepia officinalis*) and the loggerhead sea turtle (*Caretta caretta*). In our studies, we applied a multidisciplinary approach to evaluate the gonadal structure and maturation stage focusing on the possible presence of anomalies related to a stress condition. We also characterize the reproductive period, sex ratio and different maturation stages within wild populations. Recently, we are investigating the presence and possible effects of microplastics in the embryonic stage of some marine key species to identify valid biomarkers for the monitoring of microplastics effects on the marine biota.


Part of the research team (led by Prof. Ike Olivotto) is presently focusing on assessing the **physiological effects of innovative aquafeed formulations** (in terms of ingredients and attractive properties) **and on microplastic-contaminated diets in**: (i) zebrafish (*Danio rerio*), as a widely recognized model organism in aquaculture, to obtain a comprehensive overview over the whole life cycle (from larvae to adults); (ii) aquatic species of commercial interest, including crustaceans (giant freshwater prawn) and bony fish (rainbow trout, gilthead seabream, European seabass, carpione, Siberian sturgeon). The **zootechnical performance**, the gut and liver health status, and the quality of the final product are assessed through a multidisciplinary approach including histological, spectroscopic (FTIR), molecular (real-time PCR), gas chromatographic analyses, and confocal microscopy analyses. Further studies are related to the development of new equipment to sustain the early developmental phases of teleost fish as well as developing pilot actions related to fish growth and welfare as well as sustainability.


Prof. Carnevali


Prof. Olivotto


Prof. Gioacchini


Dr. Maradonna


Dr. Chemello


Dr. Zarantoniello


PhD. Giommi


PhD Conti


PhD Cattaneo


PhD Trotta


PhD Sella


PhD Mazzeo

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THE DEPARTMENT OF LIFE AND ENVIRONMENTAL SCIENCES (DiSVA)

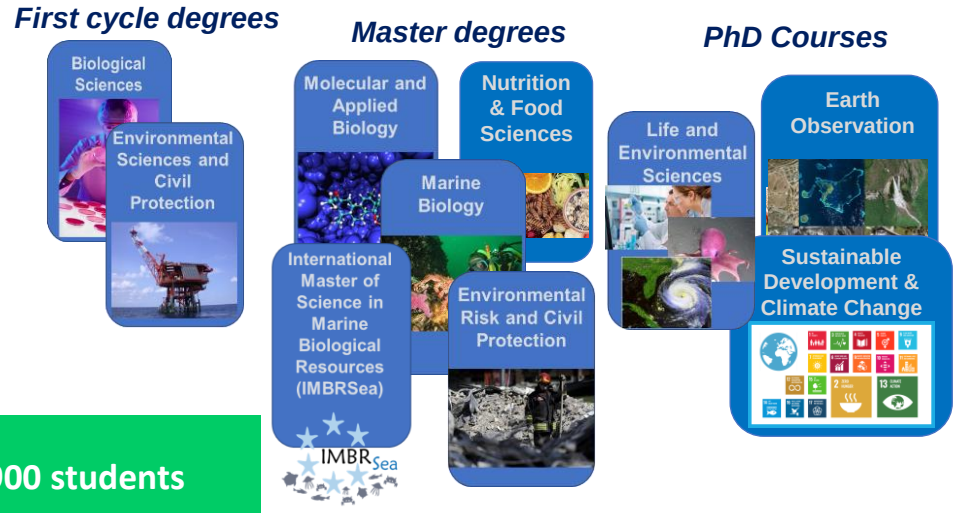
Department of Excellence

100 units of permanent staff (researchers and technicians)
80 PhD students and post-docs

in 2021-23, > 140 national and international projects for > 11 Mil €

in 2023 >220 international publications (>80% in Q1 Journals)

Teaching programmes:
2 First cycle degrees, 4 Master degrees, 3 PhD Courses

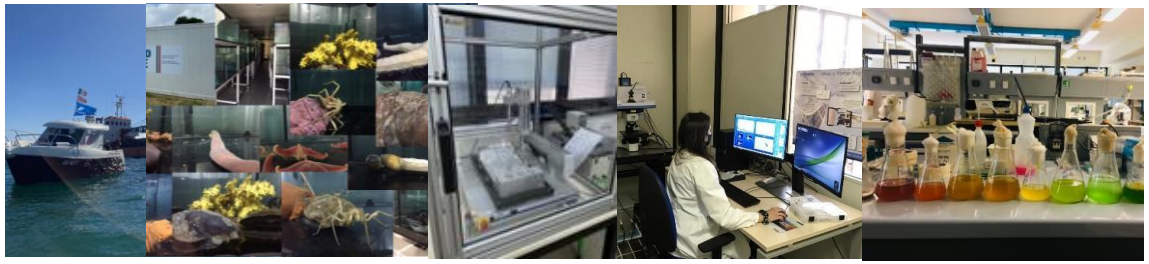


20 Professors have *h* index between 30 and >80, 15 have between 100 and 400 publications, 1 in Highly Cited Researchers (Clarivate)

> 1.900 students

Research Infrastructures & Excellence Laboratories:

- Marche Structural Biology Center (Ma.S.Bi.C.); The Aquarium-Joint Research Unit (JRU) of EMBRC ITALY (EMBRC-IT); Laboratory of Advanced Microscopy Research Instrumentation; Advanced Laboratory of Mass Spectrometry; Computing Data Center-DiSVA-HPC; Covid-19 LABC19; research vessels ACTEA and MYTILUS; Fano Marine Center (FMC), FORTUNAE Oceanographic Buoy.



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Project: **PROBIOTICS AS AN EMERGING STRATEGY TO COUNTERACT EDCs TOXICITY**

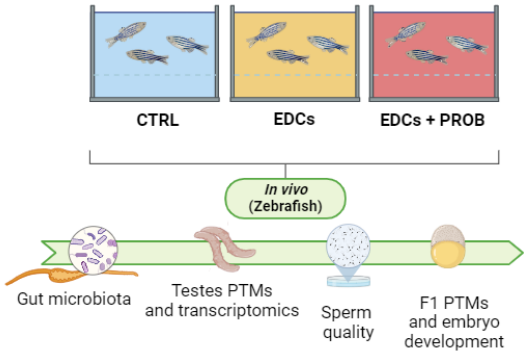
Supervisor: **Prof. Oliana Carnevali**

Project Idea: PROBIOTICS AS EMERGING TOOLS TO COUNTERACT EDCs TOXICTY (PROXY)

Backgroud: Consumer products and their underlying chemistry have been altering our planet since the industrial revolution. These alterations, caused by the release of many chemical substances, such as plasticizers and pesticides, are endangering the health of ecosystems and living organisms (Basili et al., 2023; Herráez et al., 2023). Current research is mainly focused on compounds that are able to interfere with the synthesis, secretion, transport, binding or elimination of endogenous hormones, also known as endocrine-disrupting chemicals (EDCs) (Kavlock et al., 1996). Despite the implementations of different measures to reduce human and animal exposure to BPA, new strategies are devoted to mitigating its toxicity, especially those targeting reproduction, such as the use of natural compounds (resveratrol and epigallocatechin gallate) (Bordbar et al., 2023; Lombó and Herráez, 2021) and probiotics (Giommi et al., 2021). “Probiotics are living microorganisms that, when administered in adequate amounts, confer health benefits on the host” (Dahiya and Nigam, 2022). Recently, several studies have demonstrated the potential of probiotics to counteract the harmful effects of EDCs contaminants. In rats, the probiotic mixture (*Saccharomyces boulardii*, *Lactobacillus rhamnosus*, and *L. plantarum*) reduced the systemic inflammation and had protective effects on diverse organs, improved the lipid status, and serum glucose level, in specimens exposed to phthalates and BPA (Baralić et al., 2020). Besides, the administration of *L. plantarum* decreased the apoptosis triggered by the agrochemical endosulfan in pregnant rats (Bouhafs et al., 2015).

In this respect, PROXY will develop the following research **objectives** aimed to:

1. **Establish a comprehensive atlas about the impact of EDCs on host-microbe dialogue. A high-throughput screening of the bacterial biodiversity of gut microbiota and host-microbiome interactome** will be performed ***in vivo*** (using zebrafish as model species) and in **3D *in vitro* models** (gut organoids).
2. **Evaluate the power of the probiotics to counteract the gut dysbiosis and metabolic disorders triggered by EDCs exposure *in vivo*** (using zebrafish as model)
3. Assess whether the restoration of gut microbiota by **probiotic administration is able to mitigate the disruption of gametogenesis and breeding capacity caused by EDCs, using *in vivo*** (zebrafish) **and *ex vivo*** (testicular culture) models.



Impact of the attended results

This is a multidisciplinary ambitious project aimed to determine the toxicity of contaminants of emerging concern providing information on the safety of standard doses present in daily products to which humans are constantly exposed, as well as present in the environment in which aquatic species live. The groundbreaking results consist in the identification of a mix of probiotics to mitigate the EDCs toxicity based on a multi-omics perspectives to define a solid foundation for forthcoming microbiota-based translational research from zebrafish to human. These data will be the basis for future applications in the field of reproductive and metabolic toxicology, raising awareness among citizens, stakeholders, lawmakers, and institutions.